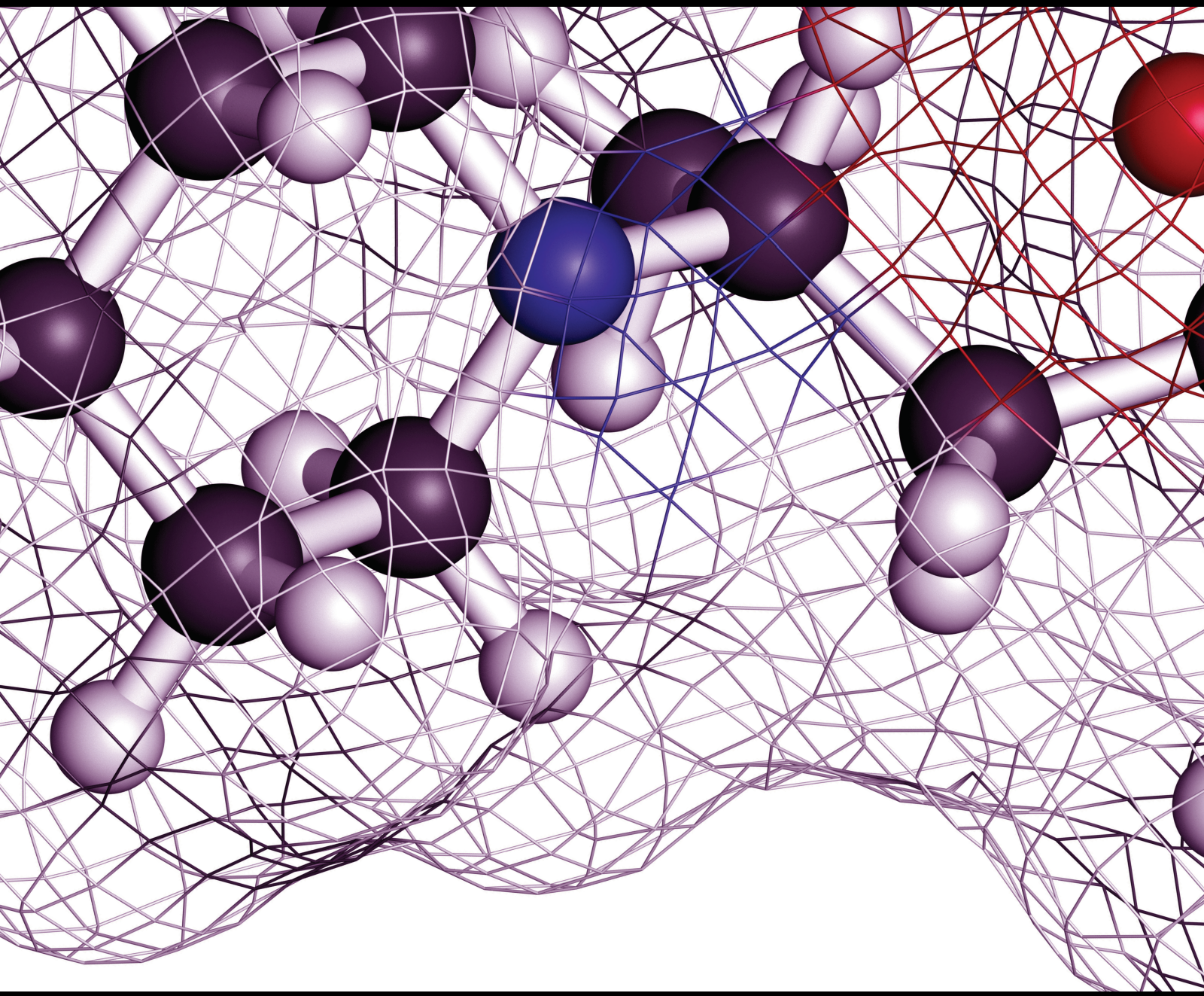
Pain Research and Management

Postoperative Pain Management of Orthopaedic Surgeries

Lead Guest Editor: Sidong Yang
Guest Editors: Pengcheng Wang, Dingjun Hao, Xiaolong Chen, and Felicity Han



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Hindawi
Pain Research and Management
Volume 2022, Article ID 1582727, 9 pages
https://doi.org/10.1155/2022/1582727

Research Article

Use of Intravenous Paracetamol Preoperatively Favors Lower Risk of Delirium and Functional Recovery in Elderly Patients with Hip Fracture: A Propensity Score-Matched Analysis

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Received 22 December 2021; Revised 12 March 2022; Accepted 18 March 2022; Published 13 April 2022

Academic Editor: Xiaolong Chen

We aimed to investigate whether the use of intravenous paracetamol (IVP) preoperatively in intertrochanteric fracture (IF) patients aged 65 years or over receiving intramedullary fixation had significantly benefits on the pain score at discharge, delirium incidence, length of hospital stay (LOS), functional outcomes, and mortality. A retrospective analysis of all surgically treated patients presenting with IF was conducted at a single Level I trauma center in China between Jan. 2016 and Jan. 2020. The data concerning patients' demographics, injury-related data, surgery-related data, operation-related data, in-hospital data, and postoperative outcomes were extracted. To minimize potential confounding and selection bias, the propensity score matching (PSM) method was performed via the caliper matching method by using a 1 : 1 ratio. After PSM, McNemar's chi-square tests were used to examine the association of using IVP with outcome analyses. The Spearman correlations of IVP using, pain scores, and the factors which may influence them were also computed. After screening 2963 consecutive patients, 2166 were included finally, including 1576 in the non-IVP group and 590 in the IVP group. After PSM, 531 remained in each group. The pain scores at discharge were significantly between the two groups before and after matching (all $p < 0.001$). The differences of delirium rate and functional outcomes became significant after propensity score-based matching ($p = 0.001$ and 0.033, respectively), although they were not significant before matching. No significant difference was observed in other operation-related data, LOS, and crude mortality rates at 30-day, 90-day, and 12-month before and after PSM. In conclusion, this study highlights the need for preoperative IVP use to optimize pain control, postoperative functional recovery, and minimize pain-related comorbidities such as delirium in elderly patients with hip fracture.

1. Introduction

As the population ages and the incidence of hip fracture rises, more hip fracture patients will receive operations and effective perioperative management. Worldwide, over 1 million hip fractures occur annually, particularly increased in the developing countries. It has been reported that the number of older adults in China, i.e., people over 60 years, has reached 249 million, accounting for nearly one-fifth of the total population by 2018, with numbers projected to reach close to 450 million, more than thirty percent of the global population by 2050 [1, 2]. Nowadays, hip fractures, especially intertrochanteric fractures, which are the most common cause of orthopedic wards admission, represent a

major public health concern in older adults due to multiple concurrent comorbidities and subsequent difficulty in achieving good outcomes, leading to a heavy socioeconomic pressure on society [3]. Despite substantial progress in this frail patients management over the past few decades, 1-year mortality remains high, ranging from 7% to 10% in 30 days and 12% to 35% in the first year [4, 5], and even with treatment, up to 10% of patients die postoperatively in hospital [6].

According to the literature [7, 8], effective pain management has been shown to be associated with significantly improved outcomes. Increasing evidence suggests that better pain control enables patients to start the rehabilitation process earlier and has shorter length of hospital stay (LOS), thus reducing total costs during the in-hospital period and mortality [9, 10]. Poor pain control, instead, predisposes hip fracture patients to delirium and disability, which impairs their ability to perform activities of daily living (ADL), and increases 1-year mortality and morbidity [3, 11]. In addition, previous researches [12, 13] have indicated that emotional problems such as depression and anxiety are also related to the intensity of acute pain after kinds of surgery. Therefore, pain management plays an important role in perioperative patient care since patient safety and comfort after surgery are of utmost importance when evaluating surgery procedures [14].

At the present stage, the existing evidence by the National Institute of Clinical Excellence guidelines suggests that the use of intravenous paracetamol (IVP) might be compared favourably to morphine and nerve block for analgesia as well as reaching a higher peak plasma concentration than its oral equivalent [15–17]. Currently, the most widely used analgesics are nonsteroidal anti-inflammatory drugs (NSAIDs) and opioids, or peripheral nerve blocking. However, patients who use morphine for patient-controlled analgesia experience many side effects related to opioids such as pruritus, tolerance, physical dependence, reward behavior, as well as contribute to serious and potentially permanent nerve damage [18–21]. However, relevant research regarding the use of IVP preoperatively in hip fracture patients is still relatively scarce. Furthermore, whether patients received IVP use have significantly lower delirium incidence, shorter LOS, higher survival rates, and particularly better functional outcomes are relatively lacking. Therefore, the aim of the present paper is to evaluate the preoperative use of IVP in elderly patients with intertrochanteric fractures (IF) and treated by intramedullary fixation on delirium incidence, LOS, and functional outcomes as well as mortality.

2. Materials and Methods

2.1. Study Design, Setting, and Population. A retrospective analysis of all IF patients undergoing intramedullary fixation by proximal femoral nail antirotation (PFNA) was conducted at a single Level I trauma center in China between Jan. 2016 and Jan. 2020. Patients who were 65 years or older, with an admission delay from initial injury <48 h, and received a minimum of one-year follow-up were included and screened. Exclusion criteria were open or pathological fractures, additional fractures of the IF and multiple injuries, patients who had inability to communicate, with mental illness, or refused surgery, and who were treated conservatively due to severe comorbidities, were excluded. The patients were divided into IVP or non-IVP groups according to whether they received IVP preoperatively. All investigations were conducted in conformity with the ethical principles of research. The study was overseen and approved by the institutional internal review board of the participating institution in compliance with the Declaration of Helsinki, and consent was waived as this is an observational study without an intervention. All collected patient data were anonymously recorded to protect patient confidentiality.

2.2. Perioperative Treatment and Surgical Procedure. Our hospital has specialized geriatric orthopedics wards. The patients in wards are assessed once daily by a multidisciplinary team including at least two orthopedists, one internal medicine consultant who is responsible for patients' perioperative management, together with an attending anesthesiologist, and nurses. Strategy in using IVP was according to the current guidelines that is given at a dose of 2000–4000 mg daily in 2–4 divided doses, which has been demonstrated had no relevant side effects on kidney and gastric function [16, 22].

Preoperative X-rays (anteroposterior and lateral view) and a Siemens 128-layer dual-source spiral CT scan (Siemens Medical System, Germany) of the injured leg were taken. Fractures were classified as stable (A1.1–A2.1) or unstable (A2.2–A3.3) according to the Orthopaedic Trauma Association classification system. The patients surgically treated by PFNA that were all following international treatment guidelines. The surgical operation was carried out under general anesthesia or region anesthesia. The position of internal fixation was checked and the wound sutured layer by layer. After the operation, early partial to full weight bearing was encouraged. The patients were followed regularly by an outpatient review or telephone interview with patients or their family members.

2.3. Data Collection. Data were retrospectively collected from our institution's electronic medical record. The data collection consisted of patients' demographics, including gender, age, body mass index (BMI), residence (rural or urban), and smoking or drinking history; injury-related data consisted of fracture type and time from initial injury to surgery; surgery-related data including general health status based on the American Society of Anesthesiologists (ASA) grade (ASA physical status are classified as I to VI) and modified Elixhauser comorbidity method (mECM); and in-hospital data including the Hb level at admission, whether received blood transfusion, the commonly used visual analog scores (VAS) and numerical rating scores (NRS) at admission [23, 24], Geriatric Depression Scale (GDS), functional independence measure (FIM), and anxiety or not. Outcome analyses consisted of operation-related data including anesthesia methods (general or regional), duration of operation, intraoperative blood loss; and in-hospital outcomes including VAS and NRS at discharge, LOS, and

postoperative delirium or not. The participants' survival status and date of death were collected during the follow-up. Beginning of follow-up was defined as enrollment in the cohort, and end point event was defined as all reasons of death or at a most recent follow-up visit, whichever was earlier. Then, 30-day, 90-day, and 12-month mortality and functional outcomes (including independent walking, use of walking aids, wheelchair, bedridden status, and death) were also recorded.

2.4. Definitions. Patients' age was classified as 65–69, 70–79, 80–89, 90–99, and over 100 years old, while BMI was grouped as normal with BMI $<24\,kg/m^2$, overweight with $24 \leq BMI < 28\,kg/m^2$, and obesity with BMI $\geq 28\,kg/m^2$. From electronic medical records, the mECM was used to assess patients' comorbidities at admission and further stratified into groups <0, 0, 1–5, 6–13, and ≥14 in this study cohort. Additionally, ASA grade is a commonly used predictor of mortality in orthopedic surgery. Thus, to ensure transparency, the authors have included both variables as we have done in our previously published studies [25, 26]. The 15-item GDS and FIM were used to determine the depression symptoms and the generic ability to perform ADL, respectively [27, 28]. Breakpoints of 8 g/dL, 10 g/dL, and 12 g/dL were used to classify the Hb level at admission.

2.5. Statistical Analysis. Continuous variables were evaluated for normality by applying the Shapiro–Wilk test. Numerical variables satisfying normality were compared using the Student *t* test to obtain group mean differences, and data are presented as mean ± standard deviation (SD). Median and interquartile range (IQR) were reported as data were non-normally distributed and done with the Mann–Whitney *U* test. Categorical variables are shown as proportions, and the differences were analyzed using the chi-square or Fisher's exact test. To reduce selection bias and potential confounding factors, propensity score matching (PSM) was adopted for the adjustment of baseline clinical by using a 1 : 1 ratio and via the caliper matching of 0.20. After PSM, paired *t* tests and paired chi-square tests were used for continuous variables and categorical variables, respectively. Finally, the Spearman correlations of IVP using, VAS, NRS, and the factors which may influence them were also computed, respectively. All data analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM, Armonk, NY, USA). The level of significance was set at $p < 0.05$.

3. Results

From Jan. 2016 to Jan. 2020, a total of 2963 consecutive patients presenting with IF were retrospectively reviewed and assessed for eligibility. A total of 797 patients were eliminated by the exclusion criteria. Among these patients, 196 were under 65 years old; 213 received conservative treatment; 186 had an admission delay of greater than or equal to 48 h; 47 had open hip fractures, pathological fractures, and multiple injuries; 89 had inability to communicate or with mental illness; and 66 were lost to follow-up. Finally, 2166 patients (including 1576 in the non-IVP group and 590 in the IVP group) who met the inclusion and exclusion criteria were enrolled (Figure 1).

Comparison of general data of patients between two groups is presented in Table 1. More than sixty percent of the participants were female, and the mean age was 79 years old in both groups. There were significant differences between the IVP group and the non-IVP group regarding gender, residence, smoking history, fracture type, VAS and NRS at admission, GDS, FIM, and anxiety incidence. There were 531 matched pairs after propensity score matching, and the two groups had similar baseline demographic and disease characteristics ($p > 0.05$) (Table 1).

Prematching and postmatching results, including operation-related data, VAS and NRS at discharge, LOS, delirium incidence, functional outcomes, and mortalities, are presented in Table 2. The statistical distribution showed that intraoperative blood loss was significantly different between the two groups before PSM; however, the difference was not significant after PSM. Although the differences in the characteristics of VAS and NRS at discharge were significantly reduced between the two groups, after matching, the characteristics of each covariate still differed. Notably, the differences of delirium rate and functional outcomes became significant after propensity score-based matching ($p = 0.001$ and 0.033, respectively); however, before matching, the differences were not significant. No significant difference was observed in other operation-related data, LOS, and crude mortality rates at 30-day, 90-day, and 12-month before and after PSM.

To examine if IVP use, VAS, and NRS were correlated with other variables, correlation analyses were performed. By using the Spearman method, although our results showed several variables were significantly associated, pain (VAS and NRS) at admission was the only variable with the weak correlation to IVP use, while smoking and drinking histories were correlated with pain experience and severity (Tables 3, 4). The overall mortality rates of patients in the non-IVP group and the IVP-group were 20.1% and 20.5%, respectively, at the end of this study.

4. Discussion

It has been reported that approximately two-thirds of patients had moderate-to-severe pain before surgery [10, 29, 30]. However, to the best of our knowledge, inconsistent and inadequate pain control is indeed due to several reasons including fearing side effects, poor treatment compliance by patients, poor consistency in prescribing medications by clinicians, and underappreciated issue in patients with cognitive impairment, which is cited as a barrier to effective pain assessment [9]. In a prospective study, Oberkircher et al. found that although all patients having significant pain before arrival to the hospital, more than seventy percent of patients received no analgesia [10].

Despite oral paracetamol with various doses has been recommended routinely given as the first step of the WHO analgesic ladder [30], its bioavailability when given orally can be reduced by hepatic first pass metabolism. Instead,

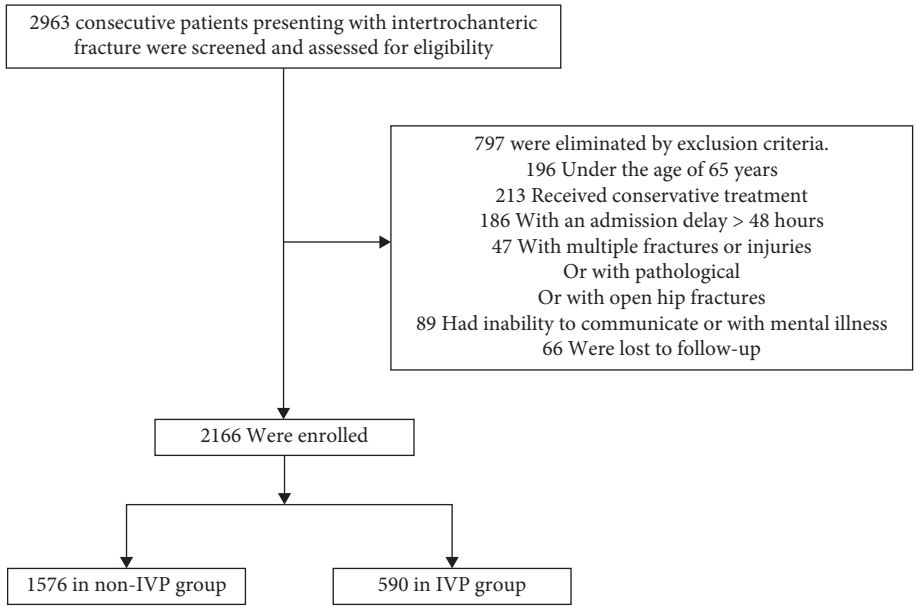

Figure 1: Flow diagram of included patients.

IVP has been proven to be a reliable and effective analgesic in managing both preoperative and postoperative pain for orthopedic patient care [31–33]. Moreover, published literatures [17, 34] have demonstrated that IVP reached a higher peak plasma concentration, with a superior opioid-sparing effect, and significantly reduced morphine requirements with no adverse effects or compromise in pain management than its oral equivalent.

This study set out to evaluate the preoperative use of IVP in elderly patients with IF and treated with intramedullary fixation, focusing on the impact of delirium incidence, LOS, functional outcomes, and mortality. Based on the results analyses performed in this study involving 2166 patients, we observed 590 patients (27.2%) received IVP treatment before surgery, and in male patients, urban living, smoking history, unstable fracture type, higher VAS, NRS, GDS at admission, anxiety, and lower FIM were independent predictors for IVP use. The intensity of acute pain after hip fracture is likely multifactorial. Numerous studies have suggested that gender [35], age [36], smoking history [35, 37], unstable fracture type [36], and anxiety [13, 37] were related factors, which are consistent with our conclusions.

Several literature focused on the use of paracetamol for pain reduction in hip fracture patients, which has been already shown to be associated with reduced delirium rate [29], mortality rate and LOS [9, 16, 29], as well as improved functional outcomes [9, 16]. Few of these studies, however, presented results that adjusted for other covariables that may confound these outcomes. Thus, we applied PSM to minimize confounding biases. The differences roughly represented the effects of gender, residence, smoking history, fracture type, VAS, NRS, GDS at admission, anxiety, and FIM on anesthesia method, intraoperative blood loss, duration of operation, VAS and NRS at discharge, LOS, delirium rate, mortality rate, and functional outcomes before PSM were eliminated in the present study. After PSM and McNemar's tests, we confirmed that IF fracture patients received IVP have advantages in terms of VAS and NRS at discharge, delirium rate, and functional outcomes than the patients who did not receive IVP before surgery. Our conclusions are in line with other literatures [10, 16] that IVP seems to have the potential to reduce delirium rate and gain better functional outcomes that possibly due to early immobilization, as a result of painless.

Previous literature [3, 16] also revealed that optimizing pain management contributed to reducing LOS while poor pain control may increase 1-year mortality. However, we did not obtain similar conclusions in this Chinese population. The fact is that there are many factors affecting LOS and mortality. Previous published articles [6, 38] studied the short-term outcomes of the elderly hip fracture patients. In this study, 437 of 2166 (20.2%) total patients died at the end of the study, and the mortality rates of the non-IVP group and IVP group in 12 months were 6.9% and 6.3% before PSM, respectively. Our findings reveal that the mortality rate is lower than previous data [5, 6, 38], which can be ascribed to the participants selection that we restricted the study population to surgical patients and excluded nonsurgical patients. Similarly, there is no significant difference in mortality rates between the two groups after PSM. Surprisingly, we found that only less than 1 in 10 of patients were restricted to a wheelchair or bedridden state requiring full assistance while most patients could walk independently/with the help of walking aids before and after PSM. Ekstrom et al. [39] demonstrated that only about 55% of patients maintain their activities of daily living and approximately 34% of patients lose their previous ability to walk. According to our results, 40.6% of non-IVP patients and 40.3% of IVP patients walked independently before PSM while the percentages were 42.7% and 44.8% after PSM, respectively. In addition, a substantial percentage of individuals are able to walk with assistive devices.

Table 1: Patient characteristics at baseline comparisons before and after propensity score matching.

Variables	Prematching			Postmatching		
	Non-IVP group ($n = 1576$)	IVP group ($n = 590$)	p value	Non-IVP group ($n = 531$)	IVP group ($n = 531$)	p value
Demographics						
Gender, n (%)						
Male	494 (31.3%)	212 (35.9%)	0.043*	187 (35.2%)	196 (36.9z5)	0.565
Female	1082 (68.7%)	378 (64.1%)		344 (64.8%)	335 (63.1%)	
Age, years	79.0 ± 7.2	79.2 ± 7.3	0.510	79.0 ± 7.4	79.3 ± 7.2	0.518
Age group, n (%)						
65–69	172 (10.9%)	60 (10.2%)		60 (11.3%)	51 (9.6%)	
70–79	639 (40.5%)	230 (39.0%)	0.142	218 (41.1%)	211 (39.7%)	0.174
80–89	655 (41.6%)	251 (42.5%)		215 (40.5%)	225 (42.4%)	
90–99	103 (6.5%)	49 (8.3%)		34 (6.4%)	44 (8.3%)	
≥100	7 (0.4%)	0 (0.0%)		4 (0.8%)	0 (0.0%)	
BMI (kg/m^2), n (%)						
Normal (BMI < 24)	1023 (64.9%)	384 (65.1%)	0.937	345 (65.0%)	347 (65.3%)	0.939
Overweight (24 ≤ BMI < 28)	431 (27.3%)	163 (27.6%)		146 (27.5%)	147 (27.7%)	
Obesity (BMI ≥ 28)	122 (7.7%)	43 (7.3%)		40 (7.5%)	37 (7.0%)	
Residence						
Rural	670 (42.5%)	189 (32.0%)	<0.001*	199 (37.5%)	212 (39.9%)	0.413
Urban	906 (57.5%)	401 (68.0%)		332 (62.5%)	319 (60.1%)	
Smoking history (Yes)	186 (11.8%)	90 (15.3%)	0.032*	87 (16.4%)	78 (14.7%)	0.446
Drinking history (Yes)	373 (23.7%)	157 (26.6%)	0.156	130 (24.5%)	134 (25.2%0	0.776
Injury-related data						
Fracture type, n (%)						
Stable (A1.1–A2.1)	928 (58.9%)	252 (42.7%)	<0.001*	244 (46.0%)	231 (43.5%)	0.422
Unstable (A2.2–A3.3)	648 (41.1%)	338 (57.3%)		287 (54.0%)	300 (56.5%)	
Time from injury to surgery, days	6.1 ± 3.1	5.9 ± 3.3	0.100	6.0 ± 3.1	6.0 ± 3.3	0.766
Surgery-related data						
ASA, n (%)						
1	306 (19.4%)	110 (18.6%)		101 (19.0%)	99 (18.6%)	
2	451 (28.6%)	184 (31.2%)	0.713	152 (28.6%0	164 (30.9%)	0.859
3	575 (36.5%)	200 (33.9%)		196 (36.9%)	181 (34.1%)	
4	206 (13.1%)	82 (13.9%)		72 (13.6%)	75 (14.1%)	
5	38 (2.4%)	14 (2.4%)		10 (1.9%0	12 (2.3%)	
mECM, n (%)						
<0	31 (2.0%)	13 (2.2%)		12 (2.3%)	13 (2.4%)	
0	804 (51.0%)	278 (47.1%)	0.580	272 (51.2%)	250 (47.1%)	0.752
1–5	257 (16.3%)	99 (16.8%)		86 (16.2%)	90 (16.9%)	
6–13	420 (26.6%)	174 (29.5%)		140 (26.4%)	155 (29.2%)	
≥14	64 (4.1%)	26 (4.4%)		21 (4.0%)	23 (4.3%)	
In-hospital data						
Hb level at admission (g/dL)						
Hb ≥ 12	454 (28.8%)	179 (30.3%)		155 (29.2%)	160 (30.1%)	
12 > Hb ≥ 10	670 (42.5%)	237 (40.2%)	0.729	219 (41.2%)	215 (40.5%)	0.962
10 > Hb ≥ 8	371 (23.5%)	146 (24.7%)		127 (23.9%)	129 (24.3%)	
Hb < 8	81 (5.1%)	28 (4.7%)		30 (5.6%)	27 (5.1%)	
Blood transfusion (Yes)	1203 (76.3%)	149 (74.7%)	0.442	413 (77.8%)	400 (75.3%)	0.346
VAS at admission	4.9 ± 1.7	6.4 ± 1.5	<0.001*	5.9 ± 1.3	6.0 ± 1.6	0.410
NRS at admission	4.9 ± 1.7	6.4 ± 1.5	<0.001*	5.9 ± 1.3	5.9 ± 1.6	0.934
GDS	3.5 ± 1.6	4.4 ± 1.3	<0.001*	4.0 ± 1.9	4.2 ± 1.7	0.109
FIM	84.6 ± 10.6	83.4 ± 10.2	0.022*	83.1 ± 10.2	83.3 ± 10.9	0.769
Anxiety (Yes)	142 (9.0%)	507 (14.1%)	0.001*	102 (19.2%)	82 (15.4%)	0.105

Values are presented as the number (%) or mean ± SD (standard deviation). * $p < 0.05$, statistical significance. BMI, body mass index; ASA, American Society of Anesthesiologists; mECM, modified Elixhauser's Comorbidity Measure; VAS, visual analog scores; NRS, numerical rating scores; GDS, Geriatric Depression Scale; FIM, functional independence measure.

Table 2: Patient outcome analyses before and after propensity score matching.

Variables	Prematching			Postmatching		
	Non-IVP group ($n = 1576$)	IVP group ($n = 590$)	p value	Non-IVP group ($n = 531$)	IVP group ($n = 531$)	p value
Type of anesthesia, n (%)			0.906			0.849
General anesthesia	592 (37.6%)	220 (37.3%)		197 (37.1%)	200 (37.7%)	
Regional anesthesia	984 (62.4%)	370 (62.7%)		334 (62.9%)	331 (62.3%)	
Duration of operation, mins	99.7 ± 34.7	97.2 ± 34.6	0.130	99.8 ± 34.5	97.8 ± 35.0	0.352
Intraoperative blood loss (mL)	200 (100, 300)	200 (100, 300)	0.012*	200 (100, 300)	200 (100, 300)	0.095
VAS at discharge	2.4 ± 1.1	1.5 ± 0.9	<0.001*	2.3 ± 1.1	1.8 ± 0.9	<0.001*
NRS at discharge	2.3 ± 1.1	1.4 ± 0.8	<0.001*	2.2 ± 1.1	1.8 ± 0.9	<0.001*
Length of hospital stay	14.7 ± 6.8	14.3 ± 6.0	0.255	14.3 ± 6.5	14.4 ± 6.1	0.815
Delirium (Yes)	128 (8.1%)	48 (8.1%)	0.992	85 (16.0%)	48 (9.0%)	0.001*
30-day mortality	14 (0.9%)	5 (0.8%)	0.928	6 (1.1%)	5 (0.9%)	0.762
90-day mortality	25 (1.6%)	8 (1.4%)	0.697	10 (1.9%)	8 (1.5%)	0.634
12-month mortality	109 (6.9%)	37 (6.3%)	0.594	39 (7.3%)	37 (7.0%)	0.812
Functional outcomes						
Independent walking	640 (40.6%)	238 (40.3%)	0.984	227 (42.7%)	238 (44.8%)	0.033*
Use of walking aids	488 (31.0%)	182 (30.8%)		158 (29.8%)	178 (33.5%)	
Use of wheelchair	92 (5.8%)	32 (5.4%)		34 (6.4%)	41 (7.7%)	
Bedridden	40 (2.5%)	17 (2.9%)		15 (2.8%)	7 (1.3%)	
Death	316 (20.1%)	121 (20.5%)		97 (18.3%)	67 (12.6%)	

Values are presented as the number (%) or mean ± SD (standard deviation) or median (interquartile range). * $p < 0.05$, statistical significance. VAS, visual analog scores; NRS, numerical rating scores.

Table 3: The association of IVP group with gender, age, residence, smoking or drinking history, fracture type, pain scores at admission, GDS, FIM, and anxiety.

Variables	Non-IVP group ($n = 1576$)	IVP group ($n = 590$)	Spearman's r statistic	p value
Gender, n (%)				
Male	494 (31.3%)	212 (35.9%)	−0.044	0.043*
Female	1082 (68.7%)	378 (64.1%)		
Age, years	79.0 ± 7.2	79.2 ± 7.3	0.016	0.451
Age group, n (%)				
65–69	172 (10.9%)	60 (10.2%)	0.026	0.235
70–79	639 (40.5%)	230 (39.0%)		
80–89	655 (41.6%)	251 (42.5%)		
90–99	103 (6.5%)	49 (8.3%)		
≥100	7 (0.4%)	0 (0.0%)		
Residence				
Rural	670 (42.5%)	189 (32.0%)	−0.096	<0.001*
Urban	906 (57.5%)	401 (68.0%)		
Smoking history (Yes)	186 (11.8%)	90 (15.3%)	0.049	0.022*
Drinking history (Yes)	373 (23.7%)	157 (26.6%)	0.033	0.126
Fracture type, n (%)				
Stable (A1.1–A2.1)	928 (58.9%)	252 (42.7%)	0.147	<0.001*
Unstable (A2.2–A3.3)	648 (41.1%)	338 (57.3%)		
VAS at admission	4.9 ± 1.7	6.4 ± 1.5	0.388	<0.001*
NRS at admission	4.9 ± 1.7	6.4 ± 1.5	0.396	<0.001*
GDS	4.4 ± 1.3	3.5 ± 1.6	−0.286	<0.001*
FIM	84.6 ± 10.6	83.4 ± 10.2	0.055	0.010*
Anxiety (Yes)	142 (9.0%)	507 (14.1%)	0.074	0.001*

Values are presented as the number (%) or mean ± SD (standard deviation). * $p < 0.05$, statistical significance. VAS, visual analog scores; NRS, numerical rating scores; GDS, Geriatric Depression Scale; FIM, functional independence measure.

Previous considerable research has assessed the factors influencing the rates of functional outcomes and mortality in hip fracture patients. Compared to these former studies, the strength of this study lies in the more recent data with a relatively large sample size. Other strengths are the sets of scoring systems we involved and the specific cohort of patients who received surgery by a single internal fixation and grouped based on whether they received IVP or not,

Table 4: The association of pain scores (VAS and NRS) with gender, age, BMI, residence, smoking or drinking history, fracture type, ASA, mECM, Hb level at admission, GDS, FIM, and anxiety.

Variables	VAS at admission	p value	NRS at admission	p value
Gender	−0.011	0.595	−0.004	0.836
Age	0.002	0.917	0.003	0.874
Age group	0.002	0.915	0.004	0.863
BMI	0.003	0.895	−0.002	0.924
Residence	−0.095	<0.001*	−0.087	<0.001*
Smoking history (Yes)	0.209	<0.001*	0.201	<0.001*
Drinking history (Yes)	0.262	<0.001*	0.292	<0.001*
Fracture type	0.015	0.474	0.015	0.497
ASA	0.008	0.726	0.010	0.638
mECM	−0.007	0.750	−0.004	0.863
Hb level at admission	0.025	0.242	0.024	0.263
GDS	−0.157	<0.001*	−0.166	<0.001*
FIM	−0.088	<0.001*	−0.099	<0.001*
Anxiety	0.010	0.644	0.020	0.348

* $p < 0.05$, statistical significance. VAS, visual analog scores; NRS, numerical rating scores; BMI, body mass index; ASA, American Society of Anesthesiologists; mECM, modified Elixhauser's Comorbidity Measure; GDS, Geriatric Depression Scale; FIM, functional independence measure.

which eliminated the effects of possible confounding variables. Finally, to the best of our knowledge, this is the first study to evaluate IVP on functional outcomes in hip fracture patients after PSM. Such quantitative analyses might increase the orthopedist's confidence in pain management for hip fracture patients and be beneficial for clinicians looking to establish probabilities for delirium and adverse functional outcomes in the future and establishing rational goals of medical care for this vulnerable population. A weakness, however, comes with the fact that it is a retrospective single-center observational study. In addition, we did not rule out other unknown factors, including perioperative laboratory values and surgeon practice, for analysis, which may potentially influence our findings. However, this is the first study including multiple relative contributions of patient demographics, injury-related, surgery-related, anesthetic, transfusion, and sets of scoring systems factors, which have not been studied together.

5. Conclusion

In conclusion, early identification of individuals with moderate-to-severe pain and using IVP preoperatively for pain killing is prone to reducing pain score at discharge, delirium incidence, and achieving better functional outcomes that benefited from accelerated care. This study highlights the need for preoperative IVP to optimize pain control and minimize pain-related comorbidity as well as postoperative functional recovery in elderly patients with hip fracture.

Abbreviations

LOS: Length of hospital stay
ADL: Activities of daily living
IVP: Intravenous paracetamol
IF: Intertrochanteric fracture
PFNA: Proximal femoral nail antirotation
BMI: Body mass index
ASA: American Society of Anesthesiologists
mECM: Modified Elixhauser comorbidity method
VAS: Visual analog scores
NRS: Numerical rating scores
GDS: Geriatric Depression Scale
FIM: Functional independence measure
PSM: Propensity score matching.

Data Availability

The data and code used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Acknowledgments

The authors gratefully acknowledge the work performed by the members of our hospital staff and laboratory. The study was financially supported by the National Key R&D Program of China (No. 2019YFC0120600) and the 2019 Hebei Provincial Department of Finance Geriatric Disease Prevention and Control Funds, and Baoding City Science and Technology and Intellectual Property Bureau (No. 2041ZF260).

References

[1] Q. Zhang, Y. Wu, T. Han, and E. Liu, "Changes in cognitive function and risk factors for cognitive impairment of the elderly in China: 2005–2014," *International Journal of Environmental Research and Public Health*, vol. 16, no. 16, 2019.

[2] L. Wang, X. Xu, Y. Zhang et al., "A model of health education and management for osteoporosis prevention," *Experimental and Therapeutic Medicine*, vol. 12, no. 6, pp. 3797–3805, 2016.

[3] J. Zanker and G. Duque, "Rapid geriatric assessment of hip fracture," *Clinics in Geriatric Medicine*, vol. 33, no. 3, pp. 369–382, 2017.

[4] S. Mundi, B. Pindiprolu, N. Simunovic, and M. Bhandari, "Similar mortality rates in hip fracture patients over the past 31 years," *Acta Orthopaedica*, vol. 85, no. 1, pp. 54–59, 2014.

[5] T. Roth, C. Kammerlander, M. Gosch, T. J. Luger, and M. Blauth, "Outcome in geriatric fracture patients and how it can be improved," *Osteoporosis International*, vol. 21, no. 4, pp. S615–S619, 2010.

[6] C. A. Brauer, M. Coca-Perraillon, D. M. Cutler, and A. B. Rosen, "Incidence and mortality of hip fractures in the United States," *Jama*, vol. 302, no. 14, pp. 1573–1579, 2009.

[7] J. Zhou, Y. Fan, J. Zhong, X. Wen, and H. Chen, "Efficacy and safety of multimodal analgesic techniques for preventing chronic postsurgery pain under different surgical categories: a meta-analysis," *Scientific Reports*, vol. 7, no. 1, p. 678, 2017.

[8] S. Vacas and B. Van de Wiele, "Designing a pain management protocol for craniotomy: a narrative review and consideration of promising practices," *Surgical Neurology International*, vol. 8, p. 291, 2017.

[9] S. R. Morrison, J. Magaziner, M. A. McLaughlin et al., "The impact of post-operative pain on outcomes following hip fracture," *Pain*, vol. 103, no. 3, pp. 303–311, 2003.

[10] L. Oberkircher, N. Schubert, D.-A. Eschbach et al., "Pre-hospital pain and analgesic therapy in elderly patients with hip fractures," *Pain Practice*, vol. 16, no. 5, pp. 545–551, 2016.

[11] K. S. Feldt, M. B. Ryden, and S. Miles, "Treatment of pain in cognitively impaired compared with cognitively intact older patients with hip-fracture," *Journal of the American Geriatrics Society*, vol. 46, no. 9, pp. 1079–1085, 1998.

[12] S. Ziehm, J. Rosendahl, J. Barth, B. M. Strauss, A. Mehnert, and S. Koranyi, "Psychological interventions for acute pain after open heart surgery," *Cochrane Database of Systematic Reviews*, vol. 7, no. 7, Article ID Cd009984, 2017.

[13] R. R. Edwards, J. A. Haythornthwaite, M. T. Smith, B. Klick, and J. N. Katz, "Catastrophizing and depressive symptoms as prospective predictors of outcomes following total knee replacement," *Pain Research and Management*, vol. 14, no. 4, pp. 307–311, 2009.

[14] P. S. Myles, D. L. Williams, M. Hendrata, H. Anderson, and A. M. Weeks, "Patient satisfaction after anaesthesia and surgery: results of a prospective survey of 10,811 patients," *British Journal of Anaesthesia*, vol. 84, no. 1, pp. 6–10, 2000.

[15] P. Cuvillon, J. Ripart, S. Debureaux et al., "Analgesia after hip fracture repair in elderly patients: the effect of a continuous femoral nerve block: a prospective and randomised study," *Annales Françaises d'Anesthesie et de Reanimation*, vol. 26, no. 1, pp. 2–9, 2007.

[16] A. J. Bollinger, P. D. Butler, M. S. Nies, D. L. Sietsema, C. B. Jones, and T. J. Endres, "Is scheduled intravenous acetaminophen effective in the pain management protocol of geriatric hip fractures?" *Geriatric Orthopaedic Surgery & Rehabilitation*, vol. 6, no. 3, pp. 202–208, 2015.

[17] J. Van der Westhuizen, P. Y. Kuo, P. W. Reed, and K. Holder, "Randomised controlled trial comparing oral and intravenous paracetamol (acetaminophen) plasma levels when given as preoperative analgesia," *Anaesthesia and Intensive Care*, vol. 39, no. 2, pp. 242–246, 2011.

[18] F. Chatigny, C. M. Creighton, and E. D. Stevens, "Intramuscular infiltration of a local anesthetic, lidocaine, does not result in adverse behavioural side effects in rainbow trout," *Scientific Reports*, vol. 8, no. 1, Article ID 10250, 2018.

[19] D. You, L. Qin, K. Li, D. Li, G. Zhao, and L. Li, "A meta-analysis on advantages of peripheral nerve block post-total knee arthroplasty," *The Korean Journal of Pain*, vol. 34, no. 3, pp. 271–287, 2021.

[20] M. A. Gandini, I. A. Souza, D. Raval, J. Xu, Y.-X. Pan, and G. W. Zamponi, "Differential regulation of Cav2.2 channel exon 37 variants by alternatively spliced μ-opioid receptors," *Molecular Brain*, vol. 12, no. 1, p. 98, 2019.

[21] L. Shen, W. Wang, S. Li, J. Qin, and Y. Huang, "NMDA receptor antagonists attenuate intrathecal morphine-induced pruritus through ERK phosphorylation," *Molecular Brain*, vol. 11, no. 1, p. 35, 2018.

[22] K. A. Candiotti, S. D. Bergese, E. R. Viscusi, S. K. Singla, M. A. Royal, and N. K. Singla, "Safety of multiple-dose intravenous acetaminophen in adult inpatients," *Pain Medicine*, vol. 11, no. 12, pp. 1841–1848, 2010.

[23] W. W. Downie, P. A. Leatham, V. M. Rhind, V. Wright, J. A. Branco, and J. A. Anderson, "Studies with pain rating scales," *Annals of the Rheumatic Diseases*, vol. 37, no. 4, pp. 378–381, 1978.

[24] D. D. Price, F. M. Bush, S. Long, and S. W. Harkins, "A comparison of pain measurement characteristics of mechanical visual analogue and simple numerical rating scales," *Pain*, vol. 56, no. 2, pp. 217–226, 1994.

[25] J. Guo, P. Ye, Q. Zhang et al., "Is there a "weekend effect" in intertrochanteric fracture surgery?" *Gerontology*, pp. 1–12, 2021.

[26] J. Guo, J. Di, X. Gao et al., "Discriminative ability for adverse outcomes after hip fracture surgery: a comparison of three commonly used comorbidity-based indices," *Gerontology*, vol. 68, no. 1, pp. 1–13, 2021.

[27] A. S. Schreiner, H. Hayakawa, T. Morimoto, and T. Kakuma, "Screening for late life depression: cut-off scores for the geriatric depression Scale and the cornell Scale for depression in dementia among Japanese subjects," *International Journal of Geriatric Psychiatry*, vol. 18, no. 6, pp. 498–505, 2003.

[28] K. Goto, H. Kataoka, A. Honda et al., "Factors Affecting Persistent Postoperative Pain in Patients with Hip Fractures," *Pain Research and Management*, vol. 2020, Article ID 8814290, 7 pages, 2020.

[29] J. Dixon, F. Ashton, P. Baker, K. Charlton, C. Bates, and W. Eardley, "Assessment and early management of pain in hip fractures: the impact of paracetamol," *Geriatric orthopaedic surgery & rehabilitation*, vol. 9, Article ID 2151459318806443, 2018.

[30] G. Vargas-Schaffer, "Is the WHO analgesic ladder still valid? Twenty-four years of experience," *Canadian Family Physician*, vol. 56, no. 6, pp. 514–517, 2010.

[31] P. F. White, "The role of non-opioid analgesic techniques in the management of pain after ambulatory surgery," *Anesthesia & Analgesia*, vol. 94, no. 3, pp. 577–585, 2002.

[32] J. Hernández-Palazón, J. A. Tortosa, J. F. Martínez-Lage, and D. Pérez-Flores, "Intravenous administration of propacetamol reduces morphine consumption after spinal fusion surgery," *Anesthesia & Analgesia*, vol. 92, no. 6, pp. 1473–1476, 2001.

[33] V. A. Peduto, M. Ballabio, and S. Stefanini, "Efficacy of propacetamol in the treatment of postoperative pain Morphine-sparing effect in orthopedic surgery," *Acta Anaesthesiologica Scandinavica*, vol. 42, no. 3, pp. 293–298, 1998.

[34] K. S. Tsang, J. Page, and P. Mackenney, "Can intravenous paracetamol reduce opioid use in preoperative hip fracture patients?" *Orthopedics*, vol. 36, no. 2, pp. 20–24, 2013.

[35] H. L. Chiang, Y.-Y. Chia, H.-S. Lin, and C.-H. Chen, "The Implications of Tobacco Smoking on Acute Postoperative

Pain: A Prospective Observational Study," *Pain Research and Management*, vol. 2016, Article ID 9432493, 7 pages, 2016.

[36] H. Y. V. Ip, A. Abrishami, P. W. H. Peng, J. Wong, and F. Chung, "Predictors of postoperative pain and analgesic consumption," *Anesthesiology*, vol. 111, no. 3, pp. 657–677, 2009.

[37] H. Ye, R. Chen, X. Lian et al., "Risk factors associated with postoperative pain and discomfort in oculoplastic surgery with general anesthesia: a prospective study," *Journal of Pain Research*, vol. 11, pp. 407–415, 2018.

[38] O. Chechik, R. Thein, G. Fichman, A. Haim, T. B. Tov, and E. L. Steinberg, "The effect of clopidogrel and aspirin on blood loss in hip fracture surgery," *Injury*, vol. 42, no. 11, pp. 1277–1282, 2011.

[39] W. Ekström, R. Miedel, S. Ponzer, M. Hedström, E. Samnegård, and J. Tidermark, "Quality of life after a stable trochanteric fracture-A prospective cohort study on 148 patients," *Journal of Orthopaedic Trauma*, vol. 23, no. 1, pp. 39–44, 2009.

Hindawi
Pain Research and Management
Volume 2022, Article ID 1639560, 11 pages
https://doi.org/10.1155/2022/1639560

Research Article

Overexpression of Aquaporin-3 Alleviates Hyperosmolarity-Induced Nucleus Pulposus Cell Apoptosis via Regulating the ERK1/2 Pathway

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Received 24 September 2021; Revised 23 October 2021; Accepted 18 March 2022; Published 9 April 2022

Academic Editor: Sidong Yang

Intervertebral disc degeneration (IDD) is closely related to osmolarity, which fluctuates with daily activities, and hyperosmolarity may be a contributor to nucleus pulposus (NP) cells apoptosis. Aquaporin-3 (AQP-3) belongs to the family of aquaporins and mainly transports water and other small molecular proteins, which is reduced with the aging of the intervertebral disc. ERK1/2 pathway is one type of mitogen-activated protein kinase (MAPK) and is associated with cellular apoptosis. This study was aimed to investigate the effects of AQP-3 on NP cells apoptosis induced by a hyperosmolarity and focused on the role of the ERK1/2 signaling pathway. We found that NP apoptosis could be induced by hyperosmolarity (550 mOsm/kg), and downregulation of AQP-3 and inhibition of ERK1/2 could be simultaneously observed. Therefore, lentivirus was used to enhance the expression of AQP-3 to compare apoptosis between AQP-3-overexpressed NP cells and the control NP cells. The results showed that apoptosis could be alleviated by overexpression of AQP-3 and the activity of ERK1/2 could also be promoted. Furthermore, we found that the inhibitor U0126 could partly aggravate apoptosis of the AQP-3-overexpressed NP cells. In summary, our results suggested that overexpression of AQP-3 could protect against hyperosmolarity-induced NP cell apoptosis via promoting the activity of the ERK1/2 pathway. This study may shed light on a better understanding of the pathologic mechanism of IDD and bring AQP-3 into the therapeutic approaches for IDD treatment.

1. Introduction

Intervertebral disc degeneration (IDD), one of the most important causes of low back pain (LBP), severely affects normal daily life and imposes a significant financial burden on society and the healthcare system [1–3]. Currently, treatments for intervertebral disc degeneration, such as bed rest, functional exercise, physical therapy, and surgery, only relieve pain and do not target the cause of the condition [4–6]. Therefore, an in-depth investigation into the pathophysiological mechanism of intervertebral disc degeneration will provide a theoretical basis for the biological repairment of degenerated intervertebral discs.

Apoptosis, also known as programmed cell death, plays an important role in facilitating IDD by directly reducing the number of nucleus pulposus (NP) cells, thereby affecting the synthesis of extracellular matrix in intervertebral disc NP tissue, such as collagen and proteoglycan [7–11]. The intervertebral disc consists of the upper and lower cartilaginous endplates, the outer annulus fibrosus, and the central

NP tissue [12]. NP tissue is highly hydrophilic due to the rich content of negatively charged glycosaminoglycans [13, 14]. Performance of day-to-day activities and changes in the spinal posture cause the NP tissue to be subjected to the constant change in axial compressive stress [15, 16]. This causes water to enter or exit the NP tissue, which in turn causes the in situ osmotic pressure of the NP tissue to fluctuate between 450 mOsm/kg and 550 mOsm/kg, a range that is much higher than the normal osmotic pressure of other extracellular fluids in the human body [17]. Studies by other research groups and our research group have shown that an environment with high osmotic pressure promotes the apoptosis of NP cells [18, 19], but the related mechanism is still unclear.

Aquaporins (AQPs) are transmembrane water channel proteins that can regulate the permeability of cells to water and other small molecules [20, 21]. Previous studies have reported that the expression of AQPs in notochord cells of mouse intervertebral discs is affected by the osmotic pressure environment and is involved in regulating notochord cell differentiation and apoptosis [22]. Aquaporin-3 (AQP-3) is one of the important members of the aquaporin family; it is expressed in rat and human NP tissues and annulus fibrosus tissues. Some studies have proven that AQP-3 expression is significantly reduced in degenerated intervertebral discs compared with normal intervertebral disc [21, 22]. The ERK pathway, one of the important components of the MAPK signaling pathway, participates in the biological processes of various cells. In a study of chondrocytes, ERK1/2 plays a role in osmotic pressure-induced apoptosis, and inhibiting ERK1/2 can increase apoptosis of NP cells in the osmotic pressure culture of intervertebral disc organ models [18, 23]. Studies have also found that AQP-3 can activate the ERK1/2 pathway [19]. The purpose of the current study is to investigate the relationship between AQP-3 expression and apoptosis in NP cells under different osmotic pressure environments and to explore the role of AQP-3 and the ERK1/2 pathway in NP cell apoptosis.

2. Methods

2.1. Disc Harvest and NP Cell Culture. Twenty-five Sprague-Dawley rats (female, 300–320 g and 12–13 weeks old) were purchased from the Animal Center of Southwest Hospital affiliated with the Army Medical University. The animal care methods were carried out according to the relevant guidelines [SYXK (YU) 2012-0012] and approved by the Ethics Committee at Southwest Hospital affiliated with the Army Medical University. After rats were sacrificed with excess carbon dioxide inhalation, the lumbar discs were separated under sterile conditions. Then, the innermost NP tissue was harvested under a dissecting microscope. NP cell pellet was obtained after sequential enzymatic digestion with 0.25% trypsin for 5–10 minutes and 0.25% Type II collagenase for 10–15 minutes at 37°C. Thereafter, NP cell pellets were resuspended with DMEM/F12 containing 10% fetal bovine serum (FBS) and 1% penicillin-streptomycin and were cultured under standard conditions (37°C, 21% O_2, and 5% CO_2). The passage 2 (P2) NP cells were used in this study. The medium osmolarity levels of 330 mOsm/kg and 550 mOsm/kg were used in this study and these defined osmolarity levels were adjusted with sodium chloride and verified with a freezing-point osmometer (FM-8P, Shanghai Medical College Instrument Co. Ltd, China).

2.2. Cell Transfection. Briefly, after NP cells seeded in the 6-well plate were grown to approximately 50–55% confluence, NP cells were incubated with the recombinant lentiviral vectors LV5-AQP-3 (GenePharma, Shanghai, China) for 48 hours to enhance AQP-3 expression (NP-AQP-3). The control NP cells were transfected with negative vectors (NP-AQP-3-NC). To further purify the transfected NP cells, all transfected NP cells were incubated with a culture medium containing additional puromycin (1 ug/ml) for 5-6 days. The transfection efficacy was verified by observation under a fluorescence microscope, real-time PCR, and western blot assays.

2.3. CCK-8 Assay. NP cell proliferation was measured with a Cell Counting Kit-8 (CCK-8, Beyotime, China). Briefly, 2×10^3 cells/well were seeded in a 96-well plate and incubated in a 5% CO_2 incubator at 37°C with the osmolarity of 330 mOsm/kg and 550 mOsm/kg, and then 20 ul of CCK-8 was added to each well after 12 h, 24 h, 48 h, and 72 h, respectively. Next, after incubation for another 2 h, the potency of cell proliferation indicated by the absorbance at a wavelength of 450 nm was detected.

2.4. Flow Cytometry. After being incubated in the osmolarity of 330 mOsm/kg and 550 mOsm/kg, NP cells were harvested with 0.25% trypsin without EDTA and washed 3 times with phosphate buffer solution (PBS). Then, NP cell apoptosis was evaluated by Annexin V-APC/PI double staining according to the manufacturer's instructions (KeyGENBioTECH, China). NP cells were suspended in binding buffer and 1×10^5 cells were incubated with 5 ul of Annexin V-APC and 10 ul of PI at room temperature in the dark for 20 min. Apoptotic cells were counted by FACS scan flow cytometer (NovaCyte, US) and the cells were stained as Annexin V(+)/PI(−) and Annexin V(+)/PI(+) were regarded as apoptotic cells in this assay.

2.5. Quantitative Real-Time PCR. Total RNA was extracted from NP cells with TRIzol reagent (Invitrogen, USA) according to the manufacturer's instructions. After determinating RNA concentration, extracted RNA was synthesized into cDNA with a reverse transcription kit (Roche, Switzerland). Subsequently, quantitative real-time PCR was performed to quantify the mRNA expression levels of Bax, Bcl-2, caspase-3, and AQP-3 with 40 cycles through a reaction system containing cDNA, primers (Table 1), and SYBR Green Mix (Roche, Switzerland). β-Actin was used as an internal reference and the relative gene expressions were calculated as $2^{-\Delta\Delta Ct}$.

Table 1: Primers of target genes.

Gene	Forward (5′-3′)	Reverse (5′-3′)
β-Actin	CCGCGAGTACAACCTTCTTG	TGACCCATACCCACCATCAC
Bcl-2	GGGGCTACGAGTGGGATACT	GACGGTAGCGACGAGAGAAG
Bax	GGCGAATTGGCGATGAACTG	CCCAGTTGAAGTTGCCGTCT
Caspase-3	GGAGCTTGGAACGCGAAGA	ACACAAGCCCATTTCAGGGT
AQP-3	AGAAGGAGTTGATGAACCGTTGCG	AACCACAGCCGAACATCACAAGG

2.6. Western Blot. To detect the protein level of apoptosis-related molecules (Bax, Bcl-2, and cleaved caspase-3) and AQP-3, a western blot was performed according to the following steps. Total protein was isolated from NP cells using RIPA lysis buffer with PMSF and phosphatase inhibitor, and the concentration of the protein sample was measured with a BCA Protein Quantification kit. The same amount of proteins in each group was subject to SDS-PAGE and transferred to PVDF membranes. After being blocked with 5% skimmed milk at room temperature for 1 h, these PVDF membranes were incubated with primary antibodies (Bax: Proteintech, 60267-1; Bcl-2: Proteintech, 12789-1-AP; cleaved-caspase3: CST, 9661T; AQP-3: Abcam, ab125219; GAPDH: Proteintein, 60004-1-Ig; β-actin: Proteintein, 60008-1; ERK1/2: Santa Cruz, sc-292838; p-ERK1/2: Santa Cruz, sc-101761) at 4°C overnight with a dilution of 1 : 1000, then washed with TBST solution 3 times, and incubated with corresponding HRP-conjugated secondary antibodies (Beyotime, diluted 1 : 2000) at room temperature for 2 h. Then, protein bands were detected using the enhanced chemiluminescent system. GAPDH and β-actin were used as the internal reference.

2.7. Immunocytochemistry. To analyze AQP-3 protein expression difference between 330 mOsm/kg culture and 550 mOsm/kgculture, immunocytochemistry staining was performed on cell slides. NP cells were cultured on cell sides for 3 days, then fixed with 4% paraformaldehyde for 30 min at room temperature, and blocked with 5% BSA for 30 min. The cell sides were incubated with AQP-3 primary antibody (1 : 100, Abcam, US) overnight at 4°C. After being washed 3 times, the cell slides were incubated with the HRP-conjugated secondary antibody (1 : 200, ZSGB-BIO, China) for 1 h. Finally, the color development was finished with DAB and the cell slides were viewed under a microscope (Olympus EX51).

2.8. Statistical Analysis. All data were expressed as mean ± SD (standard deviation) and SPSS20.0 software was used for statistical analysis. The difference between two groups was performed by Student's t-test. The comparison of multiple groups was performed by one-way analysis of variance (ANOVA), followed by a post hoc test was determined by LSD test. Values of $p < 0.05$ were considered statistically significant.

3. Results

3.1. Apoptosis of NP Cells Increased under Culture with Hyperosmolarity. CCK-8 assay results showed that compared with NP cells cultured under an osmotic pressure of 330 mOsm/kg for 12 h, 24 h, 48 h, and 72 h, the proliferation of NP cells cultured under an osmotic pressure of 550 mOsm/kg for the same durations was significantly reduced (Figure 1(a)).

Flow cytometry analysis showed that the apoptosis rate was significantly higher in NP cells at osmotic pressure of 550 mOsm/kg than at 330 mOsm/kg (Figure 1(b)). Meanwhile, western blotting and quantitative PCR results showed that compared with an osmotic pressure of 330 mOsm/kg, osmotic pressure of 550 mOsm/kg decreased the mRNA/protein expression of antiapoptotic molecule Bcl-2 and increased the mRNA/protein expression of proapoptotic molecules Bax and cleaved caspase 3/caspase-3 in NP cells (Figures 2(a) and 2(b)). These results suggest that a high osmotic pressure condition promotes apoptosis of NP cells.

3.2. AQP-3 Expression in NP Cells Decreased and ERK1/2 Pathway Activity Was Suppressed under a High Osmotic Pressure Condition. Immunocytochemical detection of AQP-3 expression in NP cells under osmotic pressures of 550 mOsm/kg and 330 mOsm/kg showed that, compared to the AQP-3 expression under an osmotic pressure of 330 mOsm/kg, the AQP-3 expression under 550 mOsm/kg was significantly reduced (Figure 3(a)). In addition, western blotting and quantitative PCR results showed that mRNA and protein expression of AQP-3 in NP cells under an osmotic pressure of 550 mOsm/kg were also significantly reduced (Figures 3(b) and 3(c)). These results suggest that a high osmotic pressure environment reduces AQP-3 expression in NP cells. In addition, western blot results showed that, compared to the osmotic pressure of 330 mOsm/kg, the ratio of p-ERK1/2 to ERK1/2 in NP cells decreased at osmotic pressure of 550 mOsm/kg, suggesting that the activity of the ERK1/2 pathway inhibited under a high osmotic pressure condition (Figure 3(d)).

3.3. Overexpression of AQP-3 Alleviated Apoptosis of NP Cells in a High Osmotic Pressure Environment. Verification of the efficacy of AQP-3 overexpression in NP cells showed that after transfection with a lentivirus overexpressing AQP-3 (NP-AQP-3), the mRNA and protein levels of AQP-3 were significantly higher than those in NP cells transfected with the negative control lentivirus (NP-AQP-3-NC) and NP cells in the blank control group (NP-CN). Furthermore, there was no statistically significant difference in the expression levels of AQP-3 mRNA and protein between NP cells transfected with negative control lentivirus (NP-AQP-3-NC) and NP

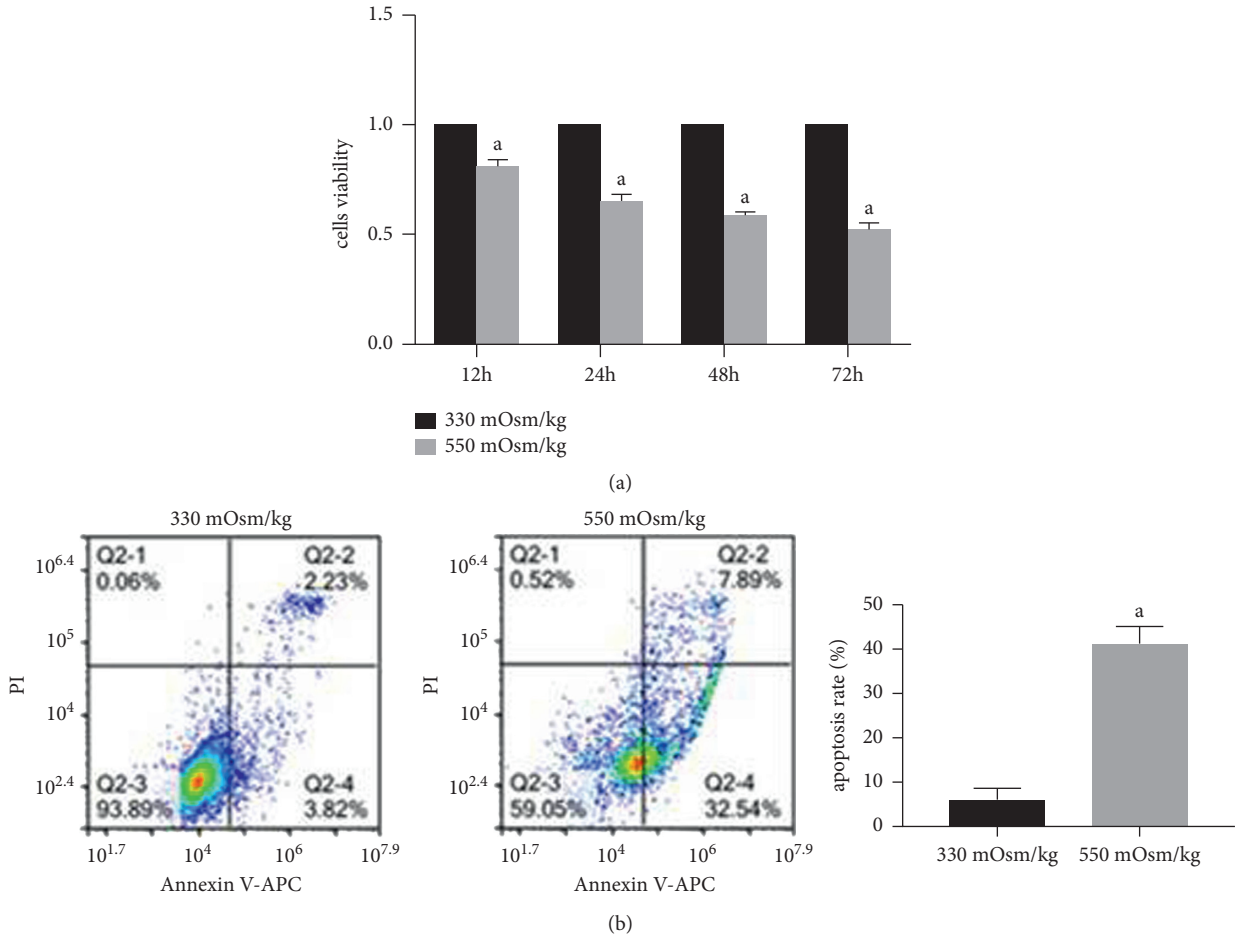

Figure 1: Hyperosmolarity inhibited NP cell proliferation and promoted NP cell apoptosis. (a) The proliferation of rat NP cells detected by CCK-8. (b) Flow cytometry analysis of cell apoptosis rate under different osmotic pressures (330 mOsm/kg and 550 mOsm/kg). Data are expressed as mean ± SD. (A) indicates a significant difference ($p < 0.05$) when compared with 330 mOsm/kg.

cells in the blank control group (NP-CN) (Figures 4(a) and 4(b)).

To observe the change in the activity of the ERK1/2 pathway after AQP-3 overexpression, we further detected protein expression of p-ERK1/2 and ERK1/2 under different osmotic pressure cultures. The western blotting showed that the ratio of p-ERK1/2 to ERK1/2 was promoted in NP-AQP-3 cultured in 550 mOsm/kg compared with NP-CN (Figure 5(a)). Flow cytometry analysis showed that, compared with the apoptosis rate of NP-AQP-3-NC, the apoptosis rate of NP-AQP-3 decreased under an osmotic pressure of 550 mOsm/kg. The western blotting and quantitative PCR results showed that the expression of the antiapoptotic molecule Bcl-2 in NP cells increased, while the expression of proapoptotic molecules Bax and cleaved caspase-3/caspase-3 decreased under an osmotic pressure of 550 mOsm/kg. However, compared with the apoptosis rate under an osmotic pressure of 330 mOsm/kg, the apoptosis rate of NP cells significantly increased, the expression of the antiapoptotic molecule Bcl-2 decreased, and the expression of proapoptotic molecules Bax and cleaved caspase-3/caspase-3 increased under an osmotic pressure condition of 550 mOsm/kg in NP-AQP-3 cells (Figures 5(b)–5(d)).

3.4. Apoptosis of AQP-3-Overexpressed NP Cells Increased after Inhibition of the ERK1/2 Pathway. Under an osmotic pressure of 550 mOsm/kg, the ERK1/2 pathway inhibitor U0126 was added to observe the apoptosis of NP cells after inhibition of the ERK1/2 pathway. Flow cytometric analysis showed that the apoptosis rate was higher in NP-AQP-3 + U0126 cells than that in the NP-AQP-3 group when both of them were cultured under an osmotic pressure of 550 mOsm/kg (Figure 6(a)). The western blotting and quantitative PCR results showed that the expression of the antiapoptotic molecule Bcl-2 in NP cells decreased, while the expression of proapoptotic molecules Bax and cleaved caspase-3/caspase-3 increased after inhibition of the ERK1/2 pathway (Figures 6(b) and 6(c)). Moreover, compared with the NP-CN + U0126 group, the apoptosis rate of NP cells was significantly decreased, the expression of the antiapoptotic molecule Bcl-2 was increased, and the expression of proapoptotic molecules Bax and cleaved caspase-3/caspase-3 was decreased in the NP-AQP-3 + U0126 group under an osmotic pressure of 550 mOsm/kg, indicating that AQP-3 overexpression has certain protective effects (Figures 6(a)–6(c)).

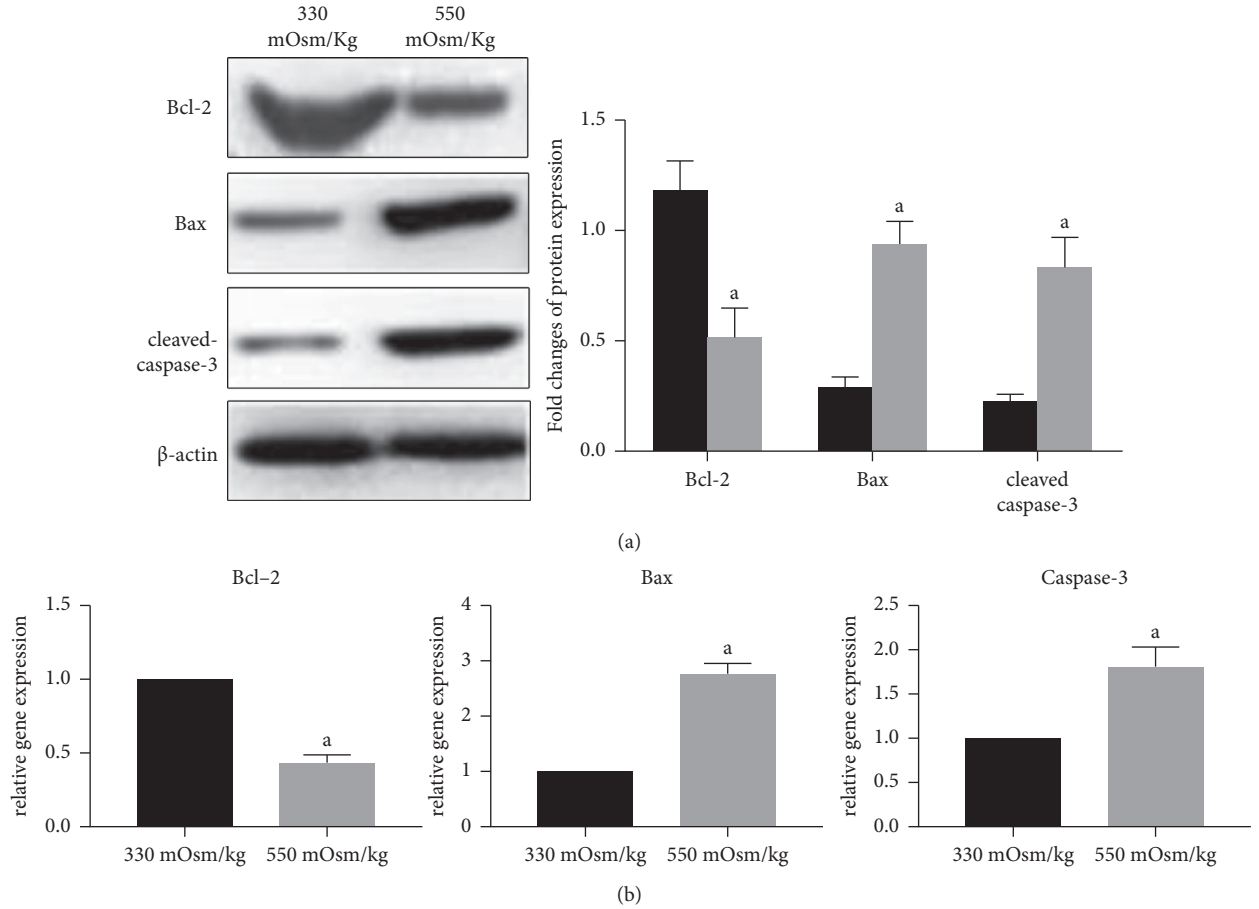

Figure 2: Hyperosmolarity increased the expression of proapoptosis molecules (Bax and caspase-3/cleaved caspase-3) and decreased the expression of antiapoptosis molecules (Bcl-2). (a,b) Real-time PCR and western blotting analysis of proapoptosis (Bax and caspase-3/cleaved caspase-3) and antiapoptosis (Bcl-2) molecules under different osmotic pressures (330 mOsm/kg and 550 mOsm/kg), respectively. Data are expressed as mean ± SD. (A) indicates a significant difference ($p < 0.05$) when compared with 330 mOsm/kg.

4. Discussion

Intervertebral disc degeneration is one of the main causes of LBP. An intervertebral disc consists of three parts, namely, the cartilaginous endplates, the annulus fibrosus, and the NP. Intervertebral disc degeneration occurs due to age, heredity, spinal biomechanics, diabetes, and autoimmunity [24]. The degeneration of the NP tissue mainly manifests by apoptosis and aging of NP cells, reduced synthesis and increased decomposition of the extracellular matrix, and microenvironment changes [25]. Previous studies have reported that high osmotic pressure of 550 mOsm/kg can cause apoptosis-like pathological changes, such as nuclear debris, chromatin condensation, and organelle destruction, while an osmotic pressure environment of 450 mOsm/kg, which is close to the in situ osmotic pressure of the NP tissue, has little influence on the apoptosis of NP cells [18]. Some studies have pointed out that ERK1/2 is involved in the apoptosis of NP cells and that inhibiting the ERK1/2 signaling pathway in these cells will increase the apoptosis rate; it has also been suggested that AQP-3 can activate the ERK1/2 signaling pathway [18].

In this study, we mainly observed the apoptosis of NP cells and the expression of AQP-3 in different osmotic pressure environments and investigated whether AQP-3 participates in the apoptosis of NP cells induced by high osmotic pressure and the role of the ERK1/2 signaling pathway therein. The results of this study showed that a high osmotic pressure significantly promoted the apoptosis of NP cells, reduced the expression of AQP-3, and suppressed ERK1/2 activity. However, AQP-3 overexpression could alleviate apoptosis of NP cells in a high osmotic pressure environment, and apoptosis was increased when the ERK1/2 signaling pathway of cells overexpressing AQP-3 was inhibited. AQP-3, a transmembrane transport protein, carries out water molecule transport by means of an osmotic pressure gradient across the cell membrane [26]. Previous studies have pointed out that AQP-3 plays a role in regulating the apoptosis of certain cells. In recent years, it has been confirmed that AQP-3 could transport H_2O_2 in keratinocytes to accelerate the progression of psoriasis [27]. H_2O_2 could induce oxidative stress, thereby leading to apoptosis of NP cells, and the overexpression of AQP-3 could alleviate H_2O_2-induced apoptosis of rat NP cells [28]. The expression of AQP-3 in NP tissue cells of degenerated

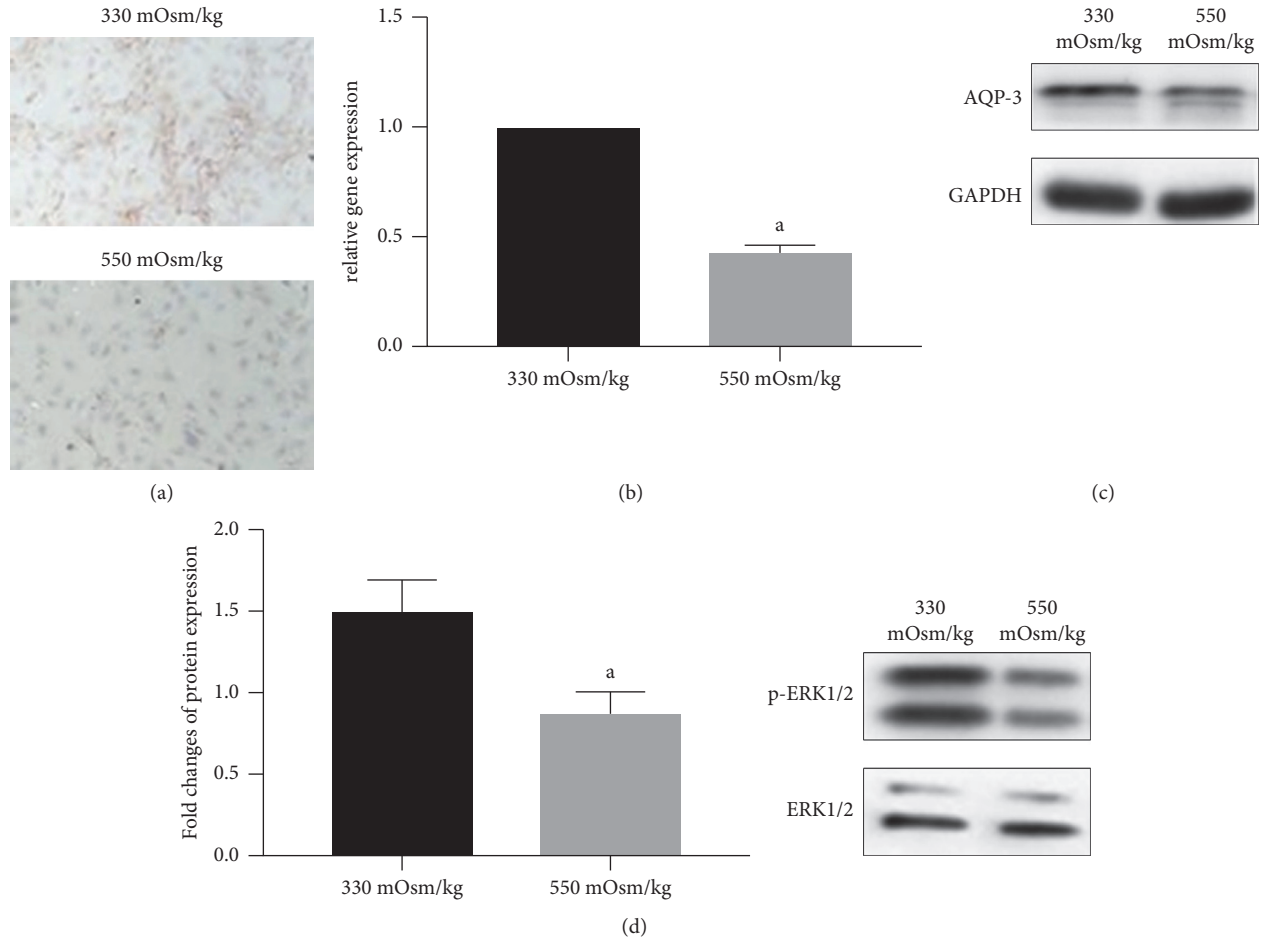

Figure 3: Hyperosmolarity decreased AQP-3 expression and inhibited activation of ERK1/2 signaling in NP cells. (a) Immunocytochemical detection of AQP-3 expression of NP cells under different osmotic pressures (330 mOsm/kg and 550 mOsm/kg). (b, c) Real-time PCR and western blotting analysis of AQP3 expression under different osmolarity (330 mOsm/kg and 550 mOsm/kg), respectively. (d) Western blotting analysis of ERK1/2 activation under different osmotic pressures (330 mOsm/kg and 550 mOsm/kg). Data are expressed as mean ± SD. (A) indicates a significant difference ($p < 0.05$) when compared with 330 mOsm/kg.

human intervertebral discs is significantly lower than that in NP tissue of normal human intervertebral discs [29]. The above research reports suggest that AQP-3 is closely associated with disc NP cell apoptosis.

Our results showed that in the high osmotic pressure environment, the proliferation of NP cells decreased, and the apoptosis increased, as determined by flow cytometry analysis, real-time PCR, and western blot. In previous studies conducted in porcine intervertebral disc organ culture models, our research group also found that the high osmotic pressure environment could reduce the matrix synthesis of NP cells and promote their apoptosis [17]. Similarly, the results of a study by Jiao S et al. are consistent with those of this study, even though 430 mOsm/kg was selected as the osmotic pressure for the control group in their experiments [30]. In this study, we also found that the AQP-3 gene and protein levels in NP cells in a high osmotic pressure environment were significantly reduced. We speculated that this decrease in AQP-3 expression may be related to the apoptosis of NP cells. Previously, Palacio-Manchenoet al. found that after intervertebral discs of C57BL/6 mice were cultured in a hypertonic environment for 14 days, the expression of AQP-3 in notochord cells was upregulated [21], which is inconsistent with the results of this study. Since notochord cells are different from NP cells with respect to sensitivity to osmotic pressure, we speculate that the different cell types used in the studies might lead to different results, but this needs to be verified via further comparative experiments. To investigate whether AQP-3 expression is related to the apoptosis of NP cells under a high osmotic pressure environment, we further generated NP cells overexpressing AQP-3 using a lentivirus with low cytotoxicity and high expression. The results showed that under 550 mOsm/kg, the apoptosis of NP cells was alleviated after AQP-3 overexpression through experiments of flow cytometry, real-time PCR, and western blotting. These results further demonstrated that in a hyperosmolarity environment, the apoptosis of NP cells is closely related to the downregulation of AQP-3 expression, and AQP-3 overexpression in these cells can reduce apoptosis in a hyperosmolarity environment. To further observe the effect of the ERK1/2 pathway, we added U0126 to inhibit ERK1/2

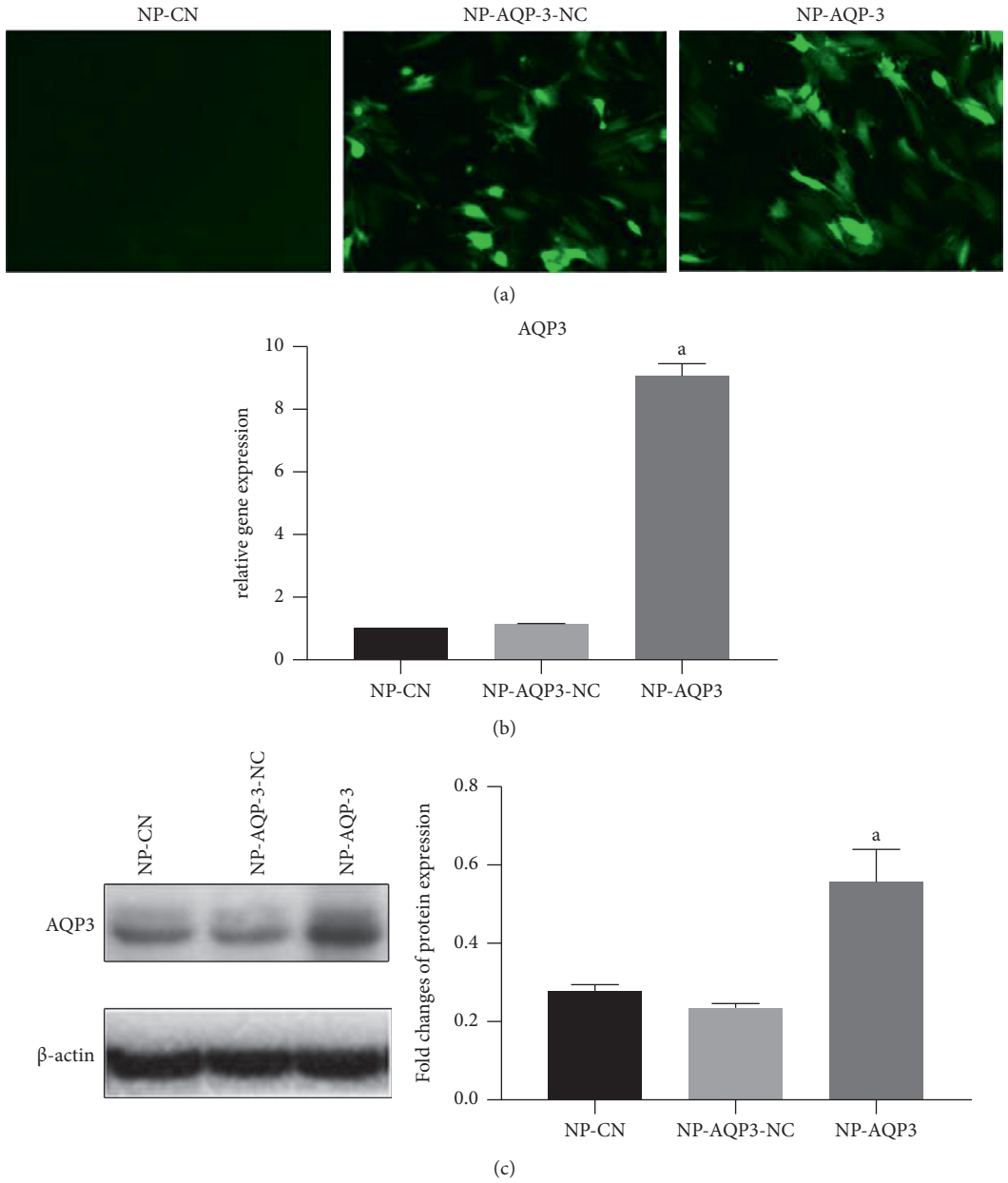

Figure 4: Verification of the efficacy of AQP-3 overexpression. (a) Observation of green fluorescent protein under an inverted fluorescence microscope. (b, c) Verification of the efficacy of AQP3 overexpression in NP cells using real-time PCR and western blotting assays. NP-CN: NP cells without transfection used as the controls. NP-AQP-3-NC: NP cells transfected with negative vectors. NP-AQP-3: NP cells with AQP-3 overexpression. Data are expressed as mean ± SD. (A) indicates a significant difference ($p < 0.05$) when compared with the control group.

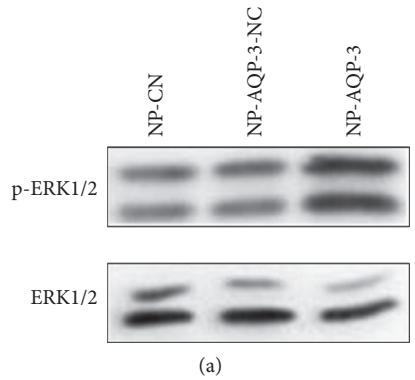

Figure 5: Continued.

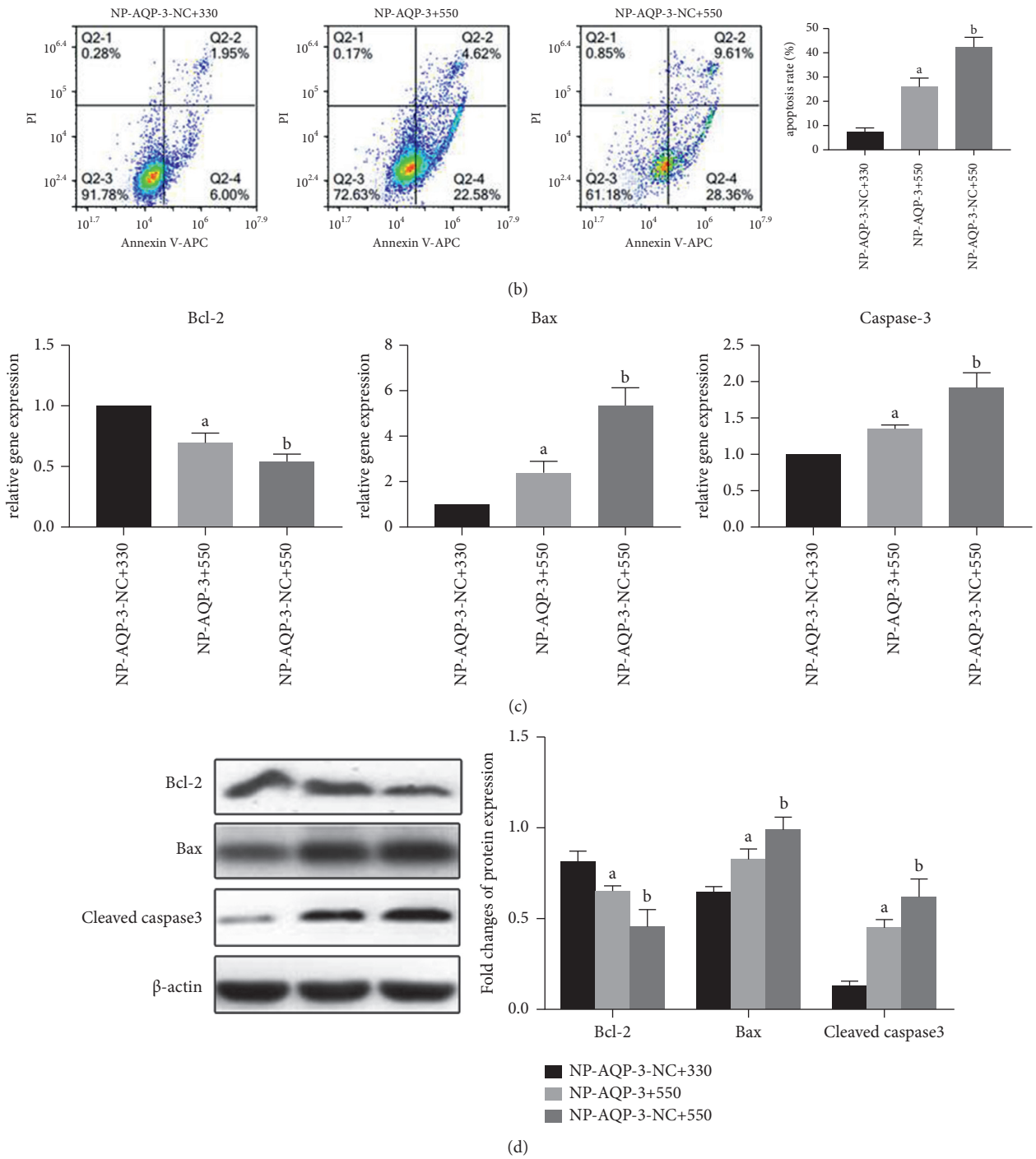

Figure 5: AQP-3 overexpression promoted activation of ERK1/2 signaling and alleviated hyperosmolarity-induced apoptosis. (a) Western blotting analysis of ERK1/2 and p-ERK1/2 expression in AQP-3 overexpressed NP cells under a hyperosmolarity (550 mOsm/kg). (b) Flowcytometry analysis of NP cell apoptosis ratio. (c) and (d): real-time PCR and western blotting analysis of proapoptosis (Bax and caspase 3/cleaved caspase 3) and antiapoptosis (Bcl-2) molecules under different osmotic pressures (330 mOsm/kg and 550 mOsm/kg), respectively. NP-AQP-3 + 330: AQP3 overexpressed NP cells cultured in 330 mOsm/kg. NP-AQP-3 + 550: AQP3 overexpressed NP cells cultured in 550 mOsm/kg. NP-AQP-3-NC + 550: NP cells without transfection (NP-CN) cultured in 550 mOsm/kg. Data are expressed as mean ± SD. (A) indicates a significant difference ($p < 0.05$) when compared with the group of NP-AQP-3 + 330. (B) indicates a significant difference ($p < 0.05$) when compared with the group of NP-AQP-3 + 550.

activity. The results of flow cytometry, western blotting, and quantitative PCR suggested that U0126 could inhibit the protective effects of AQP-3 overexpression against a hyperosmolarity-induced apoptosis, suggesting that AQP-3 may regulate apoptosis through the ERK1/2 pathway.

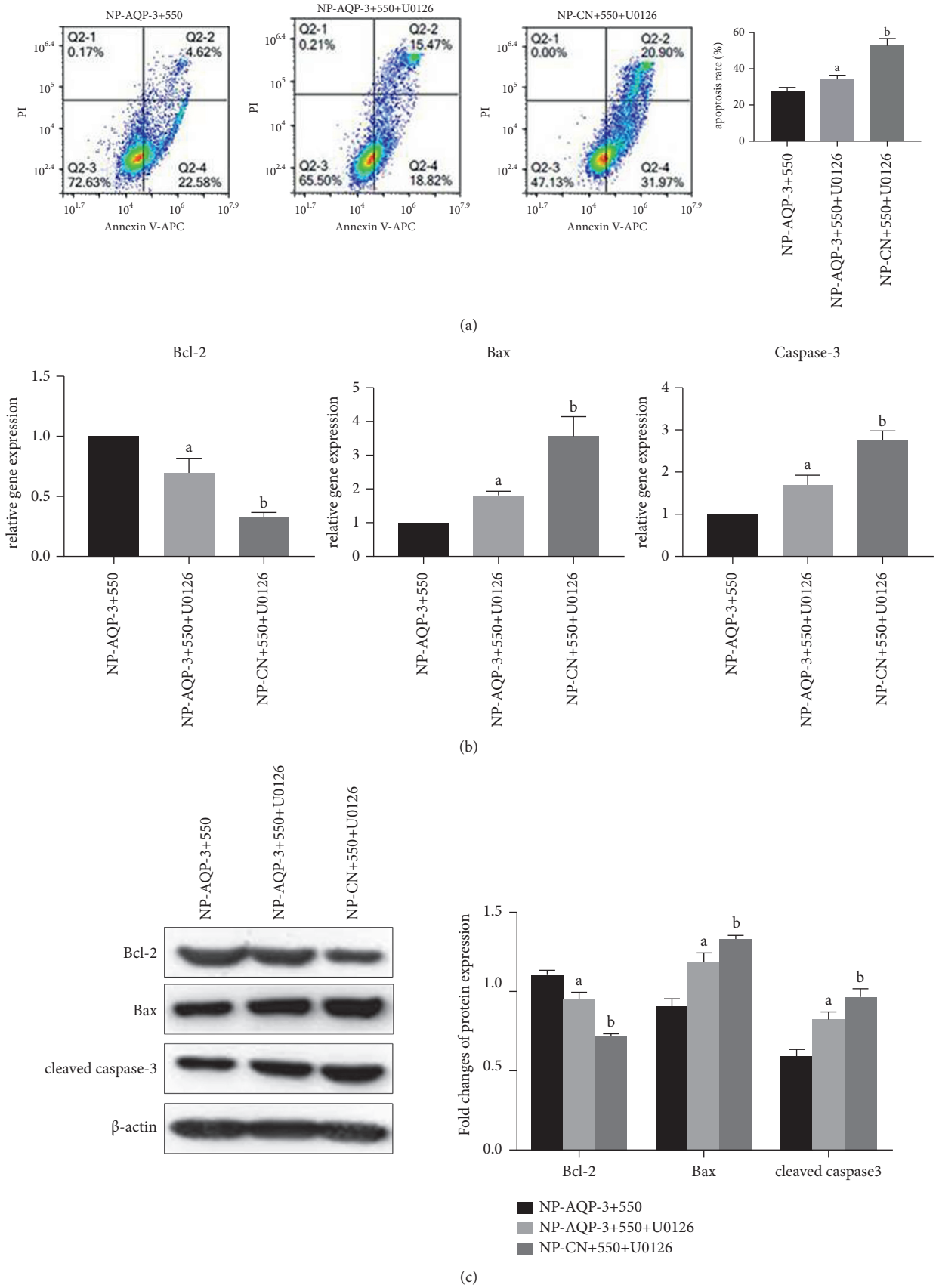

Figure 6: Inhibition of the ERK1/2 pathway promoted apoptosis of AQP-3 overexpressed NP cells under hyper-osmolarity. (a) Flow cytometry analysis of cell apoptosis rate under hyperosmolarity. (b) and (c): real-time PCR and western blotting analysis of proapoptosis (Bax and caspase-3/cleaved caspase-3) and antiapoptosis (Bcl-2) molecules under a hyperosmolarity, respectively. NP-AQP-3 + 550: AQP3 overexpressed NP cells cultured in 550 mOsm/kg; NP-AQP-3 + 550 + U0126: AQP3 overexpressed NP cells cultured in 550 mOsm/kg medium containing U0126; NP-CN + 550 + U0126: NP cells without transfection (NP-CN) cultured in 550 mOsm/kg medium containing U0126. (A) indicates a significant difference ($p < 0.05$) when compared with the group of NP-AQP-3 + 550. (B) indicates a significant difference ($p < 0.05$) when compared with the group of NP-AQP-3 + 550 + U0126.

This study also has several limitations. First, this is an in vitro study that investigated the protective effects of AQP-3 on high-osmolarity-induced NP cell apoptosis. If these results are further validated using an in vivo animal model, our study will be improved to a great extent. Second, the rat NP tissue contains NP cells and notochordal cells. Due to the uncertain cellular markers to distinguish NP cells from notochordal cells, researchers cannot assure that there are not any notochordal cells that exist in the NP cells, which are isolated using a routine cell isolation method. In the future, identification of some specific NP cell markers is helpful to obtain pure NP cells, which will avoid some interference caused by the existence of notochordal cells.

5. Conclusion

In this study, we observed the apoptosis of NP cells and the AQP-3 expression in different osmotic pressure environments and explored the specific mechanism by which AQP-3 influences a hyperosmotic stress-induced apoptosis in NP cells. Based on the results of this study, we can conclude the following: hyperosmolarity can significantly promote apoptosis of NP cells and reduce the expression of AQP-3; enhancing the expression of AQP-3 in NP cells can alleviate NP cell apoptosis under a hyperosmolarity environment, whereas inhibition of the ERK1/2 pathway partly attenuated the protective effects of AQP-3 against a hyperosmotic stress-induced NP cell apoptosis. This study has revealed the role of AQP-3 in NP cell apoptosis-mediated by a hyperosmolarity environment, which lays a theoretical foundation for further understanding the role of AQP-3 in IDD.

Data Availability

All data were included in this manuscript.

Disclosure

Zetong Zhang, Chen Zhao, and Ruijie Zhang are co-first authors.

Conflicts of Interest

There are no conflicts of interest in this study.

Acknowledgments

This study was funded by the following: the National Natural Science Foundation of China (No. 81772378 and No. 81974346); project funded by China Postdoctoral Science Foundation (2021M693925). Natural Science Foundation of Chongqing, China (No. cstc2020jcyj-msxmX0148); project supported by Chongqing Postdoctoral Research Project (2010010005061624); Basic Research and Frontier Exploration Project of Yuzhong District, Chongqing, China (No. 20200121); and Basic Research Incubation Project of the Third Affiliated Hospital of Chongqing Medical University, Chongqing, China (KY20074).

References

[1] X. Luo, R. Pietrobon, S. X Sun, G. G. Liu, and L. Hey, "Estimates and patterns of direct health care expenditures among individuals with back pain in the United States," *Spine*, vol. 29, no. 1, pp. 79–86, 2004.

[2] M. A. Adams and P. J. Roughley, "What is intervertebral disc degeneration, and what causes it?" *Spine*, vol. 31, no. 18, pp. 2151–2161, 2006.

[3] P. Li, Y. Gan, Y. Xu et al., "17beta-estradiol attenuates TNF-α-induced premature senescence of nucleus pulposus cells through regulating the ROS/NF-κB pathway," *International Journal of Biological Sciences*, vol. 13, no. 2, pp. 145–156, 2017.

[4] I. M. Shapiro, E. J. Vresilovic, and M. V. Risbud, "Is the spinal motion segment a diarthrodial polyaxial joint: what a nice nucleus like you doing in a joint like this?" *Bone*, vol. 50, no. 3, pp. 771–776, 2012.

[5] S. J. Ferguson and T. Steffen, "Biomechanics of the aging spine," *European Spine Journal*, vol. 12, no. Suppl 2, pp. S97–S103, 2003.

[6] F. Ding, Z.-W. Shao, and L.-M. Xiong, "Cell death in intervertebral disc degeneration," *Apoptosis*, vol. 18, no. 7, pp. 777–785, 2013.

[7] J.-B. Park, I.-C. Park, S.-J. Park, H.-O. Jin, J.-K. Lee, and K. D. Riew, "Anti-apoptotic effects of caspase inhibitors on rat intervertebral disc cells," *The Journal of Bone & Joint Surgery*, vol. 88, no. 4, pp. 771–779, 2006.

[8] H. Sudo and A. Minami, "Regulation of apoptosis in nucleus pulposus cells by optimized exogenous Bcl-2 overexpression," *Journal of Orthopaedic Research*, vol. 28, no. 12, pp. 1608–1613, 2010.

[9] D. Samartzis, J. Karppinen, D. Chan, K. D. K. Luk, and K. M. C. Cheung, "The association of lumbar intervertebral disc degeneration on magnetic resonance imaging with body mass index in overweight and obese adults: a population-based study," *Arthritis & Rheumatism*, vol. 64, no. 5, pp. 1488–1496, 2012.

[10] A. Di Martino, A. R. Vaccaro, J. Y. Lee, V. Denaro, and M. R. Lim, "Nucleus pulposus replacement: basic science and indications for clinical use," *Spine (Phila Pa 1976)*, vol. 30, no. 16 Suppl, pp. S16–S22, 2005.

[11] P. Li, Z. Liang, G. Hou et al., "N-Cadherin-mediated activation of PI3K/Akt-GSK-3β signaling attenuates nucleus pulposus cell apoptosis under high-magnitude compression," *Cellular Physiology and Biochemistry*, vol. 44, no. 1, pp. 229–239, 2017.

[12] J. P. Urban and J. F. McMullin, "Swelling pressure of the lumbar intervertebral discs: influence of age, spinal level, composition, and degeneration," *Spine (Phila Pa 1976)*, vol. 13, no. 2, pp. 179–187, 1988.

[13] A. Nachemson and G. Elfström, "Intravital dynamic pressure measurements in lumbar discs: a study of common movements, maneuvers and exercises," *Scandinavian Journal of Rehabilitation Medicine: Supplement*, vol. 1, pp. 1–40, 1970.

[14] K. Takeno, S. Kobayashi, K. Negoro et al., "Physical limitations to tissue engineering of intervertebral disc cells: effect of extracellular osmotic change on glycosaminoglycan production and cell metabolism," *Journal of Neurosurgery: Spine*, vol. 7, no. 6, pp. 637–644, 2007.

[15] P. Li, Y. Gan, H. Wang et al., "Dynamic compression effects on immature nucleus pulposus: a study using a novel intelligent and mechanically active bioreactor," *International Journal of Medical Sciences*, vol. 13, no. 3, pp. 225–234, 2016.

[16] P. Li, G. Hou, R. Zhang et al., "High-magnitude compression accelerates the premature senescence of nucleus pulposus cells via the p38 MAPK-ROS pathway," *Arthritis Research and Therapy*, vol. 19, no. 1, p. 209, 2017.

[17] P. Li, Y. Gan, Y. Xu et al., "Osmolarity affects matrix synthesis in the nucleus pulposus associated with the involvement of MAPK pathways: a study of ex vivo disc organ culture system," *Journal of Orthopaedic Research*, vol. 34, no. 6, pp. 1092–1100, 2016.

[18] P. Li, Y. Gan, H. Wang et al., "Role of the ERK1/2 pathway in osmolarity effects on nucleus pulposus cell apoptosis in a disc perfusion culture," *Journal of Orthopaedic Research*, vol. 35, no. 1, pp. 86–92, 2017.

[19] H. Ebi, C. Costa, A. C. Faber et al., "PI3K regulates MEK/ERK signaling in breast cancer via the Rac-GEF, P-Rex1," *Proceedings of the National Academy of Sciences*, vol. 110, no. 52, pp. 21124–21129, 2013.

[20] H. Gao, J. Gui, L. Wang et al., "Aquaporin 1 contributes to chondrocyte apoptosis in a rat model of osteoarthritis," *International Journal of Molecular Medicine*, vol. 38, no. 6, pp. 1752–1758, 2016.

[21] P. E. Palacio-Mancheno, T. W. Evashwick-Rogler, D. M. Laudier, D. Purmessur, and J. C. Iatridis, "Hyperosmolarity induces notochordal cell differentiation with aquaporin3 upregulation and reduced N-cadherin expression," *Journal of Orthopaedic Research*, vol. 36, no. 2, pp. 788–798, 2018.

[22] S. M. Richardson, R. Knowles, D. Marples, J. A. Hoyland, and A. Mobasheri, "Aquaporin expression in the human intervertebral disc," *Journal of Molecular Histology*, vol. 39, no. 3, pp. 303–309, 2008.

[23] B. Racz, D. Reglodi, B. Fodor et al., "Hyperosmotic stress-induced apoptotic signaling pathways in chondrocytes," *Bone*, vol. 40, no. 6, pp. 1536–1543, 2007.

[24] H. E. Gruber and E. N. Hanley Jr., "Analysis of aging and degeneration of the human intervertebral disc: comparison of surgical specimens with normal controls," *Spine (Phila Pa 1976)*, vol. 23, no. 7, pp. 751–757, 1998.

[25] H. E. Gruber and E. N. Hanley Jr., "Biologic strategies for the therapy of intervertebral disc degeneration," *Expert Opinion on Biological Therapy*, vol. 3, no. 8, pp. 1209–1214, 2003.

[26] Q. Chen, H. Peng, L. Lei et al., "Aquaporin3 is a sperm water channel essential for postcopulatory sperm osmoadaptation and migration," *Cell Research*, vol. 21, no. 6, pp. 922–933, 2011.

[27] M. Hara-Chikuma, H. Satooka, S. Watanabe et al., "Aquaporin-3-mediated hydrogen peroxide transport is required for NF-κB signalling in keratinocytes and development of psoriasis," *Nature Communications*, vol. 6, no. 1, p. 7454, 2015.

[28] Y. Xu, H. Yao, Q. Wang et al., "Aquaporin-3 attenuates oxidative stress-induced nucleus pulposus cell apoptosis through regulating the P38 MAPK pathway," *Cellular Physiology and Biochemistry*, vol. 50, no. 5, pp. 1687–1697, 2018.

[29] S. B. Li, K. S. Yang, and Y. T. Zhang, "Expression of aquaporins 1 and 3 in degenerative tissue of the lumbar intervertebral disc," *Genetics and Molecular Research*, vol. 13, no. 4, pp. 8225–8233, 2014.

[30] J. Shi, L. Pang, and S. Jiao, "The response of nucleus pulposus cell senescence to static and dynamic compressions in a disc organ culture," *Bioscience Reports*, vol. 38, no. 2, 2018.

Hindawi
Pain Research and Management
Volume 2022, Article ID 1507097, 20 pages
https://doi.org/10.1155/2022/1507097

Review Article

Perioperative Low-Dose Ketamine for Postoperative Pain Management in Spine Surgery: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Received 11 December 2021; Accepted 22 February 2022; Published 31 March 2022

Academic Editor: Felicity Han

Objective. Although low-dose ketamine has been shown to be generally beneficial in terms of pain control in a variety of major surgery, there is no consensus regarding the effectiveness of supplemental ketamine analgesic use exclusively in spine surgery. The objective of this systematic review and meta-analysis of randomized controlled trials (RCTs) was to assess the efficacy and safety of perioperative low-dose ketamine for pain management and analgesic consumption in patients undergoing spine surgery. *Methods*. A comprehensive literature search was performed for relevant studies using PubMed, EMBASE, Web of Science, and Cochrane Library. Patients who received perioperative low-dose ketamine were compared to the control group in terms of postoperative pain intensity, opioid consumption, and adverse events. Patients were further categorized by ages and administration times for subgroup analysis. *Results*. A total of 30 RCTs comprising 1,865 patients undergoing elective spine surgery were included. Significantly lower pain intensity and less opioid consumption at 12 h, 24 h, and 48 h postoperatively and lower incidence of postoperative nausea and vomiting (PONV) were observed in the ketamine group (all $P < 0.05$). There was no significant difference of central nervous system (CNS) adverse events between groups. However, different efficacy of low-dose ketamine was detected when patients were categorized by ages and administration times. *Conclusion*. Perioperative low-dose ketamine demonstrated analgesic and morphine-sparing effect with no increased adverse events after spine surgery. However, this effect was not significant in pediatric patients. Only postoperative or intraoperative and postoperative administration could prolong the analgesic time up to 48 h postoperatively. Further studies should focus on the optimal protocol of ketamine administration and its effect on old age participants.

1. Introduction

The postoperative pain is excessively difficult to management for patients undergoing various orthopedic surgery, particularly in spine surgery [1]. Inadequate postoperative pain control after spine surgery could impact patient well-being and rehabilitation, which remains a major clinical challenge for both spine surgeons and anesthesiologists [2].

It has been reported that spinal surgical procedures, especially in spinal fusion, always necessitate substantial pain control in the perioperative period [3]. To achieve satisfactory pain management, opioids have been the mainstay of analgesia after various spine surgery [4]. However, opioid-related adverse effects, including nausea and vomiting, pruritus, hallucination, nightmare, cardiovascular events, and even respiratory depression, frequently occurred in patients. [5–7] Also, the development of opioid-induced hyperalgesia (OIH) and/or acute opioid tolerance could consequently increase the postoperative opioid consumption and prolonged opioid-dependence that contribute substantially to the current opioid epidemic [8, 9].

Multimodal analgesia, which could achieve better postoperative pain control and reduce the need of opioid with concomitant reduction of opioid-related side effects through additive or synergistic effects of various nonopioids, has been widely reported as the leading principle of pain management after spine surgery [10–12]. Thus, finding

optimal components of multimodal analgesia is of paramount importance.

Ketamine, a nonselective antagonist of N-methyl-D-aspartate (NMDA) receptor, has been proposed as a component of multimodal analgesia for various surgical procedures, as it could inhabit the pathway of central sensitization and secondary postoperative hyperalgesia [13]. At subanesthetic doses, ketamine is effective as an adjuvant medication to standard regimen of opioids, demonstrating prominent analgesic effect and opioid-sparing effect, with no unwanted side effects of the drug [14].

Although low-dose ketamine has been shown to be generally beneficial in terms of pain control in a variety of major surgery, there is no consensus regarding the effectiveness of supplemental ketamine analgesic use exclusively in spine surgery. Also, it is unclear how the ages of patients and administration time affect the effectiveness of ketamine in pain mitigating. The objective of this systematic review and meta-analysis of randomized controlled trials (RCTs) was to assess the efficacy and safety of perioperative low-dose ketamine for pain management and analgesic consumption in patients undergoing spine surgery.

2. Materials and Methods

This study was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and registered with PROSPERO (ID: CRD42021238943) [15, 16]. As the data involved in this study are anonymized and freely available in the public domain, in which informed consent has already been obtained at the time of original data collection, this study is exempt from ethical approval.

2.1. Search Strategy. The PubMed, EMBASE, Web of Science, and Cochrane Library database were searched using the following terms: (Ketamine) AND (((((((((microdiscectomy) OR (discectomy)) OR (spine)) OR (spinal)) OR (scoliosis)) OR (disc)) OR (disk)) OR (lumbar)) OR (thoracic)).

The literature search was last updated on August 01, 2021. Two reviewers (L.Z. and H.Y.) independently screened the titles and abstracts, and any arising differences were settled by a discussion with a third party (Y.C.).

2.2. Inclusion Criteria

2.2.1. Participants. Participants undergoing elective spine surgery were included in this study. We categorized participants as pediatric (10 to 17 years of age) and adult (≥18 years of age).

2.2.2. Interventions. Patients received low-dose ketamine as

(1) An intravenous (IV) bolus dose of 0.1–0.5 mg/kg intraoperatively

(2) A continuous intravenous infusion of 1.0–10.0 $\mu g\,kg^{-1}min^{-1}$ intraoperatively and terminated in 48 h after surgery

(3) A dose of 0.1–1.0 mg/ml in intravenous patient-controlled analgesia (IV-PCA) devices postoperatively

(4) Combination of an IV bolus, an infusion, and IV-PCA devices

Ketamine in combination with a basic analgesic regimen was acceptable if such interventions were administered in a same way to both intervention and control groups.

2.2.3. Control. Control individuals comprise those who were administered an IV bolus, a continuous intravenous infusion, or IV-PCA of placebo or basic analgesic alone.

2.2.4. Outcome Measures. (1) Primary Outcomes.

(1) Pain intensity at rest and during mobilization using the Numerical Rating Scale (NRS) or Visual Analogue Scale (VAS) at 6 h, 12 h, 24 h, and 48 h postoperatively

(2) Cumulative consumption of opioids in milligrams of morphine equivalents in the first 12 h, 24 h, and 48 h postoperatively, administrated by IV-PCA devices or as rescue medication

(2) Secondary Outcomes.

(1) Time to first request for analgesia (trigger of IV-PCA) after surgery

(2) The incidence of postoperative central nervous system (CNS) adverse events and postoperative nausea and vomiting (PONV)

2.2.5. Study Design. Only the studies that described a prospective RCT were included.

2.3. Exclusion Criteria. Studies that met any of the following exclusion criteria were excluded: (1) patients not undergoing general anesthesia; (2) postoperative pain intensity or consumption of opioids was not reported; (3) reviews, case reports, and animal research; (4) duplicated publications; or (5) articles not published in English.

2.4. Assessment of Study Quality. The study quality was assessed independently by two reviewers (L.Z. and H.Y.) according to the Cochrane Handbook version 5.2.0 [17]. The specific contents of the assessment included random sequence generation, allocation of concealment, blinding, incomplete outcome data, selective outcome reporting, and other bias.

The level of certainty for the results was evaluated using the guidelines of the Recommendations, Assessment, Development, and Evaluation (GRADE) system [18]. The five domains included risk of bias, inconsistency, indirectness, imprecision, and publication bias. The level of certainty was graded using GRADEpro GDT online tool [19].

2.5. Data Extraction. Data extraction was performed by two reviewers independently (H.Y. and J.L.). The following study characteristics were recorded: demographic information, general anesthetic, bolus dosage, infusion dosage, timing of ketamine administration, interventions of control group, and primary postoperative analgesic. Continuous outcomes included pain intensity, cumulative consumption of opioids, and the time from end of surgery to first request for analgesia or first trigger of IV-PCA. Dichotomous outcomes included the postoperative CNS adverse events and PONV. Outcomes reported by at least five studies would be analyzed. The graphed data were interpolated using the tool WebPlotDigitizer.

2.6. Data Normalization. Extracted data were normalized prior to analysis. Pain intensity was assessed using various pain scores (0 = no pain) by the included studies, including Visual Analogue Scale (VAS) of 0 to 10, a Numerical Rating Scale (NRS) of 0 to 10, or a Verbal Rating Scale (VRS) of 0 to 5. We multiplied each pain score by 10 or 25 to convert them to a VAS of 0 to 100 [20]. Opioid for postoperative analgesia was administered as morphine, fentanyl, oxycodone, or hydromorphone in the included studies. Therefore, we converted the postoperative opioid consumption to morphine equivalents using conversion equations, such as 100:1 for IV fentanyl:IV morphine, 2:3 for IV oxycodone:IV morphine, 1:5 for IV hydromorphone:IV morphine, and 1:2 for IV methadone:IV morphine [21, 22]. For studies that reported opioid consumption over select time periods (e.g., 0–24 h, 24–48 h), the mean of cumulative opioid consumption was calculated, and the standard deviations were estimated according to the Cochrane Handbook.

2.7. Data Synthesis and Statistical Analysis. For studies with multiple treatment arms, the arms that involved an intervention not defined by the inclusion criteria would be excluded, and the data in other arms would be combined to create a single pair-wise comparison as described by. All statistical analysis was performed using Stata 15.1. For continuous outcomes, the weighted mean difference (WMD) was utilized for estimating effect. The effect measure of dichotomous outcomes was displayed as a risk ratio (RR). Statistical heterogeneity among studies was evaluated using the I-square test and Cochran's Q test. If the I^2 value was less than 50% and the P value was greater than 0.10, the fixed-effects model was performed; if the I^2 value was greater than 50% or the P value was less than 0.10, the random-effects model would be used.

2.8. Subgroup Analysis. The included studies were categorized for subgroup analysis:

(1) By ages: pediatric spine surgery vs. adult spine surgery

(2) By administration times of ketamine: intraoperatively (intragroup) vs. postoperatively (postgroup) vs. intraoperatively and postoperatively (intragroup + postgroup)

We restricted the subgroup analysis to the primary outcome and adverse events. Each subgroup should include at least two studies. Subgroup analysis by administration times was only performed for studies about adult spine surgery. The results of subgroup analysis were available in Supplementary Materials.

2.9. Assessment of Publication Bias. Potential publication bias was assessed by the application of Egger's test at the P value less than 0.10 level of significance. If publication bias was indicated, we further evaluated the number of missing studies in this meta-analysis by the application of the trim and fill method and recalculated the pooled WMD or RR with the addition of those missing studies [23].

3. Results

3.1. Study Selection. The systematic search yielded 6,252 articles, of which 3172 were duplicates. 3,038 studies were excluded by screening the title and abstract, and 12 studies were reasonably considered improper after full-text reviewing. Eventually, 30 studies were finally included in this meta-analysis (Figure 1) [24–53].

3.2. Characteristics of Included Studies. A total of 30 randomized controlled trials comprising 1,865 patients undergoing elective spine surgery were included. Of the patients, 1,006 cases were treated with perioperative low-dose ketamine, and 859 cases were administrated with placebo or basic analgesic alone. The characteristics of the included studies were demonstrated in Table 1. The baseline characteristics of the two groups were matched.

3.3. Quality Assessment of the Selected Studies. The majority of the studies had a "low risk" or an "unclear risk" assessment according to the Cochrane Handbook. The pooled risks of bias is presented in Figures 2(a) and 2(b).

3.4. Postoperative Pain Intensity

3.4.1. Pain Intensity at Rest at 6 h Postoperatively. A total of 16 studies reported the pain intensity at rest at 6 h postoperatively. Significant heterogeneity was detected ($I^2 = 94.6\%$, $P < 0.001$). The 16 studies included 587 patients in the ketamine group and 457 patients in the control group. The pooled results revealed significantly lower pain scores at rest at 6 h postoperatively in the ketamine than the control group (WMD, −8.93; 95% CI −13.80 to −4.06, $P < 0.001$, GRADE = moderate) (Figure 3(a)).

3.4.2. Pain Intensity at Rest at 12 h Postoperatively. A total of 13 studies reported the pain intensity at rest at 12 h postoperatively. Significant heterogeneity was detected ($I^2 = 95.1\%$, $P < 0.001$). The 14 studies included 350 patients

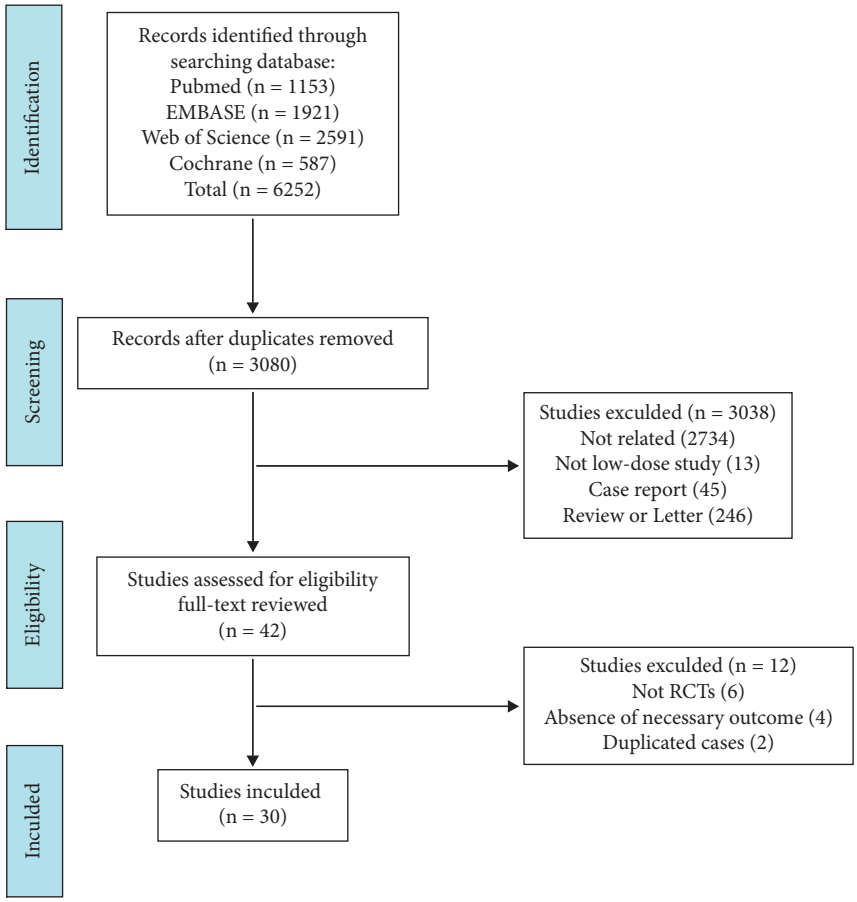


Figure 1: Flow diagram depicting the literature review, search strategy, and selection process.

in the ketamine group and 353 patients in the control group. The pooled results revealed significantly lower pain scores at rest at 12 h postoperatively in the ketamine than the control group (WMD, −8.04; 95% CI −13.69 to −2.39, $P = 0.005$, GRADE = moderate) (Figure 3(b)).

3.4.3. Pain Intensity at Rest at 24 h Postoperatively. A total of 25 studies reported the pain intensity at rest at 24 h postoperatively. Significant heterogeneity was detected ($I^2 = 70.7\%$, $P < 0.001$). The 25 studies included 907 patients in the ketamine group and 759 patients in the control group. The pooled results revealed significantly lower pain scores at rest at 24 h postoperatively in the ketamine than the control group (WMD, −10.01; 95% CI −13.09 to −6.93, $P < 0.001$, GRADE = moderate) (Figure 3(c)).

3.4.4. Pain Intensity at Rest at 48 h Postoperatively. A total of 16 studies reported the pain intensity at rest at 48 h postoperatively. Significant heterogeneity was detected ($I^2 = 56.1\%$, $P = 0.003$). The 16 studies included 565 patients in the ketamine group and 474 patients in the control group. The pooled results revealed significantly lower pain scores at rest at 48 h postoperatively in the ketamine than the control group (WMD, −4.63; 95% CI −8.34 to −0.92, $P = 0.014$, GRADE = moderate) (Figure 3(d)).

3.4.5. Pain Intensity during Mobilization at 6 h Postoperatively. A total of 9 studies reported the pain intensity during mobilization at 6 h postoperatively. Significant heterogeneity was detected ($I^2 = 44.0\%$, $P = 0.075$). The 9 studies included 239 patients in the ketamine group and 227 patients in the control group. The pooled results revealed significantly lower pain scores during mobilization at 6 h postoperatively in the ketamine than the control group (WMD, −5.48; 95% CI −9.21 to −1.75, $P = 0.004$, GRADE = low) (Figure 4(a)).

3.4.6. Pain Intensity during Mobilization at 12 h Postoperatively. A total of 8 studies reported the pain intensity during mobilization at 12 h postoperatively. Significant heterogeneity was detected ($I^2 = 87.5\%$, $P < 0.001$). The 8 studies included 204 patients in the ketamine group and 210 patients in the control group. The pooled results revealed no significant difference in pain scores during mobilization at 12 h postoperatively between groups (WMD, −7.22; 95% CI −16.44 to 2.01, $P = 0.125$, GRADE = low) (Figure 4(b)).

3.4.7. Pain Intensity during Mobilization at 24 h Postoperatively. A total of 14 studies reported the pain intensity during mobilization at 24 h postoperatively. Significant heterogeneity was detected ($I^2 = 81.7\%$, $P < 0.001$). The 14 studies

Table 1: Characteristics of the included studies.

Author	Year	Group	Sample size	Age (years)	Sex (M/F)	Weight (kg)	Mode	Bolus (mg kg^{-1})	Infusion (μg kg^{-1} min^{-1})	Dose in IV-PCA (mg ml^{-1})	Timing	Postoperative Opioid	Control
Javery	1996	Ketamine	22	37.3 ± 9.9	18/4	78.2 ± 13.1	IV-PCA			1.0	Postoperative	Morphine	Basic
		Control	20	39.5 ± 7.2	18/2	83.9 ± 10.7							
Sahin	2004	Ketamine	17	46.5 ± 7.3	9/8	80.4 ± 16.1	B	0.5			Intraoperative	Morphine	Saline
		Control	14	46.1 ± 13.3	8/6	78.7 ± 13.2							
Aveline	2006	Ketamine	23	48.3 ± 12.3	11/12	74.2 ± 6.3	B	0.15			Intraoperative	Morphine	Basic
		Control	23	44.4 ± 11.2	10/13	68.4 ± 12.8							
Engelhardt	2008	Ketamine	16	14.8 ± 1.7	2/14	59.3 ± 16.5	B+ivgtt	0.5	4.0		Intraoperative	Morphine	Saline
		Control	18	15.5 ± 1.2	3/15	56.5 ± 10.4							
Moustafa	2008	Ketamine	16	13.1 ± 5.08	7/9	39.7 ± 8.63	ivgtt		1.0		Intraoperative	Morphine	Basic
		Control	16	12.8 ± 6.07	6/10	34.6 ± 9.68							
Urban	2008	Ketamine	12	53 ± 12		80 ± 19	B+ivgtt	0.2	0.03		Intraoperative Postoperative	Hydromorphone	Saline
		Control	12	48 ± 9		78 ± 19							
Hadi	2009	Ketamine	20	22 ± 2	7/13	55 ± 15	ivgtt		1.0		Intraoperative	Morphine	Basic
		Control	20	21 ± 2	8/12	54 ± 13							
Hadi	2010	Ketamine	15	56.1 ± 10.5	7/8	66 ± 13	ivgtt		1.0		Intraoperative	Morphine	Saline
		Control	15	53.5 ± 10.2	3/12	68 ± 12							
Loftus	2010	Ketamine	52	51.7 ± 14.2	33/19	95.4 ± 17.7	B+ivgtt	0.5	10.0		Intraoperative	Morphine	Saline
		Control	50	51.4 ± 14.4	28/22	89.3 ± 23.8							
Subramaniam	2011	Ketamine	15	57.2 ± 12.2	8/7	86.2 ± 24.4	B+ivgtt	0.15	2.0		Intraoperative Postoperative	Hydromorphone	Saline
		Control	15	56.5 ± 13.6	7/8	81.4 ± 19.2							
Abrishamkar	2012	Ketamine	22	49 ± 1.32	5/18		ivgtt		8.33		Postoperative	Morphine	Basic
		Control	23	45 ± 1.64	10/12								
Pacreu	2012	Ketamine	10	52.9 ± 12.6	3/7	69.5 ± 7.2	B+ivgtt+IV-PCA	0.5	2.5	0.5	Intraoperative Postoperative	Methadone	Saline
		Control	10	61.3 ± 11.7	3/7	75.9 ± 9.8							
Yeom	2012	Ketamine	20	61.0 ± 10.0	5/15	59.1 ± 13.5	B+ivgtt	0.2	0.5		Intraoperative Postoperative	Fentanyl	Saline
		Control	20	64.5 ± 11.5	7/13	64.8 ± 10.6							
Hadi	2013	Ketamine	30	55 ± 2.5	13/17	70 ± 2.5	ivgtt		1.0		Intraoperative Postoperative	Morphine	Saline
		Control	15	51 ± 2.5	8/7	71 ± 2.6							
Kim	2013	Ketamine	35	56 ± 9.5	15/20	63.4 ± 10.5	B+ivgtt	0.5	1.0-2.0		Intraoperative Postoperative	Fentanyl	Saline
		Control	17	56 ± 13	9/8	66 ± 13							
Song	2013	Ketamine	24	52.3 ± 8.8	0/24	59 ± 7	B+ivgtt	0.3	0.04		Intraoperative Postoperative	Fentanyl	Saline
		Control	25	53.8 ± 7.8	0/25	60 ± 10							
Pestieau	2014	Ketamine	29	14.3 ± 1.8	5/24	60 ± 18	B+ivgtt	0.5	0.1-0.2		Intraoperative Postoperative	Morphine	Saline
		Control	21	14.5 ± 1.5	7/14	59 ± 14							
Minoshima	2015	Ketamine	17	15 ± 2	1/16	45 ± 6	B+ivgtt	0.5	2.0		Intraoperative Postoperative	Morphine	Saline
		Control	19	14 ± 2	0/19	46 ± 4							
Garg	2016	Ketamine	22	36.5 ± 13.4	13/9	61.5 ± 14.6	B+ivgtt	0.25	4.2		Postoperative	Morphine	Saline
		Control	22	36.3 ± 14.3	16/6	65.3 ± 15.5							

Table 1: Continued.

Author	Year	Group	Sample size	Age (years)	Sex (M/F)	Weight (kg)	Mode	Bolus (mg kg^{-1})	Infusion (μg kg^{-1} min^{-1})	Dose in IV-PCA (mg ml^{-1})	Timing	Postoperative Opioid	Control
Mitra	2017	Ketamine	14	33.9 ± 17.2	7/7	56.4 ± 10.1	B+ivgtt	0.5	4.2		Intraoperative	Fentanyl	Saline
		Control	14	33.5 ± 15.2	6/8	57.9 ± 11.3							
Nielsen	2017	Ketamine	74	57 ± 14	28/46	77 ± 14	B+ivgtt	0.5	4.2		Intraoperative	Morphine	Saline
		Control	73	55 ± 13	21/52	78 ± 18							
Perello´	2017	Ketamine	21	14.3 ± 1.9	5/16	54.3 ± 10.8	B+ivgtt	0.5	2.0		Intraoperative Postoperative	Morphine	Saline
		Control	23	14.3 ± 1.8	6/17	57.6 ± 12.6							
Boenigk	2018	Ketamine	49	54.5 ± 13.4	24/25	78.5 ± 7.2	B+ivgtt	0.2	2		Postoperative	Hydromorphone	Saline
		Control	62	55.7 ± 13.2	29/33	85.4 ± 11.5							
Czarnetzki	2019	Ketamine	80	65.8 ± 13.8	39/41	79.8 ± 4.3	B+ivgtt	0.25	1.67-4.17		Intraoperative Postoperative	Morphine	Saline
		Control	80	65.6 ± 12.6	42/38	79.7 ± 3.4							
Brinck	2020	Ketamine	127	54.2 ± 13.2	40/87	76 ± 14	B+ivgtt	0.5	2-10		Intraoperative	Oxycodone	Saline
		Control	62	55.5 ± 12	26/36	79 ± 15							
Ricciardelli	2020	Ketamine	24	13.4 ± 1.7	2/22	60.9 ± 17.4	B+ivgtt	0.5	3.33		Intraoperative Postoperative	Morphine	Saline
		Control	25	14.7 ± 2.2	8/17	61.6 ± 14.2							
Andleeb	2021	Ketamine	30	43.8 ± 14.6	15/15	57.4 ± 11.4	ivgtt		8.33		Intraoperative	Morphine	Saline
		Control	30	39.8 ± 14.1	14/16	58 ± 12.7							
Brinck	2021	Ketamine	75	60 ± 13.5	41/34	77.1 ± 14.5	IV-PCA			0.25-0.75	Postoperative	Oxycodone	Saline
		Control	25	56 ± 11	14/11	77.7 ± 15.6							
Murphy	2021	Ketamine	66	59.3 ± 16.4	32/34	64 ± 11	ivgtt		1.67-5.00		Intraoperative Postoperative	Hydromorphone	Saline
		Control	61	65.3 ± 10.6	27/34	62 ± 11							
Nikoubakht	2021	Ketamine	29	52.8 ± 12.2	17/12		ivgtt		1.67		Intraoperative	Morphine	Saline
		Control	29	53.8 ± 13.9	18/11								

B indicates intravenous bolus; ivgtt, intravenously guttae; IV-PCA, intravenous patient-controlled analgesia.

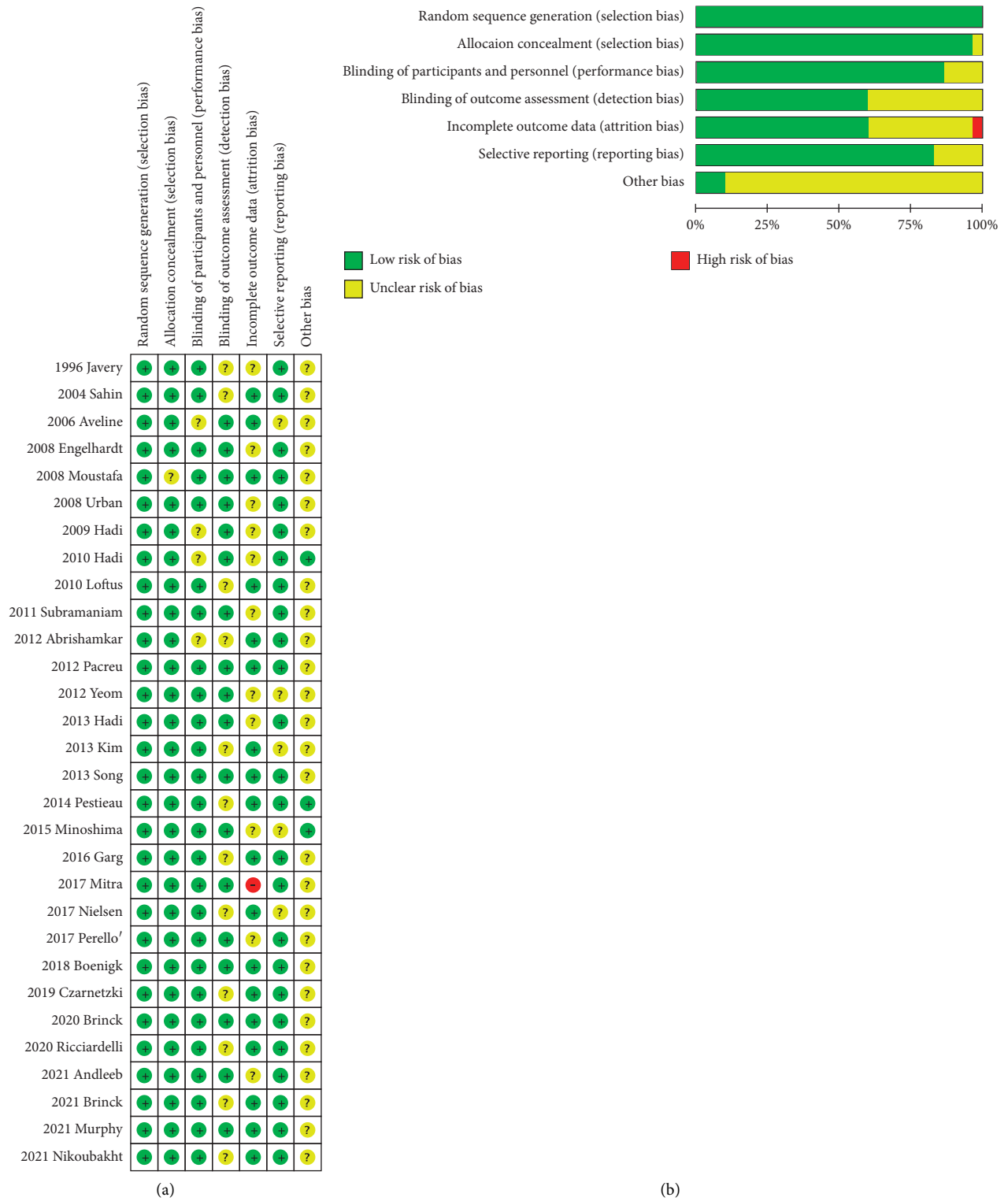
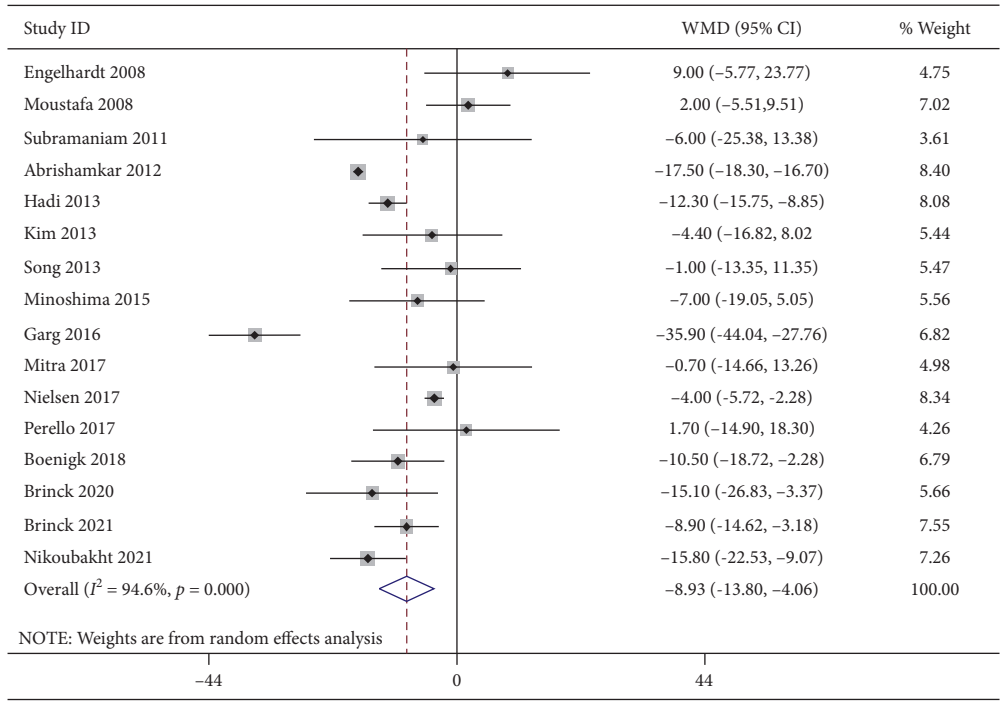
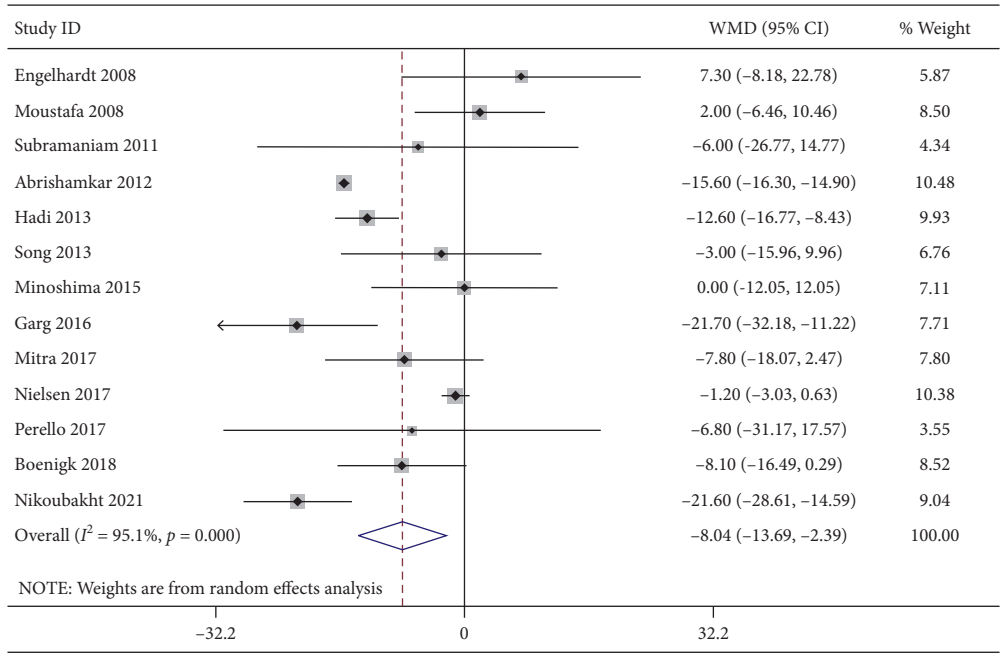


Figure 2: Risk of bias. (a) A summary table of each risk of bias item for each study; (b) a plot of the distribution of each risk of bias item. "+": low risk of bias; "?": unclear risk of bias; "−": high risk of bias.

included 425 patients in the ketamine group and 402 patients in the control group. The pooled results revealed significantly lower pain scores during mobilization at 24 h postoperatively in the ketamine than the control group (WMD, −6.72; 95% CI −12.02 to −1.43, $P < 0.001$, GRADE = moderate) (Figure 4(c)).



(a)



(b)

Figure 3: Continued.

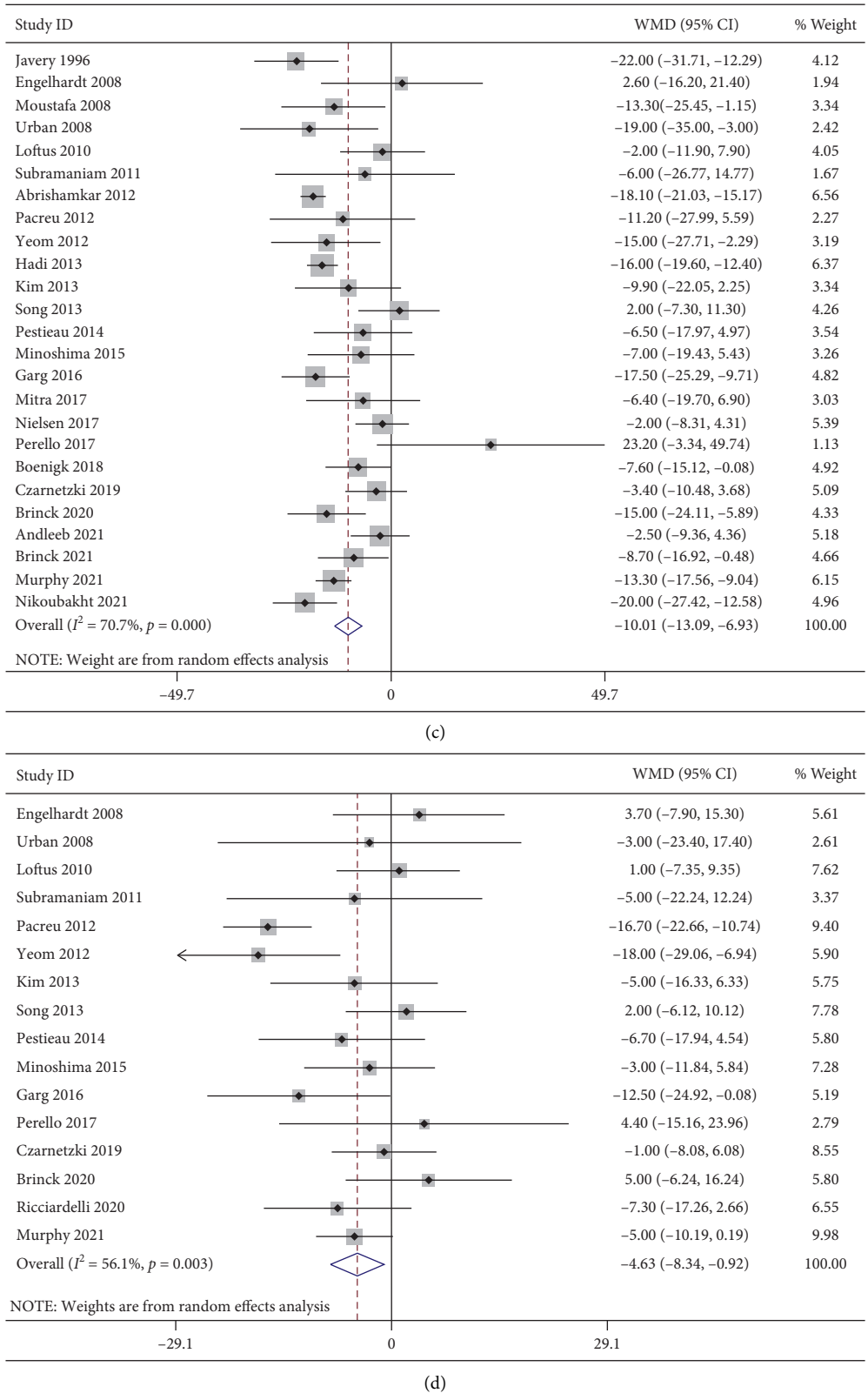
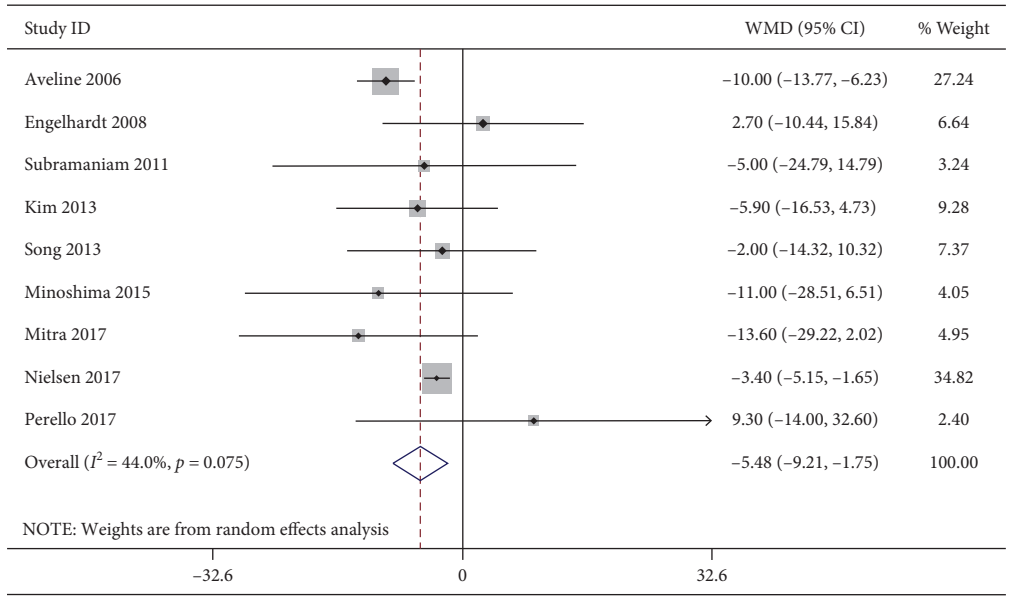
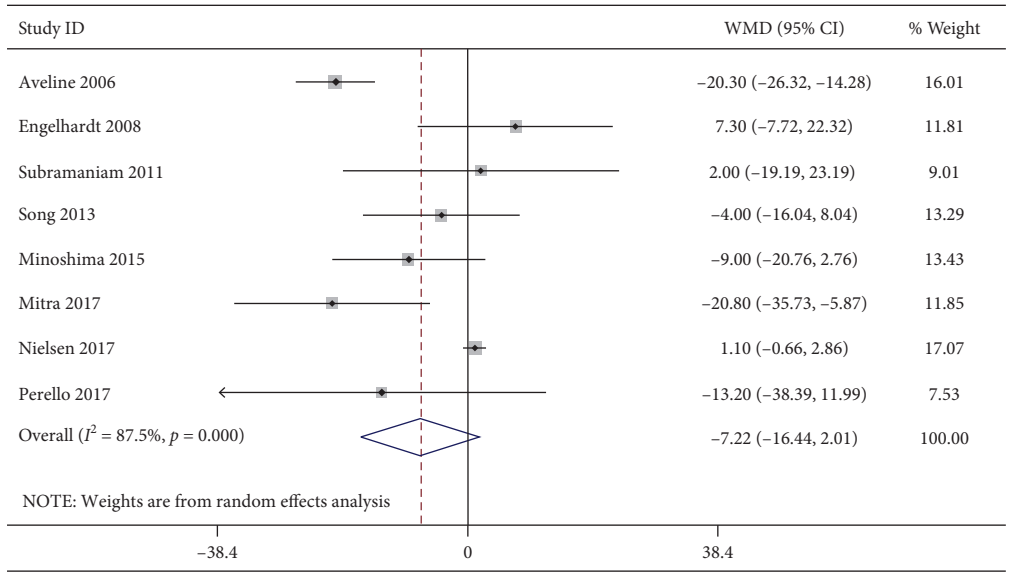


Figure 3: Forest plot of the pain intensity at rest for the ketamine group and control group. (a) 6 h; (b) 12 h; (c) 24 h; (d) 48 h.

3.4.8. Pain Intensity during Mobilization at 48 h Postoperatively. A total of 12 studies reported the pain intensity during mobilization at 48 h postoperatively. Significant heterogeneity was detected ($I^2 = 43.3\%$, $P < 0.054$). The 12 studies included 338 patients in the ketamine group and 316 patients in the control group. The pooled results revealed

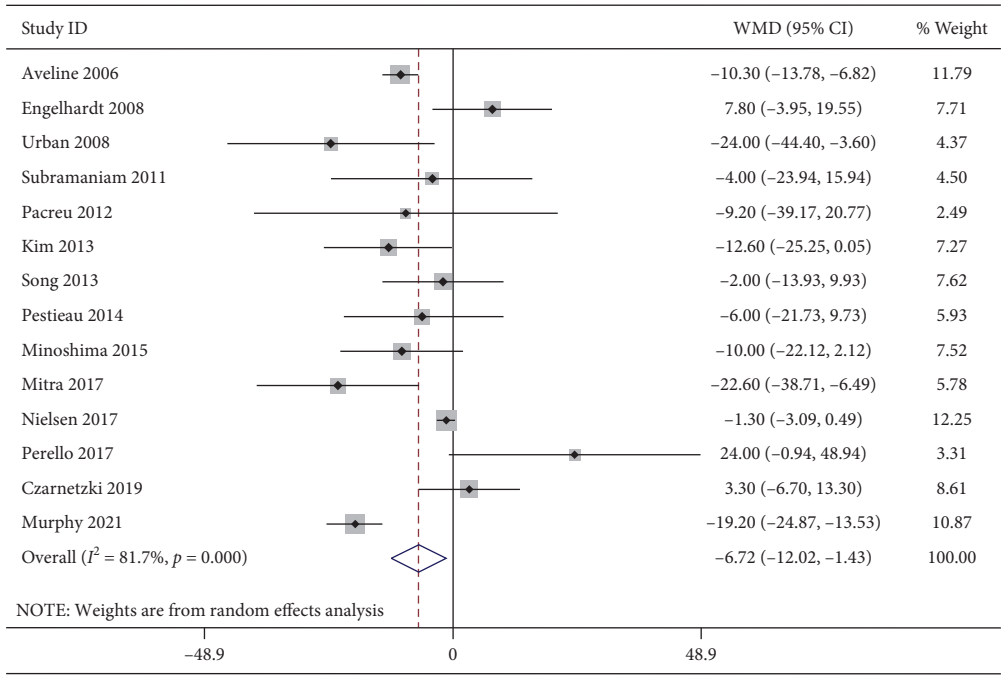


(a)

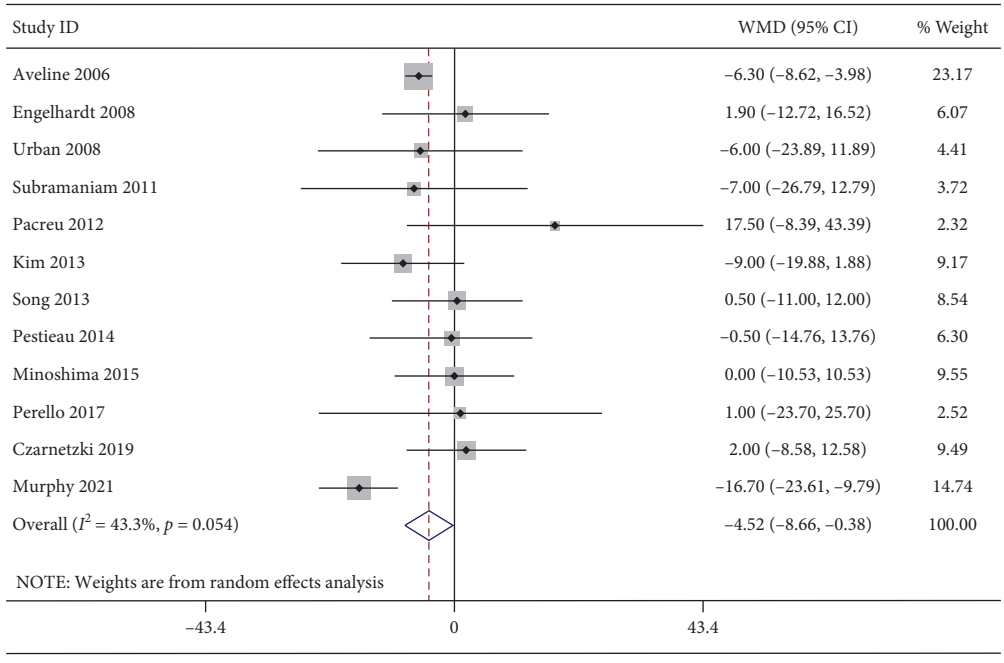


(b)

Figure 4: Continued.



(c)



(d)

Figure 4: Forest plot of the pain intensity during mobilization for the ketamine group and control group. (a) 6 h; (b) 12 h; (c) 24 h; (d) 48 h.

significantly lower pain scores during mobilization at 48 h postoperatively in the ketamine than the control group (WMD, −4.52; 95% CI −8.66 to −0.38, $P = 0.032$, GRADE = moderate) (Figure 4(d)).

3.4.9. Subgroup Analysis by Ages. The heterogeneity of pain scores was significantly decreased after categorizing the studies into pediatric studies and adult studies. For adult patients, the pooled results revealed that the pain scores at rest at 6 h (WMD, −11.73; 95% CI −17.09 to −6.38, $P < 0.001$; GRADE = moderate), 12 h (WMD, −11.21; 95% CI −17.64 to −4.78, $P = 0.001$, GRADE = moderate), 24 h (WMD, −10.86; 95% CI −14.11 to −7.62, $P < 0.001$, GRADE = moderate), 48 h (WMD, −5.37; 95% CI −10.23 to −0.50, $P = 0.031$, GRADE = moderate) and during mobilization at 6 h (WMD, −6.28; 95% CI −10.41 to −2.15, $P = 0.003$, GRADE = moderate), 24 h (WMD, −9.28; 95% CI −15.40 to −3.17,

$P = 0.003$, GRADE = moderate), and 48 h (WMD, −5.88; 95% CI −11.13 to −0.64, $P = 0.028$, GRADE = moderate) postoperatively were significantly lower in the ketamine group than the control group. However, for pediatric patients, there were no significant difference in pain scores at rest at 6 h (WMD, 1.05; 95% CI −4.47 to 6.57, $P = 0.708$, GRADE = moderate), 12 h (WMD, 1.76; 95% CI −4.36 to 7.88, $P = 0.573$, GRADE = moderate), 24 h (WMD, −4.36; 95% CI −13.04 to 4.31, $P = 0.324$, GRADE = moderate), 48 h (WMD, −3.09; 95% CI −8.03 to 1.86, $P = 0.222$, GRADE = moderate) and during mobilization at 6 h (WMD, −0.34; 95% CI −10.78 to 10.11, $P = 0.950$, GRADE = moderate), 12 h (WMD, −3.87; 95% CI −15.99 to 8.24, $P = 0.531$), 24 h (WMD, 1.67; 95% CI −10.97 to 14.31, $P = 0.796$, GRADE = moderate), and 48 h (WMD, 0.40; 95% CI −6.63 to 7.42, $P = 0.912$, GRADE = moderate) postoperatively between groups.

3.4.10. Subgroup Analysis by Administration Times. The heterogeneity of pain scores was significantly decreased after categorizing the studies into intrasubgroup, postsubgroup, and intrasubgroup + postsubgroup, according to the administration times of ketamine.

At rest, the pain scores at 6 h (WMD, −10.72; 95% CI −15.35 to −6.09, $P < 0.001$; WMD, -17.90, GRADE = moderate; 95% CI −26.23 to −9.58, $P < 0.001$, GRADE = moderate), 12 h (WMD, −13.00; 95% CI −20.44 to −5.55, $P = 0.001$, GRADE = moderate; WMD, −14.90; 95% CI −20.34 to −9.46, $P < 0.001$, GRADE = low), and 24 h (WMD, −11.51; 95% CI −15.93 to −7.08, $P < 0.001$, GRADE = moderate; WMD, −14.90; 95% CI −19.97 to −9.84, $P < 0.001$, GRADE = high) after surgery were significantly lower in the ketamine group when the drugs were administrated intraoperatively and postoperatively or solely postoperatively. However, when ketamine was administrated solely intraoperatively, the only significant difference in pain scores was detected at 24 h postoperatively (WMD, −5.01; 95% CI −9.82 to −0.19, $P = 0.042$, GRADE = moderate) and no significant difference at 6 h (WMD, −5.81; 95% CI −12.39 to 0.77, $P = 0.084$, GRADE = low) and 12 h (WMD, −2.49; 95% CI −7.61 to 2.64, $P = 0.342$, GRADE = low). As there was only one study in postsubgroup that reported the data at 48 h postoperatively, we excluded this subgroup for analysis at this terminated point. The pain scores at 48 h postoperatively were significantly lower in the ketamine group when the drugs were administrated intraoperatively and postoperatively (WMD, −6.71; 95% CI −12.39 to −1.04, $P = 0.020$, GRADE = moderate) while no significant difference in intrasubgroup (WMD, 2.42; 95% CI −4.28 to 9.13, $P = 0.479$, GRADE = low).

During mobilization, there was no data reported by studies in postsubgroup. Thus, only intrasubgroup + postsubgroup and intrasubgroup were included for analysis. The pain scores at 6 h after surgery were significantly lower in the ketamine group when the drugs were administrated intraoperatively (WMD, −7.28; 95% CI −13.29 to −1.28, $P = 0.017$, GRADE = moderate), and the pain scores at 24 h after surgery were significantly lower in the ketamine group when the drugs were administrated intraoperatively and postoperatively (WMD, −9.43; 95% CI −18.35 to −0.51, $P = 0.038$, GRADE = moderate). However, there were no significant difference in pain scores at 6 h (WMD, −4.34; 95% CI −11.80 to 3.11, $P = 0.253$, GRADE = moderate) and 12 h between groups in intrasubgroup + postsubgroup (WMD, −2.54; 95% CI −13.00 to 7.93, $P = 0.635$, GRADE = low), and there were no significant difference in pain scores at 12 h (WMD, −12.68; 95% CI −30.18 to 4.82, $P = 0.156$, GRADE = low) and 24 h (WMD, −8.62; 95% CI −17.28 to 0.05, $P = 0.051$, GRADE = moderate) between groups in intrasubgroup. We were unable to perform subgroup analysis for pain scores at 48 h after surgery because there were only one study in intrasubgroup.

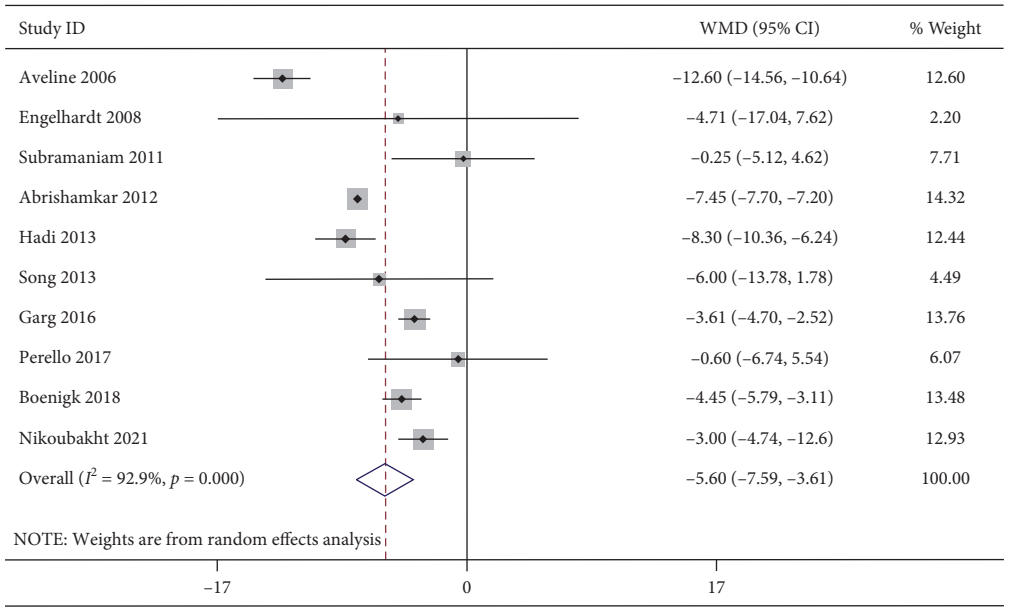
3.5. Postoperative Opioid Consumption

3.5.1. Cumulative Opioid Consumption in the First 12 h Postoperatively. A total of 10 studies reported the cumulative opioid consumption in the first 12 h postoperatively. Significant heterogeneity was detected ($I^2 = 92.9\%$, $P < 0.001$). The 10 studies included 252 patients in the ketamine group and 254 patients in the control group. The pooled results revealed significantly reduced cumulative morphine equivalent in the first 12 h postoperatively in the ketamine than the control group (WMD, −5.60; 95% CI −7.59 to −3.61, $P < 0.001$, GRADE = moderate) (Figure 5(a)).

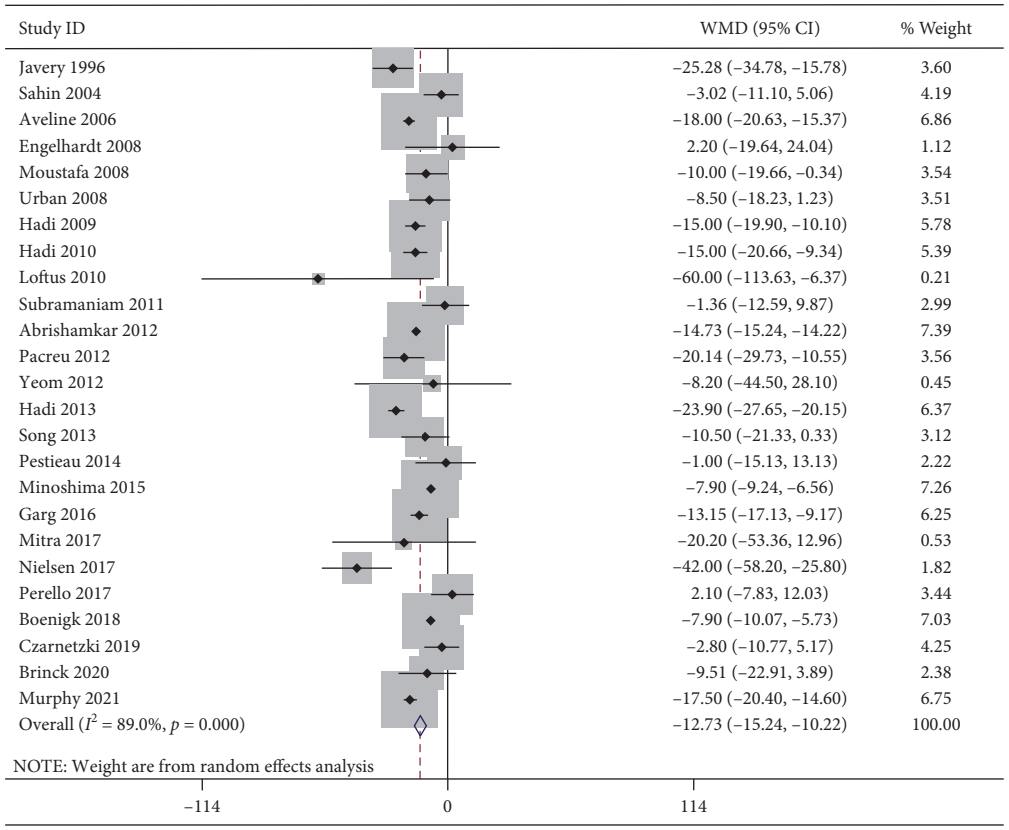
3.5.2. Cumulative Opioid Consumption in the First 24 h Postoperatively. A total of 25 studies reported the cumulative opioid consumption in the first 24 h postoperatively. Significant heterogeneity was detected ($I^2 = 89.0\%$, $P < 0.001$). The 25 studies included 759 patients in the ketamine group and 692 patients in the control group. The pooled results revealed significantly reduced cumulative morphine equivalent in the first 24 h postoperatively in the ketamine than the control group (WMD, −12.73; 95% CI −15.24 to −10.22, $P < 0.001$, GRADE = moderate) (Figure 5(b)).

3.5.3. Cumulative Opioid Consumption in the First 48 h Postoperatively. A total of 17 studies reported the cumulative opioid consumption in the first 48 h postoperatively. Significant heterogeneity was detected ($I^2 = 72.6\%$, $P < 0.001$). The 17 studies included 645 patients in the ketamine group and 505 patients in the control group. The pooled results revealed significantly reduced cumulative morphine equivalent in the first 48 h postoperatively in the ketamine than the control group (WMD, −15.42; 95% CI −20.06 to −10.78, $P < 0.001$, GRADE = moderate) (Figure 5(c)).

3.5.4. Subgroup Analysis by Ages. The heterogeneity of cumulative opioid consumption was significantly decreased after categorizing the studies into pediatric studies and adult studies. For adult patients, the pooled results revealed that the cumulative opioid consumption in the first 12 h (WMD,

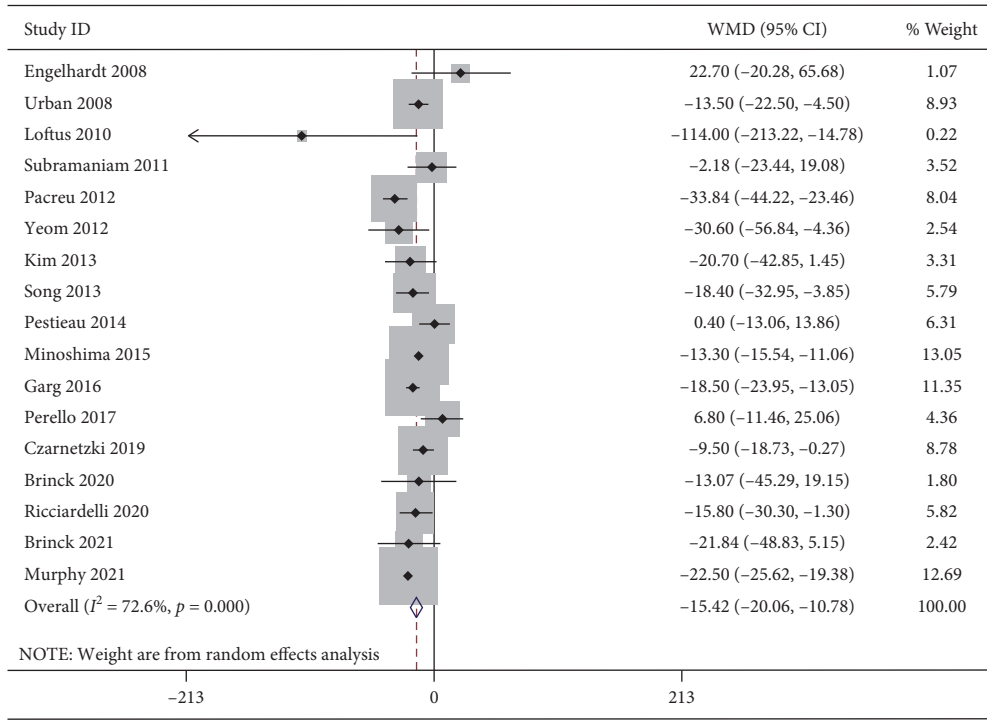


(a)



(b)

Figure 5: Continued.



(c)

Figure 5: Forest plot of the cumulative opioid consumption for the ketamine group and control group. (a) First 12 h; (b) first 24 h; (c) first 48 h.

−5.95; 95% CI −8.02 to −3.88, $P < 0.001$, GRADE = moderate), 24 h (WMD, −14.42; 95% CI −16.99 to −11.85, $P < 0.001$, GRADE = high), and 48 h (WMD, −19.24; 95% CI −24.16 to −14.32, $P < 0.001$, GRADE = high) postoperatively was significantly reduced in the ketamine group than the control group. For pediatric patients, cumulative opioid consumption in the first 24 h (WMD, −5.80; 95% CI −10.17 to −1.42, $P = 0.009$, GRADE = moderate) was significantly reduced in the ketamine group than the control group while no significant difference in the first 12 h (WMD, −1.42; 95% CI −6.91 to 4.08, $P = 0.613$, GRADE = low) and 48 h (WMD, −5.82; 95% CI −15.75 to 4.12, $P = 0.251$, GRADE = moderate) postoperatively between groups.

3.5.5. Subgroup Analysis by Administration Times:. The heterogeneity of cumulative opioid consumption was significantly decreased after categorizing the studies into intrasubgroup, postsubgroup, and intrasubgroup + postsubgroup according to the administration times of ketamine. The cumulative opioid consumption in the first 12 h (WMD, −4.48; 95% CI −8.35 to −0.61, $P = 0.023$, GRADE = moderate; WMD, −5.21; 95% CI −8.02 to −2.40, $P < 0.001$, GRADE = moderate), 24 h (WMD, -12.91; 95% CI -18.85 to -6.97, $P < 0.001$, GRADE = high; WMD, −13.41; 95% CI −17.87 to −8.95, $P < 0.001$, GRADE = moderate), and 48 h (WMD, −19.05; 95% CI −25.49 to −12.62, $P < 0.001$, GRADE = moderate; WMD, −18.63; 95% CI −23.98 to −13.28, $P < 0.001$, GRADE = low) after surgery was significantly reduced in the ketamine group when the drugs were administrated intraoperatively and postoperatively or solely postoperatively. However, for intrasubgroup, only the cumulative opioid consumption in the first 24 h was significantly reduced in the ketamine group (WMD, −16.74; 95% CI −22.73 to −10.75, $P < 0.001$, GRADE = moderate). As there was only one study in intrasubgroup that reported the data in the first 12 h postoperatively, we excluded this subgroup for analysis at this terminated point.

3.6. Time to First Request for Analgesic after Surgery. A total of 8 studies reported the time to first request for analgesic after surgery. Significant heterogeneity was detected ($I^2 = 83.5\%$, $P < 0.001$). The 8 studies included 196 patients in the ketamine group and 174 patients in the control group. The pooled results revealed significantly prolonged time to first request for analgesic after surgery in the ketamine than the control group (WMD, 6.63; 95% CI 3.99 to 9.28, $P < 0.001$, GRADE = moderate) (Figure 6).

3.7. Adverse Events with the Administration of Ketamine

3.7.1. Central Nervous System Adverse Events. CNS adverse events including hallucination, confusion, disorientation, visual disturbance, sedation, nightmare, and drowsiness were reported by 18 studies. No substantial heterogeneity was detected ($I^2 = 9.4\%$, $P = 0.342$). The incidence of CNS adverse event was 13.7% (103/752) in the ketamine group

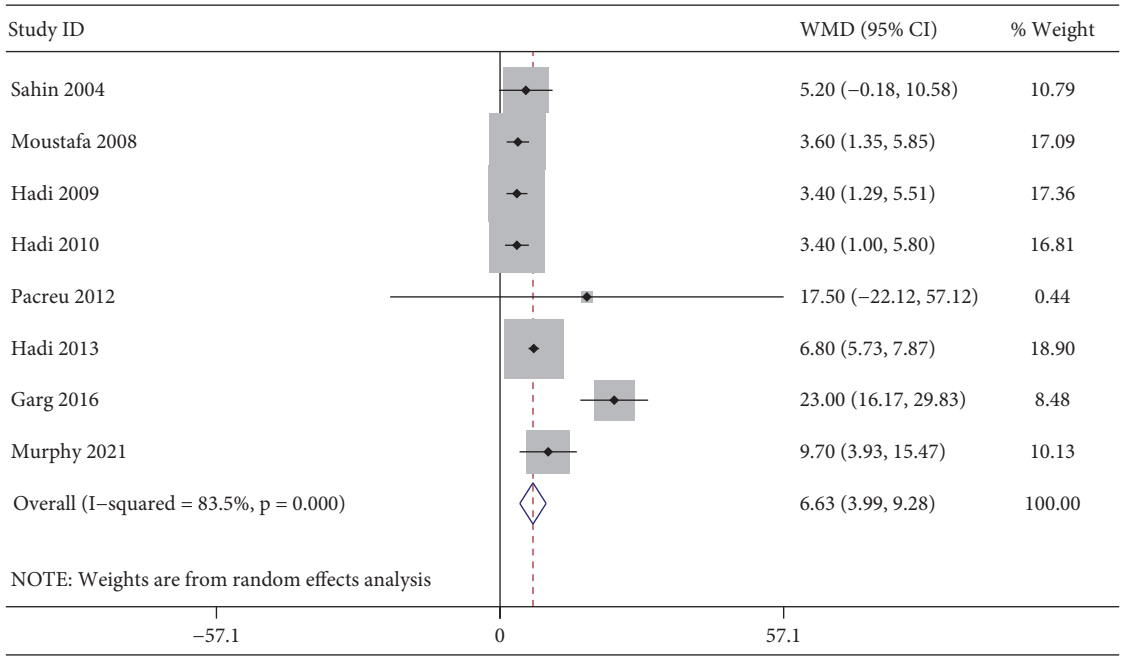


Figure 6: Forest plot of the time to first request for analgesic after surgery for the ketamine group and control group.

and 11.6% (72/623) in the control group. The pooled results revealed no significant difference in the incidence of CNS adverse event between groups (RR, 1.17; 95% CI 0.90 to 1.54, $P = 0.243$, GRADE = moderate) (Figure 7(a)).

3.7.2. Postoperative Nausea and Vomiting. PONV were reported by 21 studies. No substantial heterogeneity was detected ($I^2 = 0.8\%$, $P = 0.448$). The incidence of PONV adverse event was 27.8% (215/772) in the ketamine group and 33.9% (213/629) in the control group. The pooled results revealed a significantly lower incidence of PONV in the ketamine group than the control group (RR, 0.84; 95% CI 0.72 to 0.98, $P = 0.028$, GRADE = moderate) (Figure 7(b)).

3.7.3. Subgroup Analysis by Ages. We were unable to perform subgroup analysis for CNS adverse events because there was only one study in pediatric subgroup. The pooled results revealed no significant difference in the incidence of PONV between groups for both adult (RR, 0.87; 95% CI 0.74 to 1.02, $P = 0.083$, GRADE = moderate) and pediatric subgroup (RR, 0.68; 95% CI 0.43 to 1.09, $P = 0.113$, GRADE = low).

3.7.4. Subgroup Analysis by Administration Times. The pooled results revealed no significant difference in the incidence of CNS adverse events between groups for intrasubgroup (RR, 1.10; 95% CI 0.66 to 1.84, $P = 0.705$, GRADE = moderate), postsubgroup (RR, 1.30; 95% CI 0.65 to 2.57, $P = 0.455$, GRADE = moderate), and intrasubgroup + postsubgroup (RR, 1.13; 95% CI 0.79 to 1.63, $P = 0.504$, GRADE = moderate). Similarly, the pooled results revealed no significant difference in the incidence of PONV between groups for intrasubgroup (RR, 0.89; 95% CI 0.69 to 1.15, $P = 0.365$, GRADE = moderate), postsubgroup (RR, 0.80; 95% CI 0.33 to 1.90, $P = 0.611$, GRADE = low), and intrasubgroup + postsubgroup (RR, 0.86; 95% CI 0.69 to 1.06, $P = 0.150$, GRADE = moderate).

4. Discussion

In several previous reviews, the administration of perioperative low-dose ketamine has demonstrated an opioid-sparing effect in patients undergoing major surgery and could mitigate opioid-induced hyperalgesia and acute opioid tolerance shown to occur in these patients [2, 54, 55]. However, these literature focused on a broad range of surgical procedures, whether this hold true for spine surgery remained controversial. Although a meta-analysis by Pendi et al. has reported that supplemental perioperative ketamine was effective in pain management following spine surgery, this study did not consider the impact of patient ages and administration time of drugs [56]. As previous studies have reported an insignificant reduction in pain score and opioid consumption for pediatric patients undergoing perioperative low-dose ketamine, and only intraoperative administration could not prolong the analgesia time in adult surgery, the results by Pendi et al. may be skewed by the heterogeneous of included studies [3, 57]. In the current study, we additionally performed subgroup analysis according to ages and administration time in order to report the efficacy of perioperative low-dose ketamine more precisely.

4.1. Postoperative Pain Intensity and Cumulative Opioid Consumption. Patients administrated low-dose ketamine reported significantly less pain and corresponding decreased need for opioids up to 48 h postoperatively in the overall

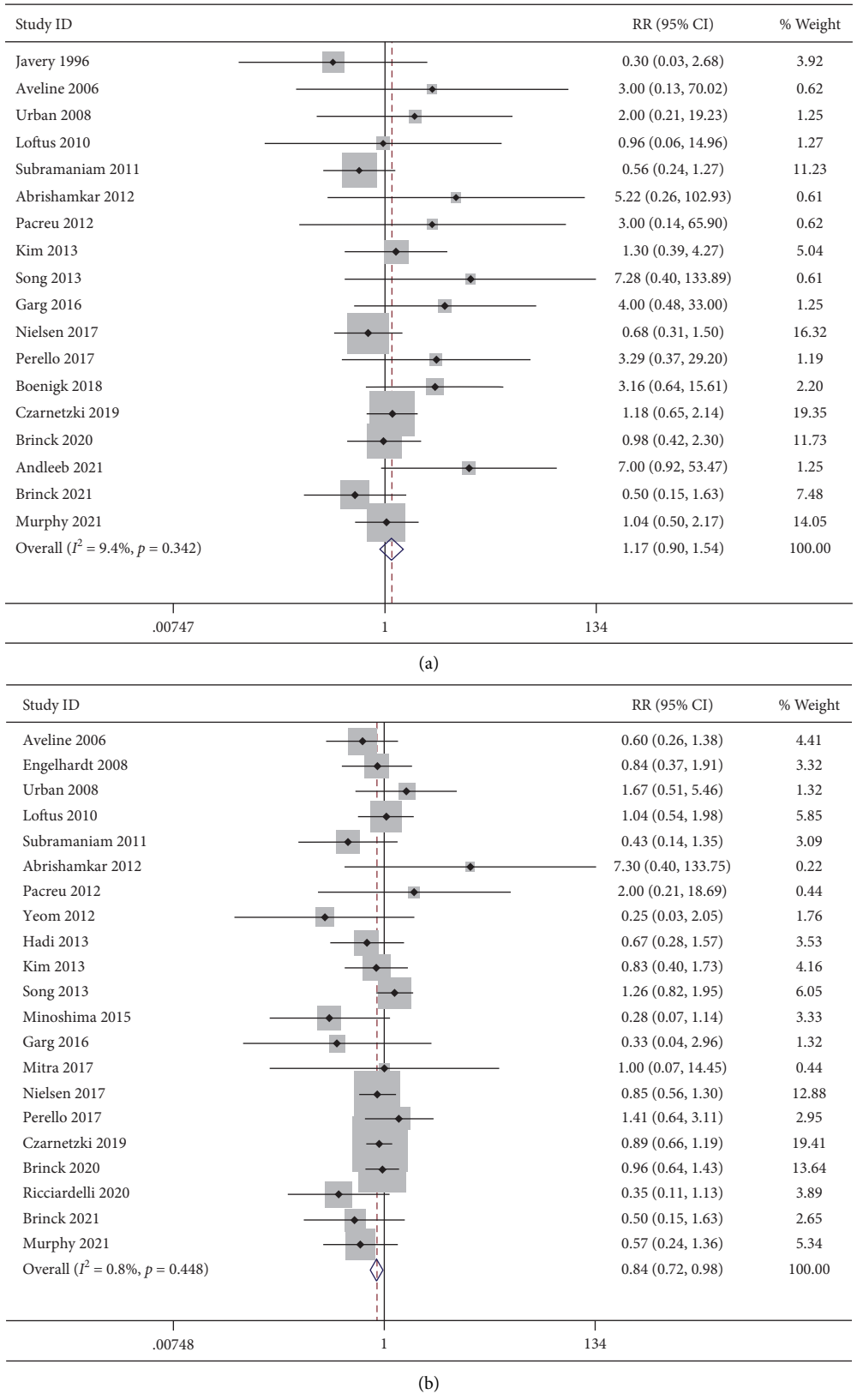


Figure 7: Forest plot of the incidence of adverse events for the ketamine group and control group. (a) CNS adverse events; (b) PONV.

analysis, which was consistent with previous studies [20]. Inconsistent with our results, a recent meta-analysis focused on spine surgery by Pendi et al. pooled the data of pediatric and adult and reported that the analgesic effect of ketamine supplementation may be only limited to the first 24 h after surgery [56]. However, the age-related differences in pharmacokinetic could impact the reliability of their results [45]. In the current study, an analgesic and morphine-sparing effect was only detected in adult patients. For pediatric patients, the low-dose ketamine failed to decrease the pain intensity and only reduced the cumulative opioid consumption in the first 24 h postoperatively. This finding was in concert with the meta-analysis by Dahmani et al., who indicated that perioperative administration of ketamine in children could not change early postoperative pain and analgesic use [58]. Pharmacokinetic studies had suggested a shorter context-sensitive half-time and a higher requirement of ketamine doses to maintain the steady-state concentrations in pediatric populations compared to adults [59, 60]. Therefore, the low-dose ketamine used in pediatric patients was not as sufficient as in adults to suppress the NMDA receptor pathway [40].

Subgroup analysis also indicated that intraoperative administration of ketamine solely was not as effective as postoperative or intraoperative and postoperative administration to prolong the analgesia time and reduced opioid consumptions, especially during 24 h to 48 h after surgery. Central sensitization was associated with hyperalgesia and opioid tolerance [44, 45]. Repetitive and high frequency noxious stimulus from C-fibers via activation of NMDA receptor could evoke this process not only during surgery but also in the postoperative period [41]. Therefore, the withdrawal hyperalgesia and acute opioid tolerance may continue and even develop long after surgery [61]. Our finding was consistent with the results of a previous meta-analysis by Wang et al., who reported that the analgesic effect and morphine-sparing effect provided by intraoperative administration of ketamine solely was very limited for adult surgery, although in the first 24 h postoperatively [62]. Thus, to obtain a beneficial effect in postoperative pain management, low-dose ketamine administrated in postoperative period or through the perioperative period may be the better choice.

4.2. Adverse Events with the Administration of Ketamine. A common concern with the use of ketamine has been its side effects including CNS adverse events and PONV [63]. Consistent with a previous large meta-analysis of ketamine adjuncts to opioid for pain control which included 130 RCTs of 4,588 participants, our results indicated that the incidence of ketamine-related adverse events has not been increased compared to those who only received opioids, in both pediatric and adult patients [20].

The meta-analysis by Wang et al. reported that the rate of psychotomimetic events was significantly higher in patients administrated low-dose ketamine intraoperatively and postoperatively [62]. However, Wang et al. pooled the data of various surgical procedures in adult patients, including hemorrhoidectomy, radical prostatectomy, laparoscopic cholecystectomy, thoracotomy, and lumbar fusion, which was highly heterogeneous and may skew the results. When solely focused on spine surgery, this study revealed that postoperative or intraoperative and postoperative administration of low-dose ketamine would not increase the risk of adverse events, in addition to its prolonged analgesic effect and morphine-sparing effect.

4.3. Limitations. We believe that this meta-analysis has presented valuable results for many anesthesiologists and spinal surgeons, although with some limitations. Firstly, although we performed subgroup analysis, there was still significant heterogeneity in most of the analyses, which might be due to different study designs, modes of delivery, dosages, and procedures. Secondly, combining multiple treatment arms may have produced a moderating effect. Thirdly, chronic opioid-dependent could magnitude the analgesic effect of ketamine; however, some studies did not clarify the usage of preoperative opioid, leaving it unclear whether opioid-tolerant patients were included [44]. Also, although this study indicated that low-dose ketamine could decrease the postoperative pain intensity and opioid use, the optimal protocol, including mode of administration, dosage, and timing, were not obtained. Later, although the participants were categorized into pediatric (10 to 17 years of age) and adult (≥18 years of age) in this study, the adult participants could not be further categorized by middle and old age due to the design of included RCTs. According to the mean age of each study, there was only one study that fulfilled the definition of old age participants (≥65 years of age) [64–66]. Considering that the old age people are more susceptible to spine disorders, further studies should focus on this population, who are the main surgical candidates. Last, although we have applied the Egger's test to assess the publication bias, the potential language bias is inevitable because clinical investigators working in non-English-speaking countries are more likely to publish their positive findings in an international English-language journal while reporting negative results in their local languages [67].

5. Conclusion

Perioperative low-dose ketamine demonstrated analgesic and morphine-sparing effect with no increased adverse events after spine surgery. However, the effect was not significant in pediatric patients. Only postoperative or intraoperative and postoperative administration could prolong the analgesic time up to 48 h postoperatively. Further studies should focus on the optimal protocol of ketamine administration and its effect on old age participants.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Lijin Zhou, Honghao Yang, and Yunzhong Cheng contributed equally to this work and should be regarded as co-first authors.

Supplementary Materials

Supplementary Figure S1: subgroup analysis of pain intensity at rest at 6 h postoperatively by ages. Supplementary Figure S2: subgroup analysis of pain intensity at rest at 12 h postoperatively by ages. Supplementary Figure S3: subgroup analysis of pain intensity at rest at 24 h postoperatively by ages. Supplementary Figure S4: subgroup analysis of pain intensity at rest at 48 h postoperatively by ages. Supplementary Figure S5: subgroup analysis of pain intensity during mobilization at 6 h postoperatively by ages. Supplementary Figure S6: subgroup analysis of pain intensity during mobilization at 12 h postoperatively by ages. Supplementary Figure S7: subgroup analysis of pain intensity during mobilization at 24 h postoperatively by ages. Supplementary Figure S8: subgroup analysis of pain intensity during mobilization at 48 h postoperatively by ages. Supplementary Figure S9: subgroup analysis of pain intensity at rest at 6 h postoperatively by administration times. Supplementary Figure S10: subgroup analysis of pain intensity at rest at 12 h postoperatively by administration times. Supplementary Figure S11: subgroup analysis of pain intensity at rest at 24 h postoperatively by administration times. Supplementary Figure S12: subgroup analysis of pain intensity at rest at 48 h postoperatively by administration times. Supplementary Figure S13: subgroup analysis of pain intensity during mobilization at 6 h postoperatively by administration times. Supplementary Figure S14: subgroup analysis of pain intensity during mobilization at 12 h postoperatively by administration times. Supplementary Figure S15: subgroup analysis of pain intensity during mobilization at 24 h postoperatively by administration times. Supplementary Figure S16: subgroup analysis of cumulative opioid consumption in the first 12 h postoperatively by ages. Supplementary Figure S17: subgroup analysis of cumulative opioid consumption in the first 24 h postoperatively by ages. Supplementary Figure S18: subgroup analysis of cumulative opioid consumption in the first 48 h postoperatively by ages. Supplementary Figure S19: subgroup analysis of cumulative opioid consumption in the first 12 h postoperatively by administration times. Supplementary Figure S20: subgroup analysis of cumulative opioid consumption in the first 24 h postoperatively by administration times. Supplementary Figure S21: subgroup analysis of cumulative opioid consumption in the first 48 h postoperatively by administration times. Supplementary Figure S22: subgroup analysis of the incidence of PONV by ages. Supplementary Figure S23: subgroup analysis of the incidence of PONV by administration times. (*Supplementary Materials*)

References

[1] C. Cozowicz, J. Bekeris, J. Poeran et al., "Multimodal pain management and postoperative outcomes in lumbar spine fusion surgery: a population-based cohort study," *Spine*, vol. 45, no. 9, pp. 580–589, 2020.

[2] J. F. García-Henares, J. A. Moral-Munoz, A. Salazar, and E. Del Pozo, "Effects of ketamine on postoperative pain after remifentanil-based anesthesia for major and minor surgery in adults: a systematic review and meta-analysis," *Frontiers in Pharmacology*, vol. 9, p. 921, 2018.

[3] P. J. Park, M. C. Makhni, M. Cerpa, R. A. Lehman, and L. G. Lenke, "The role of perioperative ketamine in postoperative pain control following spinal surgery," *Journal of Spine Surgery*, vol. 6, no. 3, pp. 591–597, 2020.

[4] M. C. Bicket, E. White, P. J. Pronovost, C. L. Wu, M. Yaster, and G. C. Alexander, "Opioid oversupply after joint and spine surgery: a prospective cohort study," *Anesthesia & Analgesia*, vol. 128, no. 2, pp. 358–364, 2019.

[5] S. Sadhasivam, V. Chidambaran, V. A. Olbrecht et al., "Opioid-related adverse effects in children undergoing surgery: unequal burden on younger girls with higher doses of opioids," *Pain Medicine*, vol. 16, no. 5, pp. 985–997, 2015.

[6] S. L. Kane-Gill, E. C. Rubin, P. L. Smithburger, M. S. Buckley, and J. F. Dasta, "The cost of opioid-related adverse drug events," *Journal of Pain & Palliative Care Pharmacotherapy*, vol. 28, no. 3, pp. 282–293, 2014.

[7] A. Soni, "Medicaid expansion and rates of opioid-related hospital use-reply," *JAMA Internal Medicine*, vol. 180, no. 10, pp. 1402-1403, 2020.

[8] S. Mercadante, E. Arcuri, and A. Santoni, "Opioid-induced tolerance and hyperalgesia," *CNS Drugs*, vol. 33, no. 10, pp. 943–955, 2019.

[9] J. Lyden and I. A. Binswanger, "The United States opioid epidemic," *Seminars in Perinatology*, vol. 43, no. 3, pp. 123–131, 2019.

[10] J. S. Yoo, J. Ahn, A. Buvanendran, and K. Singh, "Multimodal analgesia in pain management after spine surgery," *Journal of Spine Surgery*, vol. 5, no. S2, pp. S154–s159, 2019.

[11] K. Maheshwari, R. Avitsian, D. I. Sessler et al., "Multimodal analgesic regimen for spine surgery: a randomized placebo-controlled trial," *Anesthesiology*, vol. 132, no. 5, pp. 992–1002, 2020.

[12] M. Haffner, A. M. Saiz Jr., R. Nathe et al., "Preoperative multimodal analgesia decreases 24-hour postoperative narcotic consumption in elective spinal fusion patients," *The Spine Journal*, vol. 19, no. 11, pp. 1753–1763, 2019.

[13] R. Urman, N. Vadivelu, E. Schermer, V. Kodumudi, K. Belani, and A. Kaye, "Role of ketamine for analgesia in adults and children," *Journal of Anaesthesiology Clinical Pharmacology*, vol. 32, no. 3, pp. 298–306, 2016.

[14] A. Gorlin, D. Rosenfeld, and H. Ramakrishna, "Intravenous sub-anesthetic ketamine for perioperative analgesia," *Journal of Anaesthesiology Clinical Pharmacology*, vol. 32, no. 2, pp. 160–167, 2016.

[15] D. Moher, A. Liberati, J. Tetzlaff, and D. G. Altman, "Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement," *BMJ*, vol. 339, no. 1, p. b2535, 2009.

[16] S. Davies, "The importance of PROSPERO to the National Institute for Health Research," *Systematic Reviews*, vol. 1, no. 1, p. 5, 2012.

[17] M. Cumpston, T. Li, M. J. Page et al., "Updated guidance for trusted systematic reviews: a new edition of the cochrane handbook for systematic reviews of Interventions," *Cochrane Database of Systematic Reviews*, vol. 10, p. Ed000142, 2019.

[18] J. L. Brożek, E. A. Akl, P. Alonso-Coello et al., "Grading quality of evidence and strength of recommendations in clinical practice guidelines. Part 1 of 3. An overview of the GRADE approach and grading quality of evidence about interventions," *Allergy*, vol. 64, no. 5, pp. 669–677, 2009.

[19] C. A. Salazar, J. E. Basilio Flores, L. E. Veramendi Espinoza, J. W. Mejia Dolores, D. E. Rey Rodriguez, and C. Loza Munárriz, "Ranolazine for stable angina pectoris," *Cochrane Database of Systematic Reviews*, vol. 2019, no. 1, p. Cd011747, 2017.

[20] E. Brinck, E. Tiippana, M. Heesen et al., "Perioperative intravenous ketamine for acute postoperative pain in adults," *Cochrane Database of Systematic Reviews*, vol. 12, no. 12, p. Cd012033, 2018.

[21] A. E. Patanwala, J. Duby, D. Waters, and B. L. Erstad, "Opioid conversions in acute care," *The Annals of Pharmacotherapy*, vol. 41, no. 2, pp. 255–267, 2007.

[22] R. Anderson, J. H. Saiers, S. Abram, and C. Schlicht, "Accuracy in equianalgesic dosing," *Journal of Pain and Symptom Management*, vol. 21, no. 5, pp. 397–406, 2001.

[23] S. Duval and R. Tweedie, "Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis," *Biometrics*, vol. 56, no. 2, pp. 455–463, 2000.

[24] K. B. Javery, T. W. Ussery, H. G. Steger, and G. W. Colclough, "Comparison of morphine and morphine with ketamine for postoperative analgesia," *Canadian Journal of Anaesthesia*, vol. 43, no. 3, pp. 212–215, 1996.

[25] A. Sahin, O. Canbay, A. Cuhadar, N. Celebi, and U. Aypar, "Bolus ketamine does not decrease hyperalgesia after remifentanil infusion," *The Pain Clinic*, vol. 16, no. 4, pp. 407–411, 2013.

[26] C. Aveline, H. Hetet, P. Vautier, J. F. Gautier, and F. Bonnet, "Peroperative ketamine and morphine for postoperative pain control after lumbar disk surgery," *European Journal of Pain*, vol. 10, no. 7, p. 653, 2006.

[27] T. Engelhardt, C. Zaarour, B. Naser et al., "Intraoperative low-dose ketamine does not prevent a remifentanil-induced increase in morphine requirement after pediatric scoliosis surgery," *Anesthesia & Analgesia*, vol. 107, no. 4, pp. 1170–1175, 2008.

[28] A. M. Moustafa, H. H. Negmi, and M. E. Rabie, "The combined effect of ketamine and remifentanil infusions as total intravenous anesthesia for scoliosis surgery in children," *Middle East Journal of Anesthesiology*, vol. 19, no. 5, pp. 1151–1168, 2008.

[29] M. K. Urban, J. T. Ya Deau, B. Wukovits, and J. Y. Lipnitsky, "Ketamine as an adjunct to postoperative pain management in opioid tolerant patients after spinal fusions: a prospective randomized trial," *HSS Journal*, vol. 4, no. 1, pp. 62–65, 2008.

[30] B. Hadi, R. Al Ramadani, R. Daas, I. Naylor, R. Zelko, and M. Saleh, "The influence of anaesthetic drug selection for scoliosis surgery on the management of intraoperative haemodynamic stability and postoperative pain-pharmaceutical care programme," *Southern African Journal of Anaesthesia and Analgesia*, vol. 15, no. 5, pp. 10–14, 2009.

[31] B. A. Hadi, R. A. Ramadani, R. Daas, I. Naylor, and R. Zelkó, "Remifentanil in combination with ketamine versus remifentanil in spinal fusion surgery—a double blind study," *International Journal of Clinical Pharmacology and Therapeutics*, vol. 48, no. 08, pp. 542–548, 2010.

[32] R. W. Loftus, M. P. Yeager, J. A. Clark et al., "Intraoperative ketamine reduces perioperative opiate consumption in opiate-dependent patients with chronic back pain undergoing back surgery," *Anesthesiology*, vol. 113, no. 3, pp. 639–646, 2010.

[33] K. Subramaniam, V. Akhouri, P. A. Glazer et al., "Intra- and postoperative very low dose intravenous ketamine infusion does not increase pain relief after major spine surgery in patients with preoperative narcotic analgesic intake," *Pain Medicine*, vol. 12, no. 8, pp. 1276–1283, 2011.

[34] S. Abrishamkar, N. Eshraghi, A. Feizi, R. Talakoub, A. Rafiei, and P. Rahmani, "Analgesic effects of ketamine infusion on postoperative pain after fusion and instrumentation of the lumbar spine: a prospective randomized clinical trial," *Medical Archives*, vol. 66, no. 2, pp. 107–110, 2012.

[35] S. Pacreu, J. Fernández Candil, L. Moltó, J. Carazo, and S. Fernández Galinski, "The perioperative combination of methadone and ketamine reduces post-operative opioid usage compared with methadone alone," *Acta Anaesthesiologica Scandinavica*, vol. 56, no. 10, pp. 1250–1256, 2012.

[36] J. H. Yeom, M.-S. Chon, W. J. Jeon, and J.-H. Shim, "Perioperative ketamine with the ambulatory elastometric infusion pump as an adjuvant to manage acute postoperative pain after spinal fusion in adults: a prospective randomized trial," *Korean Journal of Anesthesiology*, vol. 63, no. 1, pp. 54–58, 2012.

[37] B. A. Hadi, R. Daas, and R. Zelkó, "A randomized, controlled trial of a clinical pharmacist intervention in microdiscectomy surgery—low dose intravenous ketamine as an adjunct to standard therapy," *Saudi Pharmaceutical Journal*, vol. 21, no. 2, pp. 169–175, 2013.

[38] S. H. Kim, S. I. Kim, S. Y. Ok et al., "Opioid sparing effect of low dose ketamine in patients with intravenous patient-controlled analgesia using fentanyl after lumbar spinal fusion surgery," *Korean Journal of Anesthesiology*, vol. 64, no. 6, pp. 524–528, 2013.

[39] J. W. Song, J. K. Shim, Y. Song, S. Y. Yang, S. J. Park, and Y. L. Kwak, "Effect of ketamine as an adjunct to intravenous patient-controlled analgesia, in patients at high risk of postoperative nausea and vomiting undergoing lumbar spinal surgery," *British Journal of Anaesthesia*, vol. 111, no. 4, pp. 630–635, 2013.

[40] S. R. Pestieau, J. C. Finkel, M. M. Junqueira et al., "Prolonged perioperative infusion of low-dose ketamine does not alter opioid use after pediatric scoliosis surgery," *Pediatric Anesthesia*, vol. 24, no. 6, pp. 582–590, 2014.

[41] R. Minoshima, S. Kosugi, D. Nishimura et al., "Intra- and postoperative low-dose ketamine for adolescent idiopathic scoliosis surgery: a randomized controlled trial," *Acta Anaesthesiologica Scandinavica*, vol. 59, no. 10, pp. 1260–1268, 2015.

[42] N. Garg, N. B. Panda, K. A. Gandhi et al., "Comparison of small dose ketamine and dexmedetomidine infusion for postoperative analgesia in spine surgery-A prospective randomized double-blind placebo controlled study," *Journal of Neurosurgical Anesthesiology*, vol. 28, no. 1, pp. 27–31, 2016.

[43] R. Mitra, H. Prabhakar, G. Rath, P. Bithal, and A. Khandelwal, "A comparative study between intraoperativelow-dose ketamine and dexmedetomidine, as an anaesthetic adjuvant in lumbar spine instrumentation surgery for the post-operative analgesic requirement," *Journal of Neuroanaesthesiology and Critical Care*, vol. 4, no. 2, pp. 091–098, 2017.

[44] R. V. Nielsen, J. S. Fomsgaard, H. Siegel et al., "Intraoperative ketamine reduces immediate postoperative opioid consumption after spinal fusion surgery in chronic pain patients with opioid dependency: a randomized, blinded trial," *Pain*, vol. 158, no. 3, pp. 463–470, 2017.

[45] M. Perelló, D. Artés, C. Pascuets, E. Esteban, and A. M. Ey Batlle, "Prolonged perioperative low-dose ketamine does not improve short and long-term outcomes after pediatric idiopathic scoliosis surgery," *Spine*, vol. 42, no. 5, pp. E304–E312, 2017.

[46] K. Boenigk, G. C. Echevarria, E. Nisimov et al., "Low-dose ketamine infusion reduces postoperative hydromorphone requirements in opioid-tolerant patients following spinal fusion," *European Journal of Anaesthesiology*, vol. 36, no. 1, pp. 8–15, 2019.

[47] C. Czarnetzki, J. Desmeules, E. Tessitore et al., "Perioperative intravenous low-dose ketamine for neuropathic pain after major lower back surgery: a randomized, placebo-controlled study," *European Journal of Pain*, vol. 24, no. 3, pp. 555–567, 2020.

[48] E. C. V. Brinck, K. Maisniemi, J. Kankare, L. Tielinen, P. Tarkkila, and V. K. Kontinen, "Analgesic effect of intraoperative intravenous S-ketamine in opioid-naïve patients after major lumbar fusion surgery is temporary and not dose-dependent: a randomized, double-blind, placebo-controlled clinical trial," *Anesthesia & Analgesia*, vol. 132, no. 1, pp. 69–79, 2021.

[49] R. M. Ricciardelli, N. M. Walters, M. Pomerantz et al., "The efficacy of ketamine for postoperative pain control in adolescent patients undergoing spinal fusion surgery for idiopathic scoliosis," *Spine Deformity*, vol. 8, no. 3, pp. 433–440, 2020.

[50] R. Andleeb, S. Agrawal, and P. Gupta, "Evaluation of the effect of continuous infusion of dexmedetomidine or a subanesthetic dose ketamine on transcranial electrical motor evoked potentials in adult patients undergoing elective spine surgery under total intravenous anesthesia: a randomized controlled exploratory study," *Asian Spine Journal*, 2021, In press.

[51] E. C. V. Brinck, T. Virtanen, S. Mäkelä et al., "S-ketamine in patient-controlled analgesia reduces opioid consumption in a dose-dependent manner after major lumbar fusion surgery: a randomized, double-blind, placebo-controlled clinical trial," *PLoS One*, vol. 16, no. 6, p. e0252626, 2021.

[52] G. S. Murphy, M. J. Avram, S. B. Greenberg et al., "Perioperative methadone and ketamine for postoperative pain control in spinal surgical patients: a randomized, double-blind, placebo-controlled trial," *Anesthesiology*, vol. 134, no. 5, pp. 697–708, 2021.

[53] N. Nikoubakht, M. Alimian, S. H. R. Faiz, P. Derakhshan, and M. S. Sadri, "Effects of ketamine versus dexmedetomidine maintenance infusion in posterior spinal fusion surgery on acute postoperative pain," *Surgical Neurology International*, vol. 12, p. 192, 2021.

[54] J. M. Riddell, J. M. Trummel, and I. J. Onakpoya, "Low-dose ketamine in painful orthopaedic surgery: a systematic review and meta-analysis," *British Journal of Anaesthesia*, vol. 123, no. 3, pp. 325–334, 2019.

[55] L. Pang, M. Cui, W. Dai, J. Kong, H. Chen, and S. Wu, "Can intraoperative low-dose R,S-ketamine prevent depressive symptoms after surgery? the first meta-analysis of clinical trials," *Frontiers in Pharmacology*, vol. 11, p. 586104, 2020.

[56] A. Pendi, R. Field, S.-D. Farhan, M. Eichler, and S. S. Bederman, "Perioperative ketamine for analgesia in spine surgery," *Spine*, vol. 43, no. 5, pp. E299–e307, 2018.

[57] C. S. Lee, S. Merchant, and V. Chidambaran, "Postoperative pain management in pediatric spinal fusion surgery for idiopathic scoliosis," *Pediatric Drugs*, vol. 22, no. 6, pp. 575–601, 2020.

[58] S. Dahmani, D. Michelet, P.-S. Abback et al., "Ketamine for perioperative pain management in children: a meta-analysis of published studies," *Pediatric Anesthesia*, vol. 21, no. 6, pp. 636–652, 2011.

[59] D. Dallimore, B. J. Anderson, T. G. Short, and D. W. Herd, "Ketamine anesthesia in children exploring infusion regimens," *Pediatric Anesthesia*, vol. 18, no. 8, pp. 708–714, 2008.

[60] J. Idvall, I. Ahlgren, K. F. Aronsen, and P. Stenberg, "Ketamine infusions: pharmacokinetics and clinical effects," *British Journal of Anaesthesia*, vol. 51, no. 12, pp. 1167–1173, 1979.

[61] D. D. Hood, R. Curry, and J. C. Eisenach, "Intravenous remifentanil produces withdrawal hyperalgesia in volunteers with capsaicin-induced hyperalgesia," *Anesthesia & Analgesia*, vol. 97, no. 3, pp. 810–815, 2003.

[62] X. Wang, C. Lin, L. Lan, and J. Liu, "Perioperative intravenous S-ketamine for acute postoperative pain in adults: a systematic review and meta-analysis," *Journal of Clinical Anesthesia*, vol. 68, p. 110071, 2021.

[63] C. A. Allen and J. R. Ivester Jr., "Ketamine for pain management-side effects & potential adverse events," *Pain Management Nursing*, vol. 18, no. 6, pp. 372–377, 2017.

[64] S. R. Barclay, K. B. Stoltz, and Y. B. Chung, "Voluntary midlife career change: integrating the transtheoretical model and the life-span, life-space approach," *The Career Development Quarterly*, vol. 59, no. 5, pp. 386–399, 2011.

[65] R. M. Kertzner, "The adult life course and homosexual identity in midlife gay men," *Annual Review of Sex Research*, vol. 12, pp. 75–92, 2001.

[66] W. Sanderson and S. Sherbov, "Rethinking age and aging," *Population Bulletin*, vol. 62, no. 4, pp. 3–16, 2008.

[67] C. Mao and M. Li, "Language bias among Chinese-sponsored randomized clinical trials in systematic reviews and meta-analyses-can anything Be done?" *JAMA Network Open*, vol. 3, no. 5, p. e206370, 2020.

Hindawi
Pain Research and Management
Volume 2022, Article ID 7027637, 7 pages
https://doi.org/10.1155/2022/7027637

Research Article

Retrospective Comparison of Postoperative Fascia Iliaca Block and Multimodal Drug Injection on Early Function of the Knee in Femoral Fractures Using Retrograde Intramedullary Nailing

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Received 21 December 2021; Accepted 28 February 2022; Published 19 March 2022

Academic Editor: Sidong Yang

Introduction. There is a common concern about the pain and rehabilitation of the knee after femoral retrograde intramedullary nailing. It is essential for early postoperative knee function required for physical self-maintenance in daily life. And a favorable rehabilitation of the knee usually promotes the quality of life. However, early rehabilitation is absent or insufficient for many patients in postoperative management. This retrospective study aims to evaluate the effect of early knee function improvement in comparison to postoperative fascia iliaca blocking (FIB) and multimodal drug injection (MDI). *Patients and Methods*. A retrospective analysis of 41 patients receiving femoral fracture treatment with retrograde intramedullary nailing, was performed during 2018–2020. 19 patients were treated with MDI as postoperative analgesia, and 22 patients were treated with FIB. Rehabilitation started on the first postoperative day and lasted for 3 months. Visual analog scale (VAS), the range of motion (ROM) of the knee, and single assessment numeric evaluation (SANE) were assessed. *Results*. There was no significant difference shown in any of the demographic, fracture types, and operative time. All patients performed regular and voluntary knee rehabilitation and weight-bearing at home following the instruction from the orthopedic staff. Pain in the FIB group at postoperative 1-day was milder (1.7 ± 1.1), compared with that in the MDI group (2.8 ± 1.3, $p = 0.038$). There was a significant difference in VAS between two groups at postoperative 1-month ($p = 0.031$), with a peak score in the FIB group (3.3 ± 0.9). At postoperative 3-month, both groups had pain relief with similar VAS ($p = 0.465$). The ROM of the knee in both groups was continuously improved during the first three months. The SANE in the MDI group was significantly different compared with FIB at 1-month ($p = 0.026$). However, scores of SANE were similar in both groups at 3 months ($p = 0.541$). All patients were identified as fractures union at 9-month or 12-month follow-up. *Conclusion*. The knee pain was commonly experienced in this series of retrograde femoral nailings. Both MDI and FIB provided immediate and effective pain control after femoral fracture surgery. MDI was more beneficial to continuous pain control and knee rehabilitation in the early follow-up. The extent of pain relief and knee function improvement reached the same level at postoperative 3-month.

1. Introduction

Intramedullary nailing is an effective method for femoral shaft fractures. In consideration of patients' conditions such as fractures in the distal femur, obesity, ipsilateral pelvic or hip fracture, or ipsilateral tibia fracture, the use of retrograde intramedullary nailing for femoral shaft fractures has become an attractive practice over the last decades [1–5]. However, with the entry point for retrograde nailing being within the knee, this technique may cause complaints about postoperative pain in the knee [2, 6]. Most of the studies revealed a higher rate of anterior knee pain that is more related with retrograde nailing than antegrade nailing for femoral fractures [2, 7–10]. Moreover, this pain is often exacerbated by walking, kneeling, squatting, and stair climbing. Knee function is another focus in follow-up. It

seems that there is no significant difference in knee function in the majority of reports [2, 8–10]. However, some studies found that worse knee scores and range of motion were associated with retrograde nailing [11]. Notably, the knee function in most studies was evaluated in a long-term follow-up, usually at least 1 year. The early rehabilitation of knee function seems to be ignored. The ROM is a basic indicator for knee function, for example, walking requires 67°of ROM, up- and down-stairs require 80°, and sitting in a chair requires 93°. Obviously, early postoperative knee function is an essential requirement for physical self-maintenance of daily living. A favorable functional knee rehabilitation usually promotes the life quality. Furthermore, knee function at 1 month postoperatively may indicate the likelihood of achieving the clinical goal at 12 months [12]. The changes in the knee range of flexion plateaued 3 months after total knee arthroplasty [13]. And poor knee function after knee arthroplasty can be detected through ROM data in the first few weeks [14]. Therefore, it is worthy to pay close attention to early knee rehabilitation after retrograde nailing.

A standard procedure of knee functional rehabilitation usually starts with a continuous passive motion (CPM) on the first day postoperation. Then, the active motion of the knee and weight-bearing exercise are encouraged depending on the tolerance of patients. Usually, the early knee functional rehabilitation is followed by the instructions of physical therapists. Nevertheless, early rehabilitation is absent or insufficient for many patients due to financial difficulty or a lack of home nursing. The confidence and willingness of rehabilitation in early postoperative stage were weakened due to the early pain, although orthopedic staff introduced exercise advise during hospital stay.

The authors speculated that satisfactory postoperative analgesia could facilitate the rehabilitation of the early postoperative stage and improve the knee function in retrograde nailing cases. A multimodal drug periarticular injection was found to relieve pain effectively and promote a better functional recovery among patients receiving total joint replacement [15]. Femoral nerve block has a similar analgesic effect on multimodal periarticular soft tissue injection after total knee arthroplasty as well [16]. This retrospective study is conducted to evaluate the effect of early knee function improvement in comparison with postoperative fascia iliaca blocking with multimodal drug injection.

2. Patients and Methods

2.1. Patients Information. Our institutional Ethical Review Committee reviewed and approved the study protocol. During April 2018 and November 2020, 63 patients suffering from femoral fractures were treated with retrograde intramedullary nailing (Figure 1). 3 distal femoral fractures identified as AO/OTA 33C and 4 ipsilateral tibia plateau fractures were excluded. Also 7 patients were excluded who refused or missed follow-up visits and 8 patients who performed regular exercise in rehabilitation institutions. The remaining 41 patients were retrospectively analyzed. 19 patients before April 2019 were treated with multimodal drug injection (MDI), and 22 patients were treated with fascia iliaca block (FIB) thereafter.

2.2. Operation. All patients were treated with rearmed retrograde nailing (Type B DFN, Double Medical, Xiamen, China) within an intercondylar notch approach. Through a longitudinal incision medial to the patellar tendon, the entry point was located at the anterior end of Blumensaat's line on the lateral projection, essentially at the top of the intercondylar notch, in line with the femoral shaft. After opening the canal, a threaded guidewire was inserted. The fracture was closed and reduced, and the canal was rearmed. A retrograde nailing was inserted and locked proximally and distally. Length and rotation were controlled by comparing AP knee and hip images to the contralateral side.

2.3. Perioperative Analgesia and Care. All femoral fractures were immobilized with skeletal traction, and dezocine was prescribed at the discretion of the residents. 24 hours before the operation, oral imrecoxib of 100 mg per 12 hours was prescribed. All femoral nailing operations were performed under general laryngeal mask airway anesthesia. Immediately postoperatively, the FIB group received 30 ml of 0.75% ropivacaine for an ultrasound-guided fascia iliaca block. The MDI group received a multimodal drug consisting of 10 ml of 0.75% ropivacaine, 1 ml of 40 mg triamcinolone, 1 ml of 30 mg ketorolac tromethamine, 1 ml of 100 mg pethidine hydrochloride, and saline to make up 50 ml in total. 20 ml of the mixture was injected at the fracture site, 10 ml at the subcutaneous fascia around the incision, and the remanent 20 ml was injected intraarticular after the incision was closed.

Rehabilitation was started on the first postoperative day with CPM of the hip and knee joints. The CPM machine was set to range from 40 degrees of knee flexion to full extension, with attempts to increase by 5–10 degrees of flexion to a maximum of 90°, as the patients tolerated. On the third postoperative day, the patients were encouraged to perform straight leg-raising exercises and active flexion of the hips and knees, from a tolerable range followed by a gradual increase. Partial weight bearing with crutches started as soon as the pain became tolerable. All patients were familiar with early knee rehabilitation following the instruction from the orthopedic staff. They were discharged on the seventh to ninth postoperative day and performed knee rehabilitation voluntarily at home without further professional instruction.

2.4. Data Collection. For each patient, the authors recorded knee pain in the visual analog scale (VAS) and the range of motion (ROM) of the knee on the first day, 1 week, 1 month, and 3 months postoperatively. Single assessment numeric evaluation (SANE) of the knee was recorded for knee functional recovery. Radiographs were recorded at 1, 3, 6, 9, and 12 months postoperatively. Callus formation on three out of four cortices and fracture line fading in radiographs were considered as signs of fracture union.

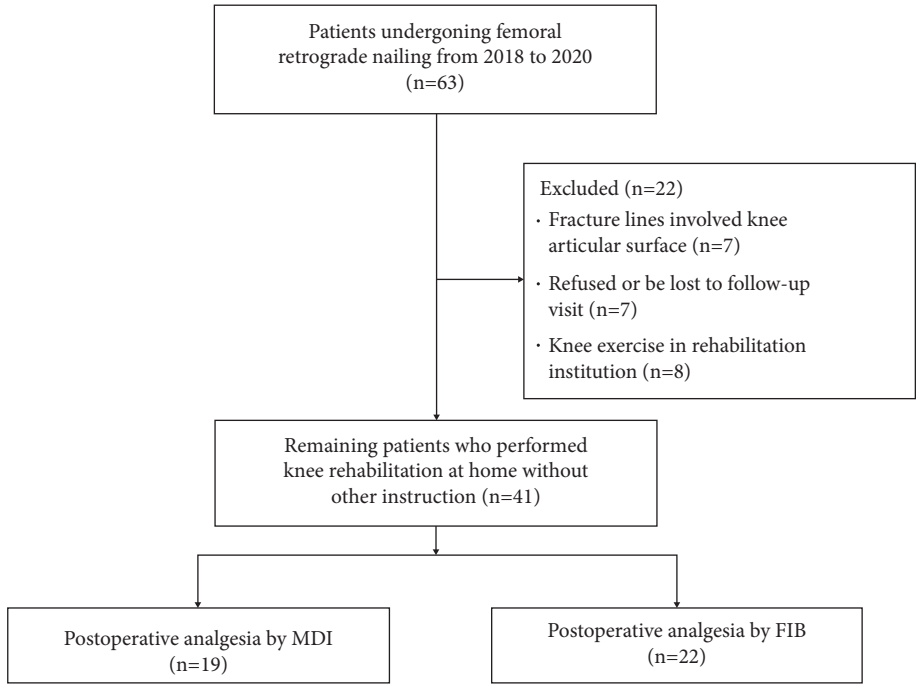

Figure 1: Enrollment flow diagram.

2.5. Statistical Analyses. Statistical analysis was performed using SPSS 20.0 software. The Chi-square test to identify differences in sex and fracture types. Student's *t*-test was used to identify differences in age, operative time, VAS, ROM, and SANE of the knee. Statistical significance was accepted for p values of <0.05.

3. Results

Demographics for patients are presented in Table 1. No significant differences were noted in any of the demographics, fracture types, or operative time. All patients reported regular and voluntary knee rehabilitation and weight-bearing at home according to previous instruction.

The comparison of VAS and knee function for the two groups was presented in Figure 2. Knee pain came out in a trend of anesis in the MDI group. Pain in the FIB group at postoperative 1-day was milder (VAS, 1.7 ± 1.1), compared with that in the MDI group (2.8 ± 1.3, $p = 0.038$). Then, the VAS of the FIB group ascended to 2.9 ± 1.2 at postoperative 1-week, although there was no significant difference between MDI (2.1 ± 1.1, $p = 0.078$). There was a significant difference in VAS between the two groups at postoperative 1-month ($p = 0.031$), with a peak score in the FIB group (3.3 ± 0.9). At 3 months, both groups had pain relief with similar VAS ($p = 0.465$). ROM of the knee in both groups was continuously improved during early rehabilitation, with the exception of stagnant in the FIB group at 1-week and 1-month ($p = 0.381$). And ROM in MDI ($92^\circ \pm 12^\circ$) was better than that in FIB ($75^\circ \pm 18^\circ$, $p = 0.009$). SANE of the knee in the FIB group (63.4 ± 9.4) was better than that in MDI (50.4 ± 14.2, $p = 0.012$). The comparison between the two groups was reversed at 1-week, although no significant ($p = 0.165$). SANE in the MDI group was significantly different compared with FIB at 1-month ($p = 0.026$). Finally, both groups got similar scores of SANE at 3-month ($p = 0.541$).

There was no secondary surgery performed such as exchange nailing, bone grafting, or screw removal in present study. All cases are identified as fractures union at 9-month (Figure 3) or 12-month follow-up (Figure 4).

4. Discussion

As a part of the golden standard for adult femoral shaft fracture treatment, the retrograde nailing technique is an attractive option available to orthopedists, as is the antegrade nailing technique. A common concern is focused on postoperative knee pain and function due to the introduction through the intercondylar notch of the femur [6, 17, 18]. It is universally accepted that retrograde nailing presents satisfactory results in knee function and pain, both in medium and long-term follow-up [2, 8]. MDI and FIB are popular methods for postoperative pain control after lower extremity surgery [15, 19–21]. However, early rehabilitation of knee function seems to be ignored in many studies. Pain relief and knee function recovery play a significant role in self-care ability, such as wearing socks and shoes, washing feet, going to the toilet, and so on. This study retrospectively compared the effects of MDI and FIB on early pain relief and rehabilitation of the knee after retrograde femoral nailing surgery, specially focused on patients who performed voluntary exercise at home.

Of the 63 cases, we excluded seven cases as having the femoral supracondylar fracture of the AO 33C type or with concomitant ipsilateral tibia plateau fractures. These complicated fractures damage the knee surface and, usually combined with severe soft tissue injury, may

Table 1: Patients information.

Patients information			
Variable	MDI group ($n = 19$)	FIB group ($n = 22$)	p
Age, y	43.5 ± 18.1	39.3 ± 17.0	0.557
Sex (M/F)	12/7	16/6	0.737
AO classification			
Femoral shaft	17	21	0.769
A	6	5	
B	6	6	
C	5	8	
Femoral supracondylar	5	6	
A	5	6	
Multi-segmental fractures	3	5	0.703
Operation time (minutes)	145.5 ± 36.1	130.9 ± 31.2	0.291

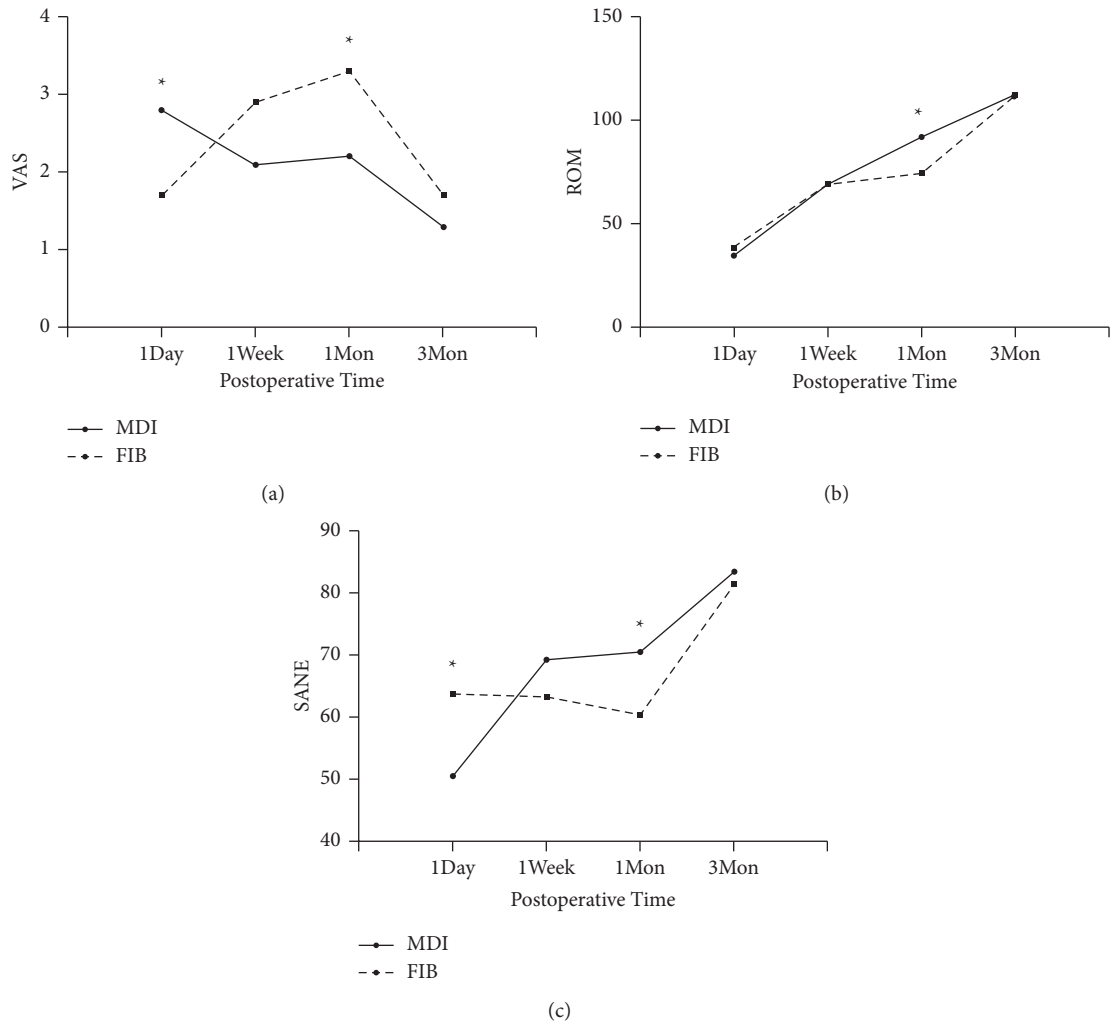

Figure 2: Changes in VAS (a), ROM of knee (b), SANE of knee (c). Data are shown as mean, $^{*}p < 0.05$.

deteriorate knee function and cause pain. Eight cases who performed rehabilitation in professional institutions were excluded due to incompatibility with the purpose of this study. SANE is an effective tool for knee function assessment and is friendly to both patients and medical staff [22].

Koehler et al. reported that multimodal drug injections presented immediate pain anesis across a diverse orthopedic trauma population undergoing operative intervention for femoral fractures [21]. The surgical-site injection with a multimodal analgesic cocktail provided the improved pain control at the 4, 8, and 12-hour postoperative time points.

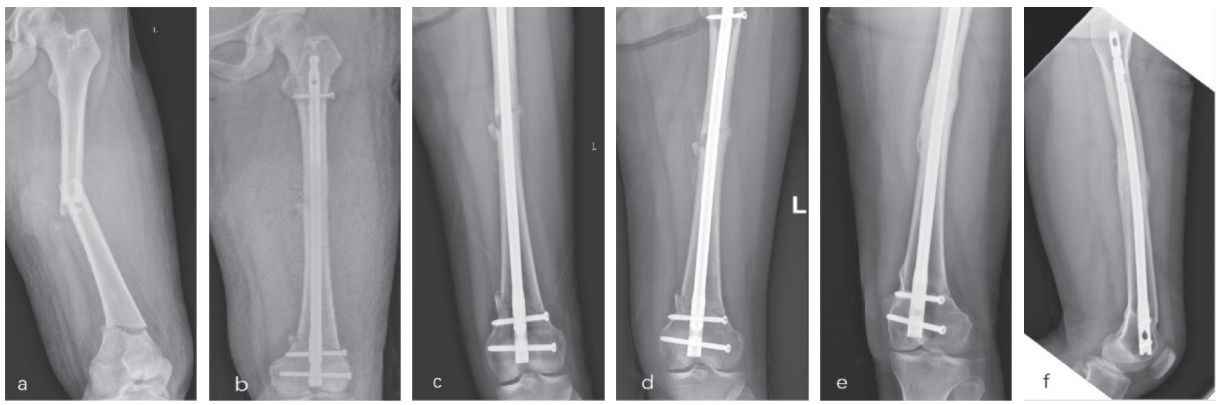

Figure 3: Female, 33, multi-fragment fracture of left femur with AO classification A3 in shaft, and A1 in distal part (a). Treated with retrograde nailing and postoperative FIB, 1-day postoperative radiograph (b). 1 month (c), 3-month (d) follow-up radiographs. 9-month follow-up radiographs indicated union (e, f).

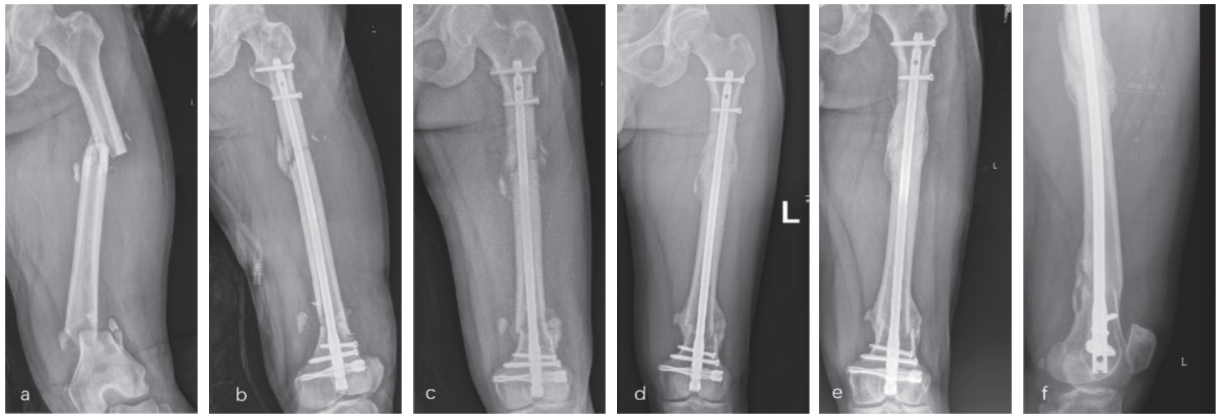

Figure 4: Male, 33, multi-fragment fracture of left femur with AO classification B3 in shaft, and A2 in distal part (a). Treated with retrograde nailing and postoperative MDI, 1-day postoperative radiograph (b). 1 month (c), 3-month (d) follow-up radiographs. 1-year follow-up radiographs indicated union (e, f).

Cocktail treatment was more popular in arthroplasty. Multimodal periarticular injection provided comparable analgesia to continuous femoral nerve block after total knee arthroplasty [16]. In our study, the MDI group presented satisfactory pain control during hospital stay and continuously improved pain relief during 3 months of follow-up. The knee function improved in the similar trend.

FIB and femoral nerve block provided similar analgesia after femoral fracture surgery [23]. Femoral nerve blocks for tibial plateau fractures operations demonstrated a similar pain relief compared with patients controlled analgesia (PCA), as reported by Cooke et al. [24]. In our study, the FIB group presented immediate analgesia effects after retrograde nailing and got the same level of pain relief at postoperative 3 months. However, pain rebounded when patients were discharged and performed voluntary knee rehabilitation at home. The knee function improvement came to a standstill at the same time.

The results revealed that FIB provided immediate pain relief rather than long-lasting analgesia. Indeed, the major component for FIB injection was ropivacaine, which provided pain relief for 12–24 hours [25]. Coincidently, most studies concerning FIB or femoral nerve block recorded the score of pain in less than 3 days [20, 26]. The short-term analgesic effect may be one of the explanations for VAS rebounded. Another explanation was the increased active exercise for knee and weight bearing. Angers et al. revealed that femoral nerve block had a negative influence on recovery at 6 weeks and 6 months following total knee replacement [27]. As an important part of knee extensional apparatus, weakened quadriceps may be responsible to the slow rehabilitation of the knee.

For the MDI group, pain and function of the knee displayed continuous relief and improvement. Recent research claimed that intraoperative periarticular injection of multimodal drugs could alleviate the inflammatory response and enhance joint function recovery after hip arthroplasty in elderly patients [19]. Similar multimodal drugs may have equally beneficial effects for the MDI group.

The limitations of our study were attributed to the retrospective analysis and could be underpowered. It was a single center study with a small number of cases, and conclusions could not be generalized. Furthermore, we did not use other scoring systems which were more reliable and comprehensive, such as the Lysholm scale and the American Academy of Orthopedic Surgeons hip and knee scale. The

life quality should be quantitatively recorded and analyzed in further study. The correlation of pain and knee function was not quantitatively analyzed. In the future, randomized controlled trials with high quality are needed.

5. Conclusion

The knee pain was commonly experienced in this series of retrograde femoral nailings. Both MDI and FIB provided immediate and satisfactory pain control after femoral fracture surgery, but pain rebounded after discharge in the FIB group. MDI was more beneficial to continuously pain control and knee rehabilitation during the first month postoperative. Pain relief and knee function improvement reached the same level at postoperative 3-month.

Data Availability

The data supporting the findings of the study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

Acknowledgments

This study was funded by the Fund of Guangxi Key laboratory of Metabolic Diseases Research (grant number 20-065-76). The authors would like to thank Dr. Gaoxiang Huang and Meiling Ye for their wise advice in discussing and writing.

References

[1] M. Bisaccia, A. Caraffa, G. Rinonapoli et al., "Feasibility and value of non-locking retrograde nail vs. Locking retrograde nail in fixation of distal third femoral shaft fractures: radiographic, bone densitometry and clinical outcome assessments," *Medicinski Glasnik : Official Publication of the Medical Association of Zenica-Doboj Canton, Bosnia and Herzegovina*, vol. 17, no. 1, pp. 163–169, 2020.

[2] J. Brewster, G. Grenier, B. C. Taylor et al., "Long-term comparison of retrograde and antegrade femoral nailing," *Orthopedics*, vol. 43, no. 4, pp. e278–e282, 2020.

[3] P. J. Dougherty, P. Gherebeh, M. Zekaj, S. Sethi, B. Oliphant, and R. Vaidya, "Retrograde versus antegrade intramedullary nailing of gunshot diaphyseal femur fractures," *Clinical Orthopaedics and Related Research*, vol. 471, no. 12, pp. 3974–3980, 2013.

[4] R. F. Ostrum, J. DiCicco, R. Lakatos, and A. Poka, "Retrograde intramedullary nailing of femoral diaphyseal fractures," *Journal of Orthopaedic Trauma*, vol. 12, no. 7, pp. 464–468, 1998.

[5] P. Tornetta 3rd and D. Tiburzi, "Antegrade or retrograde reamed femoral nailing," *Journal of Bone & Joint Surgery*, vol. 82-B, no. 5, pp. 652–654, 2000.

[6] M. El Moumni, P. Schraven, H. J. ten Duis, and K. Wendt, "Persistent knee complaints after retrograde unreamed nailing of femoral shaft fractures," *Acta Orthopaedica Belgica*, vol. 76, no. no. 2, pp. 219–225, 2010.

[7] M. Brewster, "Does fixation of femoral fractures using retrograde intramedullary nailing cause long-term knee pain: a systematic Review of the literature," *European Journal of Orthopaedic Surgery and Traumatology*, vol. 19, no. 1, pp. 27–31, 2009.

[8] H. Nasir, N. Farrah, S. Corey, and K. Hera, "Antegrade versus retrograde nailing techniques and trochanteric versus piriformis intramedullary nailing entry points for femoral shaft fractures: a systematic Review and meta-analysis," *Canadian Journal of Surgery*, vol. 22, 2017.

[9] J.-W. Kim, C.-W. Oh, J.-K. Oh et al., "Treatment of infra-isthmal femoral fracture with an intramedullary nail: is retrograde nailing a better option than antegrade nailing?" *Archives of Orthopaedic and Trauma Surgery*, vol. 138, no. 9, pp. 1241–1247, 2018.

[10] B. Daglar, E. Gungor, O. M. Delialioglu et al., "Comparison of knee function after antegrade and retrograde intramedullary nailing for diaphyseal femoral fractures: results of isokinetic evaluation," *Journal of Orthopaedic Trauma*, vol. 23, no. 9, pp. 640–644, 2009.

[11] P. Murray, P. Bergin, P. Labropoulos, and S. Gunther, "Retrograde femoral nailing and knee function," *Orthopedics*, vol. 31, no. 10, 10 pages, 2008.

[12] T. Oka, O. Wada, T. Asai, H. Maruno, and K. Mizuno, "Importance of knee flexion range of motion during the acute phase after total knee arthroplasty," *Physical Therapy Research*, vol. 23, no. 2, pp. 143–148, 2020.

[13] H. Mutsuzaki, R. Takeuchi, Y. Mataki, and Y. Wadano, "Target range of motion for rehabilitation after total knee arthroplasty," *Journal of Rural Medicine : JRM*, vol. 12, no. no. 1, pp. 33–37, 2017.

[14] A. Kornuijt, G. J. L. de Kort, D. Das, A. F. Lenssen, and W. van der Weegen, "Recovery of knee range of motion after total knee arthroplasty in the first postoperative weeks: poor recovery can Be detected early," *Musculoskeletal Surgery*, vol. 103, no. 3, pp. 289–297, 2019.

[15] N. Tammachote, S. Kanitnate, S. Manuwong, and P. Panichkul, "Periarticular multimodal drug injection is better than single anesthetic drug in controlling pain after total knee arthroplasty," *European Journal of Orthopaedic Surgery and Traumatology*, vol. 28, no. 4, pp. 667–675, 2018.

[16] F.-Y. Ng, J. K.-F. Ng, K.-Y. Chiu, C.-H. Yan, and C.-W. Chan, "Multimodal periarticular injection vs continuous femoral nerve block After total knee arthroplasty," *The Journal of Arthroplasty*, vol. 27, no. 6, pp. 1234–1238, 2012.

[17] A. Davidson, S. S. Houri, J. Cohen et al., "Initial definitive treatment of open femoral shaft fractures with retrograde nailing - is it safe? a retrospective analysis comparing antegrade to retrograde nailing," *Injury*, vol. 22, 2021.

[18] W. M. Ricci, C. Bellabarba, B. Evanoff, D. Herscovici, T. DiPasquale, and R. Sanders, "Retrograde versus antegrade nailing of femoral shaft fractures," *Journal of Orthopaedic Trauma*, vol. 15, no. 3, pp. 161–169, 2001.

[19] Z. Xiong, S. Cao, L. Zhou et al., "Intraoperative periarticular injection can alleviate the inflammatory response and enhance joint function recovery after hip arthroplasty in elderly patients with osteoporotic femoral neck fractures," *Medicine (Baltimore)*, vol. 100, no. 7, 2021.

[20] H. Zhong, X. Deng, and Z. Wang, "Effects of fascia iliaca compartment block combined with general laryngeal mask airway anesthesia in children undergoing femoral fracture surgery: a randomized trial," *Journal of Pain Research*, vol. 11, pp. 2821–2826, 2018.

[21] D. Koehler, J. L. Marsh, M. Karam, C. Fruehling, and M. Willey, "Efficacy of surgical-site, multimodal drug injection following operative management of femoral fractures,"

Journal of Bone and Joint Surgery, vol. 99, no. 6, pp. 512–519, 2017.

[22] G. N. Williams, D. C. Taylor, T. J. Gangel, J. M. Uhorchak, and R. A. Arciero, "Comparison of the single assessment numeric evaluation method and the Lysholm score," *Clinical Orthopaedics and Related Research*, vol. 373, pp. 184–192, 2000.

[23] M. Bantie, S. Mola, T. Girma, Z. Aweke, D. Neme, and A. Zemedkun, "Comparing analgesic effect of intravenous fentanyl, femoral nerve block and fascia iliaca block during spinal anesthesia positioning in elective adult patients undergoing femoral fracture surgery: a randomized controlled trial," *Journal of Pain Research*, vol. 13, pp. 3139–3146, 2020.

[24] M. E. Cooke, T. Welch, O. Gusakov, and P. Tornetta 3rd., "Are continuous femoral nerve catheters beneficial for pain management after operative fixation of tibial plateau fractures? A randomized controlled trial," *Journal of Orthopaedic Trauma*, vol. 33, no. 12, pp. e447–e451, 2019.

[25] R. D. Kasibhatla and K. Russon, "Femoral nerve blocks," *Journal of Perioperative Practice*, vol. 19, no. 2, pp. 65–69, 2009.

[26] J. E. Paul, A. Arya, L. Hurlburt et al., "Femoral nerve block improves analgesia outcomes after total knee arthroplasty," *Anesthesiology*, vol. 113, no. 5, pp. 1144–1162, 2010.

[27] M. Angers, É. L. Belzile, J. Vachon, P. Beauchamp-Chalifour, and S. Pelet, "Negative influence of femoral nerve block on quadriceps strength recovery following total knee replacement: a prospective randomized trial," *Orthopaedics and Traumatology: Surgery & Research*, vol. 105, no. 4, pp. 633–637, 2019.

Hindawi
Pain Research and Management
Volume 2022, Article ID 7769775, 13 pages
https://doi.org/10.1155/2022/7769775

Research Article

Classification and Treatment for Cervical Spine Fracture with Ankylosing Spondylitis: A Clinical Nomogram Prediction Study

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Received 7 December 2021; Revised 17 January 2022; Accepted 25 January 2022; Published 3 March 2022

Academic Editor: Xiaolong Chen

Objective. Through the follow-up analysis of cervical spine fracture cases with ankylosing spondylitis (AS), a treatment-oriented fracture classification method is introduced to evaluate the clinical efficacy guided by this classification method. *Method*. A retrospective analysis was performed on 128 AS patients who underwent comprehensive treatment in the Spine Surgery Department of Qingdao University Hospital from January 2009 to May 2018. Statistics of patient demographic data, distribution of different fractures corresponding to surgical methods, 3-year follow-up outcomes, and summary of objective fracture classification methods were analyzed. A prospective 5-year follow-up study of 90 patients with AS cervical spine fractures from June 2015 to August 2020 was also included. Statistical differences on the distribution of factors such as case information, cervical spine sagittal sequence parameters, and fracture classification were assessed. Correlations between surgical information, American Spinal Injuries Association grade (ASIA), modified Japanese Orthopaedic Association scores (mJOA), and other factors were analyzed to establish a nomogram predictive model for curative effect outcomes. Overall, three major types and the four subtypes of AS cervical spine fractures were evaluated based on the clinical efficacy of the classification and the selection of surgical treatment methods. *Result*. The most common type of fracture was type II (30 cases, 33.33%), most of the subtypes were A (37 cases), followed by B (36 cases) and C (17 cases). Twenty-four of 28 patients with type I underwent anterior surgery, and 47 of 62 patients with type II and III underwent posterior surgery. The average follow-up time was 25.76 ± 11.80 months. The results of predicting clinical variables are different but include factors such as fracture type and subtype, type of operation, and age. The predictor variables include the above-mentioned similar variables, but survival is more affected by the fracture type of the patient. *Conclusion*. This predictive model based on follow-up information delineation points out the impact of ankylosing spondylitis cervical spine fracture classification on surgical selection and clinical efficacy.

1. Introduction

Ankylosing spondylitis (AS) is a progressive inflammatory rheumatic spondyloarthropathy affecting nearly 0.5% of the global population [1, 2]. The rigid segment becomes stiff; the lever arm deforms and is more likely to fracture following a small amount of force. It is estimated that the relative risk of AS vertebral fractures is thrice that of the global population. About 14% of AS patients experience a fracture in their lifetime [3, 4]. More than 80% of fractures in AS patients are associated with the lower cervical spine and the cervicothoracic junction [1, 5]. Although various sophisticated surgical techniques have been developed to explore the treatment of cervical spine fractures in AS, the management of patients with AS may still be complicated by the presence of high risk of limited spinal motion, osteoporosis, potential clinical complications, or neurological injury [1, 3, 6, 7]. In addition, the incidence of cervical spine fractures in AS is low, and some patients even lose their lives early in the trauma due to direct spinal cord injury. The basis for clinical

management of cervical fractures in AS is staging, but unfortunately, the classification is still ambiguous and tends to separate from actual clinical observations. So far, there is a lack of cumulative clinical predictive analysis and classification-related surgical methods and outcome selection criteria [8]. This adds uncertainty to the effective intervention of AS cervical spine fractures and surgical expectations. Also, there are often unexpected results and improper surgical applications caused by the "the injury of both people and money" phenomenon.

In this study, we adopted the AS cervical spine fracture classification method based on the combination of surgical experience and clinical surgical observation. We considered both a neurological condition and a radiological assessment [2]. With the accumulated cases, we attempted to analyze and predict the treatment situation under the new classification by reviewing the previous treatment expectations. This provided a new basis for the clinical treatment of AS.

2. Materials and Methods

2.1. Retrospective Demographics. We retrieved 128 inpatient and outpatient electronic medical records from January 2009 to May 2018 in Qingdao University Affiliated Hospital for cervical spine fractures with imaging diagnosis of AS. All patients were hospitalized to have received surgical cervical spine interventions or cervical rehabilitation treatment. Data collected included basic statistics of patients, symptoms, and intervention options. This leads to a summary of the types of surgery and fracture types. This study has been approved by the Medical (Ethics) Committee of the Affiliated Hospital of Qingdao University (QDFY WZ 2015-15-07), and all participating patients are in compliance with ethical standards.

2.2. Prospective Demographics. We conducted a prospective 5-year follow-up study on 90 patients with AS cervical spine fractures from June 2015 to August 2020. The hospital ethics committee approved each intervention and research project. Before the operation, the patients were treated according to the new classification summarized through retrospective analysis. Patients signed an informed consent statement either by themselves or by family members. Data collected included patient case information, imaging cervical spine sagittal sequence parameters, and fracture classification. Results included surgical information, ASIA score, mJOA score, and so on.

2.3. Inclusion and Exclusion Criteria. For prospective studies, inclusion and exclusion criteria are established. The inclusion criteria were patients with clear clinical evidence of AS combined with cervical fracture, and all study data were recorded in the hospital electronic information system. The clinical diagnostic criteria for ankylosing spondylitis are: (1) restricted chest expansion with a maximum difference between expiration and inspiration of less than 2.5 cm; (2) sacroiliac arthritis seen on X-ray, bilateral grade II, unilateral grade III, or higher; (3) restricted range of motion in three directions, including forward bending, backward bending, and lateral bending of the lumbar spine; and (4) painful stiffness in the lower back for more than three months that does not improve with rest. The diagnosis of ankylosing spondylitis can be confirmed if one of the fourth plus 1 to 3 items is present. Patients with an unconfirmed AS diagnosis, upper cervical fracture, and significant spinal deformity were excluded, as were patients with injuries sustained earlier during the disease progression when the spine was still flexible [9]. All the patients were evaluated using X-rays, CT, and MRI before surgery to describe the circumstance of the injury site and the details of the spinal cord.

2.4. Classification and Treatment of Fracture. CT scan was used as an important examination for fracture staging, using 128-row medical spiral CT equipment (GE, Milwaukee, Wisconsin, USA), setting scan parameters: tube current, 200 mA; layer thickness and reconstruction interval, 5 mm and 5 mm, respectively; display field of view (DFOV), 20 cm; interval, 0.531:1; pixel interval, 0.430 mm; and spiral transient switching between 140 kVp and 80 kVp. Image reconstruction and analysis were performed using an advanced workstation (AW 4.7; GE Healthcare, USA), and all organ unit scans were performed according to routine procedures for scanning major pathological units, with informed consent from the family and the patient himself and ethical approval on file by the hospital.

Prior to further treatment, the fracture was classified into three types based on the fracture line and severity: type I, disc injury; type II, vertebral body injury; and type III, vertebral body and disc injury. Four subtypes were also defined as follows: (A) fracture without dislocation, (B) fractures with dislocation without obvious bone defects, (C) fractures with obvious dislocation or severe bone gap, and (D) fractures with epidural hematoma or CSF leakage (Figure 1). Pre- and intraoperative skull tractions were used to immobilize the spine especially when the fracture was unstable.

All these patients underwent intraoperative neurophysiologic monitoring (IONM) including sensory and motor-evoked potentials during surgery [10]. Patients with incomplete neurological deficits were treated urgently (within 24 hours), whereas those with complete and central cord syndrome were surgically treated at a later time [2]. Surgical procedures were determined according to the different individual factors, such as fracture location, numbers of involved segments, fracture types, neurological deficits, among others.

Anterior decompression and fusion (AF) were conducted on at least one segment above and below the fracture site if anatomical access was permitted. A tricortical iliac graft was placed into the disc or fracture defects, and a plate internal fixation was then performed [5]. The posterior approach (PF) was conducted with long segments fixation in cases of instability, using the Mayfield head holder for traction and locking [8]. A combined laminectomy was performed on cases involving neurological deficit or epidural hematoma.

Halo-vest, sterno-occipital mandibular immobilization device (SOMI), or cervical collar was given to obtain cervical immobilization for 1–1.5 months after surgery.

All surgeries are performed by a unified team of six surgeons of equal level and appropriate rank and clinical background, and more importantly, the surgeons are fully executed intraoperatively with a consensus team preoperative discussion as the established plan for the surgery.

2.5. Evaluation Index. The clinical follow-up examinations were performed up to 5 years postoperatively. CT scans and X-rays evaluations were taken at each follow-up. The clinical outcomes were assessed using the ASIA grade and mJOA score. The ASIA grading scale is a neurological assessment of spinal cord injury developed by the American Spinal Cord Injury Association (ASIA), which classifies spinal cord injuries into grades A–E, with the degree of injury decreasing as the grade increases, focusing on the evaluation of neurological structure and function, while the modified Japanese Orthopaedic Association cervical spinal cord scoring system (mJOA) focuses more on the clinical evaluation of neurological function, with a total score of 18 points, involving the motor function of the upper extremity (5 points), lower extremity (7 points), sensation (3 points), and urination (3 points), with lower scores indicating more severe disability and impairment of spinal cord function. Secondly, injury site, fracture patterns, surgical procedures, fixation levels, operation time and blood loss, fusion rate, and complications were also documented. Complications were categorized as general (such as infection, respiratory failure, or death) and surgical (such as early implant failure or screw loosening).

Imaging measurements are measured by standard X-rays in the corresponding position, and the measurement parameters and methods are: (1) C_{2-7} COBB (°): C_{2-7} COBB's angle is the angle between the lower endplate of C_2 and the upper endplate of C_7 (anterior convexity is negative), (2) cSVA (mm): cervical sagittal vertical axis is the C_2 vertebral body midpoint vertical axis to the distance of C_7 vertebral body posterior superior angle, and (3) T_1 slope (°): T_1 tilt angle is the angle between the tangent line of the upper endplate of T_1 vertebral body and the horizontal plane.

2.6. Statistical Analysis. Continuous data were presented as the mean ± standard deviation or median, the interquartile range, whereas the categorical data were presented as counts (percentages). According to the specific results, the sample size was calculated dependent on the regional incidence rate. Due to the five-year follow-up, all subjects had quality of life follow-up results. Multivariate logistic regression was used to establish a binary outcome prediction model, while multiple variables were used to establish a numerical outcome prediction model linear regression. The candidate variable of each model was a screening step where the P value was less than 0.3 in the univariate analysis. For the relaxation of the linear assumptions of numerical predictors, we used a restricted cubic spline function model [11]. Calibration was conducted by plotting the predicted patient proportion for each outcome and developing the actual proportion sample (obvious) and guide sample (bias correction) on each outcome for the original outcome. Appearance closely following the 45° equivalence line (ideal line) indicated high model calibration. For the numerical results, each final model reached the maximum deviation correction consistency correlation coefficient (pressure reduction CCC R software package). It represents the model fit through the adjusted coefficient of determination (R^2).

3. Results

3.1. Descriptive Data. Of the 128 patients, 90 (81 males and 9 females) were enrolled and subjected to follow-up consecutively. Their mean age was 52.1 ± 10.4 years (range, 29–77). Three patients (3.33%) had 1 vertebral body or disc involved, whereas 87 patients (96.67%) involved 2 or more bodies. Notably, C6, C7 body, and C6-C7 disc were the most frequently involved (84 patients, 93.33%).

3.2. Surgical Approach Related to Classification. Here, 82 patients underwent surgery according to our classification except for one patient who was subjected to revision surgery (AF + PF) because of early AF failure, and another three patients who underwent posterior surgery combined anterior surgery (PF + AF) owing to a sizeable anterior gap after posterior fixation (Figure 2).

An anterior-only approach was performed on 31 patients including the 1 patient mentioned above who underwent anterior surgery firstly, followed by AF + PF for revision. Besides, 48 patients underwent a posterior-only approach. The fixation segments related to classification are summarized in Table 1.

In type I (a total of 28 patients), 24 patients underwent anterior surgery, whereby 1 patient needed revision surgery after AF, while posterior surgery was performed on one patient. In type II (a total of 30 patients), 27 patients underwent posterior surgery, whereas anterior surgery was performed on 1 patient (type IIA). In type III (total 32 patients), 20 patients underwent posterior surgery with the fixation on more than 3 segments, whereas anterior surgery was performed on 6 patients; in addition, three patients received PF + AF. In addition, we have followed the principle of individualized surgical protocols, giving priority to: (1) maximum release of the spinal cord injury, (2) least traumatic and most mechanically stable fixation, and (3) best survival expectations and postoperative needs.

Using the anterior-only approach, the operation time was 130 ± 41.7 minutes (range: 80 to 305 min) on average and 185.9 ± 46.5 minutes (range: 110 to 280 min) in the posterior-only approach with significant difference ($P < 0.001$). Intraoperative blood loss during the anterior-only approach was 177.6 ± 138.0 cc on average (range: 50 to 800 ml), and 494.4 ± 313.6 cc (range: 100 to 1500 ml) in the posterior-only approach with significant difference ($P < 0.001$). There was a statistical difference in operation time and blood loss among type I, II, and III groups ($P = 0.020$ and 0.027, respectively; Figure 2). The average

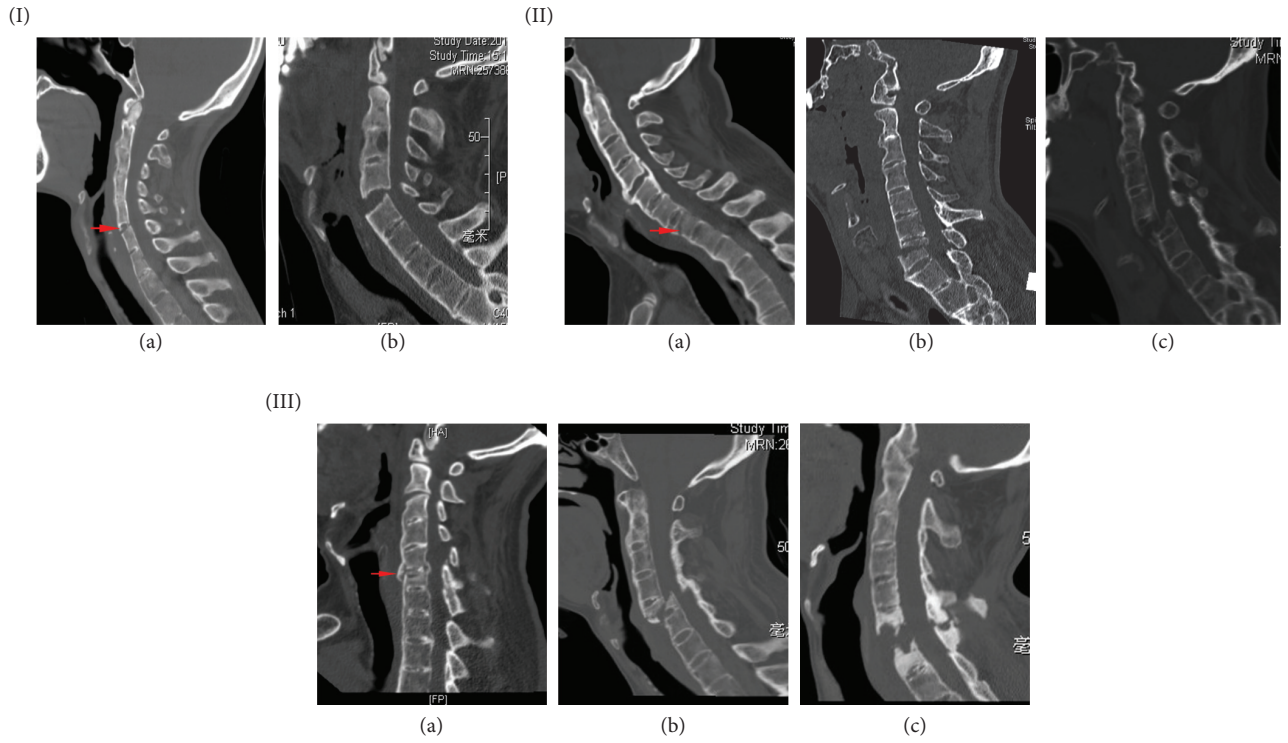

Figure 1: Fracture classification.

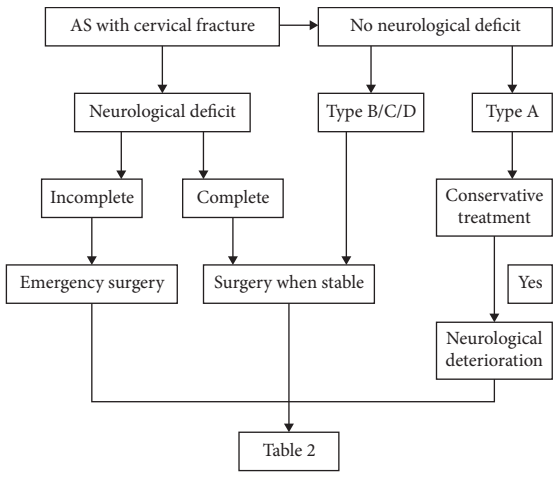

Figure 2: Treatment basis diagram.

operation time was 140.6 ± 49.7 minutes in type I, 178.3 ± 37.5 in type II, and 176.3 ± 62.4 in type III. In type I, the average blood loss was 231.4 ± 247.5 cc, whereas it was 485.8 ± 237.3 in type II and 447.5 ± 336.2 in type III. However, there was no statistical difference in average operation time and blood loss among subtype A, B, and C groups ($P = 0.534$ and 0.444, respectively).

3.3. Distribution of Fracture Types in Retrospective Analysis. According to our classification, different type and subtype of these fractures were recorded, including type I (28 patients, 31.11%), type II (30 patients, 33.33%), and type III (32 patients, 35.56%). The most common fracture pattern was type IIA (15 patients, 50%), and the majority of subtype was A (37 patients), followed by B (36 patients) and C (17 patients; Figure 3).

3.4. Basic Information in Prospective Research. In the prospective analysis, a total of 90 patients were selected, including 81 males and 9 females. The specific information of these 90 patients is given in Table 1.

3.5. Classification and Predictors of Treatment Outcomes. Prediction of clinical outcome was mainly classified as follows (Figure 4): the patients who were followed up for 36 months were classified according to the main classification, and the survival curve was generated according to the survival situation of the patients. It is evident that the survival rates of type I and II patients in the main classification are basically the same; there is a slight decline in the first 6 months, whereas the survival rate remains unchanged during the remaining time (Figure 4). However, the survival rate of type III was significantly different from the first 2 types. In the first 12 months, the survival rate of patients of this type dropped sharply, especially in the first 6 months; the decline was more obvious. After 12 months, the patient's survival rate remained constant at about 60%, which was much lower than that of type I and II patients. Comparing the survival rates of the 3 types of fractures in pairs, there was no significant difference between types I and II ($P > 0.05$),

Table 1: Basic information.

Variable	N (%) or median (IQR)	Total number
Sex		90
Female	9 (10%)	
Male	81 (90%)	
Age		90
≥60	20 (22.2%)	
<60	70 (77.8%)	
BMI		90
<25	46 (51.1%)	
≥25	44 (48.9%)	
Smoking		90
Yes	34 (37.8%)	
No	56 (62.2%)	
COBB		90
<10°	58 (64.4%)	
≥10°	32 (35.6%)	
cSVA	7.8 (6.25–9.15)	89
*T*1 slope	34.2 (30.05–38)	
Fracture site	6 (2–8)	90
Single	27 (30%)	
Multi	63 (70%)	
Fracture type		90
I	28 (31.1%)	
II	30 (33.3%)	
III	32 (35.6%)	
Subtype		90
A	37 (41.1%)	
B	36 (40%)	
C	17 (18.9%)	
Preoperative ASIA		90
A, B, C	47 (52.2%)	
D, E	43 (47.8%)	
Preoperative mJOA		90
Operation time	155 (120–210)	81
Blood loss	300 (150–500)	81
Treatment		90
PF	48 (53.3%)	
PF + AF	3 (3.3%)	
Conservative treatment	8 (8.9%)	
AF	31 (34.4%)	

while type III was highly significantly different whether it is type I or II ($P < 0.05$).

Prediction of subtype clinical outcome (Figure 5): the 36-month follow-up patients were classified according to subtypes, and survival curves were made according to the survival conditions of patients. By drawing a survival curve based on subtypes, we reported a certain degree of difference in the survival rates of the 3 types of patients. The survival rate of type A patients dropped slightly in the first 3 months; the survival rate of type B patients dropped to a certain extent within 6 months; and the survival rate of type C patients dropped significantly within 12 months. The survival rate of patients with types A and B was relatively small ($P > 0.05$) but could be maintained above 90%, and the main decline time was in the first 6 months. However, the survival

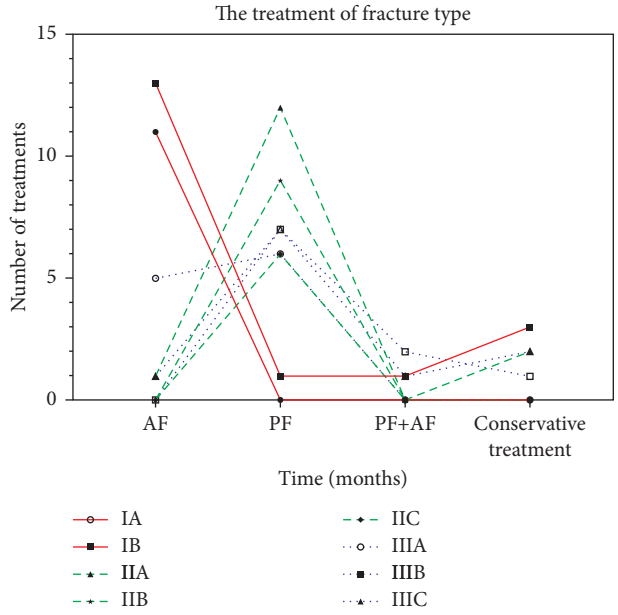

Figure 3: Statistics of fracture types and treatment methods.

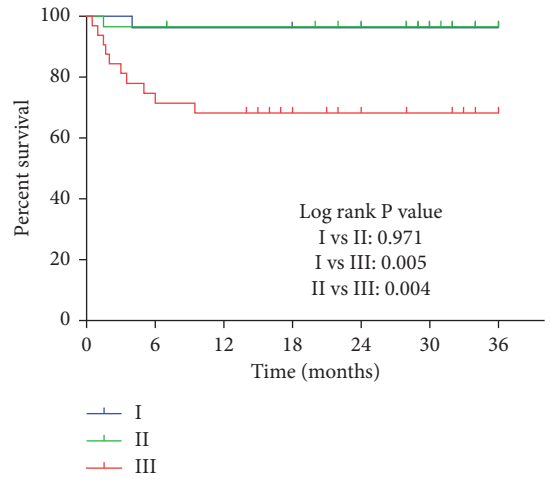

Figure 4: Prediction of clinical outcomes of main classification (survival curve).

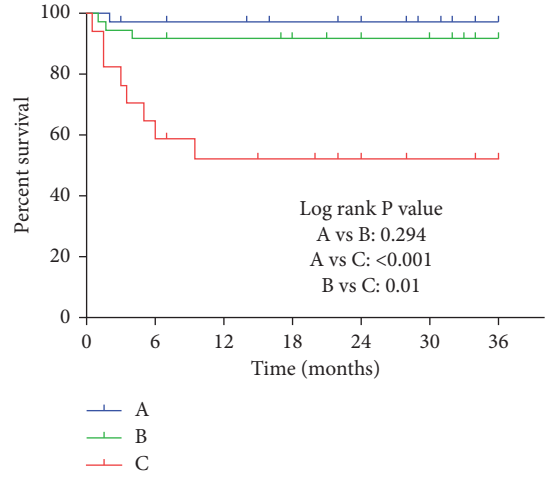

Figure 5: Prediction of subtype clinical outcomes (survival curve).

rate of type C decreased significantly in the first 12 months, especially in the first 6 months where the survival rate of patients dropped sharply. Besides, the survival rate of type C patients was maintained at about 50% after 12 months, which was much lower than types A and B. Notably, the survival rate of type C patients was significantly different from that of type A or B ($P < 0.05$).

Based on the above results, we constructed a predictive evaluation nomogram for fracture classification and clinical evaluation (Figure 6), which was validated using a calibration curve (Figure 7). The deviation-corrected c-index of the one-year survival rate was 0.63. For the QOL index, $R^2 = 0.4$ after deviation correction adjustment.

3.6. Predictors of ASIA. After analyzing data of the collected cases, 13 factors such as gender, age, and BMI were compared. Compiled results are presented in Table 2. The data mainly elucidated the type of fracture risk and 95% confidence interval. Thereafter, the obtained data were calibrated using a uniform standard to obtain the most valuable results with the smallest variables. To evaluate the impact of the ASIA score on the occurrence and development of fractures, the surgical method was inferred.

Notably, factors including gender, smoking or not, COBB angle, and *T*1 tilt rate were not statistically significant in the risk of fracture ($P > 0.05$; Table 2). The difference between BMI and ASIA scores may be attributed to the different risks of fracture ($P < 0.05$). A larger BMI index indicated a worse ASIA score, which increased the probability of fracture. Moreover, the ASIA score was more closely related to the occurrence of fractures and had a higher correlation. Of note, the 95% confidence interval of the ASIA score was 3.79–433.73, which could correlate the fracture classification with the ASIA score.

3.7. Predictors of mJOA. Similar to the ASIA score, the factors related to the mJOA score are presented in Table 3. Among them, gender, COBB angle, *T*1 tilt rate, and fracture type and risk were not statistically significant ($P > 0.05$). Moreover, mJOA had a high correlation with the type and probability of fracture ($P < 0.05$). Similarly, in comparison to the data related to the ASIA score, BMI was not statistically significant at this time ($P > 0.05$). Although slight differences in specific values were reported (Tables 2 and 3), the overall trend was the same. This demonstrated that the type of fracture is not only related to the ASIA score but also to mJOA. The 95% confidence interval of mJOA was 0.5–0.84 (see Table 3). Thus, we speculated that this would be more accurate in predicting the type of fracture and the risk of occurrence. Compared with other factors, the significance of mJOA in the data may be more significant. Through a comprehensive comparison, in the fracture classification, the ASIA score may also have a certain correlation with mJOA.

3.8. Cox Regression Analysis of Fracture Predictors. Through COX regression analysis, we revealed the factors that may be attributed to different fracture types (Table 4).

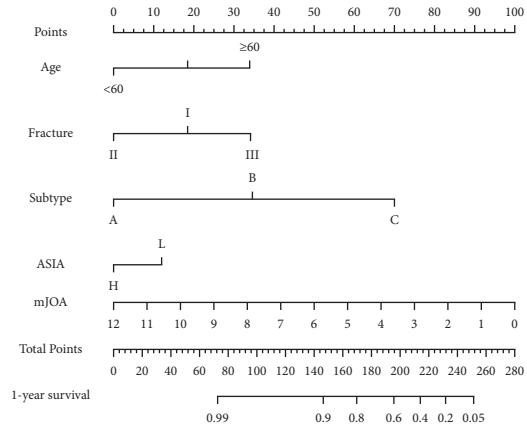

Figure 6: Predictive evaluation nomogram for fracture classification and clinical evaluation.

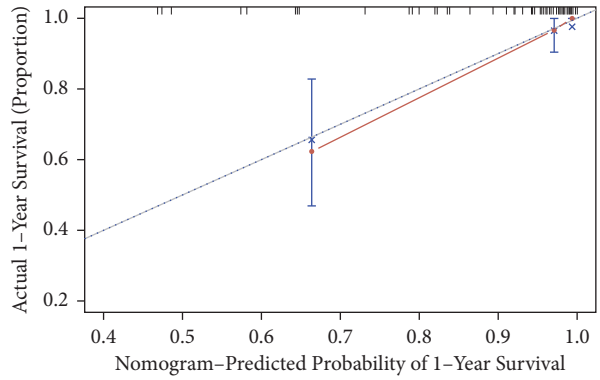

Figure 7: Calibration curve for one-year survival prediction.

Among them, age, ASIA score, and mJOA score significantly had a huge impact on the predictive factors of fracture ($P < 0.05$). There is no doubt that age had a definite influence on the occurrence of fractures. With the increase of age, especially the elderly above 60 years, the risk of fracture inevitably increased, and the type of fracture was more severe.

At the same time, the role of the ASIA score and mJOA score in the types of fractures could not be ignored. As the degree of fracture worsened, severe spinal cord injury inevitably led to more obvious sensorimotor disorders. We validated this phenomenon using COX regression analysis. Results demonstrated that ASIA score and mJOA score were important predictors; thus, their influence cannot be ignored, and they were highly correlated. Among them, the 95% confidence interval of the ASIA score was 1.48–88.85, whereas that for the mJOA was 0.47–0.83, indicating their highly significant correlation with the type of fracture.

4. Discussion

4.1. Cervical Fracture Characteristics and Classification Related to AS. AS, which is a chronic disease, typically starts before the age of 30 with a slow but steady progression [11, 12]. In the present study, patients suffering from AS for

Table 2: Logistic and ASIA.

Variable	Unadjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Sex (female vs. male)	0.51 (0.1–2.63)	0.423		
Age (≥60 vs. <60)	7.28 (2.42–21.88)	0	2.31 (0.35–15.21)	0.383
BMI (≥25 vs. <25)	0.3 (0.12–0.76)	0.011	0.26 (0.06–1.2)	0.084
Smoking (yes vs. no)	0.69 (0.28–1.73)	0.435		
COBB score (≥10° vs. <10°)	1.01 (0.41–2.49)	0.992		
cSVA (every 1 increment)	1.2 (1–1.43)	0.051	1.23 (0.89–1.69)	0.205
*T*1 slope (every 1 increment)	0.94 (0.87–1.03)	0.187		
Fracture site (single vs. multiple)	0.16 (0.04–0.57)	0.005	—	—
Fracture type		<0.001		0.821
I	Reference		Reference	
II	0.33 (0.08–1.45)	0.142	—	—
III	5.73 (1.86–17.63)	0.002	1.8 (0.29–11.35)	0.53
Subtype		0.072		0.869
A	Reference		Reference	
B	1.19 (0.43–3.28)	0.739	1 (0.17–6.08)	0.997
C	3.86 (1.15–12.91)	0.029	1.64 (0.23–11.44)	0.62
ASIA (A, B, and C vs. D and E)	74.12 (9.35–587.66)	<0.001	40.52 (3.79–433.73)	0.002
mJOA (every 1 increment)	0.68 (0.57–0.81)	<0.001	0.91 (0.69–1.2)	0.495
Treatment				
AF	Reference	0.741		
PF	1.34 (0.51–3.56)	0.556		
PF + AF	1.22 (0.1–15.23)	0.876		
Conservative treatment	2.44 (0.5–11.97)	0.27		

Table 3: Logistic and mJOA.

Variable	Unadjusted OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Sex (female vs. male)	1 (0.25–4)	1		
Age (≥60 vs. <60)	10.69 (2.3–49.59)	0.002	4.73 (0.45–49.46)	0.194
BMI (≥25 vs. <25)	0.76 (0.33–1.74)	0.51		
Smoking (yes vs. no)	0.47 (0.2–1.13)	0.091	0.24 (0.06–0.95)	0.043
COBB score (≥10° vs. <10°)	0.96 (0.4–2.28)	0.922		
cSVA (every 1 increment)	0.95 (0.8–1.11)	0.507		
*T*1 slope (every 1 increment)	0.99 (0.92–1.07)	0.821		
Fracture site (single vs. multiple)	0.21 (0.08–0.56)	0.002	0.05 (0–1.28)	0.07
Fracture type		0.003		0.538
I	Reference		Reference	
II	0.33 (0.08–1.45)	0.142	3.68 (0.15–88.42)	0.421
III	5.73 (1.86–17.63)	0.002	0.61 (0.1–3.56)	0.578
Subtype		0.001		0.053
A	Reference	0.04	Reference	
B	1.19 (0.43–3.28)	0.739	2.29 (0.56–9.37)	0.25
C	3.86 (1.15–12.91)	0.029	16.73 (1.62–172.93)	0.018
ASIA (A, B, and C vs. D and E)	8.54 (3.29–22.18)	<0.001	2.93 (0.75–11.45)	0.123
mJOA (every 1 increment)	0.64 (0.54–0.77)	<0.001	0.65 (0.5–0.84)	0.001
Treatment				
AF	Reference	0.866		
PF	1.06 (0.43–2.63)	0.902		
PF + AF	0.41 (0.03–5.03)	0.487		
Conservative treatment	1.37 (0.28–6.78)	0.697		

an average of 25–28 years at the time of injury [5, 13] were enrolled for analysis. Notably, the age distribution indicated that cervical fracture in AS is, in most cases, associated with patients between the age of 40 and 60 years (58 patients, 71.60%). Previous reports demonstrated that 75% to 81% of cervical fractures with AS involved lower cervical spine (C5–C7) [3, 14], a finding that was nearly consistent with our results.

Due to the long lever arms and biomechanics of the ankylosed spine, the classical three columns were not applicable for managing cervical fracture in AS patients [8, 15]. Although the new AO spine fracture classification system introduced the modifier M2 to mark the severity of the fracture with AS, it is only applicable for thoracolumbar fracture [16]. Recently, three classifications have been developed concerning AS-related cervical fractures [4, 9, 17].

Table 4: COX and OS.

Variable	Unadjusted HR (95% CI)	*P* value	Adjusted HR (95% CI)	*P* value
Sex (female vs. male)	0.04 (0–130.87)	0.44		
Age (≥60 vs. <60)	13.09 (3.53–48.49)	0	2.93 (0.6–14.32)	0.185
BMI (≥25 vs. <25)	0.46 (0.14–1.53)	0.205		
Smoking (yes vs. no)	1.2 (0.38–3.78)	0.756		
COBB score (≥10° vs. <10°)	0.38 (0.12–1.21)	0.101		
cSVA (every 1 increment)	1.01 (0.81–1.26)	0.931		
*T*1 slope (every 1 increment)	0.95 (0.85–1.07)	0.381		
Fracture site (single vs. multiple)	0.2 (0.03–1.55)	0.124		
Fracture type		0.01		0.59
I	Reference		Reference	
II	0.95 (0.06–15.17)	0.971	0.55 (0.03–11.43)	0.701
III	10.33 (1.32–80.74)	0.026	1.65 (0.14–19.59)	0.69
Subtype		0.001		0.085
A	Reference		Reference	
B	3.16 (0.33–30.33)	0.32	3.01 (0.3–29.73)	0.346
C	21.47 (2.68–171.94)	0.004	9.24 (1.04–82.06)	0.046
ASIA (A, B, and C vs. D and E)	11.46 (1.48–88.85)	0.02	1.46 (0.11–18.56)	0.773
mJOA (every 1 increment)	0.63 (0.47–0.83)	0.001	0.77 (0.53–1.11)	0.155
Treatment		0.741		
AF	Reference			
PF	172324.78 (0–2.994*E* + 144)	0.941		
PF + AF	—	—		
Conservative treatment	386706.5 (0–6.727*E* + 144)	0.937		

Metz-Stavenhagen et al. described two subtypes for cervical fracture in AS: type I, the complete disruption of anterior and posterior bony and ligamentous structures, and type II, the sintering fracture, often after a minor injury, unnoticed by the patient [8, 9]. Elsewhere, de Peretti et al. described a classification of four fracture types according to radiographic dislocation: type I with anterior opening, type II with horizontal dislocation, type III non-displaced, and type IV being similar to spinal fracture and unrelated to AS6. In addition, the classification introduced by Caron et al. involved the radiographic course of the fracture line (type I, disc injury; type II, body injury; type III, anterior body or posterior disc injury; and type IV, anterior disc or posterior body injury). Collectively, these classifications remained academic, and no impact of fracture type on patient treatment or outcome has been described until now [8]. Thus, we assessed the radiographic fracture severity and presented a new classification for further treatment and prediction of outcomes. The classification was as follows: type I, disc injury; type II, body injury; and type III, body and disc injury, and three subtypes were added (A, fracture without dislocation; B, obvious dislocation without bone defects; and C, obvious dislocation and bone defect in the vertebral body). Types I, II, and III presented the transverse diaphyseal long bone fracture with different fracture lines, whereas subtypes A, B, and C revealed cervical fracture severity complicated with dislocation or bone defect in the vertebral body. We also revealed that type III and subtypes B and C may be the most unstable patterns, which should be taken into thoughtful consideration before the surgical approach; however, fixed segments were chosen.

In addition, this study combined the characteristics of the three original typologies to combine clinical prognosis and spinal cord functional recovery, presenting not only the anatomical characteristics of AS cervical fractures but also taking into account the risk factors of spinal cord injury, making the typology closely related to the choice of treatment, which is the advantage of this study's typology.

4.2. Choice of Treatment Related to Different Fracture Classifications. Treatment for this kind of fracture was controversial. It has been described that the fracture without dislocation or neurological deficit may be the gold standard for conservative treatment. This typically involved bed rest, axial traction, and immobilization with halo-vest [5]. Once an unstable cervical fracture was confirmed, patients could be managed with axial traction or through immobilization [18]. Of note, these conservative treatments were associated with significant problems: risk of skin ulcerations, local septic, and respiratory problems, worsening of the regional kyphosis with loss of reduction, risk of non-union because of the shearing forces on the fracture site [19], and risk of neurological aggravation [20]. Overall, we suggest that conservative treatment only may not be suitable for this kind of fracture, particularly, in patients with severe neurological symptoms and unstable patterns such as type III and subtypes B and C. Furthermore, we strongly recommend surgery for a cervical fracture in AS, which is presently widely used [11, 21–26]. The procedures had been described including anterior approach, posterior approach, and combined approach, and the surgical procedures in relation to classification were analyzed as described below.

4.3. Anterior Approach. Although the anterior approach may pose less trauma, blood loss, and operation time and minimize risks of displacement during positioning and postoperative infections [15], the anterior-only approach

was not recommended for transverse, rotationally unstable fractures in AS [27]. Beyond that, many patients with AS were kyphotic, and the anterior access was anatomically impossible especially when the fracture was located at the cervicothoracic junction [8]. Therefore, the inferiority of the anterior-only surgery was reflected by the finding from several previous studies, in which implant failure occurred in the anterior-only treated patients [28, 29]. For instance, Kouyoumdjian et al. [5] suggested that anterior plate fixation may provide sufficient stability if the hardware is long enough to avoid significant moment arms.

In our series, 36 patients underwent an anterior-only approach, and most of them were type I (30 patients, 83.3%) with transdiscal fracture, located between the former endplates. We considered that this type of fracture may preserve the bone stock of the anterior column with fair contact between the fragments without adding the anterior graft. Although we tried a shorter fixation in patients with the mild transdiscal fracture (type IA) who were treated with SOMI postoperatively for additional immobilization and showed satisfactory outcomes (Table 1), we still recommended a longer segment fixation in type I in case of implant failure (Figure 8).

4.4. Posterior Approach. Multilevel posterior-only approach for lower cervical fracture seemed biomechanically reasonable, even if the posterior approach may have considerable bleeding and more risk of infection. Posterior-only fixation was strong and stable with few implant failures, and the fixed region was sufficient with two segments above and two below the fracture segment [30, 31].

In our series, 42 patients underwent posterior-only approach, most of them were treated with long-segment fixation (39 patients, 92.9%), and only 3 patients in type IIA were treated with fixation equal to or less than 3 segments (Table 1). We have found that posterior fixation alone for lower cervical fracture was sufficient to obtain fusion if the fixation was long enough (Figure 9). Postoperatively, an additional cervical collar was mandatory with long-segment fixation, whereas SOMI for immobilization was initially preferred in patients with shorter segment fixation [18].

4.5. Combined Approach. A combined approach may be necessary only when the structural integrity of the vertebral body has been significantly compromised. Circumferential fusion should be a suitable method for these reasons: three-column instability, poor bone quality, and severe kyphosis [28].

In our experience, posterior decompression or fixation was performed combined with the anterior surgery when posterior compression and instability or epidural hematoma were noted on MRI with persistent neurological deficits after anterior surgery, or revision surgery was needed [5]. Similarly, anterior decompression and fixation were conducted after posterior surgery when anterior compression, significant instability, or severe anterior bone defect was revealed; notably, neurological deficits did not completely regress after posterior surgery. In our series, we conducted revision surgery (AF + PF) in one patient with early implant failure. Posterior surgery combined anterior surgery (PF + AF) was performed in three patients who underwent an anterior autologous iliac bone interbody fusion because of a sizeable anterior gap after posterior surgery.

In a nutshell, we do not recommend a one-stage combined approach as the first choice owing to increased blood loss, operation time, and complication. Thus, we preferred a unique approach most of the time. In type I, we preferred an anterior-only approach ($>$ 3 segments) if anatomical access permitted. In types II and III, we recommended the posterior-only approach ($>$ 3 segments) as the first choice. However, if long posterior instrumentation was performed, the anterior access became obsolete, since stabilized fractures related to AS had a tendency to heal, even if slight anterior defects were present. The fixation allowed early rehabilitation with molded collar or SOMI for stronger immobilization postoperatively. Thus, we preferred the anterior-only approach in type I most of the time, whereas the posterior-only approach in types II and III, and fixations were long but not systematically circumferential.

4.6. Outcomes and Complications. In our series, the criteria for determining bone fusion on CT are: (1) the presence of bridging bone trabeculae around the fracture line on the thin scan, (2) the presence of bridging bone trabeculae through the fusion device, (3) the presence of the above fracture healing signs in at least two vertical null straight scan planes, and (4) the presence of both of the above. All living patients achieved bone fusion confirmed by CT scan at last follow-up and improved or maintained their neurological status except for three patients who suffered deterioration in neurological status after surgery. The fracture subtype related to fracture severity may be predictive of neurological status and outcomes. Also, patients with subtype C may have more severe neurological symptoms and poor recovery, followed by patients with subtypes B and A. This indicated that subtypes may be related to neurological deficits and outcomes.

Moreover, AS Patients with cervical fractures were extremely prone to complications after surgical intervention. In another study, Einsiedel et al. [28] revealed that early implant failures occurred exclusively after single-session anterior stabilization (50%). In our series, two patients developed early implant failure or screw loosening after anterior stabilization alone. Implant failure may be attributed to difficult anatomy and osteoporosis of the spine and the surgeon's misunderstanding of biomechanics. For such predictable implant failures, we have taken compensatory measures in the form of adjunctive external fixation in all postoperative cases and opted for compensatory measures in the form of reoperation for endograft failures that may endanger neurological function.

As with other published reports [1, 5], the overall mortality rate in this injury was higher (33%), and related to the initial medullary involvement, the death in our series was in one patient (type IIIC, ASIA B before the surgery), who had significant medulla injuries visible on MRI. The patient was aged above 70 years with poor condition and died of

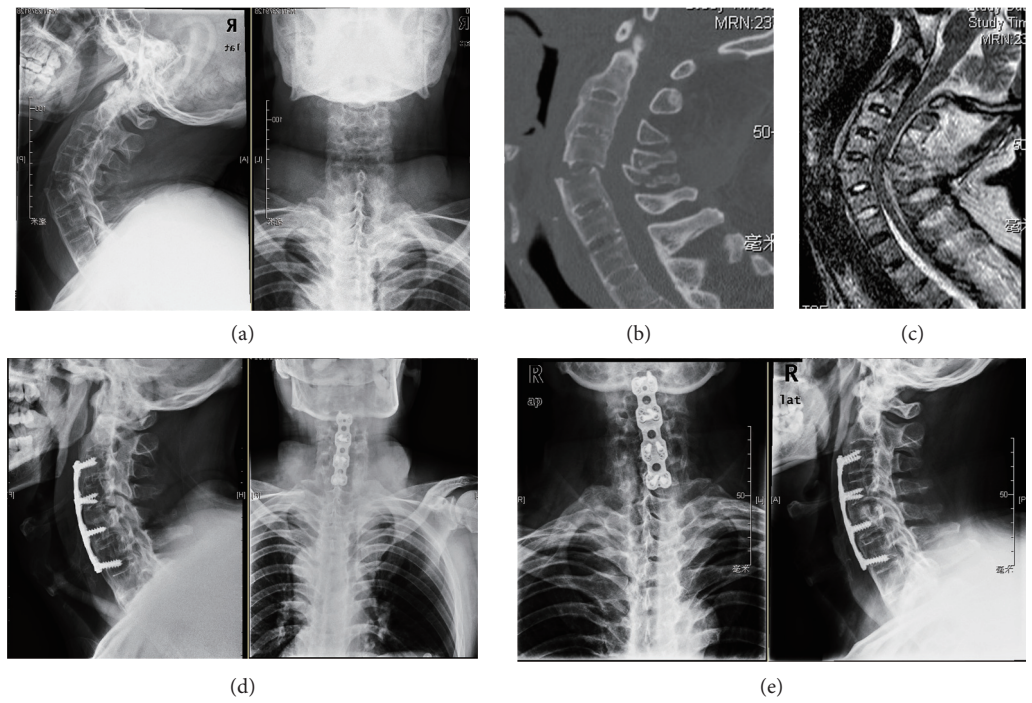

Figure 8: Type I fracture. An anterior approach is adopted. The length of the plate should be extended by more than two segments.

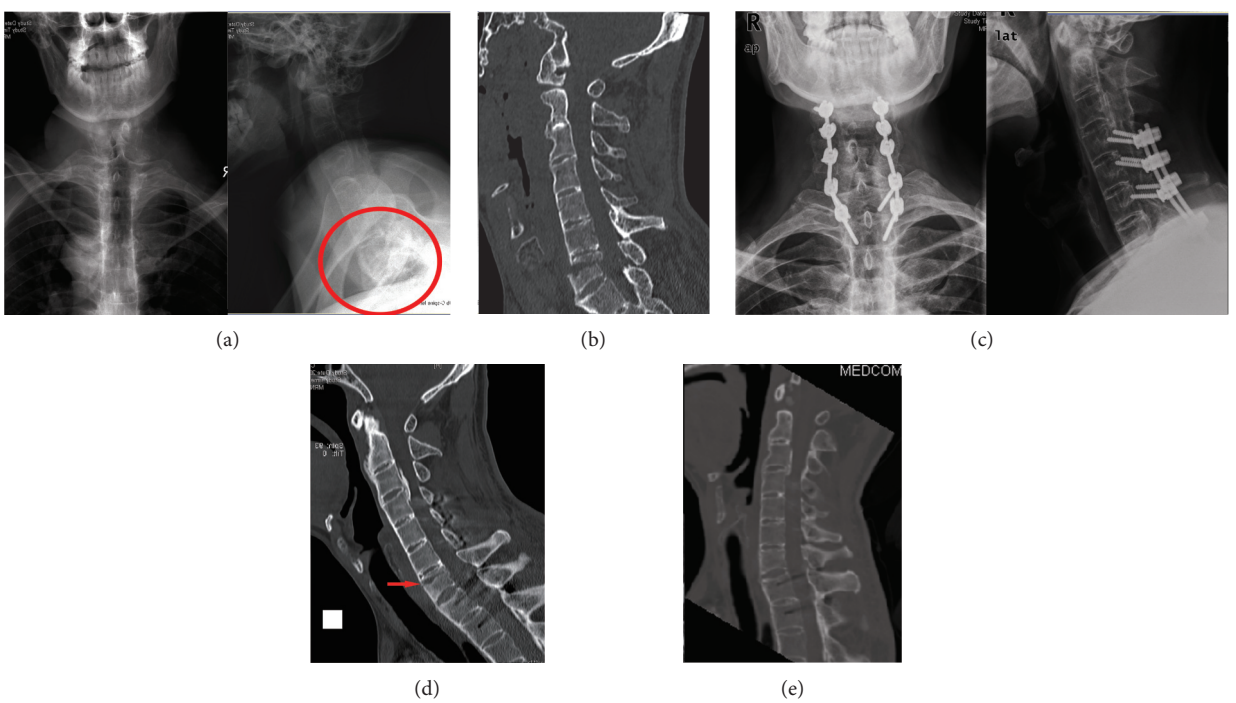

Figure 9: Treatment of type IIA; most fracture patients can be treated with posterior surgery, which is safer.

respiratory failure and infection. These fetal complications may necessitate making difficult decisions regarding post-operative immobilization to avoid chest compressions and significantly interfere with the surgical strategy [18].

In the present study, the obvious epidural hematoma was identified on neuroimaging or during operation in nine patients (Figure 1), with a higher risk than in the non-AS population. All these patients presented with severe

neurologic deficits (ASIA A or B). Although they experienced an improvement in their clinical status after surgery, there were still severe neurological deficits at the last follow-up. Thus, the hematoma could be a key factor in AS patients with cervical fracture as being predictive of severe neurological deficits and poor recovery.

4.7. Limitations. The limitations of this study are as follows: (1) the partial time overlap between the retrospective and prospective studies resulted in some patients appearing in different studies, and there may be a small bias in the summary of experience in the time frame; (2) the postoperative medical treatment of ankylosing spondylitis fractures may have an impact on the prognosis and partially influence the experimental results; and (3) the uncontrollable out-of-hospital rehabilitation and the uneven postoperative rehabilitation exercise methods had some influence on the clinical efficacy assessment of this study, which needs to be further extended and controlled by improving the experimental follow-up methods.

5. Conclusions

The present study demonstrated that patients with AS are highly susceptible to cervical fracture and extensive neurological injury caused by even mild traumatic force. X-ray, CT, and MRI imaging were strongly recommended regardless of whether minor initial clinical findings are present. Since conservative treatment alone is inadequate for this kind of fracture, we assessed the severity of the fracture based on radiological findings and presented a new classification to assist surgeons in their efforts to provide optimal surgical treatment.

Notably, the anterior-only approach is preferable in type I as it presents satisfactory results, whereas the posterior-only approach in types II and III, and fixation is long but not systematically circumferential. Also, the fracture subtypes especially B and C often indicated a more severe neurological status. It was revealed that S patients with a cervical fracture are extremely prone to complications after surgical intervention, which is related to the severity of the initial neurological presentation, and the epidural hematoma may be a key factor in AS patients with cervical fracture as being predictive of severe neurological deficits and poor recovery.

To better show our improved fracture classification, a nomogram was introduced in data analysis. The nomogram as an important data analysis tool may be of great significance to clinical research. This analysis method has been applied in many fields such as oncology and cervical diseases. It enables clinicians and patients to choose more reasonable treatment plans for specific diseases in a systematic manner based on data [32, 33].

Unfortunately, there was still no high-level evidence to guide the treatment, and the current data was based on our sentinel experience and small cases. Patients with obvious kyphosis or deformity were not in our series; thus, further studies are warranted to confirm these early findings.

Abbreviations

AS: Ankylosing spondylitis
mJOA: Modified Japanese Orthopaedic Association
ASIA: American Spinal Cord Injury Association
AF: Anterior cervical decompression and fusion
PF: Posterior cervical decompression and fusion.

Data Availability

The basic information of clinical objects data used to support the findings of this study is included within the supplementary information file. Detailed imaging information and original case images can be obtained from the corresponding authors and provided by e-mail after approval by the local ethics committee.

Disclosure

All funders did not participate in the content of this experiment; they had given different levels of support in the project funding and equipment.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Nana Shen and Xiaolin Wu contributed equally to this work.

Acknowledgments

The authors thank Professor Bohua Chen for his helpful advice regarding researching the unpublished literature. This work was supported by the Young Taishan Scholars Program (tsqn201909190); National Natural Science Foundation of China (82172478, 81802190, and 81772412); Postdoctoral Science Foundation of China (2021M701813); National Key Research and Development Project (2019YFC0121404); Shandong Provincial Natural Science Foundation, China (ZR2019BH084); Qingdao Postdoctoral Applied Research Project (2020); and Innovation Fund of National Orthopedics and Sports Rehabilitation Clinical Medicine Research Center (2021-NCRC-CXJJ-ZH-02).

Supplementary Materials

In Section 3.4, the article shows the statistical table of 90 patients selected for prospective analysis, including 81 males and 9 females. We summarize and count the specific information of 90 patients including "sex, age, BMI, SMOK, $C_{2\text{-}7}$ COBB, cSVA, *T*1 slope, fracture site, fracture type, ASIA, mJOA, treatment, fixation level, operation time, blood loss, fusion, last follow-up time, ASIA at last follow-up, mJOA at last follow-up, and complication," a total of 20 indicators, see Table S1 for details. (*Supplementary Materials*)

References

[1] V. Gilard, S. Curey, S. Derrey, A. Perez, and F. Proust, "Cervical spine fractures in patients with ankylosing spondylitis: importance of early management," *Neurochirurgie*, vol. 60, no. 5, pp. 239–243, 2014.

[2] A. S. Kanter, M. Y. Wang, and P. V. Mummaneni, "A treatment algorithm for the management of cervical spine fractures and deformity in patients with ankylosing spondylitis," *Neurosurgical Focus*, vol. 24, no. 1, p. E11, 2008.

[3] F. Anwar, A. Al-Khayer, G. Joseph, M. H. Fraser, M. V. Jigajinni, and D. B. Allan, "Delayed presentation and diagnosis of cervical spine injuries in long-standing ankylosing spondylitis," *European Spine Journal*, vol. 20, no. 3, pp. 403–407, 2011.

[4] T. Caron, R. Bransford, Q. Nguyen, J. Agel, J. Chapman, and C. Bellabarba, "Spine fractures in patients with ankylosing spinal disorders," *Spine*, vol. 35, no. 11, pp. E458–E464, 2010.

[5] P. Kouyoumdjian, P. Guerin, C. Schaelderle, G. Asencio, and O. Gille, "Fracture of the lower cervical spine in patients with ankylosing spondylitis: retrospective study of 19 cases," *Orthopaedics and Traumatology: Surgery & Research*, vol. 98, no. 5, pp. 543–551, 2012.

[6] A. Grisolia, R. L. Bell, and L. F. Peltier, "Fractures and dislocations of the spine complicating ankylosing spondylitis. 1967," *Clinical Orthopaedics and Related Research*, vol. 422, pp. 129–134, 2004.

[7] W. B. Jacobs and M. G. Fehlings, "Ankylosing spondylitis and spinal cord injury: origin, incidence, management, and avoidance," *Neurosurgical Focus*, vol. 24, no. 1, p. E12, 2008.

[8] Y. Robinson, A.-L. Robinson, and C. Olerud, "Complications and survival after long posterior instrumentation of cervical and cervicothoracic fractures related to ankylosing spondylitis or diffuse idiopathic skeletal hyperostosis," *Spine*, vol. 40, no. 4, pp. E227–E233, 2015.

[9] P. Metz-Stavenhagen, S. Krebs, and O. Meier, "Cervical fractures in conjunction with spondylitis ankylosans," *Orthopäde, Der*, vol. 30, no. 12, pp. 925–931, 2001.

[10] P. S. Schneider, J. Bouchard, K. Moghadam, and G. Swamy, "Acute cervical fractures in ankylosing spondylitis," *Spine*, vol. 35, no. 7, pp. E248–E252, 2010.

[11] M. Koizumi, J. Iida, H. Shigematsu et al., "Posterior fixation of a cervical fracture using the RRS loop spine system and polyethylene tape in an elderly ankylosing spondylitis patient: a case report," *Asian Spine Journal*, vol. 6, no. 1, pp. 60–65, 2012.

[12] N. E. El Tecle, K. O. Abode-Iyamah, P. W. Hitchon, and N. S. Dahdaleh, "Management of spinal fractures in patients with ankylosing spondylitis," *Clinical Neurology and Neurosurgery*, vol. 139, pp. 177–182, 2015.

[13] E. Feldtkeller, M. Khan, D. van der Heijde, S. van der Linden, and J. Braun, "Age at disease onset and diagnosis delay in HLA-B27 negative vs. positive patients with ankylosing spondylitis," *Rheumatology International*, vol. 23, no. 2, pp. 61–66, 2003.

[14] H. Alaranta, S. Luoto, and Y. T. Konttinen, "Traumatic spinal cord injury as a complication to ankylosing spondylitis. An extended report," *Clinical & Experimental Rheumatology*, vol. 20, pp. 66–68, 2002.

[15] C.-E. Heyde, J. K. Fakler, E. Hasenboehler et al., "Pitfalls and complications in the treatment of cervical spine fractures in patients with ankylosing spondylitis," *Patient Safety in Surgery*, vol. 2, no. 1, p. 15, 2008.

[16] A. R. Vaccaro, C. Oner, C. K. Kepler et al., "AOSpine thoracolumbar spine injury classification system," *Spine*, vol. 38, no. 23, pp. 2028–2037, 2013.

[17] F. de Peretti, J.-C. Sane, G. Dran, C. Razafindratsiva, and C. Argenson, "Fractures du rachis sur ankylose étendue par spondylarthrite ou hyperostose vertébrale: diagnostic et complications," *Revue de Chirurgie Orthopédique et Réparatrice de l'Appareil Moteur*, vol. 90, no. 5, pp. 456–465, 2004.

[18] J.-Y. Lazennec, H. d'Astorg, and M.-A. Rousseau, "Cervical spine surgery in ankylosing spondylitis: review and current concept," *Orthopaedics and Traumatology: Surgery & Research*, vol. 101, no. 4, pp. 507–513, 2015.

[19] J. Mountney, A. J. Murphy, and J. L. Fowler, "Lessons learned from cervical pseudoarthrosis in ankylosing spondylitis," *European Spine Journal*, vol. 14, no. 7, pp. 689–693, 2005.

[20] L. A. Westerveld, J. J. Verlaan, and F. C. Oner, "Spinal fractures in patients with ankylosing spinal disorders: a systematic review of the literature on treatment, neurological status and complications," *European Spine Journal*, vol. 18, no. 2, pp. 145–156, 2009.

[21] S.-B. An, K.-N. Kim, D.-K. Chin, K.-S. Kim, Y.-E. Cho, and S.-U. Kuh, "Surgical outcomes after traumatic vertebral fractures in patients with ankylosing spondylitis," *Journal of Korean Neurosurgical Society*, vol. 56, no. 2, pp. 108–113, 2014.

[22] D.-J. Jo, S.-M. Kim, K.-T. Kim, and E.-M. Seo, "Surgical experience of neglected lower cervical spine fracture in patient with ankylosing spondylitis," *Journal of Korean Neurosurgical Society*, vol. 48, no. 1, pp. 66–69, 2010.

[23] J. Ma, C. Wang, X. Zhou, S. Zhou, and L. Jia, "Surgical therapy of cervical spine fracture in patients with ankylosing spondylitis," *Medicine (Baltimore)*, vol. 94, no. 44, Article ID e1663, 2015.

[24] G. Sapkas, K. Kateros, S. A. Papadakis et al., "Surgical outcome after spinal fractures in patients with ankylosing spondylitis," *BMC Musculoskeletal Disorders*, vol. 10, no. 1, p. 96, 2009.

[25] F. H. Shen and D. Samartzis, "Surgical management of lower cervical spine fracture in ankylosing spondylitis," *The Journal of Trauma, Injury, Infection, and Critical Care*, vol. 61, no. 4, pp. 1005–1009, 2006.

[26] L.-B. Xiang, H.-L. Yu, J. Liu, Y. Chen, and H.-F. Yang, "One-stage surgery by a combined anterior-posterior approach to treat ankylosing spondylitis complicated by a multiple-level cervical vertebral chance fracture," *Modern Rheumatology*, vol. 25, no. 2, pp. 282–285, 2015.

[27] M. F. Dvorak, C. G. Fisher, M. G. Fehlings et al., "The surgical approach to subaxial cervical spine injuries," *Spine*, vol. 32, no. 23, pp. 2620–2629, 2007.

[28] T. Einsiedel, A. Schmelz, M. Arand et al., "Injuries of the cervical spine in patients with ankylosing spondylitis: experience at two trauma centers," *Journal of Neurosurgery: Spine*, vol. 5, no. 1, pp. 33–45, 2006.

[29] M. Zdichavsky, M. Blauth, C. Knop, U. Lange, C. Krettek, and L. Bastian, "Ankylosierende spondylitis," *Chirurg, Der*, vol. 76, no. 10, pp. 967–976, 2005.

[30] M. Cornefjord, M. Alemany, and C. Olerud, "Posterior fixation of subaxial cervical spine fractures in patients with ankylosing spondylitis," *European Spine Journal*, vol. 14, no. 4, pp. 401–408, 2005.

[31] D. A. Taggard and V. C. Traynelis, "Management of cervical spinal fractures in ankylosing spondylitis with posterior fixation," *Spine*, vol. 25, no. 16, pp. 2035–2039, 2000.

[32] D. Lubelski, V. Alentado, A. S. Nowacki et al., "Preoperative nomograms predict patient-specific cervical spine surgery

clinical and quality of life outcomes," *Neurosurgery*, vol. 83, no. 1, pp. 104–113, 2018.

[33] D. W. Rowed, "Management of cervical spinal cord injury in ankylosing spondylitis: the intervertebral disc as a cause of cord compression," *Journal of Neurosurgery*, vol. 77, no. 2, pp. 241–276, 1992.

Hindawi
Pain Research and Management
Volume 2022, Article ID 3489160, 7 pages
https://doi.org/10.1155/2022/3489160

Research Article

Clinical Efficacy of Percutaneous Kyphoplasty Combined with Calcitriol and Calcium in the Treatment of Traumatic Nonosteoporotic Vertebral Compression Fractures

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Received 4 December 2021; Accepted 28 January 2022; Published 27 February 2022

Academic Editor: Sidong Yang

Objective. The present study investigated the clinical efficacy of percutaneous kyphoplasty (PKP) combined with calcitriol and calcium in the treatment of traumatic nonosteoporotic vertebral compression fractures (TNVCFs). *Methods*. The patients were equally divided into a control group and a treatment group by a random number table. The patients in the control group underwent PKP surgery, and the patients in the treatment group received calcitriol and calcium on the basis of PKP surgery. The visual analog scale (VAS) pain scores, Oswestry Disability Index (ODI) scores, the height of the anterior edge of the vertebral body, Cobb's angle, and the level of the bone mineral density of the two groups of TNVCF patients before surgery were recorded and compared, one and six months after surgery. *Results*. Thirty-six inpatients with TNVCFs admitted to the trauma center of the First Affiliated Hospital of Soochow University from January 2019 to January 2020 were recruited. There were no significant differences in the VAS and ODI scores, the height of the anterior edge of the injured vertebral body, Cobb's angle, and bone mineral density between the two groups before surgery ($P > 0.05$). The VAS scores, ODI scores, the height of the anterior edge of the injured vertebral body, and Cobb's angle of the two groups of patients after surgery were significantly better than those before surgery. One and six months after surgery, the VAS and ODI scores, the height of the anterior edge of the injured vertebral body, Cobb's angle, and the bone mineral density of the patients in the treatment group improved significantly compared to those in the control group ($P < 0.05$). *Conclusions*. PKP combined with calcitriol and calcium medications could significantly relieve pain, alleviate the loss of compressed vertebral height and kyphosis, and improve the spinal function and the life quality of the TNVCF patients.

1. Introduction

Trauma is the leading cause of death in the youngest and most productive individuals and the fourth leading cause of mortality in all age groups [1]. Death, disability, and loss of productivity imposed by trauma have imposed significant economic burden and rehabilitation costs on the society and families. Trauma often damages the musculoskeletal system, including traumatic spinal fractures. As increasingly more such injuries occur every day, traumatic spinal fractures can lead to devastating consequences, including pain, deformity, and paralysis [2–5]. Among the spinal fractures caused by this high-energy impact, there is a special type of traumatic nonosteoporotic vertebral compression fracture (TNVCF), which is different from the osteoporotic vertebral compression fractures (OVCFs) in osteoporotic patients, with the latter generally caused by low-energy impacts. Treatment for patients with vertebral compression fractures usually includes bed rest, open reduction, internal fixation, and minimally invasive percutaneous kyphoplasty (PKP).

Since Garfin et al. [6] first reported the clinical application of PKP in 1998, it has been widely used to correct spinal deformities, relieve pain, and maintain spinal stability and has gradually become the most popular surgical treatment for OVCFs. In addition to surgical treatment, active anti-osteoporosis treatment is the basis for OVCF treatment since it can improve the therapeutic effect of PKP and reduce long-term complications. Calcitriol and calcium are the most commonly used clinical antiosteoporosis drugs. Calcium is the basic raw material for bone synthesis, and calcitriol can promote bone formation, increase the absorption of calcium in the intestine, and play a crucial role in OVCF treatment. However, the effectiveness of calcitriol and calcium in TNVCFs remains controversial. There is still no unanimous consensus on the management of TNVCFs with PKP.

This study enrolled 36 TNVCF patients admitted to the trauma center of our hospital and explored the effect of combined calcitriol and calcium on TNVCF patients undergoing PKP. Our research tried to provide evidence for clinicians to choose optimal treatment for TNVCF patients.

2. Materials and Methods

2.1. Inclusion and Exclusion Criteria. The inclusion criteria were as follows: (1) patients presenting with spinal trauma (an accident or severe fall); (2) X-ray and CT scans indicating vertebral compression fractures, with the MRI showing that the injured vertebrae had T1-weighted low signal and T2-weighted high signal, consistent with a diagnosis of fresh vertebral fracture; (3) normal bone mineral density (BMD) (t-value ≥ -1); (4) patients' cooperation with the research and effective communication with the researcher; (5) subjects signing an informed consent form.

The exclusion criteria were as follows: (1) patients with severe heart, liver, lung, and other organ diseases or mental and nervous system conditions; (2) vertebral osteomyelitis, vertebral tuberculosis, pathological fractures, and acute infections; (3) neurological impairment, such as spinal cord injury or cauda equina injury; (4) a history of osteoporosis; (5) patients who could not cooperate, could not be followed up, or could not perform imaging examinations on time.

2.2. Patient Population. According to the inclusion and exclusion criteria, 36 TNVCF patients were recruited from those hospitalized in the trauma center of the First Affiliated Hospital of Soochow University from January 2019 to January 2020. Thirty-six patients were divided into the control and treatment groups by a random number table ($n = 18$). Each case only had a single-segment lesion. In the control group, there were 6 males and 12 females, 18–56 years of age (average = 35.8 ± 7.4). All the involved vertebral segments were the thoracic (T) and lumbar (L) vertebrae: two cases of T10, three cases of T11, five cases of T12, four cases of L1, two cases of L2, and two cases of L3. In the treatment group, there were eight males and ten females, 19–59 years of age (average = 36.7 ± 8.3). The involved vertebral segments were as follows: three cases of T10, four cases of T11, five cases of T12, three cases of L1, one case of L2, and two cases of L3. There was no statistically significant difference in general information between the two groups ($P > 0.05$); therefore, the two groups were matched and could be compared. All the patients signed informed consent forms, which were approved by the Medical Ethics Committee of our hospital.

2.3. Surgical Procedure in the Control Group. In this study, all the PKP procedures were performed by the same spine surgeon in the trauma center. Patients in the control group were treated with a standard PKP surgical procedure [7] and postoperative management. Under C-arm fluoroscopy, the pedicle approach was used for a bilateral vertebral puncture, and then a puncture trocar was gently tapped into the vertebral body through a bone hammer. When the C-arm fluoroscopy showed that the tip of the puncture needle was located at the inner edge of the pedicle and the posterior edge of the vertebral body, the puncture needle was moved forward about 0.5 cm; then, the inner core of the puncture needle was pulled out, and the K-wire was inserted. A working cannula was inserted to obtain a small amount of bone for pathological examination. Then, two expansion balloons were inserted, expanded sequentially, and withdrawn after satisfactorily reducing the compressed vertebral body. The prepared bone cement was slowly pushed into the working sleeve from both sides. C-arm fluoroscopy confirmed that the bone cement penetrated well, with no leakage. The working casing was removed after the bone cement solidified.

2.4. Medications in the Treatment Group. After the PKP procedure, the patients in the treatment group were prescribed calcitriol (Rocaltrol, no. J20150011, Shanghai Roche Pharmaceutical Co., Ltd.), 0.25 μg twice daily, and calcium (Caltrate D, no. H10950029, Wyeth Pharmaceuticals Co., Ltd.), 0.6 g daily for six months.

2.5. Clinical and Radiographic Evaluation. During the entire treatment period, the visual analog scale (VAS) score and Oswestry Disability Index (ODI) score, the height of the anterior edge of injured vertebrae, Cobb's angle, and bone mineral density (BMD) levels of the two groups of patients were recorded before the PKP procedure and one and six months after the procedure. A typical case of a 44-year-old female patient with TNVCFs is shown in Figure 1.

2.6. Statistical Analysis. All data conforming to the normal distribution were expressed as means ± standard deviations ($x \pm s$). Statistical analyses were performed using SPSS 22.0. Comparisons before and after treatment were performed using paired-sample t-test, and intergroup comparisons were performed with independent-sample t-test. $P < 0.05$ indicated statistical significance.

3. Results

3.1. VAS and ODI Scores between the Two Groups. Table 1 indicates no significant differences in the preoperative VAS scores between the two groups of TNVCF patients ($P > 0.05$). Compared with the baseline, the VAS scores of the two groups of patients decreased significantly ($P < 0.05$).

Table 1: Comparisons of VAS scores between the two groups of TNVCF patients before and after the PKP procedure ($x \pm s$).

Time	Control group ($n = 18$)	Treatment group ($n = 18$)	t	P
Preoperative	7.98 ± 0.83	7.56 ± 0.67	1.671	0.104
One month after surgery	$3.45 \pm 0.56^*$	$2.99 \pm 0.69^*$	2.196	0.035
Six months after surgery	$2.66 \pm 0.45^*$	$2.18 \pm 0.56^*$	2.835	0.008

$^*p < 0.05$ compared with the preoperative period.

At 1- and 6-month postoperative intervals, the VAS scores of the patients in the treatment group were significantly lower than those in the control group ($P < 0.05$).

As shown in Table 2, there were no significant differences in the preoperative ODI scores between the two groups ($P > 0.05$). Compared with the baseline, the ODI scores of the two groups of patients decreased significantly ($P < 0.05$). At 1- and 6-month postoperative intervals, the ODI scores of the patients in the treatment group were significantly lower than those in the control group ($P < 0.05$).

3.2. Comparison of the Height of the Anterior Edge of Injured Vertebrae and Cobb's Angles between the Two Groups. Table 3 shows no significant difference in the preoperative height of the anterior edge of the injured vertebrae between the two groups ($P > 0.05$). Compared with the baseline, the height of the anterior edge of the injured vertebral body increased significantly in the two groups ($P < 0.05$). At 1- and 6-month postoperative intervals, the height of the anterior edge of the injured vertebrae in the treatment group significantly increased compared with the control group ($P < 0.05$).

Data in Table 4 show no significant difference in the preoperative Cobb's angle between the two groups of TNVCF patients ($P > 0.05$). Compared with the baseline, Cobb's angles in the two groups of patients decreased significantly ($P < 0.05$). At 1- and 6-month postoperative intervals, Cobb's angles of patients in the treatment group decreased significantly compared with the control group ($P < 0.05$).

3.3. BMD between the Two Groups. Table 5 shows no significant difference in the preoperative BMD between the two groups ($P > 0.05$). There was no significant difference between preoperative and postoperative BMDs in the control group ($P > 0.05$). In the treatment group, postoperative BMD increased significantly compared with the preoperative BMD ($P < 0.05$). At 1- and 6-month postoperative intervals, the BMDs of the patients in the treatment group increased significantly ($P < 0.05$) compared with the control group.

4. Discussion

Traumatic spine fractures most commonly occur in the thoracolumbar vertebrae (especially the T10-L2 region) and can be divided into several types, including compression fractures, stable or unstable burst fractures, flexion-distraction fractures, and fracture dislocations. These patients' need for surgery depends on several factors: the degree of bone compromise, neurological involvement, and the integrity of the posterior ligamentous complex. OVCF is an important factor leading to morbidity and even death of the elderly, and one of its characteristics is low-energy impacts. However, TNVCF, often occurring in young and middle-aged individuals, is often caused by high-energy impacts. TNVCF patients usually experience a high level of pain and disability.

The treatment goals of TNVCFs are to reduce pain, restore vertebral height and mobility, and reduce the risk of vertebral collapse. Treatment options include conservative treatment, PKP, vertebroplasty, open reduction, and internal fixation [8–12]. Conservative treatment includes bed rest, waist protection, functional exercises, and appropriate medications. In the past few decades, minimally invasive PKP has become a popular treatment worldwide for patients with vertebral compression fractures without neurological impairment [13–15]. Many clinical studies have confirmed that PKP fills the balloon in the vertebrae before injecting bone cement to achieve partial reduction [16], relieving pain and stabilizing the fractured vertebral body [17–19]. In this study, all TNVCF patients successfully completed the PKP surgical procedure, and the patients' postoperative VAS and IDO scores were significantly reduced. The heights of the anterior edge of the injured vertebrae and Cobb's angles were restored significantly, indicating that PKP is a safe and effective treatment option for TNVCF patients. Actually, over the last decade, increasingly more surgeons have selected PKP as a viable approach to treat posttraumatic compression fractures [20–22], although PKP was mainly used to treat OVCF initially. The current study confirmed earlier findings. One prospective single-arm study found that percutaneous cement augmentation (PVP and PKP) in TNVCF patients could rapidly relieve pain and significantly improve physical and social functions [23]. In a retrospective study, the authors explored the evolution of vertebral and regional kyphosis in TNVCF patients treated with PKP, reporting that PKP was an efficient and reliable procedure to treat posttraumatic vertebral compression fractures, although there was a slight deterioration of kyphosis correction over time. However, some patients still have a poor prognosis after PKP surgery, accompanied by chronic pain or gradual vertebral collapse. This may be related to the lack of active drug treatment after surgery in some TNVCF patients, which is exactly the focus of this study.

Vitamin D and calcium supplementation is essential to prevent and treat osteoporosis and secondary OVCF. Vitamin D helps absorb calcium and phosphorus from the intestines and maintain bone mineralization and muscle mass and has potential benefits for other organs and systems [24]. Vitamin D can be synthesized in the skin after exposure to the sun and can

Table 2: Comparisons of ODI scores between the two groups of TNVCF patients before and after the PKP procedure ($\bar{x} \pm s$).

Time	Control group ($n = 18$)	Treatment group ($n = 18$)	t	P
Preoperative	50.67 ± 7.28	52.34 ± 7.21	0.692	0.494
One month after surgery	$34.71 \pm 6.08^*$	$30.31 \pm 5.15^*$	2.343	0.025
Six months after surgery	$15.44 \pm 3.07^*$	$13.02 \pm 2.76^*$	2.487	0.018

$^*p < 0.05$ compared with the preoperative period.

Table 3: Comparisons of the height of the anterior edge of injured vertebrae between the two groups of TNVCF patients before and after the PKP procedure ($\bar{x} \pm s$, cm).

Time	Control group ($n = 18$)	Treatment group ($n = 18$)	t	P
Preoperative	1.49 ± 0.11	1.47 ± 0.14	0.477	0.637
One month after surgery	$1.96 \pm 0.16^*$	$2.08 \pm 0.19^*$	2.050	0.048
Six months after surgery	$1.91 \pm 0.15^*$	$2.05 \pm 0.16^*$	4.256	0.011

$^*p < 0.05$ compared with the preoperative period.

Table 4: Comparisons of Cobb's angle between the two groups of TNVCF patients before and after the PKP procedure ($\bar{x} \pm s$, °).

Time	Control group ($n = 18$)	Treatment group ($n = 18$)	t	P
Preoperative	25.27 ± 3.19	25.09 ± 2.99	0.175	0.862
One month after surgery	$17.48 \pm 2.21^*$	$15.66 \pm 2.11^*$	2.527	0.016
Six months after surgery	$17.55 \pm 2.05^*$	$15.83 \pm 1.78^*$	2.688	0.011

$^*p < 0.05$ compared with the preoperative period.

Table 5: Comparisons of BMD between the two groups of TNVCF patients before and after the PKP procedure ($\bar{x} \pm s$, g/cm^3).

Time	Control group ($n = 18$)	Treatment group ($n = 18$)	t	P
Preoperative	0.98 ± 0.09	0.94 ± 0.11	1.194	0.241
One month after surgery	1.03 ± 0.11	$1.11 \pm 0.12^*$	2.085	0.045
Six months after surgery	1.01 ± 0.14	$1.16 \pm 0.15^*$	3.102	0.004

$^*p < 0.05$ compared with the preoperative period.

also be taken in through a balanced diet. With changes in modern lifestyles (reduced outdoor activities and unbalanced diets), in addition to the elderly, some young and middle-aged individuals may also suffer from vitamin D deficiency. Vitamin D deficiency causes osteopenia and osteoporosis in men and women, resulting in bone mineralization defects and muscle weakness, which increases the risk of fractures and refractures after surgery. This is especially true in patients with hip fractures and spine VCFs [25]. Therefore, for the elderly, middle-aged, and young people, especially patients with OVCF or TNVCF, adequate vitamin D levels are a requisite for the efficacy of surgical treatment and comprehensive drug treatment. In addition, it is also important to ensure adequate calcium intake through a balanced diet. Calcium and vitamin D supplements can reduce secondary hyperparathyroidism in the elderly, decreasing the risk of proximal femoral fractures [26].

BMD is a method of measuring bone mass and mineralization by dual-energy X-ray absorptiometry. Past meta-analyses have shown that oral vitamin D3 and calcium supplements in postmenopausal women can increase BMD in the spine, body, femoral neck, and total hip, while oral vitamin D3 supplementation alone is not effective [27]. This sampling test was mainly for menopausal and postmenopausal women, in which the subjects were given 800 IU of vitamin D3 and 500 mg of dietary calcium. In addition, researchers have also found that 400 IU of vitamin D3 and 1000 mg of calcium can significantly increase hip BMD levels [28].

The present study explored the effect of the combined use of calcitriol and calcium on the surgical efficacy and BMD levels in TNVCF patients after PKP surgery. In this study, we administered 0.5 μg of calcitriol (active vitamin D) and 600 mg of calcium per day to the treatment group. The postoperative indicators of both groups were significantly better than the baseline one and six months after surgery. We also found that compared with the control group at the same time intervals, the VAS and ODI scores of the patients in the treatment group decreased significantly after surgery. In addition, the height of the anterior edge of the injured vertebrae and Cobb's angle of the injured vertebrae were restored significantly, and the BMD levels increased significantly. There is growing evidence that vitamin D and calcium are indispensable for bone mineralization, with a key role in fracture healing [29, 30]. A fracture could cause systemic bone loss and reduce 2–15% of total bone mass compared to age-matched controls without fractures [31, 32]. Since secondary posttraumatic bone loss might affect bone mineralization and bone repair and daily dietary vitamin D and calcium supply may not meet the body's requirement for

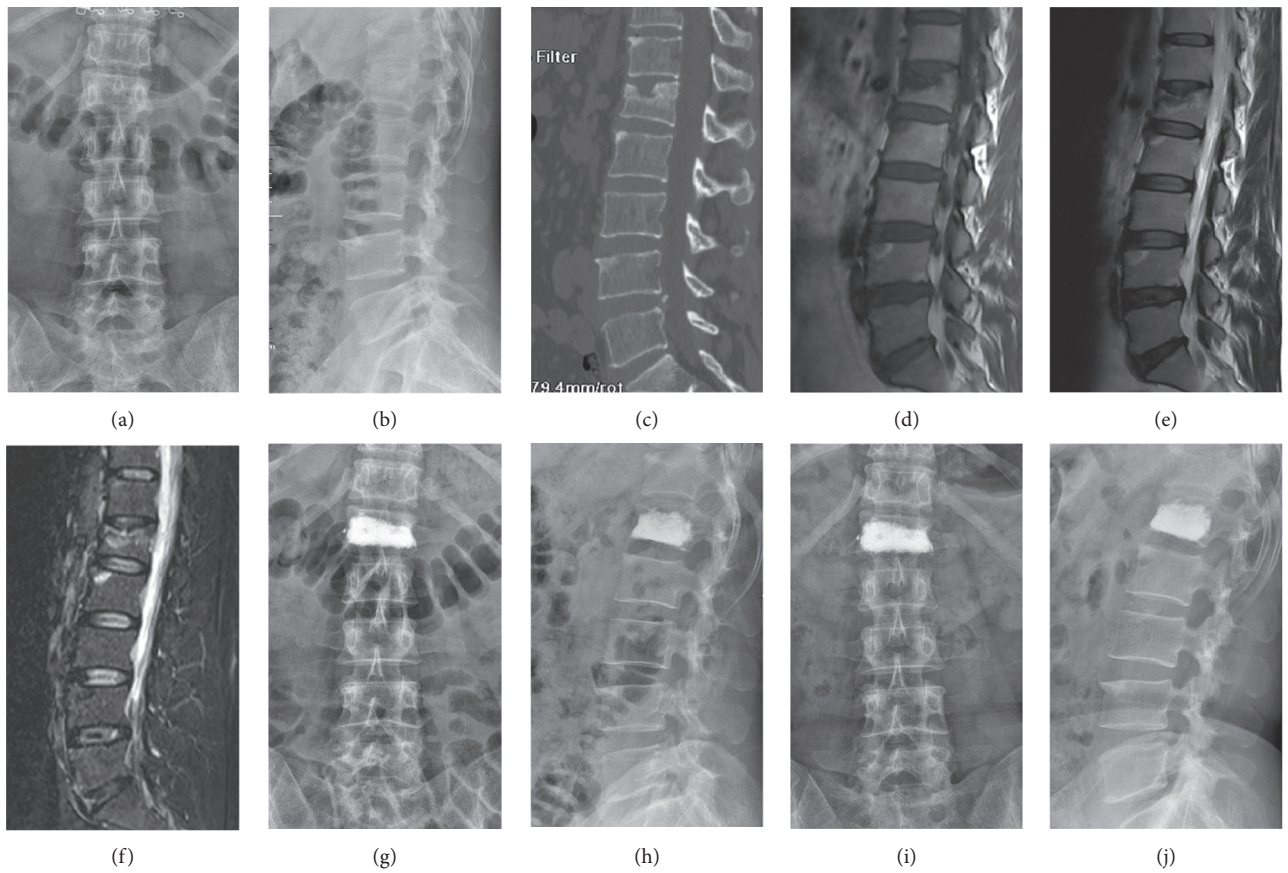

Figure 1: A 44-year-old female patient with TNVCF at L1 in the treatment group. (a) Anteroposterior X-ray film before surgery. (b) Lateral X-ray film before surgery. (c) Vertebral compression fracture shown in the sagittal CT view before surgery. (d) A low-signal intensity in the injured vertebrae shown in the sagittal T1-weighted MRI image before surgery. ((e), (f)) A high-signal intensity in the injured vertebrae shown in the sagittal T2-weighted and short tau inversion recovery (STIR) MRI image before surgery. (g) Anteroposterior X-ray film one month after surgery. (h) Lateral X-ray film one month after surgery. (i) Anteroposterior X-ray film six months after surgery. (j) Lateral X-ray film six months after surgery.

callus mineralization, additional vitamin D and calcium supplements are necessary when a fracture occurs. This partly explains why the postoperative recovery in the treatment group in the present research was significantly better than that in the control group.

However, the present study had some important limitations. First, only small groups of TNVCF patients were included; therefore, a large-scale study of PKP is warranted to reach more convincing conclusions. Second, the duration of the follow-up period was only six months, with possible negative impacts on our findings. Third, we did not determine the levels of vitamin D3 and calcium in blood before and after surgery. Serum calcium concentrations should be better monitored to avoid hypercalcemia.

5. Conclusions

PKP can significantly relieve the pain, alleviate the loss of compressed vertebral height and kyphosis, and improve the spinal function and the quality of life of TNVCF patients. The therapeutic effect of PKP combined with calcitriol and calcium medications is significantly better than that of PKP alone, and it is incumbent on surgeons to choose the best strategy to treat patients with TNVCFs.

Data Availability

The datasets used during the current study are available from the corresponding author upon reasonable request.

Ethical Approval

This study was approved by the ethics committee of the First Affiliated Hospital of Soochow University.

Consent

Written informed consent for publication was obtained from patients.

Disclosure

The funding body did not influence the design of the study, the collection, analysis, or interpretation of the data, or the writing of the manuscript.

Conflicts of Interest

All authors declare that they have no conflicts of interest.

Authors' Contributions

Feng Xu contributed to the study design. Shouqian Dai and Xin Lu prepared the manuscript. Ningning Dai, Xiu Shi, and Peng Yang collected the data. Peng Peng performed the data analysis. All authors read and approved the manuscript. Shouqian Dai, Xin Lu, and Ningning Dai contributed equally to this work.

Acknowledgments

This work was funded by the Natural Science Foundation of the First Affiliated Hospital of Soochow University Boxi Training Program (BXQN202108) and Jiangsu Special Research Project (JSYGY-3-2021-JZ71).

References

[1] L. L. Maerz, K. A. Davis, and S. H. Rosenbaum, "Trauma," *International Anesthesiology Clinics*, vol. 47, no. 1, pp. 25–36, 2009.

[2] J. J. Diaz Jr., D. C. Cullinane, D. T. Altman et al., "Practice management guidelines for the screening of thoracolumbar spine fracture," *The Journal of Trauma, Injury, Infection, and Critical Care*, vol. 63, no. 3, pp. 709–718, 2007.

[3] Y. R. Rampersaud, N. Annand, and M. B. Dekutoski, "Use of minimally invasive surgical techniques in the management of thoracolumbar trauma: current concepts," *Spine (Phila Pa*, vol. 31, no. 11, pp. S96–S102, 1976.

[4] S. D. Gertzbein, "Multicenter spine fracture study," *Spine*, vol. 17, no. 5, pp. 528–540, 1992.

[5] A. M. Levine, P. C. McAfee, and P. A. Anderson, "Evaluation and emergent treatment of patients with thoracolumbar trauma," *Instructional Course Lectures*, vol. 44, pp. 33–45, 1995.

[6] S. R. Garfin, H. A. Yuan, and M. A. Reiley, "New technologies in spine: kyphoplasty and vertebroplasty for the treatment of painful osteoporotic compression fractures," *Spine (Phila Pa*, vol. 26, no. 14, pp. 1511–1515, 1976.

[7] S.-Q. Dai, R.-Q. Qin, X. Shi, and H.-l. Yang, "Percutaneous vertebroplasty versus kyphoplasty for the treatment of neurologically intact osteoporotic Kümmell's disease," *BMC Surgery*, vol. 21, no. 1, p. 65, 2021.

[8] S. Boonen, D. A. Wahl, L. Nauroy et al., "Balloon kyphoplasty and vertebroplasty in the management of vertebral compression fractures," *Osteoporosis International*, vol. 22, no. 12, pp. 2915–2934, 2011.

[9] S. Boonen, J. Van Meirhaeghe, L. Bastian et al., "Balloon kyphoplasty for the treatment of acute vertebral compression fractures: 2-year results from a randomized trial," *Journal of Bone and Mineral Research*, vol. 26, no. 7, pp. 1627–1637, 2011.

[10] I. D. Papanastassiou, F. M. Phillips, J. Meirhaeghe et al., "Comparing effects of kyphoplasty, vertebroplasty, and non-surgical management in a systematic review of randomized and non-randomized controlled studies," *European Spine Journal*, vol. 21, no. 9, pp. 1826–1843, 2012.

[11] P. Vanek, O. Bradac, R. Konopkova, P. de Lacy, J. Lacman, and V. Benes, "Treatment of thoracolumbar trauma by short-segment percutaneous transpedicular screw instrumentation: prospective comparative study with a minimum 2-year follow-up," *Journal of Neurosurgery: Spine*, vol. 20, no. 2, pp. 150–156, 2014.

[12] S. R. Gnanenthiran, S. Adie, and I. A. Harris, "Nonoperative versus operative treatment for thoracolumbar burst fractures without neurologic deficit: a meta-analysis," *Clinical Orthopaedics and Related Research*, vol. 470, no. 2, pp. 567–577, 2012.

[13] J.-T. Liu, C.-s. Li, C.-S. Chang, and W.-J. Liao, "Long-term follow-up study of osteoporotic vertebral compression fracture treated using balloon kyphoplasty and vertebroplasty," *Journal of Neurosurgery: Spine*, vol. 23, no. 1, pp. 94–98, 2015.

[14] C. Bouza, T López-Cuadrado, N Almendro, and J. M Amate, "Safety of balloon kyphoplasty in the treatment of osteoporotic vertebral compression fractures in Europe: a meta-analysis of randomized controlled trials," *European Spine Journal : Official Publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*, vol. 24, no. 4, pp. 715–723, 2015.

[15] J. Du, X. Li, and X. Lin, "Kyphoplasty versus vertebroplasty in the treatment of painful osteoporotic vertebral compression fractures: two-year follow-up in a prospective controlled study," *Acta Orthopaedica Belgica*, vol. 80, no. 4, pp. 477–486, 2014.

[16] Y. Robinson and C. Olerud, "Vertebroplasty and kyphoplasty-A systematic review of cement augmentation techniques for osteoporotic vertebral compression fractures compared to standard medical therapy," *Maturitas*, vol. 72, no. 1, pp. 42–49, 2012.

[17] L. Chen, H. Yang, and T. Tang, "Unilateral versus bilateral balloon kyphoplasty for multilevel osteoporotic vertebral compression fractures: a prospective study," *Spine (Phila Pa*, vol. 36, no. 7, pp. 534–540, 1976.

[18] R. S. Taylor, P. Fritzell, and R. J. Taylor, "Balloon kyphoplasty in the management of vertebral compression fractures: an updated systematic review and meta-analysis," *European Spine Journal*, vol. 16, no. 8, pp. 1085–1100, 2007.

[19] S. R. Garfin, "Balloon kyphoplasty for symptomatic vertebral body compression fractures results in rapid, significant, and sustained improvements in back pain, function, and quality of life for elderly patients," *Spine Phila Pa*, vol. 31, no. 19, pp. 2213–2220, 2006.

[20] D. Wardlaw, S. R. Cummings, J. Van Meirhaeghe et al., "Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE): a randomised controlled trial," *The Lancet*, vol. 373, no. 9668, pp. 1016–1024, 2009.

[21] J. T. Ledlie and M. Renfro, "Balloon kyphoplasty: one-year outcomes in vertebral body height restoration, chronic pain, and activity levels," *Journal of Neurosurgery*, vol. 98, no. 1, pp. 36–42, 2003.

[22] M. E. Majd, S. Farley, and R. T. Holt, "Preliminary outcomes and efficacy of the first 360 consecutive kyphoplasties for the treatment of painful osteoporotic vertebral compression fractures," *The Spine Journal*, vol. 5, no. 3, pp. 244–255, 2005.

[23] R. N. Joseph, A. J. Swift, and P. J. Maliakal, "Single centre prospective study of the efficacy of percutaneous cement augmentation in the treatment of vertebral compression fractures," *British Journal of Neurosurgery*, vol. 27, no. 4, pp. 459–464, 2013.

[24] R. Rizzoli, S. Boonen, M.-L. Brandi et al., "Vitamin D supplementation in elderly or postmenopausal women: a 2013

update of the 2008 recommendations from the European society for clinical and economic aspects of osteoporosis and osteoarthritis (ESCEO)," *Current Medical Research and Opinion*, vol. 29, no. 4, pp. 305–313, 2013.

[25] H. A. Bischoff-Ferrari, U. Can, H. B. Staehelin et al., "Severe vitamin D deficiency in Swiss hip fracture patients," *Bone*, vol. 42, no. 3, pp. 597–602, 2008.

[26] B. M. Tang, G. D. Eslick, C. Nowson, C. Smith, and A. Bensoussan, "Use of calcium or calcium in combination with vitamin D supplementation to prevent fractures and bone loss in people aged 50 years and older: a meta-analysis," *The Lancet*, vol. 370, no. 9588, pp. 657–666, 2007.

[27] M. Chung, E. M Balk, M Brendel et al., "Vitamin D and calcium: a systematic review of health outcomes," *Evidence Report/technology Assessment*, vol. 183, pp. 1–420, 2009.

[28] R. D. Jackson, A. Z LaCroix, M Gass et al., "Calcium plus vitamin D supplementation and the risk of fractures," *New England Journal of Medicine*, vol. 354, no. 7, pp. 669–683, 2006.

[29] L. Claes, S. Recknagel, and A. Ignatius, "Fracture healing under healthy and inflammatory conditions," *Nature Reviews Rheumatology*, vol. 8, no. 3, pp. 133–143, 2012.

[30] T. A. Einhorn and L. C. Gerstenfeld, "Fracture healing: mechanisms and interventions," *Nature Reviews Rheumatology*, vol. 11, no. 1, pp. 45–54, 2015.

[31] L. A. Ahmed, J. R. Center, A. Bjørnerem et al., "Progressively increasing fracture risk with advancing age after initial incident fragility fracture: the Tromsø Study," *Journal of Bone and Mineral Research*, vol. 28, no. 10, pp. 2214–2221, 2013.

[32] K. W. Lyles, A. P. Schenck, and C. S. Colón-Emeric, "Hip and other osteoporotic fractures increase the risk of subsequent fractures in nursing home residents," *Osteoporosis International*, vol. 19, no. 8, pp. 1225–1233, 2008.

Hindawi
Pain Research and Management
Volume 2022, Article ID 9052246, 8 pages
https://doi.org/10.1155/2022/9052246

Research Article

The Impact of Perioperative Multimodal Pain Management on Postoperative Outcomes in Patients (Aged 75 and Older) Undergoing Short-Segment Lumbar Fusion Surgery

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Received 24 November 2021; Revised 26 January 2022; Accepted 31 January 2022; Published 27 February 2022

Academic Editor: Sidong Yang

Background. Due to the presence of multimorbidity and polypharmacy, patients aged 75 and older are at a higher risk for postoperative adverse events after lumbar fusion surgery. More effective enhanced recovery pathway is needed for these patients. Pain control is a crucial part of perioperative management. The objective of this study is to determine the impact of multimodal pain management on pain control, opioid consumption, and other outcomes. *Methods*. This is a retrospective review of a prospective collected database. Consecutive patients who underwent elective posterior lumbar fusion surgery (PLF) from October 2017 to April 2021 in our hospital were reviewed. Perioperative multimodal pain management (PMPM) group (from January 2019 to April 2021) in which patients received multimodal analgesia was case-matched to the control group (from October 2017 to December 2018) in which patients were treated under the conventional patient-controlled analgesia (PCA) method. Postoperative visual analogue scale (VAS), opioid consumption, complications within 3 months, and other outcomes were collected and compared between groups. *Results*. A total of 122 consecutive patients (aged 75 and older) were included in the PMPM group and compared with previous 122 patients. The PMPM group had a lower maximal VAS score (3.0 ± 1.7 vs. 3.7 ± 2.0, $p < 0.001$) and frequency of additional opioid consumption (6.6% vs. 19.7%, $p = 0.001$) on POD3 than the control group. The rates of postoperative complications were lower in the PMPM group compared with the control group (25% vs. 49%, $p = 0.006$) during a 3-month follow-up period. *Conclusions*. This study demonstrates that the PMPM protocol is effective in pain control and reducing additional opioid consumption when compared with conventional analgesia, even for patients aged 75 and older. Moreover, these improvements occur with a lower incidence of postoperative complications within three months after PLF surgery.

1. Introduction

With rapid population aging in many countries, the incidence of lumbar degenerative disease is gradually increasing and seriously deteriorating the quality of life of patients [1, 2]. Short-segment (one- or two-level) posterior lumbar interbody fusion (PLF) surgery with or without depression is an important way to treat lumbar degenerative diseases such as lumbar disk herniation (LDH), lumbar spinal stenosis, and lumbar spondylolisthesis [3]. Age is a risk factor for increased incidence of postoperative complications after PLF; however, age is not associated with worse patient-reported outcomes [4]. Due to the presence of multimorbidity and polypharmacy, patients with age 75 and older are at a higher risk for postoperative adverse events, which increases the costs of hospitalization [5]. Efforts are needed to accelerate recovery after surgery and improve these patient's clinical outcomes and experience.

Poor pain control is associated with patients' dissatisfaction [6], postoperative complications [7], and excessive opioid consumption [8]. Patient-controlled analgesia (PCA) and perioperative multimodal pain management (PMPM) (also known as multimodal analgesia) relive unnecessary suffering after fusion surgery [9]. PCA is a conventional method that allows the patients to self-administer intravenous opioid medication to control pain [10]. Perioperative opioid use was associated with gastrointestinal complications [8, 11], more extended hospital stays [12], and long-term opioid use [13] after surgery. Multimodal pain management involves a combination of acetaminophen, pregabalin, gabapentin, cyclooxygenase-2 (COX-2) inhibitors, steroids, and neuraxial anesthesia with different mechanisms of action to reduce the use of opioids and the incidence of opioid-related adverse events [14]. Since Kehlet et al. [15] proposed the effects of multimodal analgesia, multimodal pain management had been implemented in animal studies and perioperative pain control. Durand et al. [16] found that multimodal analgesia was more effective in long-term pain management following castration in sheep. Coutens et al. [17] also found that the combination of morphine with ketamine or ketoprofen produced antinociceptive responses in animals with severe nociceptive acute pain induced by a closed tibial fracture.

At present, despite great advances in medicine and infusion devices in recent decades, opioids remain the primary drug to achieve adequate pain control. Given the side effects of opioids, effective multimodal medication regimens are needed to reduce postoperative opioid use and improve outcomes without increasing pain levels in older patients. Previous studies had demonstrated the associations between PMPM and outcomes including cost reduction, less morphine consumption, shorter length of hospitalization, and lower complications rates in various patient cohorts with an average age range of 50–70 years [9, 18–21]. However, few studies reported PMPM implementation in older patients undergoing lumbar fusion surgery. To our knowledge, this is the first report on the role of PMPM in patients aged 75 and older. Our primary aim was to compare the efficiency of our multimodal pain management program (i.e., reducing postoperative pain levels and opioid use during hospitalization) to a traditional pain management method, and the secondary aim was to evaluate the impact of multimodal pain management on length of hospital stays (LOS), postoperative complications, and readmission within three months in patients (aged 75 and older) undergoing short-segment lumbar fusion surgery.

2. Materials and Methods

This was a single-center retrospective study. We reviewed consecutive patients who underwent elective posterior lumbar fusion surgery for degenerative lumbar spinal stenosis, lumbar disc herniation, and lumbar spondylolisthesis. The same surgical team performed surgery from October 2017 to April 2021 in our hospital, and data from the electric medical records' system and prescription records were collected. Approval was obtained from the ethics committee of our hospital (permit data 2018.4.3; no. 2018086).

2.1. Inclusion and Exclusion Criteria. The inclusion criteria were as follows: (1) age 75 and older; (2) short-segment fusion surgery for lumbar degenerative disease. The exclusion criteria were as follows: (1) revision surgery; (2) emergency surgery; (3) lumbar tuberculosis and tumor; (4) incomplete perioperative clinical data.

2.2. Surgical Technique. We reviewed all patients who underwent depression with standard posterior lumbar fusion. Under general anesthesia, the patient was placed on the operating table in a prone position. The surgical approach was chosen depending on the planned range of decompression. A midline incision was made for all patients. For patients undergoing the traditional approach, the erector spinae muscles were separated from lumbar bony elements to expose the lamina and facet joints and transverse as needed for the levels that must be visualized. For patients undergoing open-Wiltse approach, only the plane between the multifidus and longissimus muscles was exposed by blunt dissection. The vertebral pedicle screws of surgical segments were implanted according to preoperative radiography and intraoperative fluoroscopy. The nerve roots were decompressed by hemilaminectomy or laminectomy according to the preoperative lumbar symptoms and radicular symptoms and MRI. After removal of the intervertebral disc, the bone graft was placed at the anterior part of the intervertebral space, the cage filled with the bone graft was also implanted into the intervertebral space, and at last, the remaining part of autogenous bone grafts from the decompression laminectomy was placed in the bone bed. Once the position and direction of implants were satisfactory, the wound was flushed, and the drainage tube was placed, incision was sutured layer by layer.

2.3. Perioperative Pain Management. An enhanced recovery after surgery (ERAS) protocol was applied in our institute from January 2019 with the multimodal analgesia as the only pain management method, and the patients were divided into a control group (from October 2017 to December 2018) in which patients were treated with the conventional PCA method and a case-matched PMPM group (from January 2019 to April 2021). Intraoperatively, both groups received general anesthesia with intravenous propofol and remifentanil according to patients' weight and operation time. In the PMPM group, all patients were given 150 mg of pregabalin 2 h before surgery. A mixture of 10 ml 2% lidocaine and 10 ml 1% ropivacaine was infiltrated around the surgical incision before incision and after skin closure. All patients received an intravenous cyclooxygenase-2 (COX-2) infusion on postoperative day 0 (POD0), POD1, and POD2. In the PMPM group, pain medications were prescribed according to the World Health Organization's (WHO) three-step analgesic ladder protocol. Oral or intravenous drugs were used to improve perioperative analgesia with the nonopioid drug as the first choice (which differed from the control group). In the control group, pain medications were prescribed according to the experience of the attending

physicians, and PCA (containing sufentanil and other agents in 100 mL saline) was used for anesthesia on POD0, POD1, and POD2 (Table 1).

2.4. Outcome Measure. We extracted age, gender, body mass index (BMI), comorbidities, primary diagnosis, American Society of Anesthesiologists score (ASA score), and visual analogue scale (VAS) of the leg and lower back. Operation-related variables from the electronic medical records' system and perioperative opioid prescription information from the prescription monitoring program were collected. The primary outcomes were additional oral opioids' doses and postoperative maximal VAS score on postoperative days 1, 2, and 3. The secondary outcomes were the day of first ambulation and postoperative complications within three months of surgery, postoperative LOS, and readmissions within 3 months. Two independent researchers analyzed all data.

2.5. Statistical Analysis. All continuous variables (e.g., age) were presented as mean ± standard deviation and analyzed using the two-tailed Student's *t*-test and one-way ANOVA. For nonnormally distributed data, data conversion or the Mann–Whitney test was used. Qualitative variables (such as gender) were represented as frequency (percentages) and analyzed using Fisher's exact or chi-square tests. SPSS software (version 22.0; SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Significance was set at $p < 0.05$.

3. Results

A total of 122 consecutive patients in the PMPM group received multimodal analgesia protocol at our institute. Baseline data for these patients were compared to the previous 122 consecutive patients (from October 2017 to December 2018), and no differences were observed in age, gender, BMI, and fused levels; therefore, further matching was not attempted. In the PMPM group, 62.3% of patients were female, with an average age of 77.9 years. The average age was 77.9 years in the control group, and 59.0% were female. No significant differences were observed between two groups in ASA scores or surgery-related variables (Table 2).

The pain level was defined as the maximal VAS score in the current study. The VAS scores were similar on POD1 between groups and were higher in the PMPM group than in the control group on POD2 (however, without reaching statistical significance). The maximal VAS score was significantly lower on POD3 in the PMPM group than the control group (3.0 ± 1.7 vs. 3.7 ± 2.0, $p < 0.001$) (Figure 1). No significant differences were observed in the frequency of additional oral opioid prescriptions between the two groups on POD1 and POD2; however, the frequency and percentages were significantly lower in the PMPM group than in the control group on POD3 (6.6% vs. 19.7%, $p = 0.001$) (Figure 2), and total oral opioid consumption was lower in the PMPM group (213 mg vs. 655 mg) (Table 3).

The rates of postoperative complications were lower in the PMPM group than the control group (25% vs. 49%, $p = 0.006$) during the 3-month follow-up. The most common complications in both groups were constipation and hypoalbuminemia. The PMPM group had a lower incidence than the control group for constipation (18% vs. 28.7%, $p = 0.049$) and hypoalbuminemia (13% vs. 38%, $P = 0.012$); however, there were no differences in other complications including surgical site infection (SSI) and urine retention. The rates of 3-month readmission and transferring to rehabilitation were similar between the groups, with shorter postoperative LOS (7.7 ± 3.9 vs. 9.0 ± 4.1, $p = 0.013$) and frequency of extended LOS (28% vs. 42%, $p = 0.023$) in the PMPM group. The average time of first bedside ambulation was 1.7 days in the PMPM group and 4.1 days in the control group after surgery (Table 4).

4. Discussion

Due to the presence of more significant risks of frailty and comorbidity, the incidences of postoperative complications and mortality are higher in patients aged 75 and older; for these reasons, careful perioperative management protocol of these patients is needed [22]. Postoperative pain control is an essential component of ERAS. Inadequate pain control is detrimental to early mobilization and recovery and is associated with increased LOS, costs of hospitalization, and incidence of postoperative complications [23, 24]. Although many nonopioid analgesics were prescribed for pain management after orthopedic surgery, the use of opioids continues to increase. Opioid overdoses are associated with a higher risk of death and postoperative complications, including constipation, nausea, vomiting, and urinary retention [8]. The minimization of postoperative opioid consumption relies on the comprehensive analgesia protocol and is critical in the context of the opioid epidemic. Traditional analgesia methods include nurse-controlled analgesia and PCA. PCA is effective for pain control; however, it increases the use of opioid and opioid-related side effects [10]. In the current study, we hoped to evaluate the effects of the multimodal analgesia pathway on pain control and other outcomes in older patients in China.

Multimodal analgesia is an alternative to PCA and is based on concurrent use of primary nonopioid agents. Nonsteroidal anti-inflammatory drugs (NSAIDs) are effective analgesics for musculoskeletal pain control; they inhibit cyclooxygenase (COX) isozymes and decrease prostaglandin generation. Acetaminophen produces an analgesic effect through peripheral and central COX inhibition like NSAIDs. Jirarattanaphochai and Jung [25] reviewed 17 randomized controlled trials and found that the addition of NSAIDs to opioid analgesics provided better pain control than opioid analgesics alone. However, a previous study had shown that NSAIDs had dose-dependent and duration-dependent effects on fusion rates, and high-dose COX inhibitors decreased fusion rates [26]. As structural analogues of gamma-aminobutyric acid, gabapentin and pregabalin could relieve acute and chronic neuropathic pain through reducing neuronal excitability. A systematic review and meta-analysis

Table 1: Two different perioperative pain management protocols.

	Control group	PMPM group	Time
Preoperatively	No intervention	Step one: acetaminophen and/or NSAIDs and/or gabapentin, PO Step two: opioids, PO	After admission, PRN PRN
Intraoperatively	— Propofol, IV Sufentanil, IV —	150 mg of pregabalin, PO Propofol, IV Sufentanil, IV A mixture of 10 ml 2% lidocaine and 10 ml 1% ropivacaine, local anesthesia	2 h before surgery During surgery During surgery Before incision and after skin closure
Postoperatively	PCA No intervention	Cyclooxygenase-2 (COX-2) inhibitors, IV Step one: acetaminophen and/or NSAIDs and/or gabapentin, PO Cyclooxygenase-2 (COX-2) inhibitors, IV Step two: opioids, PO	Day 0–day 2 PRN PRN PRN

PMPM: perioperative multimodal pain management; IV: intravenous; NSAIDs: nonsteroidal anti-inflammatory drugs; PO: peros (oral); PRN: as required.

Table 2: Baseline characteristics of patients in the two groups.

Variable	PMPM group ($n = 122$)	Control group ($n = 122$)	p value
Female, n (%)	76 (62.3)	72 (59.0)	$p = 0.600$
Age (yr)	77.9 (74.0–81.8)	78.7 (74.8–82.6)	$p = 0.230$
Height (cm)	161 (153–169)	161 (153–169)	$p = 0.075$
Weight (kg)	65.1 (54.8–75.4)	64.8 (54.1–75.5)	$p = 0.896$
BMI (kg/m^2)	25.1 (21.4–28.8)	24.9 (21.3–28.5)	$p = 0.723$
Comorbidities, n (%)			
Hypertension	86 (70)	82 (67)	$p = 0.580$
Coronary heart disease	30 (25)	32 (26)	$p = 0.769$
Diabetes disease	41 (33)	32 (26)	$p = 0.208$
Mental disease	2 (2)	4 (3)	$p = 0.320$
Digestive disease	8 (7)	7 (6)	$p = 0.790$
Old cerebral infarction	14 (11)	8 (7)	$p = 0.180$
Pulmonary disease	4 (3)	6 (5)	$p = 0.518$
Osteoporosis	17 (14)	18 (15)	$p = 0.855$
Preoperative opioid	7 (6)	9 (7)	$p = 0.605$
Diagnosis			$p = 0.900$
LSS	64 (52.4%)	63 (51.6%)	
LDH	39 (32.0%)	40 (32.8%)	
Lumbar spondylolisthesis	19 (15.6%)	19 (15.6%)	
VAS (lower back)	5.3 (3.2–7.4)	5.6 (3.7–7.5)	$p = 0.485$
VAS (leg)	7.3 (5.9–8.7)	7.2 (5.7–8.7)	$p = 0.718$
ODI	60.0 (46.6–73.4)	58.3 (44.8–71.8)	$p = 0.543$
Procedure-related			
Fusion level			$p = 0.433$
1	52 (42.6%)	46 (37.8%)	
2	70 (57.4%)	76 (62.2%)	
Operative time (min)	190.7 (131.9–249.5)	192.6 (145.2–240.0)	$p = 0.068$
EBL (ml)	240.9 (68.2–412.0)	279.0 (115.1–443.0)	$p = 0.549$

BMI: body mass index; LSS: lumbar spine stenosis; LDH: lumbar disc herniation; VAS: visual analogue scale; ODI: Oswestry Disability Index; EBL: estimated blood loss.

performed by Hurley et al. showed that patients receiving preoperative pregabalin had a significant decrease in postoperative neuropathic pain significantly [27]. Combining these drugs with different mechanisms of action has synergistic analgesic effects on postoperative pain and reduces the dose of single-agent doses.

PMPM is a comprehensive protocol including multiple analgesic strategies. Schotanus et al. [28] performed a randomized controlled trial and found that single-shot local infiltration analgesia with ropivacaine alone resulted in clinical acceptable adequate pain control in patients undergoing total knee arthroplasty. In the present study, preemptive analgesia and local infiltration analgesia were applied in patients of the PMPM group. Our PMPM protocol improved pain control on postoperative day 3, which was consistent with previous studies. Rajpal et al. [19] reported that preventative multimodal analgesia improved pain control on all four postoperative days in patients undergoing lumbar fusion surgery, and Choi et al. [9] found that multimodal analgesia reduced additional opioid use on postoperative day 2 without increasing pain levels in patients with one- or two-level posterior lumbar fusion surgery

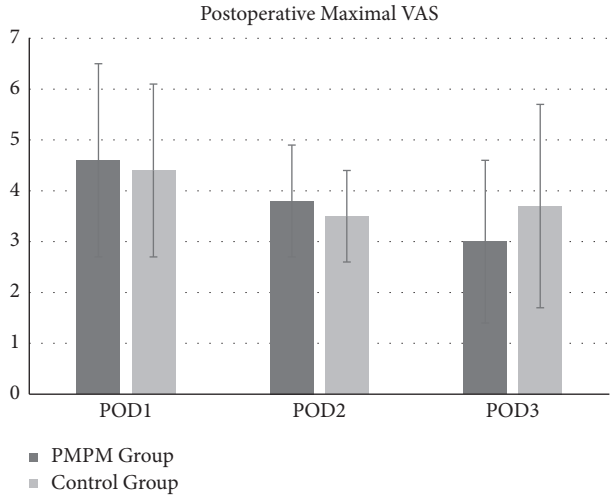

Figure 1: The maximal VAS score on POD1, POD2, and POD3 of patients in the PMPM group and control group.

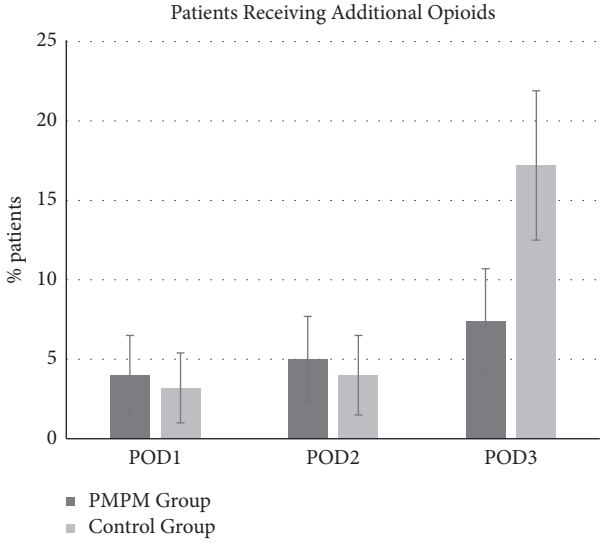

Figure 2: Percentages of patients receiving additional oral opioids on POD1, POD2, and POD3 for the PMPM group and control group.

Table 3: Postoperative pain level and opioid consumption.

	PMPM group ($n = 122$)	Control group ($n = 122$)	p value
Maximal VAS score			
POD1	4.7 (2.8–6.6)	4.6 (2.8–6.4)	$p = 0.690$
POD2	3.9 (2.8–5.0)	3.6 (2.6–4.6)	$p = 0.149$
POD3	3.0 (1.2–4.6)	3.7 (1.7–5.7)	$p = 0.001^*$
Additional opioid consumption, n (%)			
POD1	6 (4.9)	4 (3.3)	$p = 0.518$
POD2	6 (4.9)	5 (4.1)	$p = 0.758$
POD3	8 (6.6)	24 (19.7)	$p = 0.001^*$
Total oral opioid consumption (mg)	213	655	

VAS: visual analogue scale; POD1: postoperative day 1; POD2: postoperative day 2; POD3: postoperative day 3; $^* P < 0.05$.

compared to a PCA group. In our study, more physical activity might contribute to the slightly increased VAS score and additional opioids' prescription on POD3 in the PMPM group; the analgesic pump would be turned off on POD3, which might contribute to a significantly increased VAS score in the control group. A previous study reported that opioid requirements were lower in the older patients but were associated with more adverse events [29].

In the present study, we identified that the PMPM group had less use of opioids without increasing the level of

Table 4: Other outcomes of the two groups.

	PMPM group ($n = 122$)	Control group ($n = 122$)	p value
Postoperative LOS	7.7 (3.8–11.6)	9.0 (4.9–13.1)	$p = 0.013^*$
Extended LOS, n (%)	35 (28)	52 (42)	$p = 0.023^*$
The day of first ambulation	1.7 (0.8–2.7)	4.1 (2.4–5.8)	$p = 0.001^*$
Complications	30 (25%)	60 (49%)	$p = 0.006^*$
Cardiovascular disease	1 (1%)	2 (2%)	$p = 0.561^*$
Acute cerebral infarction	0	0	
Delirium	1 (1%)	2 (2%)	$p = 0.561$
SSI	5 (4%)	8 (7%)	$p = 0.392$
Pneumonia	2 (2%)	1 (1%)	$p = 0.561$
Hematoma	1 (1%)	2 (2%)	$p = 0.561$
DVT	3 (2%)	3 (2%)	$p = 0.100$
Urinary tract infection	2 (2%)	3 (3%)	$p = 0.006$
Nausea/vomiting	6 (4.9%)	15 (12.3%)	$p = 0.006$
Retention of urine	1 (1%)	4 (3%)	$p = 0.175$
Constipation	22 (18%)	35 (28.7%)	$p = 0.049^*$
Hypoalbuminemia	28 (13%)	46 (38%)	$p = 0.012^*$
The rate of readmission, n (%)	2 (2%)	7 (6%)	$p = 0.089$
Transfer to rehabilitation center, n (%)	2 (2)	6 (5)	$p = 0.150$

LOS: length of stay; SSI: surgical site infection; DVT: deep vein thrombosis; $^* p < 0.05$.

postoperative pain and incidence of severe complications in patients (75 years or older). Compared with the control group, the incidences of postoperative complications in the PMPM group were lower (especially opioid-related complications, such as postoperative constipation and nausea/vomiting). The use of opioid has a suppressive effect on the respiratory center and provoked nausea and vomiting by activation of central chemoreceptors. Poor pain control is also associated with postoperative complications [7]. The reduction of opioid use and adequate pain control may contribute to a low incidence of opioid-related complications [8, 14]. There was no difference between the groups in deep venous thrombosis, urinary tract infections, and wound infections. A retrospective study conducted by Pirkle et al. [30] found that chronic opioid use was associated with surgical wound infections; however, the underlying mechanisms for this observation remain unclear. The present study found that the multimodal analgesia pathway was associated with less postoperative hypoproteinemia. The reasons for this result might be as follows: firstly, patients in the PMPM group had a lower risk for gastrointestinal complications after surgery, and secondly, improved pain control may make patients feel more at ease than the control group. Our PMPM program achieved the goal of early mobilization without increasing postoperative pain levels. A retrospective study found that early ambulation was associated with decreased postoperative adverse events [31]; in our study, most patients were more likely to ambulate on POD1 in the PMPM group and on POD4 in the control group. Previous studies demonstrated an association between opioid agonists and serious postoperative complications following orthopedic procedures [32, 33]. The safety of PMPM had been validated in other studies; the rates of respiratory depression, acute renal failure, and central nervous system complications were not higher in the PMPM group than in the non-PMPM group after spinal surgery and total knee arthroplasty [21, 34]. In the present study, the rates of postoperative delirium, acute myocardial infarction, and acute cerebral infarction were similar between groups.

Because of the higher risk for extending postoperative LOS in patients aged 75 and older, the average LOS of patients in our study was more prolonged than shown in other studies; however, patients in the PMPM group had a shorter postoperative LOS. Tank et al. [12] found that opioid dependence was associated with prolonged LOS following lumbar fusion. Our multimodal analgesia protocol combined opioid and nonopioid analgesic mechanisms to achieve additive or synergistic effects on pain control. ERAS pain management protocols emphasize a multidisciplinary and comprehensive approach across the operative episode to enhance postoperative recovery and minimize opioids' consumption [14]. A previous study showed that ERAS reduced LOS and hospital costs significantly in older adults [25]; however, little attention has been paid to the contribution that ERAS and multimodal analgesia might make to achieving the same goals considerably in older patients (aged 75 or older). In the present study, we identified that PMPM resulted in clinical acceptable adequate pain control in patients undergoing short-segment fusion surgery with less opioids' consumption, which contributed to maximization of early mobilization and recovery in older patients.

Our PMPM strategy included preemptive analgesia and multimodal analgesia and ensured that the nonopioid agent was preferentially used for postoperative pain control according to the three-step analgesic ladder protocol. A randomized placebo-controlled study conducted by Fujita et al. [36] showed that administration of 150 mg of pregabalin before spine surgery decreased morphine consumption and postoperative pain intensity, but Trung Kien et al. [37] found that preoperative pregabalin combined with celecoxib orally had a good preemptive analgesic effect in lumbar spine surgery. Vasigh et al. [38] also showed that the effect of gabapentin plus celecoxib on pain was better than gabapentin alone after laminectomy. Further research

should attempt to establish a better combination of preemptive analgesia and nonopioid analgesia based on recent advancements in analgesics and synergistic effects of various narcotics.

There are several limitations to the present study. First, this was not a randomized controlled study and was subject to inherent limitations associated with retrospective analyses; nevertheless, it is unethical to perform a randomized controlled study, given that opioids have been proven to be correlated with numerous adverse events. Second, only the impact of multimodal analgesia on pain levels and opioid use on POD1, POD2, and POD3 were evaluated. The VAS scores or opioid prescription doses were not acquired after discharge. Longer follow-up is needed to determine the long-term effects of the PMPM protocol. The ways of pedicle screw implantation and the procedures of surgical decompression have an impact on postoperative lower back pain; however, we did not have a detailed record of surgical approach of each individual. Despite these limitations, our retrospective review and analysis of a prospectively collected database was the first to evaluate the effect of multimodal analgesia on patients aged 75 years and older.

5. Conclusions

This study demonstrates that the PMPM protocol is effective in pain control and reducing additional opioid consumption when compared with conventional analgesia, even for patients with age 75 and older, and these improvements occur with a lower incidence of postoperative complications within three months after PLF surgery. The implementation of multimodal analgesia combined with nonopioid analgesia could be recommended for accelerating recovery after fusion surgery. Further research should attempt to establish better pain management protocol-based recent advancements in analgesics and synergistic effect of different narcotic drugs.

Data Availability

The underlying data supporting the results of this study could be obtained by contacting the corresponding author.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Authors' Contributions

Shuaikang Wang and Tongtong Zhang contributed equally to this work.

Acknowledgments

The authors would like to thank all participants who took part in this study. This research received grant from Beijing Municipal Medical Research Institute Public Welfare Development and Reform Pilot Project (Grant no. jingyiyan2019-2).

References

[1] T. M. O'Lynnger, S. L. Zuckerman, P. J. Morone, M. C. Dewan, R. A. Vasquez-Castellanos, and J. S. Cheng, "Trends for spine surgery for the elderly: implications for access to healthcare in North America," *Neurosurgery*, vol. 77, pp. S136–S141, 2015.

[2] S. Yang, F. Zhang, J. Ma, and W. Ding, "Intervertebral disc ageing and degeneration: the antiapoptotic effect of oestrogen," *Ageing Research Reviews*, vol. 57, Article ID 100978, 2020.

[3] P. Endler, P. Ekman, I. Berglund, H. Möller, and P. Gerdhem, "Long-term outcome of fusion for degenerative disc disease in the lumbar spine," *The Bone & Joint Journal*, vol. 101-B, no. 12, pp. 1526–1533, 2019.

[4] J. M. Khan, B. A. Basques, G. K. Harada et al., "Does increasing age impact clinical and radiographic outcomes following lumbar spinal fusion?" *The Spine Journal*, vol. 20, no. 4, pp. 563–571, 2020.

[5] S. Rosas, Z. O. Knio, A. K. Gowd, T. D. Luo, C. L. Emory, and T. J. O'Gara, "Cost and complications of single-level lumbar decompression in those over and under 75," *Spine*, vol. 46, no. 1, pp. 29–34, 2021.

[6] S. Chotai, A. Sivaganesan, S. L. Parker, M. J. McGirt, and C. J. Devin, "Patient-specific factors associated with dissatisfaction after elective surgery for degenerative spine diseases," *Neurosurgery*, vol. 77, no. 2, pp. 157–163, 2015.

[7] S.-D. Yang, W.-Y. Ding, D.-L. Yang et al., "Prevalence and risk factors of deep vein thrombosis in patients undergoing lumbar interbody fusion surgery," *Medicine*, vol. 94, no. 48, Article ID e2205, 2015.

[8] C. Cozowicz, A. Olson, J. Poeran et al., "Opioid prescription levels and postoperative outcomes in orthopedic surgery," *Pain*, vol. 158, no. 12, pp. 2422–2430, 2017.

[9] S.-W. Choi, H.-K. Cho, S. Park et al., "Multimodal analgesia (MMA) versus patient-controlled analgesia (PCA) for one or two-level posterior lumbar fusion surgery," *Journal of Clinical Medicine*, vol. 9, no. 4, Article ID 1087, 2020.

[10] A. A. Patel, C. T. Walker, V. Prendergast et al., "Patient-controlled analgesia following lumbar spinal fusion surgery is associated with increased opioid consumption and opioid-related adverse events," *Neurosurgery*, vol. 87, no. 3, pp. 592–601, 2020.

[11] M. E. Menendez, D. Ring, and B. T. Bateman, "Preoperative opioid misuse is associated with increased morbidity and mortality after elective orthopaedic surgery," *Clinical Orthopaedics & Related Research*, vol. 473, no. 7, pp. 2402–2412, 2015.

[12] A. Tank, J. Hobbs, E. Ramos, and D. S. Rubin, "Opioid dependence and prolonged length of stay in lumbar fusion: a retrospective study utilizing the national inpatient sample 2003–2014," *Spine*, vol. 43, no. 24, pp. 1739–1745, 2018.

[13] A. Hockley, D. Ge, D. Vasquez-Montes et al., "Predictors of long-term opioid dependence in transforaminal lumbar interbody fusion with a focus on pre-operative opioid usage," *European Spine Journal*, vol. 29, no. 6, pp. 1311–1317, 2020.

[14] E. C. Wick, M. C. Grant, and C. L. Wu, "Postoperative multimodal analgesia pain management with nonopioid analgesics and techniques: a review," *JAMA Surgery*, vol. 152, no. 7, pp. 691–697, 2017.

[15] H. Kehlet and J. B. Dahl, "The value of multimodal or balanced analgesia in postoperative pain treatment," *Anesthesia and Analgesia*, vol. 177, pp. 1048–1056, 1993.

[16] D. Durand, M. Faure, A. de la Foye, and D. des Roches, "Benefits of a multimodal analgesia compared to local

anesthesia alone to alleviate pain following castration in sheep: a multiparametric approach," *Animal*, vol. 13, pp. 2034–2043, 2019.

[17] B. Coutens, C. Derreumaux, F. Labaste et al., "Efficacy of multimodal analgesic treatment of severe traumatic acute pain in mice pretreated with chronic high dose of buprenorphine inducing mechanical allodynia," *European Journal of Pharmacology*, Article ID 172884, 2020.

[18] K. H. Thybo, D. Hägi-Pedersen, J. B. Dahl et al., "Effect of combination of paracetamol (acetaminophen) and ibuprofen vs either alone on patient-controlled morphine consumption in the first 24 hours after total hip arthroplasty: The PANSAID randomized clinical trial," *JAMA*, vol. 321, no. 6, pp. 562–571, 2019.

[19] S. Rajpal, S. L. Hobbs, E. L. Nelson et al., "The impact of preventative multimodal analgesia on postoperative opioid requirement and pain control in patients undergoing lumbar fusions," *Clinical Spine Surgery: A Spine Publication*, vol. 33, no. 3, pp. E135–E140, 2020.

[20] M. Haffner, A. M. Saiz, R. Nathe et al., "Preoperative multimodal analgesia decreases 24-hour postoperative narcotic consumption in elective spinal fusion patients," *The Spine Journal*, vol. 19, no. 11, pp. 1753–1763, 2019.

[21] C. Cozowicz, J. Bekeris, J. Poeran et al., "Multimodal pain management and postoperative outcomes in lumbar spine fusion surgery," *Spine*, vol. 45, no. 9, pp. 580–589, 2020.

[22] M. Umekawa, K. Takai, and M. Taniguchi, "Complications of sine surgery in elderly Japanese patients: implications for future of world population aging," *Neurospine*, vol. 16, no. 4, pp. 780–788, 2019.

[23] C. Thompson, D. G. French, and I. Costache, "Pain management within an enhanced recovery program after thoracic surgery," *Journal of Thoracic Disease*, vol. 10, no. S32, pp. S3773–S3780, 2018.

[24] B. Holm, M. T. Kristensen, L. Myhrmann et al., "The role of pain for early rehabilitation in fast track total knee arthroplasty," *Disability and Rehabilitation*, vol. 32, no. 4, pp. 300–306, 2010.

[25] K. Jirarattanaphochai and S. Jung, "Nonsteroidal antiinflammatory drugs for postoperative pain management after lumbar spine surgery: a meta-analysis of randomized controlled trials," *Journal of Neurosurgery: Spine*, vol. 9, no. 1, pp. 22–31, 2008.

[26] A. Sivaganesan, S. Chotai, G. White-Dzuro, M. J. McGirt, and C. J. Devin, "The effect of NSAIDs on spinal fusion: a cross-disciplinary review of biochemical, animal, and human studies," *European Spine Journal*, vol. 26, no. 11, pp. 2719–2728, 2017.

[27] R. Hurley, S. Cohen, K. A. Williams, A. J. Rowlingson, and C. Wu, "The analgesic effects of perioperative gabapentin on postoperative pain: a meta-analysis," *Regional Anesthesia and Pain Medicine*, vol. 31, no. 3, pp. 237–247, 2006.

[28] M. G. M. Schotanus, Y. F. L. Bemelmans, P. H. M. van der Kuy, J. Jansen, and N. P. Kort, "No advantage of adrenaline in the local infiltration analgesia mixture during total knee arthroplasty," *Knee Surgery, Sports Traumatology, Arthroscopy*, vol. 25, no. 9, pp. 2778–2783, 2017.

[29] V. Dagenais-Beaulé, J.-F. Tourigny, and L. Papillon-Ferland, "Opioid use and pain control in the elderly after elective or urgent orthopaedic surgery: a retrospective cohort study," *Clinical Drug Investigation*, vol. 39, no. 3, pp. 301–308, 2019.

[30] S. Pirkle, S. Reddy, S. Bhattacharjee, L. L. Shi, and M. J. Lee, "Chronic opioid use is associated with surgical site infection after lumbar fusion," *Spine*, vol. 45, no. 12, pp. 837–842, 2020.

[31] O. Adogwa, A. A. Elsamadicy, J. Fialkoff, J. Cheng, I. O. Karikari, and C. Bagley, "Early ambulation decreases length of hospital stay, perioperative complications and improves functional outcomes in elderly patients undergoing surgery for correction of adult degenerative scoliosis," *Spine*, vol. 42, no. 18, pp. 1420–1425, 2017.

[32] M. Boom, M. Niesters, E. Sarton, L. Aarts, T. W. Smith, and A. Dahan, "Non-analgesic effects of opioids: opioid-induced respiratory depression," *Current Pharmaceutical Design*, vol. 18, no. 37, pp. 5994–6004, 2012.

[33] R. D. Urman, A. K. Khanna, S. D. Bergese et al., "Postoperative opioid administration characteristics associated with opioid-induced respiratory depression: results from the PRODIGY trial," *Journal of Clinical Anesthesia*, vol. 70, Article ID 110167, 2021.

[34] P. L. Fu, J. Xiao, Y. L. Zhu et al., "Efficacy of a multimodal analgesia protocol in total knee arthroplasty: a randomized, controlled trial," *Journal of International Medical Research*, vol. 38, no. 4, pp. 1404–1412, 2010.

[35] B. Garg, N. Mehta, T. Bansal, S. Shekhar, P. Khanna, and D. K. Baidya, "Design and implementation of an enhanced recovery after surgery (ERAS) protocol in elective lumbar spine fusion by posterior approach," *Spine*, vol. 46, no. 12, pp. E679–E687, 2020.

[36] N. Fujita, M. Tobe, N. Tsukamoto, S. Saito, and H. Obata, "A randomized placebo-controlled study of preoperative pregabalin for postoperative analgesia in patients with spinal surgery," *Journal of Clinical Anesthesia*, vol. 31, pp. 149–153, 2016.

[37] N. Trung Kien, P. Geiger, H. V. Chuong et al., "Preemptive analgesia after lumbar spine surgery by pregabalin and celecoxib: a prospective study," *Drug Design, Development and Therapy*, vol. 13, pp. 2145–2152, 2019.

[38] A. Vasigh, M. Jaafarpour, J. Khajavikhan, and A. Khani, "The effect of gabapentin plus celecoxib on pain and associated complications after laminectomy," *Journal of Clinical and Diagnostic Research*, vol. 10, pp. UC04–UC08, 2016.

Hindawi
Pain Research and Management
Volume 2022, Article ID 6835219, 10 pages
https://doi.org/10.1155/2022/6835219

Research Article

Bibliometric and Visualized Analyses of Research Studies on Different Analgesics in the Treatment of Orthopedic Postoperative Pain

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Received 21 December 2021; Accepted 28 January 2022; Published 24 February 2022

Academic Editor: Sidong Yang

Background. Pain following orthopedic surgery has always been a critical issue, which caused great distress to the patients. Analgesics in the treatment of postoperative pain following orthopedic surgery have aroused great attention from scholars, and numerous studies have been published in recent years. Bibliometrics could assist scholars in understanding the scope of research topics better, identifying research focuses and key literature, and analyzing the development and trend of analgesics in the treatment of postoperative pain following orthopedic surgery. *Methods*. Literature data were retrieved from the Science Citation Index Expanded (SCI-E) of Web of Science (WOS) Core collection database. The articles from 1992 to December 2021 on analgesics in the treatment of postoperative pain following orthopedic surgery were recruited. The citation reports including the publication numbers, h-index, total citations, and average citations in terms of authors, organizations, and countries were obtained. Top 20 research directions, funds, and journals with the most publications were charted. The co-authorship relations in the analysis units of authors, organizations, and countries were analyzed by the online bibliometric tool and VOSviewer software. The author's keywords co-occurrence overlay map was visualized by the VOSviewer software. *Results*. A total of 406 articles were retrieved from 1992 to December 4th, 2021, with 11,655 times cited, average citations of 28.57 per item, and an h-index of 55. The most high-yield publication year, authors, organizations, countries, research directions, funds, and journals were 2020 ($n = 887$), Ilfeld BM from University of California San Diego ($n = 7$), University of California System ($n = 21$), the USA ($n = 178$), Anesthesiology ($n = 161$), National Institutes of Health (NIH), USA, and United States Department of Health Human Services ($n = 12$), and Anesthesia and Analgesia ($n = 29$), respectively. Similarly, co-authoring analysis of publications regarding on different analgesics showed that the authors and countries with the most co-authorship strength were Carr Daniel B (total link strength = 6) and the USA (total link strength = 30), respectively. The highest occurrence keywords were "postoperative pain" with 135 occurrences (total link strength = 784). The future research hotspots might be "acute pain," "outcomes," "oxycodone," "total hip," "replacement," and "United States." *Conclusion*. Analgesics in the treatment of postoperative pain following orthopedic surgery can be observed in this study by employing the online bibliometric tool and VOSviewer software, which established the relationship between the units of analysis. It can provide a meaningful resource with detailed information for orthopedic surgeons who would like to understand the trend in this field better. They can also benefit from the emphasis on citation count to carry out high-level research in the future.

1. Introduction

Postoperative pain has always been a problem plaguing clinical treatment. In addition to the pain of the incision, many other factors can also cause pain, especially following the orthopedic operations, such as periosteal irritation, swelling of the affected limb, increased bone fascia tension, postoperative compression bandaging, and external fixation

[1]. More importantly, pain after orthopedic surgery becomes more common and more severe. What is worse, pain can increase cortisol, blood sugar, tea phenolamine in the body, and tissue metabolism, which is not conducive to wound healing. Therefore, the management of postoperative analgesia following orthopedic surgery is very important [2].

There are more than 53 million records and 1.18 billion cited references in the Science Citation Index Expanded (SCI-E) of Web of Science (WOS) Core collection database, which is an important resource for scientific statistics and evaluation [3]. More frequent citations of the article play a more important role in the field [4]. A bibliometric analysis and visualization tool can effectively assess the thematic development of structural contents and help readers understand a field comprehensively [5].

However, no bibliometric research on different analgesics in the treatment of postoperative pain following orthopedic surgery has been performed. This study aims to outline the intellectual connections within the dynamic changing of scientific knowledge in orthopedic postoperative analgesia using the WOS Core Collection database and the VOSviewer software.

2. Methods

The literature data were retrieved through SCI-E of WOS Core Collection database, which is widely applied in bibliometric research using an advanced search strategy. The search query was "(((((TS = (Orthopedic OR Orthopedic Procedure OR Orthopedic Surgery OR Orthopedic Surgical Procedure)) AND TS = (Postoperative OR Postoperative Periods)) AND TS = (Pain OR Physical Suffering OR Ache)) AND TS = (Analgesics OR anodyne OR Analgesic Drugs OR Analgesic OR Analgesic Agents OR Antinociceptive Agents)) AND LA = (English) AND DT = (Article)." Timespan = all years. All articles were evaluated by two independent reviewers in order to confirm their relevance. Full records of all articles were searched on December 4th, 2021.

The trends of publications and citations were charted annually. The distribution of the bibliographic records per year in different countries was also obtained. The top 20 most cited articles were recorded and analyzed by the following information: first author, article title, journals of publication, year of publication, total number of citations, and average citations. The records, h-index, total citations, and average citations in terms of authors, organizations, and countries were tabulated directly. The top 20 research directions, funds, and journals with the most publications were charted. The co-authorship relations in the analysis units of authors, organizations, and countries were mapped by the online bibliometric tool (https://bibliometric.com/) and VOSviewer 1.6.11 software (Nees Jan van Eck and Ludo Waltman, 2019). The author's keywords co-occurrence overlay map was implemented by VOSviewer, setting the minimum occurrences of a keyword to 5 times.

3. Results

3.1. Publication Outlines. A total of 406 articles were retrieved in the SCI-E of WOS Core Collection database from 1992 to December 4th, 2021, with 11,655 times cited, average citations of 28.57 per item, and an h-index of 55. Figure 1 shows the annual publications and sum of times cited per year on analgesics in the treatment of postoperative pain following orthopedic surgery. The first article was published in 1992, and the year with the most publications ($n = 29$) was 2020. The citation started in 1992, and the year with the most times cited was 2020 ($n = 887$). The results showed a fluctuating increase year by year.

The USA had contributed 178 articles (43.842%) at the top. Canada was the second contributing country with 25 articles (6.157%), followed by England with 22 articles (5.419%) and France and Germany both with 20 articles (4.926%). China only ranked 9th with 13 articles (3.186%). Only two countries contributed articles in 1992. However, more and more countries published articles yearly, and the number of involved countries increased to ten in 2021. The USA dominates in this field almost every year. The distribution of the bibliographic records each year of the top 10 countries on analgesics in the treatment of postoperative pain following orthopedic surgery is shown in Figure 2.

3.2. Top 20 Most Cited Articles on Different Analgesics. This search collected a total of 406 articles between 1992 and 2021 from WOS. The top 20 most cited articles are given in Table 1, including first author, article title, journals of publication, year of publication, total number of citations, and average citations. The total citations of the top 20 articles ranged from 101 to 1013. The average citations of the top 20 articles ranged from 4.21 to 40.52. The most cited article had 1013 citations and was published in 1997 by Collins et al. [6], followed by Chung et al. [7] with 271 citations in 1997 and Sinatra et al. [8] with 252 citations in 2005. The first two published articles were by Laitinen and Nuutinen [9] and Baker [10] in February 1992, and the most recent articles were published in December 2021 by De Biase et al. [11] and Rajput et al. [12].

3.3. Contribution of Authors, Organizations, and Countries. There were 1,961 authors, 745 organizations, and 46 countries contributing to this field. Table 2 provides the top 5 high-yield authors (Ilfeld Brian M, Lauretti Gabriela Rocha, Carr Daniel B, Liu Spencer S, and Capdevila Xavier [13–17]), organizations (University of California System, Pennsylvania Commonwealth System of Higher Education Pcshe, Universidade De São Paulo, University of Pennsylvania, and Cleveland Clinic Foundation), and countries (the USA, Canada, England, France, and Germany), with the corresponding records, h-index, total citations, and average citations.

3.4. Contribution of Research Directions, Funds, and Journals. There were 37 research directions, 154 funds, and 174 journals contributing to this topic. Figure 3 shows the top 20 high-yield research directions, the top is Anesthesiology with 161 publications, followed by Neurosciences Neurology with 65 publications and Orthopedics with 55 publications. In the top 20 high-yield funds, National Institutes of Health

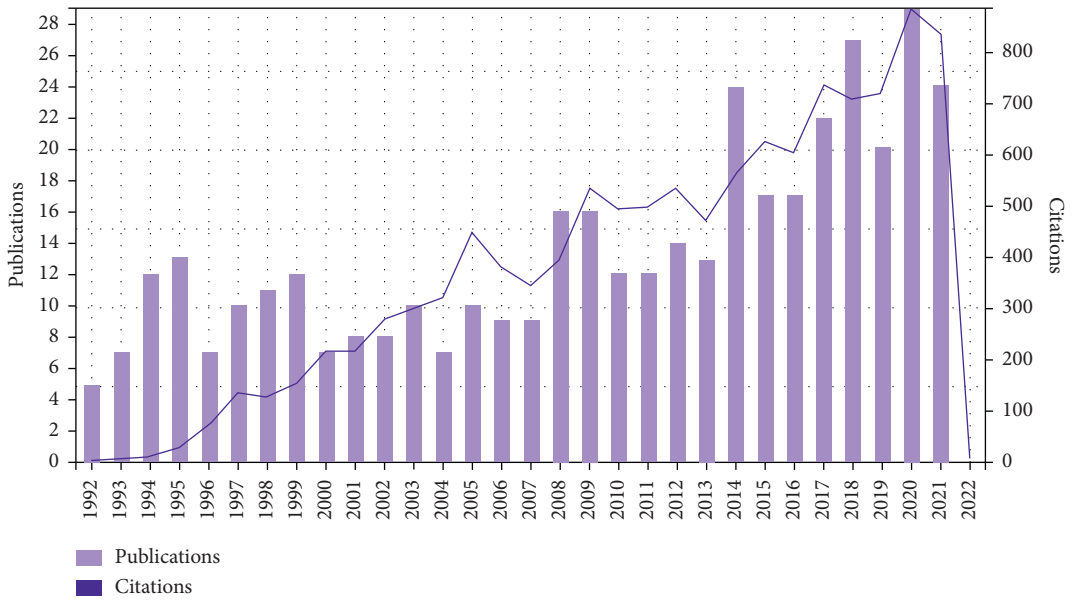

Figure 1: Annual publications (column chart) and sum of times cited per year (curve line) on analgesics in the treatment of orthopedic postoperative pain from 1992 to 2021.

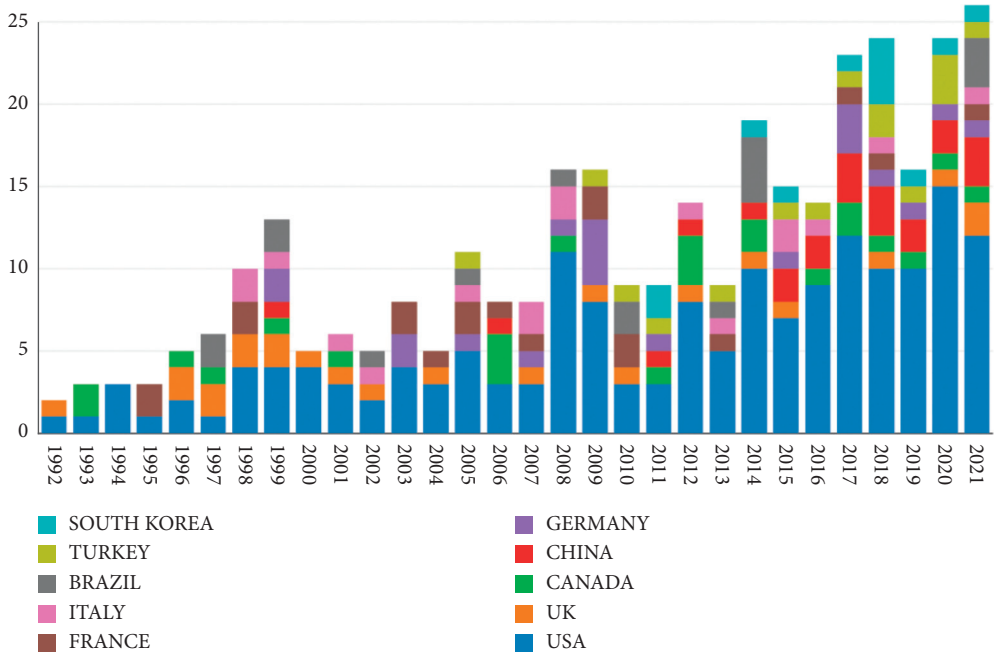

Figure 2: The distribution of the bibliographic records per year of the top 10 countries on analgesics in the treatment of orthopedic postoperative pain.

(NIH), USA, and United States Department of Health Human Services were tied for first place with 12 publications, followed by European Commission and NIH National Center for Advancing Translational Sciences (NCATS) both with 4 publications (Figure 4). Figure 5 shows the top 20 high-yield journals. Anesthesia and Analgesia had contributed 29 articles (7.108%) at the top. Journal of Clinical Anesthesia was the second contributing journal with 19 articles (4.657%), followed by Anesthesiology and British Journal of Anesthesia both with 12 articles (2.941%).

3.5. Co-Authoring Analysis of Publications regarding Different analgesics. The authors with the most co-authorship strength were Carr Daniel B, Daniels et al. [18], Viscusi et al. [19], and Lauretti and Reis [20] (Table 3). The strongest collaborative country was the USA with 4,411 citations (total link strength = 30), followed by France with 599 citations (total link strength = 9), Canada with 997 citations (total link strength = 8), Germany with 530 citations (total link strength = 8), and Sweden with 279 citations (total link strength = 7) (Figure 6).

Table 1: Top 20 most cited articles on analgesics in the treatment of orthopedic postoperative pain.

First author	Article title	Journal	Publication year	Total citations	Average citations
Collins SL	The visual analogue pain intensity scale: What is moderate pain in millimetres?	Pain	1997	1013	40.52
Chung F	Postoperative pain in ambulatory surgery	Anesthesia and Analgesia	1997	271	10.84
Sinatra RS	Efficacy and safety of single and repeated administration of 1 g intravenous acetaminophen injection (paracetamol) for pain management after major orthopedic surgery	Anesthesiology	2005	252	14.82
Feldt KS	Treatment of pain in cognitively impaired compared with cognitively intact older patients with hip-fracture	Journal of the American Geriatrics Society	1998	192	8.00
Lascelles BDX	Efficacy and kinetics of carprofen, administered preoperatively or postoperatively, for the prevention of pain in dogs undergoing ovariohysterectomy	Veterinary Surgery	1998	173	7.21
Reuben SS	Postoperative analgesic effects of celecoxib or rofecoxib after spinal fusion surgery	Anesthesia and Analgesia	2000	169	7.68
Briggs M	A descriptive study of the use of visual analogue scales and verbal rating scales for the assessment of postoperative pain in orthopedic patients	Journal of Pain and Symptom Management	1999	168	7.3
Rapp SE	Acute pain management in patients with prior opioid consumption: a case-controlled retrospective review	Pain	1995	161	5.96
Moore A	Deriving dichotomous outcome measures from continuous data in randomised controlled trials of analgesics	Pain	1996	158	6.08
Hebl JR	A preemptive multimodal pathway featuring peripheral nerve block improves perioperative outcomes after major orthopedic surgery	Regional Anesthesia and Pain Medicine	2008	153	10.93
White PF	The use of a continuous popliteal sciatic nerve block after surgery involving the foot and ankle: Does it improve the quality of recovery?	Anesthesia and Analgesia	2003	134	7.05
Liu SS	Patient-controlled epidural analgesia with bupivacaine and fentanyl on hospital wards: prospective experience with 1,030 surgical patients	Anesthesiology	1998	129	5.38
Gwirtz KH	The safety and efficacy of intrathecal opioid analgesia for acute postoperative pain: Seven years' experience with 5969 surgical patients at Indiana University Hospital	Anesthesia and Analgesia	1999	125	5.43
Dohoo SE	Postoperative use of analgesics in dogs and cats by Canadian veterinarians	Canadian Veterinary Journal-Revue Veterinaire Canadienne	1996	125	4.81
Gimbel JS	Efficacy and tolerability of celecoxib versus hydrocodone/acetaminophen in the treatment of pain after ambulatory orthopedic surgery in adults	Clinical Therapeutics	2001	114	5.43
Hernandez-Palazon J	Intravenous administration of propacetamol reduces morphine consumption after spinal fusion surgery	Anesthesia and Analgesia	2001	109	5.19
Collins SL	Seeking a simple measure of analgesia for mega-trials: Is a single global assessment good enough?	Pain	2001	108	5.14
Marino J	Continuous lumbar plexus block for postoperative pain control after total hip arthroplasty a randomized controlled trial	Journal of Bone and Joint Surgery-American Volume	2009	105	8.08
Grisneaux E	Comparison of ketoprofen and carprofen administered prior to orthopedic surgery for control of postoperative pain in dogs	Journal of the American Veterinary Medical Association	1999	101	4.39
Peduto VA	Efficacy of propacetamol in the treatment of postoperative pain: morphine-sparing effect in orthopedic surgery	Acta Anaesthesiologica Scandinavica	1998	101	4.21

Table 2: The top five high-yield countries, organizations, and authors on analgesics in the treatment of orthopedic postoperative pain from 1985 to 2021.

Category	Rank	Items	Records	H-index	Total citations	Average citations
Author	1	Ilfeld BM, University of California San Diego	7	5	226	32.29
	2	Lauretti GR, University of São Paulo	6	4	171	28.5
	3	Carr DB, Tufts University	5	5	77	15.4
	3	Liu SS, Virginia Mason Medical Center	5	5	220	44
	4	Capdevila X, CHU de Montpellier Anesthesiol and Crit Care Dept	4	4	197	49.25
Organization	1	University of California System	21	12	602	28.67
	2	Pennsylvania Commonwealth System of Higher Education Pcshe	9	5	160	17.78
	2	Universidade De Sao Paulo	9	5	206	22.89
	3	University of Pennsylvania	8	6	124	15.5
	4	Cleveland Clinic Foundation	7	3	120	17.14
Country	1	USA	178	36	4777	26.84
	2	Canada	25	18	1272	50.88
	3	England	22	16	2064	93.82
	4	France	20	13	667	33.35
	4	Germany	20	13	531	26.55

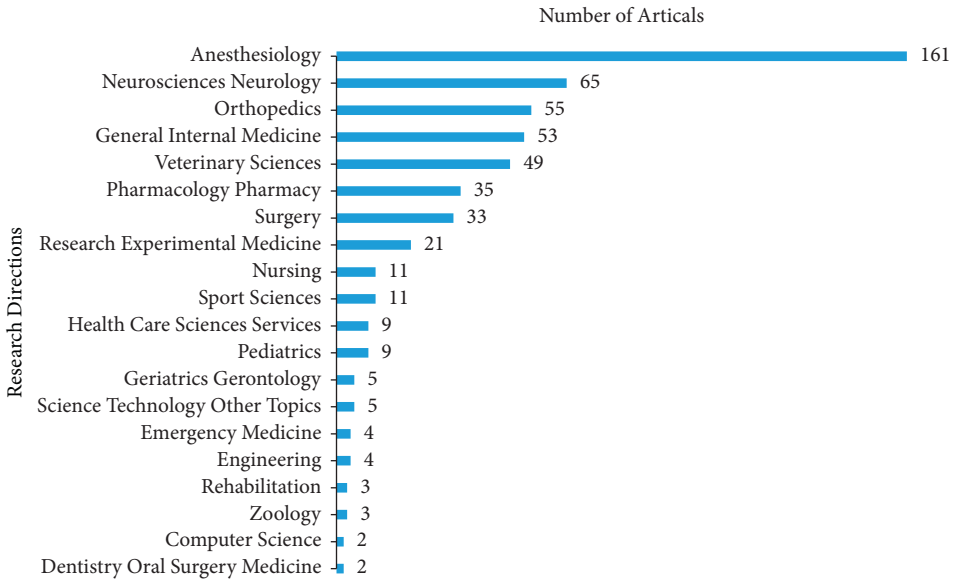

Figure 3: Top 20 research directions with the most publications on analgesics in the treatment of orthopedic postoperative pain.

3.6. Keywords Co-Occurrence. The overlay visualization of the top 162 co-occurrence keywords is shown in Figure 7. The highest occurrence keyword was "postoperative pain" with 135 occurrences (total link strength = 784), followed by "morphine" with 91 occurrences (total link strength = 616), "orthopedic-surgery" with 91 occurrences (total link strength = 582), "analgesia" with 85 occurrences (total link strength = 550), and "pain" with 83 occurrences (total link strength = 522). The most recent keywords were "acute pain," "outcomes," "oxycodone," "total hip," "replacement," and "United States."

4. Discussion

Bibliometrics mainly collects bibliographic databases and bibliometric features and uses mathematical and statistical methods to qualitatively and quantitatively analyze the relevant information of the literature, such as the distribution of countries, authors, journals, institutions, and funds. It also helps researchers grasp the development trend of this field intuitively and quickly [21, 22]. Using visual analysis software to analyze the literature further, researchers can find current research hotspots

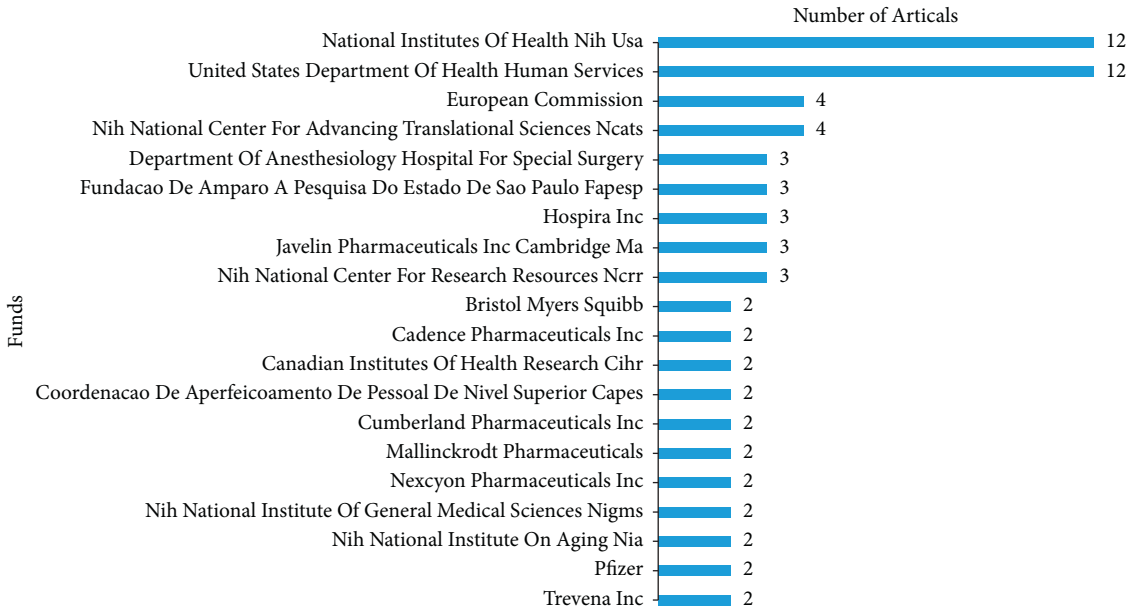

Figure 4: Top 20 funds for the most publications on analgesics in the treatment of orthopedic postoperative pain.

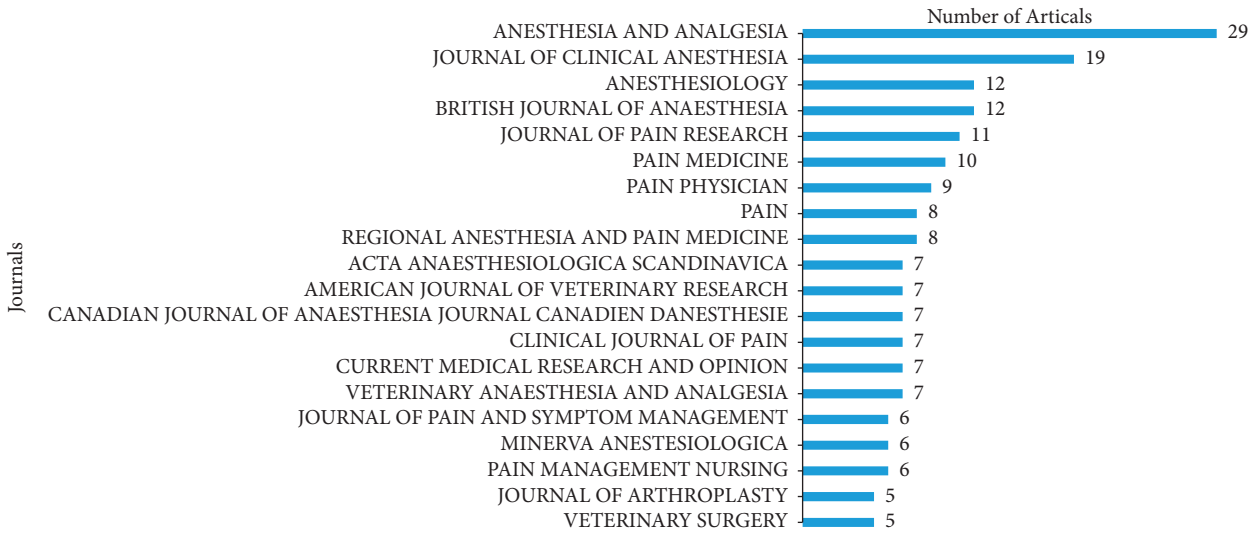

Figure 5: Top 20 journals with the most publications on analgesics in the treatment of orthopedic postoperative pain.

Table 3: Co-author analysis of publications regarding analgesics in the treatment of orthopedic postoperative pain.

Author	Number of articles	Citations	Total link strength
Carr DB	5	77	6
Daniels SE	4	124	6
Singla N	4	83	6
Lauretti GR	5	171	4
Reis MP	4	167	4
Turan A	4	60	3
Ilfeld BM	4	82	2
Minkowitz HS	4	169	1

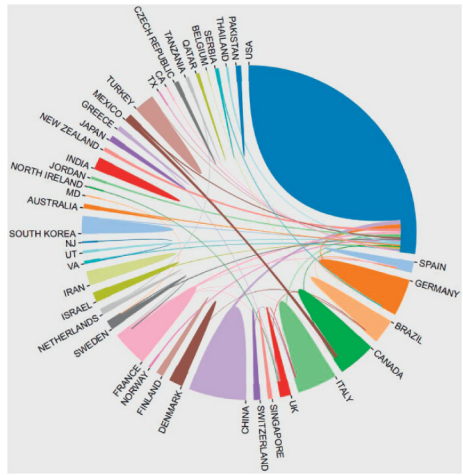

Figure 6: Country co-authoring analysis of publications regarding analgesics in the treatment of orthopedic postoperative pain.

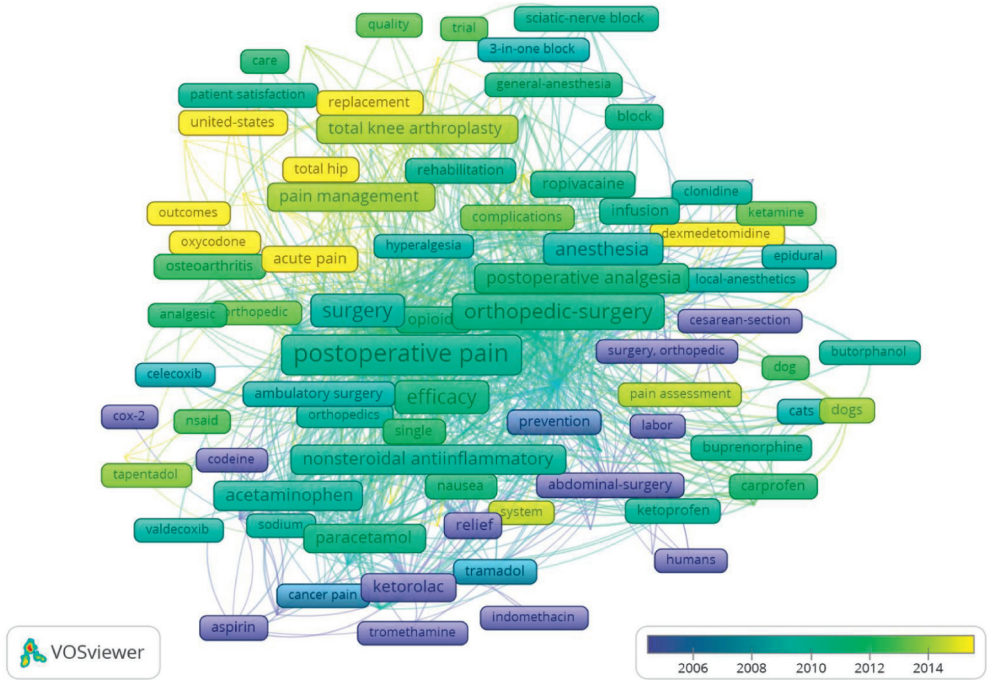

Figure 7: Keywords co-occurrence overlay mapping on analgesics in the treatment of orthopedic postoperative pain. Each frame indicates a keyword. The rainbow color marks the average publication year from violet (further year) to yellow (recent year) in the range of spectrum. The larger scale of a keyword is according to the higher frequency, while the closer distance between the two keywords represents the stronger co-occurrence.

and directions in this field. These methodologies have been widely applied in orthopedic research studies [23, 24].

4.1. Analysis on Publication Outlines. The popularity of a specific topic can be reflected by the number of publications. The study on analgesics in the treatment of postoperative pain following orthopedic surgery was initially published in 1992. The number of articles published fluctuated around ten from 1992 to 2007 and increased significantly from 2008 to 2021. Meanwhile, the quality of a specific topic can be judged by the number of citations [25]. There was an exponential growth in the citation times from 1992 to 2021. From Figure 1, we can learn that the future trend on analgesics in treating orthopedic postoperative pain looks promising.

As shown in Figure 2, the number of articles published from the USA is dominant in this field, followed by the UK and Canada. The article initially published from China was in 1999. The number of articles published from China is far less than that in the USA, which may be due to less attention paid to this field by Chinese scholars.

4.2. Analysis on Top 20 Most Cited Articles on Different Analgesics. Citation analysis is a systematic method to evaluate the influence of scientific research [26]. An article with more frequent citation can be recognized as more influential in the specific field [4]. As given in Table 1, the total citation of each article on different analgesics was more than 100. The most cited article was a clinical trial by Collins et al. in 1997 in Pain [6], focusing on visual analogue scales (VAS). The results indicate that if a patient records a VAS score over 30 mm at baseline, they would probably have recorded at least moderate pain on a 4-point categorical scale. After that, the VAS score has been more widely used by many scholars, which may explain why this article was ranked at the top with 1013 citations.

The second most cited article was a retrospective review by Chung et al. in 1997 in Anesthesia and Analgesia [7], focusing on the pattern of pain in ambulatory surgical patients and determining those factors that predict postoperative pain. The final results of the article showed that anesthesiologists give adequate analgesia by taking into consideration the body mass index of the patient, the duration of anesthesia, and the type of surgery. Better methods of postoperative pain treatment, such as using NSAIDs, regional techniques, and multimodal analgesia techniques, are needed. The third most cited article was a clinical trial by Sinatra et al. in 2005 in Anesthesiology [8], focusing on pain intensity, pain relief, and morphine use. The results indicate that intravenous acetaminophen, 1 g, administration over a 24-h period in patients with moderate to severe pain after orthopedic surgery could be well tolerated with rapid and effective analgesia.

The latest literature was a randomized controlled trial by Marino et al. in 2009 in Journal of Bone and Joint Surgery, paying attention to continuous lumbar plexus block for postoperative pain control after total hip arthroplasty. The conclusion was that continuous lumbar plexus and femoral blocks significantly reduce the need for opioids and decrease related side effects [27]. Another literature was a retrospective research by Hebl JR in 2008 in Regional Anesthesia and Pain Medicine, suggesting that a preemptive multimodal pathway featuring peripheral nerve block improves perioperative outcomes after major orthopedic surgery [28].

4.3. Analysis on Contribution of Authors, Organizations, and Countries. H-index refers to h articles in the literature that have been cited at least h times by other scholars, which is a measure to evaluate an author or country by the number of academic output and the index of the academic output level [29, 30]. The total number of references cited refers to the number of times a document has been cited in a certain period, an important indicator for evaluating individual national influence [31].

Among the top five high-yield authors, three come from the USA, Ilfeld BM from University of California San Diego, Carr DB from Tufts University, and Liu SS from Virginia Mason Medical Center. Similarly, four were in the USA among the top five high-yield organizations, including University of California System, Pennsylvania Commonwealth System of Higher Education Pcshe, University of Pennsylvania, and Cleveland Clinic Foundation. This may explain why the USA was ranked at the top one with a total of 178 records, which is far more than that in other countries (Table 2).

4.4. Analysis on Contribution of Research Directions, Funds, and Journals. As shown in Figures 3–5, anesthesiology, neurosciences, neurology, and orthopedics were the hot research directions, which will help orthopedic physicians to catch the right directions better.

In addition, National Institutes of Health (NIH), USA, and United States Department of Health Human Services were the most high-yield funds. Both of them belong to the USA. This was a good reason to explain why the USA was dominant in this field.

Identifying the dominant journals in a specific topic can help scholars construct scientific achievement. Anesthesia and Analgesia, Journal of Clinical Anesthesia, Anesthesiology, and British Journal of Anesthesia were the most high-yield journals. Paying more attention to high-yield journals can assist scholars in accessing the most authoritative knowledge framework and the orientation of manuscript submitting. The publishers of these journals belong to the USA, while the rest one is from the UK. Researchers may benefit from this important information and realize the deficiencies when high-level articles appear [32].

4.5. Analysis on Co-Authoring Analysis of Publications regarding Different Analgesics. VOSviewer was used for cooperation network analysis of authors, organizations, and countries [33]. Carr DB, Daniels SE, and Singla N were the authors with the most link strength. However, the most link strength was only six, which indicated that the cooperation between the authors was less (Table 3).

As shown in Figure 6, the strongest collaborative countries were the USA with 4,411 citations (total link strength = 30), followed by France with 599 citations (total link strength = 9) and Canada with 997 citations (total link strength = 8). The rest were mainly from developed countries. The result showed that the USA have the most cooperation with other countries.

4.6. Analysis on Keywords Co-Occurrence. VOSviewer was also used to generate a keyword co-occurrence map [34]. The highest occurrence keyword was "postoperative pain" with 135 occurrences (total link strength = 784), followed by "morphine" with 91 occurrences (total link strength = 616) and "orthopedic-surgery" with 91 occurrences (total link strength = 582). The most recent keyword was "acute pain," "outcomes," "oxycodone," "total hip," "replacement," and "United States," which indicated that these keywords might be the future research hotspots (Figure 7).

5. Limitations

As all we know, bibliometric analysis has been widely used to measure the impact of articles in recent years. However, there are still some limitations to this method. First and foremost, we only used the core collection of WOS to search literature, which is a single database. The more databases we use, the more information we can get and analyze. Other databases such as InCites and MEDLINE should be considered in the future. Second, the main language of WOS is English. Articles written in other languages are excluded, which means some relevant articles be omitted. Third, the citation number of each study is time-dependent. For different time points to search the articles, different citations may be obtained. However, the trend of citation number of each study is nearly the same.

This study has several advantages despite the limitations mentioned. It is the first study using the bibliometric method to search and identify literature on analgesics in the treatment of postoperative pain following orthopedic surgery, which has attracted increasing attention in recent years. Most importantly, our study provides valuable information for orthopedic surgeons and researchers in this field.

6. Conclusion

To conclude, we researched and analyzed the literature information regarding authors, organizations, countries, research directions, funds, and journals and analyzed the thematic development and future research hotspots. Our research observes the raising concern on analgesics in the treatment of orthopedic postoperative pain in recent years. Anesthesia and Analgesia, Journal of Clinical Anesthesia, Anesthesiology, and British Journal of Anesthesia are the most influential journals. The future research hotspots might be "acute pain," "outcomes," "oxycodone," "total hip," "replacement," and "United States."

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Disclosure

Yunzhong Cheng and Honghao Yang are the co-first authors of this study.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Yunzhong Cheng took part in data collection and wrote the article; Honghao Yang was responsible for data analysis and contributed all the figures; Aixing Pan reviewed and edited the article; and Li Guan and Yong Hai supervised the study. All authors have read and approved the content of the manuscript.

References

[1] H. Kehlet and J. B. Dahl, "Anaesthesia, surgery, and challenges in postoperative recovery," *Lancet*, vol. 362, no. 9399, pp. 1921–1928, 2003.

[2] M. H. Bourne, "Analgesics for orthopedic postoperative pain," *American Journal of Orthopedics (Belle Mead, N.J.)*, vol. 33, no. 3, pp. 128–135, 2004.

[3] W. Xu, H.-K. Choi, and L. Huang, "State of panax ginseng research: a global analysis," *Molecules*, vol. 22, no. 9, p. 1518, 2017.

[4] A. Eyre-Walker and N. Stoletzki, "The assessment of science: the relative merits of post-publication review, the impact factor, and the number of citations," *PLoS Biology*, vol. 11, no. 10, Article ID e1001675, 2013.

[5] L. Wang, W. Feng, J. Duan, and J. Liang, "Pharmacovigilance bibliometrics: visualizing thematic development in the category of pharmacology and pharmacy in Web of science," *Frontiers in Pharmacology*, vol. 12, Article ID 731757, 202.

[6] S. L. Collins, R. A. Moore, and H. J. McQuay, "The visual analogue pain intensity scale: what is moderate pain in millimetres?" *Pain*, vol. 72, no. 1-2, pp. 95–97, 1997.

[7] F. Chung, E. Ritchie, and J. Su, "Postoperative pain in ambulatory surgery," *Anesthesia and Analgesia*, vol. 85, no. 4, pp. 808–816, 1997.

[8] R. S. Sinatra, J. S. Jahr, L. W. Reynolds, E. R. Viscusi, S. B. Groudine, and C. Payen-Champenois, "Efficacy and safety of single and repeated administration of 1 gram intravenous acetaminophen injection (paracetamol) for pain management after major orthopedic surgery," *Anesthesiology*, vol. 102, no. 4, pp. 822–831, 2005.

[9] J. Laitinen and L. Nuutinen, "Intravenous diclofenac coupled with PCA fentanyl for pain relief after total hip replacement," *Anesthesiology*, vol. 76, no. 2, pp. 194–198, 1992.

[10] A. B. Baker, "Analgesia for day surgery," *Medical Journal of Australia*, vol. 156, no. 4, pp. 274–280, 1992.

[11] G. De Biase, S. E. Gruenbaum, J. L. West et al., "Spinal versus general anesthesia for minimally invasive transforaminal lumbar interbody fusion: implications on operating room time, pain, and ambulation," *Neurosurgical Focus*, vol. 51, no. 6, p. E3, 2021.

[12] K. Rajput, C. B. Reid, D. Yanez, D Shiwlochan, S Ohanyan, and R Chow, "Patterns of use of opioid sparing adjuncts for perioperative pain management of patients on chronic opioids," *Pain Physician*, vol. 24, no. 8, pp. 577–586, 2021.

[13] B. M. Ilfeld, A. Plunkett, A. M. Vijjeswarapu et al., "Percutaneous peripheral nerve stimulation (neuromodulation) for postoperative pain: a randomized, sham-controlled pilot study," *Anesthesiology*, vol. 135, no. 1, pp. 95–110, 2021.

[14] G. R. Lauretti, F. S. Veloso, A. T. Kitayama, and A. L. Mattos, "Low-dose spinal neostigmine further enhances the analgesic effect of spinal bupivacaine combined with epidural dexamethasone, following orthopedic surgery," *Journal of Research in Medical Sciences: The Official Journal of Isfahan University of Medical Sciences*, vol. 19, no. 9, pp. 801–806, 2014.

[15] T. Gan, N. Singla, S. E. Daniels et al., "Postoperative opioid sparing with injectable hydroxypropyl-β-cyclodextrin-diclofenac: pooled analysis of data from two Phase III clinical trials," *Journal of Pain Research*, vol. 20, no. 10, pp. 15–29, 2016.

[16] S. S. Liu, J. J. Bae, M. Bieltz, B. Wukovits, and Y. Ma, "A prospective survey of patient-controlled epidural analgesia with bupivacaine and clonidine after total hip replacement," *Anesthesia & Analgesia*, vol. 113, no. 5, pp. 1213–1217, 2011.

[17] X. Capdevila, C. Dadure, S. Bringuier et al., "Effect of patient-controlled perineural analgesia on rehabilitation and pain after ambulatory orthopedic surgery," *Anesthesiology*, vol. 105, no. 3, pp. 566–573, 2006.

[18] S. E. Daniels, T. J. Gan, D. A. Hamilton et al., "A pooled analysis evaluating renal safety in placebo- and active comparator-controlled phase III trials of multiple-dose injectable HPβCD-diclofenac in subjects with acute postoperative pain," *Pain Medicine*, vol. 17, no. 12, pp. 2378–2388, 2016.

[19] E. R. Viscusi, F. Skobieranda, D. G. Soergel, E. Cook, D. A. Burt, and N. Singla, "APOLLO-1: a randomized placebo and active-controlled phase III study investigating oliceridine (TRV130), a G protein-biased ligand at the μ-opioid receptor, for management of moderate-to-severe acute pain following bunionectomy," *Journal of Pain Research*, vol. 12, no. 12, pp. 927–943, 2019.

[20] G. Lauretti and M. Reis, "Postoperative analgesia and antiemetic efficacy after subarachnoid neostigmine in orthopedic surgery," *Regional Anesthesia and Pain Medicine*, vol. 22, no. 4, pp. 337–342, 1997.

[21] D. Xing, Y. Zhao, S. Dong, and J. Lin, "Global research trends in stem cells for osteoarthritis: a bibliometric and visualized study," *International Journal of Rheumatic Diseases*, vol. 21, no. 7, pp. 1372–1384, 2018.

[22] W.-J. Zhang, W. Ding, H. Jiang, Y.-F. Zhang, and J.-L. Zhang, "National representation in the plastic and reconstructive surgery literature," *Annals of Plastic Surgery*, vol. 70, no. 2, pp. 231–234, 2013.

[23] H. Wu, K. Cheng, Q. Guo et al., "Mapping knowledge structure and themes trends of osteoporosis in rheumatoid arthritis: a bibliometric analysis," *Frontiers in Medicine*, vol. 8, no. 8, Article ID 787228, 2021.

[24] K. Vishwanathan, S. B. S. Kambhampati, M. K. Patralekh, A. Vaish, and R. Vaishya, "Bibliometric analysis of the top 50 most cited publications of the Journal of Clinical Orthopaedics and Trauma," *Journal of Clinical Orthopaedics and Trauma*, vol. 22, no. 22, Article ID 101590, 2021.

[25] H. Lin, X. Wang, M. Huang et al., "Research hotspots and trends of bone defects based on Web of Science: a bibliometric analysis," *Journal of Orthopaedic Surgery and Research*, vol. 15, no. 1, p. 463, 2020.

[26] H. F. Moed, "New developments in the use of citation analysis in research evaluation," *Archivum Immunologiae et Therapiae Experimentalis*, vol. 57, no. 1, pp. 13–18, 2009.

[27] J. Marino, J. Russo, M. Kenny, R. Herenstein, E. Livote, and J. E. Chelly, "Continuous lumbar plexus block for postoperative pain control after total hip arthroplasty," *Journal of Bone and Joint Surgery American Volume*, vol. 91, no. 1, pp. 29–37, 2009.

[28] J. R. Hebl, J. A. Dilger, D. E. Byer et al., "A pre-emptive multimodal pathway featuring peripheral nerve block improves perioperative outcomes after major orthopedic surgery," *Regional Anesthesia and Pain Medicine*, vol. 33, no. 6, pp. 510–517, 2008.

[29] M. V. Root Kustritz and A. J. Nault, "Measuring productivity and impact of veterinary education-related research at the institutional and individual levels using the H-index," *Journal of Veterinary Medical Education*, vol. 47, no. 4, pp. 414–420, 2020.

[30] M. T. Kalcioglu, Y. Ileri, O. I. Ozdamar, U. Yilmaz, and M. Tekin, "Evaluation of the academic productivity of the top 100 worldwide physicians in the field of otorhinolaryngology and head and neck surgery using the Google Scholar h-index as the bibliometrics ranking system," *The Journal of Laryngology & Otology*, vol. 132, no. 12, pp. 1097–1101, 2018.

[31] Y. Le, S. Cao, M. Wang, X. Lin, and B. Qian, "A bibliometric and visualized analysis of nursing informatics competencies in China (2000–2020)," *Studies in Health Technology and Informatics*, vol. 15, no. 284, pp. 403–407, 2021.

[32] M. Yin, C. Xu, and W. Mo, "The 100 most cited articles on lumbar spinal stenosis: a bibliometric analysis," *Global Spine Journal*, vol. 1, no. 11, Article ID 2192568220952074, 2020.

[33] X. Mao, L. Guo, P. Fu, and C. Xiang, "The status and trends of coronavirus research," *Medicine (Baltimore)*, vol. 99, no. 22, Article ID e20137, 2020.

[34] A.-R. Kim and H. Y. Park, "Theme trends and knowledge-relationship in lifestyle research: a bibliometric analysis," *International Journal of Environmental Research and Public Health*, vol. 18, no. 14, p. 7503, 2021.

Hindawi
Pain Research and Management
Volume 2022, Article ID 8110896, 7 pages
https://doi.org/10.1155/2022/8110896

Research Article

Application of a Knowledge, Attitude, Belief, and Practice Model in Pain Management of Patients with Acute Traumatic Fractures and Alcohol Dependence

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Received 23 December 2021; Accepted 28 January 2022; Published 15 February 2022

Academic Editor: Sidong Yang

Objective. To evaluate the outcome of a knowledge, attitude, belief, and practice mode (KABP) in the pain management in patients with acute traumatic fractures complicated with alcohol dependence. *Methods*. Twenty-nine alcohol-dependent male patients with acute traumatic fractures and who received surgical treatment between January 2019 and December 2020 were included in this retrospective case-control study. The age range was 30–65 years (average 50.03 ± 7.94). *Fracture Type*. Six cases of spinal burst fractures and 23 cases of limb trauma fractures. Ten patients were treated with routine nursing (control group), and 19 patients were treated with pain management in KABP mode (experimental group). The control group received traditional pain care, including the conventional numerical rating scale (NRS) pain score system, with focus on symptomatic treatment. On this basis, the experimental group managed pain using KABP, including cognitive behavioral intervention, optimization programs, modification of personal beliefs, and behavior patterns. NRS, self-rated anxiety/depression scale (SAS), and quality of life (SF-36) scale were applied at admission, 1 day before surgery, and 3 months after surgery. *Results*. The perioperative NRS score of the KABP group was lower than that of the control group, and the postoperative anxiety levels improved. Discharge satisfaction was significantly higher than that in the control group ($p < 0.05$). There were behaviors promoting health in the experimental group, and five patients expressed abstinence behavior after discharge ($p < 0.05$). *Conclusion*. Patients with alcohol dependence represents a unique set of cases for perioperative pain management. To ensure patient safety, individualized pain management through the application of KABP can significantly reduce postoperative pain and promote the generation of healthy behaviors in patients.

1. Introduction

Perception and knowledge of pain increased substantially in the past two decades. In August 2002, at the International Pain Society (IASP)'s 10th World Congress on Pain in San Diego, California, USA, a consensus was reached that pain is the fifth vital sign, after blood pressure, body temperature, respiration, and pulse [1]. Alcohol is a psychoactive substance with toxic and addictive properties and fast distribution after absorption. Alcohol dependence is also commonly known as "alcohol addiction." A large number of patients with alcohol dependence on long-term drinking may present slow response, poor concentration and memory, and may seriously impair the nervous system [2]. Patients with alcohol dependence and acute trauma fractures, due to sudden interruption of alcohol stimulation after admission, demonstrate withdrawal symptoms [3].

Significant postoperative pain is often experienced in trauma-related orthopedic surgeries. Patients with alcohol dependence often experience greater pain, compared to the ordinary population [4], as conventional analgesic measures are often ineffective. Such patients often resist surgery, due to alcohol withdrawal symptoms or fear of significant postoperative pain. This often results in a series of physical and psychological problems. Therefore, individualized pain control and management are essential for patients with acute traumatic fractures and alcohol dependence. There are no clinical pain management protocols for patients with alcohol

dependence. Behavioral studies [5] show that there is a strong association between knowledge and behavior, but it is not entirely causal. A person's behavior is multifactorial, being related to knowledge, values, beliefs, living environment, and personal experience [6]. The knowledge, attitude, belief, and practice mode (KABP) hold that knowledge and information are the basis for establishing positive and correct beliefs and attitudes, thus promoting health-related behaviors, while beliefs and attitudes are the driving forces for behavior change [7]. To this end, we conducted a retrospective case-control study to evaluate the outcomes of KABP and traditional nursing modes in the perioperative pain management of patients with acute traumatic fractures complicated by alcohol dependence.

2. Materials and Methods

Inclusion criteria were as follows: (1) patients with alcohol dependence and demonstration of alcoholic withdrawal syndromes; (2) no history of compulsory abstinence therapy prior to admission; (3) no signs of delirium and cognitive impairment. The exclusion criteria were as follows: (1) patients with Alzheimer's disease, disturbance of consciousness, mental illness, and poor cooperation; (2) malignant tumor and severe hepatic and renal failure.

A total of 29 patients with acute traumatic fractures complicated by alcohol dependence were included, all of whom were men. The age ranged from 30 to 65 years (50.03 ± 7.94) years. Fracture type: six cases of spine burst fracture and 23 cases of limb trauma fracture. Ten patients were treated with conventional nursing (control group), and 19 patients were treated with pain management in the KABP mode (experimental group). There was no statistically significant difference in baseline data between the two groups ($P > 0.05$), indicating a good comparability (Table 1). Written informed consent was obtained from all patients. This study was approved by the Medical Ethics Committee of the First Affiliated Hospital of Soochow University.

2.1. Nursing Methods

2.1.1. Control Group. The routine orthopedic pain management mode was used. Upon admission, the bed nurse performed pain assessment using the NRS pain assessment scale. Analgesic treatments were performed according to the evaluation results. A stepwise analgesic drug use principle was adopted. All patients received general symptomatic treatment.

2.1.2. The Experimental Group. On the basis of conventional nursing, KABP mode was applied for all patients, including the following:

(1) Cognitive intervention: cognitive intervention is an effective measure to improve the quality of pain management and occupies an important position in the perioperative nursing of orthopedic surgery [8]. Preoperatively, medical staff should provide patients with a general understanding of the surgical procedure and timely communication with the patient, so that the patient can change the initial cognition of perioperative pain as well as correct cognition of the operation. The influence of alcohol on perioperative pain is shown in Figure 1. Therefore, KABP mode reduces the risk of postoperative complications and enhances patient recovery.

Cognitive intervention for alcohol withdrawal syndromes: Alcohol withdrawal syndrome mainly includes mental and somatic symptoms. Somatic symptoms generally occur within 7–48 hours after reducing alcohol intake or complete withdrawal, mainly demonstrating symptoms of tremor, sweating, tachycardia, elevated blood pressure, and other aspects, while the threshold of pain is reduced [9]. Psychiatric symptoms usually occur 48–72 hours after alcohol consumption is reduced, or withdrawn, and are characterized by severe confusion, loss of orientation, vivid daydream-like delusions and hallucinations, accompanied by anxiety, insomnia, and hypersympathetic activity. Cognitive intervention measures at this stage mainly include knowledge education and targeted treatment, explaining the withdrawal symptoms to patients, alleviating the occurrence of withdrawal symptoms, and reducing their anxiety and fear through rational use of drugs. Commonly used drugs include benzodiazepines, vitamins, and naloxone [10].

(2) Changes in beliefs and attitudes: beliefs come from four factors: knowledge, environment, happenstance, and successful experience [11]. Optimization of postoperative pain management is the main method to reduce patients' fear of surgery and refusal of treatment. Alcohol-dependent patients have reduced thresholds to pain and sensitivity to pain medications. Intense pain experience will bring detrimental emotions to patients, which will affect their attitude toward intervention, or even reject the implementation of intervention measures. For such patients, the optimization strategy recommended the principles of multimodal analgesia, advanced analgesia, and individualized analgesia (medication on demand instead of on-time).

The 2012 American Society of Anesthesiologists recommended that multiple modes of analgesia should be used as much as possible [12]. Multimode analgesia refers to the combined use of analgesic drugs. It also involves the use of different methods or mechanisms of action to achieve additive or synergistic effects without increasing complications. Simultaneously, the dosage of each drug is steadily reduced, as are the adverse reactions. The objective is to achieve the maximum balanced analgesic effect that is conducive to patients with surgical pain.

Advanced analgesia: the objective of preventive analgesia is to reduce or eliminate sensitization that is caused by harmful stimuli in the perioperative period. Preventive analgesia can inhibit peripheral and central sensitization, reduce postoperative pain intensity, and reduce the demand for analgesics [13].

Medications: medications that rapidly cross the blood-brain barrier to inhibit central sensitization, including selective COX-2 inhibitors.

Individualized analgesia: on-demand symptomatic treatment is transformed into on-time and on-volume analgesia treatment [14]. The treatment plan mainly includes

Table 1: General information.

Group	Cases	Age	Fracture type		Level of education				Daily alcohol intake (ml)
			All	Spine	College	Junior school	Primary school	Illiteracy	
Control group	10	48.50 ± 9.54	8	2	3	4	1	2	475 ± 118.43
Experimental group	19	50.84 ± 7.12	4	15	8	6	3	2	484 ± 162.49
T/χ^2	—	−0.749	0.004			1.040			−0.158
P	—	0.461	0.947			0.791			0.876

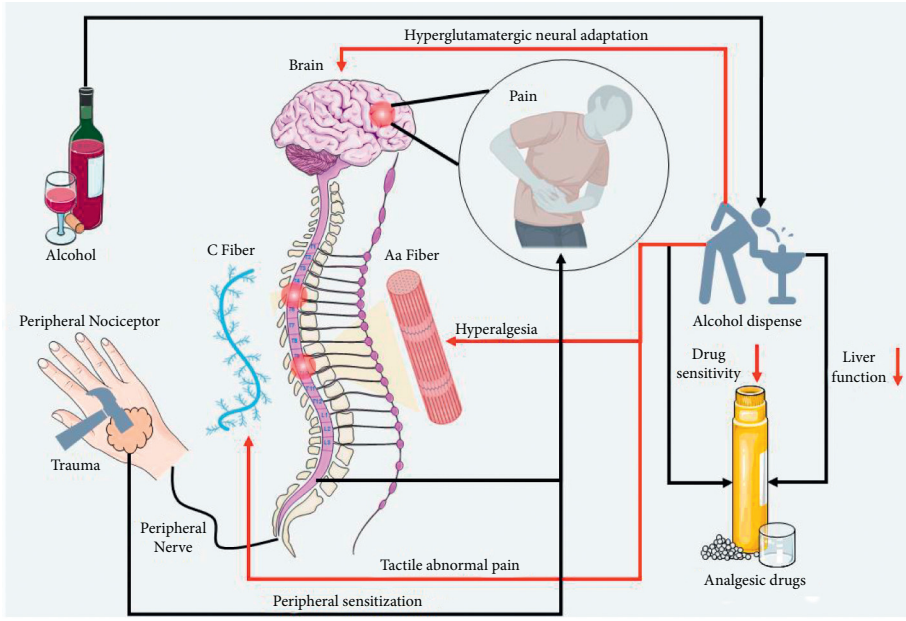

Figure 1: Alcohol and pain mechanisms.

the following: after 1-2 days of parecoxib sodium alone after mild pain, oral Celebrex 200 mg bid 5–7 days after PCA after moderate pain, combined with parecoxib sodium 2-3 days, oral Celebrex 200 mg bid for 5–7 days. If PCA is not used, tramadol plus parecoxib should be used for 2-3 days. PCA was used after severe pain surgery, and Celebrex 200 mg bid for 5–7 days after the combined use of parecoxib sodium for 3–7 days. A combination of peripheral nerve block, plexus block, and sustained-release opioid analgesics was used when necessary.

(3) Behavioral interventions: by increasing the cognitive behavior intervention, an optimized scheme to set up faith to change the behavior of patients was sought [15]. The experimental group was encouraged to participate in pain management through the intervention of pain and alcohol withdrawal cognition during the perioperative period, and self-pain score was performed. The analgesic program should be optimized to increase patients' confidence in pain control through successful analgesic experience or their own experience so that patients can carry out healthy behaviors.

On the premise of alleviating pain in patients, optimization of rehabilitation programs for patients. Functional exercise was performed under pain control, supplemented by dietary education, to improve the comfort of patients and enhance recovery.

2.2. Observation Indicators. (1) The NRS digital scoring scale was used to compare the pain scores of patients in the two groups on admission, 1 day before surgery, 1 day after surgery, and 3 months after surgery. (2) SAS anxiety/depression scale was used to compare the anxiety curve of the two groups at admission, 1 day before surgery, and 3 months after surgery. (3) The changes in health behaviors in the two groups were compared using the quality of life scale. (4) Nursing satisfaction was compared between the two groups. When the patients were discharged, a satisfaction questionnaire was issued. It included the following information: satisfaction with the intervention measures, functional exercise guidance, health education, and other contents, with a total score of 100 points, 80–100 points were very satisfied, 60–79 points were satisfied, and <60 points were not satisfied. Overall satisfaction was calculated as follows: (very satisfied + satisfied)/total number of cases × 100%.

2.3. Statistical Analysis. The application of SPSS 23.0, the Shapiro–Wilk method to normality test data, accorded with normal distribution, according to measurement data to mean + SD group comparison between the two independent samples t-tests; measurement data that did not conform to normal distribution were represented by M (Q1, Q3), and

the rank sum test was used for comparison of groups. Statistical data were expressed as percentages and the χ^2 test was used for comparison between groups. Statistical significance was set at $p < 0.05$.

3. Results

3.1. The NRS Scoring Scale. The NRS scoring scale was used at 1 day preoperatively, on the day of operation, 1 day, and 3 months postoperatively to compare between the control group and the experimental group. The results are given in Table 2.

There was no statistically significant difference between the two groups in pain score at admission and 1 day preoperatively. Significant differences were observed on the day of surgery and postoperatively. The NRS pain.

Scores were significantly lower than the control group, indicating that the KABP intervention is effective and can significantly reduce the patient's pain.

3.2. The SAS Anxiety/Depression Scale. The SAS anxiety/depression scale was used to compare the anxiety curve of the two groups on admission, 1 day before surgery, and 3 months after surgery. The results are given in Table 3 and Figure 2.

No statistical difference in psychological anxiety at admission was observed between the experimental and control groups. The application of cognitive intervention showed that anxiety level was significantly alleviated in the experimental group, compared to the control group 1 day before and 3 months after surgery ($p < 0.05$).

3.3. The SF-36 Health Status Questionnaire. The SF-36 health status questionnaire was used to evaluate the patients' quality of life from eight aspects, including physical function, physical role, physical pain, general health, vitality, social function, emotional function, and mental health. The quality of life assessment scale (SF-36) was used at admission and 3 months after surgery to compare the differences in quality of life between the two groups. The results are given in Tables 4 and 5.

The results showed that the scores of the two groups at admission were not statistically significant. However, due to fracture trauma, the quality of the patients' life in both groups decreased to varying degrees within three months of surgery. Comparatively speaking, the scores of the control group were lower, and the results were statistically significant. In comparison within the same group, the quality of life of the control group was significantly reduced, and the results were significant ($p < 0.05$). No significant decrease in SF-36 scores was observed in the experimental group ($p < 0.05$). In addition, in this study, there were five patients in the experimental group who took the initiative to express abstinence determination and/or action.

3.4. Comparison of Nursing Satisfaction. Comparison of nursing satisfaction between the two groups is given in Table 6.

The satisfaction of the experimental group was significantly higher than that of the control group, and the results were statistically significant ($p < 0.05$).

4. Discussion

The sharp increase of alcohol consumption in China since the 1980s and a series of social and economic problems were caused by excessive drinking [16]. Alcohol abuse is the fifth major risk factor for premature death and disability globally and is the leading cause of death and disability in developing countries. The WHO Global Action Plan for the Prevention and Control of Noncommunicable Diseases (2013–2020) formulated that the voluntary global target was to reach a 10% reduction in the harmful use of alcohol, as appropriate, within the national context [17]. However, through numerous literature reviews, the authors found that there is still a lack of large-scale national epidemiological investigations on the Chinese alcoholic population, and there are only investigations and studies on the organic damage caused by alcohol dependence, such as alcoholic hepatitis in foreign countries [18]. The foundation of alcohol control is weak, and a complete working system has not yet been formed.

4.1. Pain Management. Pain management remains a critical public health issue worldwide, particularly for orthopedic surgery patients. Patients with acute traumatic fractures and alcohol dependence require specific pain management techniques. However, these patients do not receive sufficient clinical attention, and ordinary conventional analgesic measures are often insufficient for pain relief. They often increase unpleasant or even painful emotional experiences, which leads to patients being depressed and refuse to get treated, thus affecting their rehabilitation. Clinical nursing work urgently needs to adopt safe and effective pain management modes for these patients. In this study, patients in the experimental group correctly understood pain and surgery through early cognitive intervention. Patients were encouraged to participate in pain management and self-pain assessment. Through the analgesia optimization strategy, patients' pain score in the perioperative period was significantly lower than that in the control group.

4.2. Knowledge, Attitude, Belief, and Practice Mode (KABP). The KABP divides the change of human behavior into three continuous processes: knowledge, generating belief, and forming behavior [18]. In clinical trials, the goal of the model is ensure patients' consistent compliance after considering their best interests and ensure the efficiency and quality of the trial. The results of this study indicate that the establishment of beliefs and change of attitudes is essential and directly related to the stability of patient compliance.

Table 2: Comparison of pain scores between the two groups (NRS) ($\bar{x} \pm s$).

Group	Number of cases	Admission	Preoperative 1 day	Surgery	Postoperative 1 day	Postoperative 3 months
Control group	10	5.10 ± 0.994	4.30 ± 0.675	5.80 ± 1.135	6.10 ± 1.101	4.30 ± 0.823
Experimental group	19	5.00 ± 1.00	3.47 ± 0.612	4.84 ± 1.068	4.95 ± 1.079	2.89 ± 1.197
t		0.256	3.339	2.248	2.717	3.310
P		0.800	0.002**	0.033*	0.011*	0.003**

Table 3: Comparison of patient anxiety.

Group	Number of cases	Admission			Preoperative 1 day			Postoperative 3 months		
		Mild	Moderate	Severe	Mild	Moderate	Severe	Mild	Moderate	Severe
Control group	10	2 (20)	6 (60)	2 (20)	0 (0)	5 (60)	5 (40)	1 (10)	6 (60)	3 (30)
Experimental group	19	4 (21.05)	11 (57.90)	4 (21.05)	3 (10.53)	14 (73.68)	2 (15.79)	13 (68.42)	5 (26.32)	1 (5.26)
χ^2			0.020			0.424			0.497	
P			0.994			0.041*			0.009**	

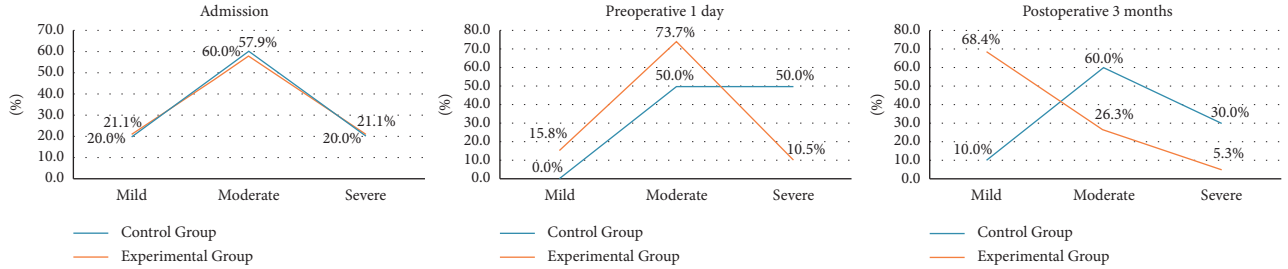

Figure 2: Comparison of patient anxiety.

Table 4: Comparison of quality of life scores between the two groups (SF-36).

Group	Number of cases	Admission	Postoperative 3 months
Control group	10	88.20 ± 7.21	77.50 ± 6.33
Experimental group	19	89.74 ± 10.47	88.37 ± 12.42
t		−0.414	−2.581
P		0.682	0.016

Table 5: Comparison of quality of life scores of patients in the same group (SF-36).

Group	Number of cases	Control group	Experimental group
Admission	10	88.20 ± 7.21	89.74 ± 10.47
Postoperative 3 months	19	77.50 ± 6.33	88.37 ± 12.42
t		3.527	0.367
P		0.002	0.716

Table 6: Comparison of satisfaction.

Group	Number of cases	Great satisfaction	Satisfaction	Dissatisfaction
Control group	10	3 (30)	5 (50)	2 (20)
Experimental group	19	16 (84.21)	2 (10.53)	1 (5.26)
χ^2			8.594	
P			0.014	

4.3. The KABP Pattern Is Beneficial to Patient Knowledge Mastery and Cognitive Improvement. Long-term, heavy drinking can lead to mental and physical dependence and cognitive dysfunction. Studies have shown that patients with alcohol dependence have impaired cognitive functions (e.g., memory, visual space, and executive function),

whereas their general intelligence and familiar knowledge are relatively intact [19]. In this study, patients in the experimental group displayed improved cognitive level and reduced anxiety and fear through repeated cognitive reinforcement in the KABP mode. Regarding anxiety, between the control and experimental groups, there was no difference at admission, a significant difference before surgery, and a significant difference three months after surgery; this indicates that early and repeated interventions of knowledge, belief, and action modes are conducive to anxiety relief in patients.

4.4. The KABP Mode Is Conducive to the Establishment of Healthy Behaviors. Multidirectional communication is conducive to patients' understanding of knowledge and mastery of exercise methods. Under the encouragement and guidance of medical staff, it is easier to transform knowledge, methods, and beliefs into healthy behaviors. In this study, the change in patient anxiety, improvement of their sense of participation, and the degree of treatment cooperation indicate that the health education in the KABP mode make patients more receptive. According to the SF-36 health status scores, the quality of life in the experimental group did not significantly decrease three months after surgery, whereas the quality of life in the control group significantly decreased. In the later investigation, five patients in the experimental group took the initiative to express the willingness or action of abstaining from alcohol, reflecting the intervention's positive effect and promoting the establishment of patients' healthy behaviors.

4.5. The KABP Mode Is Conducive to Improving Patient Satisfaction. In this study, 30% of patients in the control group and 84.2% in the experimental group were highly satisfied. The education in the KABP mode takes the needs of patients as the starting point, attaches importance to communication and interaction with patients in the intervention process to significantly improve the degree of attention they feel, and increases patients' satisfaction with nursing work.

In conclusion, on the basis of ensuring safety, individualized pain management programs can significantly reduce patients' pain and promote the generation of healthy behaviors through the application of knowledge, belief, and action mode [20]. This study provides practical guidance for pain management in patients with acute traumatic fractures and alcohol dependence and lays a foundation for the study of surgical pain management in other special populations.

Data Availability

The data generated or analyzed during this study are included within the article.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

YD, HG, YQJ, and JZ conceptualized the study. YD, JZ, YH, and YQJ developed methodology. HG, ZYJ, and JZ investigated the study. Visualization: HG and JZ visualized the study. YD, HG, and ZYJ wrote the original draft. YQJ and JZ reviewed and edited the article. YD and HG contributed equally.

References

[1] J. R. Volpicelli, "Naltrexone in alcohol dependence," *Lancet (London, England)*, vol. 346, no. 8973, p. 456, 2019.
[2] M. T. Murray and J. Nowicki, Alcohol Dependence[M], 2020.
[3] A. Gb and D. Kaa, "A machine learning approach to risk assessment for alcohol withdrawal syndrome," *European Neuropsychopharmacology*, vol. 6, 70 pages, 2020.
[4] E. L. Zale, L. R. Larowe, and J. Boissoneault, "Gender Differences in Associations between Pain-Related Anxiety and Alcohol Use Among Adults with Chronic pain," *The American Journal of Drug and Alcohol Abuse*, vol. 18, pp. 1–9, 2019.
[5] M. T. Murray and F. Aleksandr, BEHAVIOROLOGY AND DIALECTICAL MATERIALISM: ON THE WAY TO DIALOGUE[M], 2015.
[6] M. Harrison, "Drinking behavior and risk factors related to the work place: implications for research and prevention," *The Journal of Applied Behavioral Science*, vol. 24, no. 4, 2016.
[7] P. Erwin and Bettinghaus, "Health promotion and the knowledge - attitude - behavior continuum -- science direct," *Preventive Medicine*, vol. 22, no. 2, pp. 475–491, 2004.
[8] H. Pushparaj and A. Bhatia, "Perioperative pain management for orthopedic and spine surgery," *Anesthesia & Analgesia*, vol. 129, 2019.
[9] Y. T. Kim, J. H. Shim, and S. Kim, "Diffusion tensor imaging analysis of subcortical gray matter in patients with alcohol dependence," *Applied Magnetic Resonance*, vol. 52, no. 1, 2021.
[10] J. R. Volpicelli, *Naltrexone in Alcohol Dependence*, Lancet, (London, England), 2019.
[11] P. Niraj, B. S. Glenn, and L. D. Scherer, "Evaluating the cognitive reflection test as a measure of intuition/reflection, numeracy, and insight problem solving, and the implications for understanding real-world judgments and beliefs," *Journal of Experimental Psychology. General*, vol. 148, no. 12, pp. 2129–2153, 2020.
[12] S. P. Parameters, J. L. Apfelbaum, and R. T. Connis, "Practice advisory for preanesthesia evaluation: an updated report by the American society of Anesthesiologists task force on preanesthesia evaluation," . *Anesthesiology*, vol. 116, no. 3, pp. 522–538, 2012.
[13] J. Simpson, X. Bao, and A. Agarwala, "Pain management in enhanced recovery after surgery (ERAS) protocols," *Clinics in Colon and Rectal Surgery*, vol. 32, no. 02, pp. 121–128, 2019.
[14] M. Echeverria-Villalobos, N. Stoicea, and A. B. Todeschini, "Enhanced recovery after surgery (eras): a perspective review of postoperative pain management under eras pathways and its role on opioid crisis in United States," *The Clinical Journal of Pain*, vol. 36, no. 3, p. 1, 2019.
[15] C.-Y. Hsu, H.-E. Liao, and L.-C. Huang, "Exploring smoking cessation behaviors of outpatients in outpatient clinics," *Medicine*, vol. 99, no. 27, Article ID e20971, 2020.
[16] E. Yakovlev: Alcohol Consumption and Mortality. 2019.

[17] B. Banerjee, Chapter-31 WHO Global Action Plan and Monitoring Framework for Prevention and Control of Non-Communicable Diseases[M], 2017.
[18] X. Gu and W. Cheng, "Chinese oncologists' knowledge, attitudes and practice towards palliative care and end of life issues," *BMC Medical Education*, vol. 16, no. 1, pp. 1–7, 2016.
[19] D. Stewart, H. Lu, and T. Doran, "Alcohol consumption and all-cause mortality: an analysis of general practice database records for patients with long-term conditions," *Journal of Epidemiology & Community Health*, vol. 71, no. 8, 2017.
[20] C. Angus, J. Brown, and E. Beard, "Socioeconomic inequalities in the delivery of Brief Interventions for smoking and excessive drinking: findings from a cross-sectional household survey in England," *BMJ Open*, vol. 9, no. 4, 2019.

Hindawi
Pain Research and Management
Volume 2022, Article ID 3353810, 8 pages
https://doi.org/10.1155/2022/3353810

Research Article

Comparison of Radiographic Reconstruction and Clinical Improvement between Artificial Cervical Disc Replacement and Anterior Cervical Discectomy and Fusion

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Received 15 November 2021; Accepted 22 December 2021; Published 24 January 2022

Academic Editor: Sidong Yang

Background. The surgical management of cervical degenerative disc degeneration (CDDD) has not reached a consensus. Artificial cervical disc replacement (ACDR) has been shown to be efficient in reducing symptoms after CDDD, although the topic remains highly controversial in this field. This study aimed to evaluate the effectiveness of ACDR on the treatment of CDDD on the aspect of radiographic reconstruction and clinical improvement compared with anterior cervical discectomy and fusion (ACDF). *Methods*. This was a retrospective comparative study with 47 patients who underwent single-level ACDR and 46 patients who underwent single-level ACDF. The radiographic reconstruction was assessed by the cervical sagittal alignment parameters, consisting of two aspects, distance and angle, such as cervical sagittal vertical axis (cSVA), cervical lordosis (CL), T1 slope (T1s), and intervertebral space height (ISH). The clinical improvement was assessed by patient-related outcomes (PROs), consisting of two aspects, relief of axial neck pain and recovery of cervical dysfunction, measured through the Visual Analogue Scale (VAS), Neck Disability Index (NDI), and Japanese Orthopedic Association (JOA). *Results*. Significant variations were achieved on aspects of radiographic reconstruction and clinical improvement after ACDR ($P < 0.05$), which were similar to that of the ACDF group ($P < 0.05$). A significantly larger postoperative range of motion (ROM) was found in patients less than 45 years of age in the ACDR group ($P < 0.05$). In addition, a significantly better postoperative JOA was found in patients with a preoperative ISH less than 4 mm in the ACDF group than that in the ACDR group ($P < 0.05$). Other than that mentioned above, no significant variations in radiographic and clinical outcomes were found between the two groups ($P > 0.05$). *Conclusions*. Overall, this study showed that a similar capability in terms of radiographic reconstruction and clinical improvement was found between the two methods. Specific concerns should be analyzed while choosing between an ACDR and an ACDF. It should be pointed out that, based on our experience, if the patient is younger, ACDR is recommended; for patients with preoperative ISH less than 4 mm, ACDF is more recommended.

1. Background

Myelopathy, radiculopathy, or both can be caused by cervical degenerative disc disease (CDDD) which can induce severe axial neck pain [1]. It has been decades since anterior cervical discectomy and fusion (ACDF) was first introduced and has been regarded as the gold standard procedure to treat CDDD [2–5]. Despite its proven success, ACDF may interfere with cervical sagittal alignment and lead to adjacent segment disease (ASD) [6, 7] due to a decreased range of motion (ROM) at the index level and an increased ROM at the adjacent segment [8–11].

With its improved preservation of the spinal kinematic, artificial cervical disc replacement (ACDR) has been offered as an alternative technique [12, 13], which is supported by both clinical and biomechanical research [14, 15]. In earlier research, ACDF was used as a control group to explore the efficacy of ACDR. However, even on this premise, the optimum treatment remains in dispute [16–24].

The cervical sagittal alignment has a crucial role in transferring axial loads, maintaining horizontal gaze and global spinal balance [25, 26]. It has been shown that dysfunction of the neck and severe axial neck pain is related to abnormal cervical sagittal alignment [27, 28]. To quantify the cervical sagittal alignment, the cervical sagittal vertical axis (cSVA), cervical lordosis (CL), T1 slope (T1s), intervertebral space height (ISH), etc. were assessed in previous research [6, 7, 25, 26]. However, the cervical sagittal alignment has been fiercely disputed, with some studies showing it to be closely associated with patient-reported outcomes (PROs) and others having ambiguous views on the matter [26].

It was, therefore, decided to compare the effect on the aspects of radiographic reconstruction and clinical improvement for patients with CDDD between ACDR and ACDF. The results were expected to be used to provide suitable guidance to surgeons and to assist the prescription for patients.

2. Methods

2.1. Study Design. The patients diagnosed with CDDD who underwent ACDR or ACDF performed by a single surgeon team from February 2016 to February 2019 in our center were screened for enrollment. All the medical records, radiographic examinations, and clinically functional outcomes were reviewed retrospectively. The present study was approved by the institutional review board of Beijing Chao-Yang Hospital, and written consent was obtained from all the patients preoperatively.

2.2. Inclusion and Exclusion Criteria. Inclusion criteria: (1) received either single-level ACDR or ACDF treatment in which the follow-up period was at least twelve months; (2) age: 18–65 years; (3) index level occurred between C3 and C7; and (4) conservative therapy with ineffectiveness.

Exclusion criteria: (1) traumatic injury; (2) tumor; (3) ossification of the posterior longitudinal ligament (OPLL); (4) autoimmune or metabolic bone disease such as ankylosing spondylitis and rheumatoid arthritis; (5) osteoporosis (T-score ≤ -2.5); (6) kyphotic deformity; and (7) prior surgery.

2.3. Surgical Indication and Procedure. The indications of ACDR were anterior cervical decompression was required for radiculopathy and/or myelopathy; the contraindications of ACDR were malalignment of the cervical spine, severe kyphosis, obvious instability, advanced age, and disc space collapse. Patients with the contraindication mentioned above underwent ACDF, whereas those without underwent ACDR [29, 30]. Also, the surgical procedure and details of ACDR (Mobi-C: Zimmer Biomet) and ACDF (Cage: Medtronic) in this study by the same surgeon team were in accordance with previous studies [14, 30–33].

2.4. Clinical Measurement. The clinical improvement was assessed by patient-related outcomes (PROs), consisting of two aspects: relief of axial neck pain evaluated by the Visual Analogue Scale (VAS) and recovery of cervical dysfunction assessed via the score of Neck Disability Index (NDI) and the Japanese Orthopedic Association (JOA) score. For the VAS and NDI, a decrease represents an improvement, whereas for the JOA, an increase indicates an improvement.

2.5. Radiographic Measurement. The radiographic reconstruction was assessed by the cervical sagittal alignment parameters, consisting of two aspects, distance and angle, such as cervical sagittal vertical axis (cSVA), cervical lordosis (CL), T1 slope (T1s), and intervertebral space height (ISH) (Figure 1). Preoperative and postoperative radiographs were obtained, as well as at the follow-up.

2.6. Statistical Analysis. Mean and standard deviation was used to represent results in the study. Student's *t*-test and ANOVA were utilized in this study. It was deemed statistically significant if the two-tailed $P < 0.05$. All statistical analyses were performed using GraphPad Prism 8.

3. Results

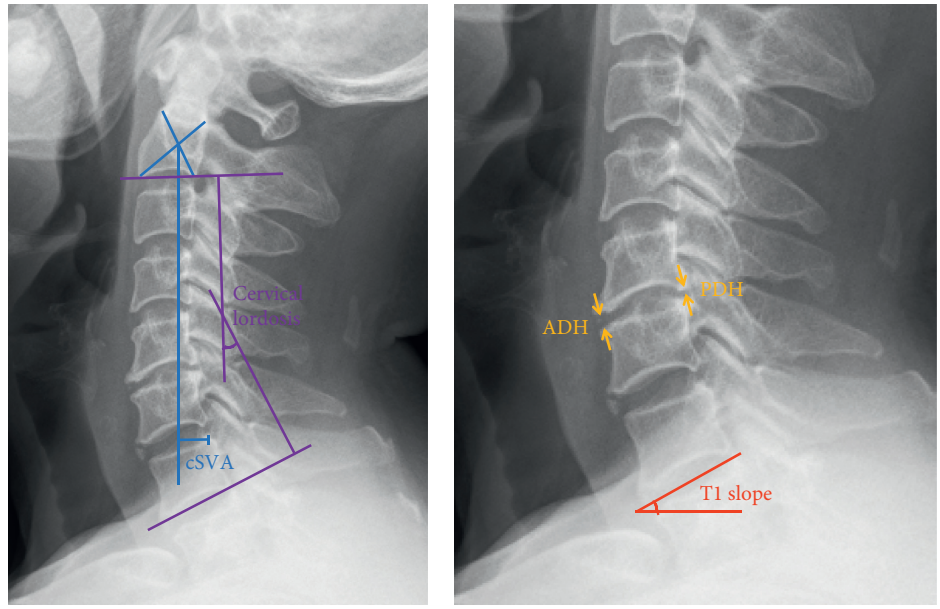
3.1. Patients' Baseline Characteristics. Demographic information and surgical data are reported in Table 1.

Patients in this study consisted of 93 individuals with complete baseline and follow-up data. The mean patient age was 48.73 ± 11.31 years, mean body mass index (BMI) was $25.30 \pm 3.903\,\text{kg/m}^2$, mean follow-up was 47.40 months (from 30 to 66 months) (Table 2), and 39% of patients were female. The series in the ACDR group was younger than that in the ACDF group ($P < 0.05$). A total of 62 patients had an index level of C5 to C6, who are most likely to develop CDDD based on previous research.

3.2. Clinical Improvement Outcomes. After surgery, both groups of patients received significant relief of neck pain and improvement of dysfunction of the cervical spine, and the results are summarized in Table 3.

The preoperative VAS was 7.617 ± 1.114 and 7.674 ± 1.055 in the ACDR and ACDF groups. Both of the two groups achieved significant pain relief to 1.511 ± 0.5053 and 1.435 ± 0.5437, respectively ($P < 0.05$). In addition, the preoperative NDI was 80.68 ± 5.129 and 79.30 ± 5.219 in the ACDR and ACDF groups, respectively. The value of NDI in the ACDR and ACDF groups decreased considerably at the follow-up to 26.26 ± 17.210 and 27.70 ± 14.250, respectively ($P < 0.05$). Furthermore, a similar clinical improvement result was found in the value of the JOA score. The JOA in the ACDR group improved from 6.120 ± 1.156 to 11.850 ± 1.609, and that improved from 6.554 ± 1.671 to 12.460 ± 1.807 in the ACDF group ($P < 0.05$). However, no significant differences were found between the two groups at the time point of the follow-up ($P > 0.05$).

3.3. Radiographic Reconstruction Outcomes. Radiographic reconstruction improved similarly in both two groups and is reported in Tables 4 and 5. Cervical alignment parameters



(a) (b)

Figure 1: Radiographic measurement of the cervical sagittal alignment parameters. (a) cSVA: the distance between the plumb line from the center of C2 and the superior posterior corner of C7; CL: the angle between C2 (the inferior endplate) and C7 (the inferior endplate); (b) T1s: the angle between T1 (the superior endplate) and a horizontal line; ISH: average of anterior disc height (ADH) and posterior disc height (PDH). Abbreviations: cSVA, cervical sagittal vertical axis; CL, cervical lordosis; T1s, T1 slope; ISH, intervertebral space height; ADH, anterior disc height; and PDH, posterior disc height.

Table 1: General information of the patients[a].

Variable	ACDR	ACDF	Total	P value
Number of cases	47	46	93	
Gender (female/male)	12/35	24/22	36/57	
Age (years)	45.68 ± 9.255	51.85 ± 12.43	48.73 ± 11.31	0.048
BMI (kg/m^2)	25.28 ± 3.860	25.33 ± 3.989	25.30 ± 3.903	0.95
Follow-up (months)	48.72 ± 10.39	46.04 ± 10.82	47.40 ± 10.63	0.23
Surgical level				
C3/4	6	6	12	0.62
C4/5	1	2	3	0.50
C5/6	28	32	62	0.26
C6/7	12	4	16	0.052

[a]Values are presented as mean ± standard deviation or number of cases. Abbreviations: ACDR, artificial cervical disc replacement; ACDF, anterior cervical discectomy and fusion.

Table 2: Age and postoperative ROM outcome[a].

Age	ACDR		ACDF	
	N	Postoperative ROM	N	Postoperative ROM
≤45	24	10.31 ± 3.499	23	7.282 ± 3.189
≥46	23	8.293 ± 2.573	24	6.590 ± 3.673
P value		0.0274[b]		0.5210

[a]Values are presented as mean ± standard deviation. [b]Significant difference between the age ≤45 group and age ≥46 group. Abbreviations: ROM, range of motion.

such as cSVA, CL, T1s, and ISH were significantly improved ($P < 0.05$). The follow-up also found that they were significantly improved than those before surgery ($P < 0.05$). Although a significant difference of cervical alignment parameters (cSVA, CL, T1s, and ISH) was found in each group at each time point, there were no significant differences between the two groups ($P > 0.05$).

Referring to motion preservation, ACDR was designed for the maintenance of ROM at the original. With no surprises, a significant improvement was found among all

Table 3: Pain relief and dysfunction improvement[a].

Group		ACDR	ACDF
VAS	Preoperative	7.617 ± 1.114	7.674 ± 1.055
	Follow-up	1.511 ± 0.5053	1.435 ± 0.5437
	P value (preop vs. follow-up)	<0.001[b]	<0.001[b]
NDI	Preoperative	80.68 ± 5.129	79.30 ± 5.219
	Follow-up	26.26 ± 17.210	27.70 ± 14.250
	P value (preop vs. follow-up)	<0.001[b]	<0.001[b]
JOA	Preoperative	6.120 ± 1.156	6.554 ± 1.671
	Follow-up	11.850 ± 1.609	12.460 ± 1.807
	P value (preop vs. follow-up)	<0.001[b]	<0.001[b]

[a]Values are presented as mean ± standard deviation or number of cases. [b]Significant difference compared with preoperative values. Abbreviations: VAS, Visual Analogue Scale; NDI, Neck Disability Index; JOA, Japanese Orthopedic Association.

Table 4: Cervical sagittal alignment parameters[a].

ACDR	Preoperative	Postoperative	Follow-up	P value (preop vs. postop)	P value (preop vs. follow-up)	P value (postop vs. follow-up)
cSVA (mm)	10.37 ± 3.816	7.906 ± 3.197	8.558 ± 3.312	0.0058[b]	0.0084[b]	0.0062[b]
CL (°)	15.97 ± 11.55	20.58 ± 12.31	19.00 ± 11.62	0.0014[b]	0.0056[b]	0.0062[b]
T1s (°)	20.44 ± 6.057	26.52 ± 4.954	24.79 ± 4.937	0.0022[b]	0.0055[b]	0.0051[b]
ISH (mm)	4.200 ± 0.7466	6.726 ± 1.071	6.100 ± 0.9377	0.0078[b]	0.0040[b]	0.0044[b]
ROM (°)	4.745 ± 2.253	10.29 ± 3.335	9.151 ± 3.133	0.0037[b]	0.0053[b]	0.0027[b]
ACDF	Preoperative	Postoperative	Follow-up	P value (preop vs. postop)	P value (preop vs. follow-up)	P value (postop vs. follow-up)
cSVA (mm)	12.59 ± 6.798	9.509 ± 6.582	10.40 ± 6.613	0.0085[b]	0.0090[b]	0.0018[b]
CL (°)	15.56 ± 8.636	21.92 ± 9.998	19.96 ± 9.166	0.0046[b]	0.0038[b]	0.0049[b]
T1s (°)	21.13 ± 5.696	27.72 ± 5.777	25.82 ± 5.477	0.0097[b]	0.0036[b]	0.0025[b]
ISH (mm)	4.229 ± 1.177	6.408 ± 1.344	5.770 ± 1.186	0.0056[b]	0.0015[b]	0.0086[b]
ROM (°)	5.467 ± 3.952	7.457 ± 3.797	6.846 ± 3.482	0.0157[b]	0.0793 0.0002[c]	0.4234 0.0011[c]

[a]Values are presented as mean ± standard deviation. [b]Significant difference between preoperative, postoperative, or follow-up values. [c]Significant difference between ACDR and ACDF. Abbreviations: cSVA, cervical sagittal vertical axis; CL, C2-7 lordosis; T1s, T1 slope; ISH, intervertebral space height; ROM, range of motion.

the time points (preoperative, postoperative, and follow-up) in the ACDR group ($P < 0.05$). However, the statistical improvement was only found from preoperative to postoperative in the ACDF group, no significant differences were found neither from postoperative to follow-up nor from preoperative to follow-up ($P > 0.05$). Furthermore, a statistical difference at the time point of postoperative and follow-up between the two groups was found, indicating that there was an advantage in ACDR compared with ACDF on the aspect of ROM maintenance, which was in line with our expectations.

4. Discussion

The cervical sagittal alignment has gained great attention as an important factor to determine axial neck pain and dysfunction of the cervical spine. Modifications to the cervical sagittal alignment might increase tiredness and neck discomfort [34, 35]. For this reason, it is important to maintain or reconstruct cervical sagittal alignment after spine surgery. This is also the reason why the cervical sagittal alignment has been used to evaluate the reconstruction of the cervical spine.

Except for the intrinsic difference between the above-mentioned two surgeries, the present study estimated the effect on cervical sagittal alignment and PROs of the ACDR versus ACDF and discovered that both the two methods could do well for the treatment of CDDD.

Regarding the aspect of the patient-related outcomes, the value of VAS, NDI, and JOA scores showed statistically significant improvement in both ACDR and ACDF groups which were in accordance with the findings of diverse kinds of ACDR studies. But the two groups were evenly matched in terms of this aspect in this study [36–41].

When it comes to determining cervical sagittal alignment, the value of cSVA is often used as a key metric. With C7 as the foundation of support, cSVA stands for cervical spine offset. In addition, postoperative cSVA >40 mm has been observed to be associated with poor PROs [42]. Furthermore, Iyer et al. believed that cSVA is an independent predictor of preoperative NDI [28]. Similarly, the present study found that preoperative ISH is associated with postoperative JOA.

It has to be said that the disadvantage of ACDR, in the beginning, is the inability to restore the sagittal curvature of the cervical spine. Kim et al. conducted retrospective research on the utilization of the ACDR prosthesis and

Table 5: Preoperative ISH and postoperative JOA outcome[a].

Preoperative ISH (mm)	ACDR		ACDF		P value
	N	Postoperative JOA	N	Postoperative JOA	
≤4	20	11.88 ± 1.700	21	12.95 ± 1.516	0.0383[b]
>4	27	11.72 ± 1.631	25	12.04 ± 1.952	0.5259

[a]Values are presented as mean ± standard deviation. [b]Significant difference between ACDR and ACDF. Abbreviations: ISH, intervertebral space height; JOA, Japanese Orthopedic Association.

reported that only 36% of the patients retained CL 33 months after the operation [43]. With technological advancement, studies have shown that the prosthesis can maintain the sagittal curvature of the cervical spine compared with that preoperative, through strict criteria and improved operation, but it can only maintain but not reconstruct the cervical alignment. In the ACDR group in this study, the value of CL was improved from 15.97 ± 11.55 preoperatively to 20.58 ± 12.31 postoperatively and 19.00 ± 11.62 at follow-up with a significant difference compared with baseline. The result of this study showed that CL could be reconstructed well through ACDR. The authors analyzed the reasons and considered that it may be due to the absolute removal of osteophyte, repairment of the endplate bed, and suitable choice of the prosthesis.

According to a prospective study by Lee et al. [44], the greater value of CL was associated with a greater value of T1s, which had a key role to preserve the physiological neck tilting and horizontal gaze and determine the sagittal balance of the cervical spine. The forward inclination of T1 can lead to the forward movement of the center of gravity of the cervical spine. In addition, the stability of the posterior cervical muscle makes the cervical lordosis increase and the head move backward, to make the balance center of gravity forward. As a result, a greater T1 inclination requires a larger CL to maintain the cervical sagittal alignment balance, representing the relationship between the T1s and global sagittal alignment [45]. In the present study, the value of T1s achieved significant improvement from 20.44 ± 6.057 preoperative to 26.52 ± 4.954 postoperative in the ACDR group and 21.13 ± 5.696 preoperative to 27.72 ± 5.777 postoperative in the ACDF group. Both the two groups had a certain degree of loss, which was 24.79 ± 4.937 and 25.82 ± 5.477 at follow-up, respectively. The changing trend between T1s, cSVA, and CL in this study was consistent with that of previous studies [44–47].

It is also necessary to note that restoring and maintaining the value of ISH is of importance to reconstruct the cervical sagittal alignment. It is closely associated with axial neck pain, adjacent segment degeneration, and neurologic symptoms [48]. Liu et al. conducted a clinical study on the aspect of the association between ISH and ROM to explore the efficacy of ACDR.

No correlation was found between the cervical sagittal alignment parameters (cSVA, CL, T1s, and ISH) and PROs (VAS, NDI, and JOA) in previous studies [49], except that patients with preoperative ISH < 4 mm exhibited increased postoperative ROM, while those with preoperative ISH > 4 mm remained the same [48], which was similar with the study of Basques et al. [50]. However, in this study, no similar results were found in the ACDR group. The authors in this study considered that it might be due to the difference in the prosthesis, Bryan was utilized in theirs while Mobi-C was used in the present study. Additionally, a significantly better postoperative JOA was found in patients with a preoperative ISH < 4 mm in the ACDF group than the ACDR group in this study. These results may interpret that patients with more preoperative loss of ISH may suffer from low quality of life such as intolerable severe axial neck pain and need more thorough decompression during the operation, even including the resection of the posterior longitudinal ligament; as a result, the improvement postoperative may be changed significantly compared with that with less preoperative loss of ISH. For the abovementioned reasons, the authors believed that, in patients with preoperative ISH less than 4 mm, ACDF was more recommended.

In addition to the abovementioned findings, the results of this study also showed a difference in the baseline of age. Reviewing the data, the authors found that the median age of enrolled patients in this study was exactly 45 years. The author analyzed and considered that it may due to the different surgical indications of the ACDR and ACDF in daily clinical practice. Also, this study aimed to compare the radiographic reconstruction and clinical improvement between the two procedures, so the author held that it would not unduly affect the pooled results and conclusions. Additionally, the author divided the enrolled patients into groups of less than 45 years of age and more than 46 years of age to verify whether the daily clinical experience of recommending ACDR for younger patients and ACDF for elderly patients should continue to be followed. The result showed that patients with age less than 45 years received a significantly larger postoperative ROM than patients with age more than 46 years in the ACDR group ($P < 0.05$). However, a similar result was not found in the ACDF group ($P > 0.05$).

There were also limitations in the present study. Only the Mobi-C prosthesis was included in this study, and the results may be modified by diverse kinds of different prostheses, and the sequential studies were still needed and went on. Also, prospective cohorts with various types of prosthesis as well as higher sample sizes might support stronger findings.

5. Conclusions

Overall, according to the results mentioned above, both the two methods could do well for the treatment of CDDD, and a similar capability in terms of radiographic reconstruction and clinical improvement was found between the two methods. Specific concerns should be analyzed while

choosing between an ACDR and an ACDF. It should be pointed out that, based on our experience, if the patient is younger, ACDR is recommended; for patients with preoperative ISH less than 4 mm, ACDF is more recommended.

Data Availability

The data analyzed during the current study are not publicly available due to the data being confidential; however, they are available from the corresponding author on reasonable request.

Ethical Approval

This study was approved by the ethics committee of Beijing Chao-Yang Hospital of Capital Medical University (2016-Department-187-1).

Conflicts of Interest

The authors declare no conflicts of interest.

Authors' Contributions

Yuxiang Chen and Yue Li contributed equally to this work. PY and YH conceptualized and designed the study; YzL, QjS, and JcY provided study materials or patients; YL and YxC collected and assembled data; and YxC and YL analysed and interpreted data. All authors read and approved the final manuscript.

Acknowledgments

This work was supported by the Natural Science Foundation of Beijing, China (7204264), and the National Key Research and Development Program of China (2019YFC0120604).

References

[1] M. A. Hollyer, E. C. Gill, S. Ayis, and A. K. Demetriades, "The safety and efficacy of hybrid surgery for multilevel cervical degenerative disc disease versus anterior cervical discectomy and fusion or cervical disc arthroplasty: a systematic review and meta-analysis," *Acta Neurochirurgica*, vol. 162, no. 2, pp. 289–303, 2020.

[2] H. H. Bohlman, S. E. Emery, D. B. Goodfellow, and P. K. Jones, "Robinson anterior cervical discectomy and arthrodesis for cervical radiculopathy. Long-term follow-up of one hundred and twenty-two patients," *The Journal of Bone and Joint Surgery*, vol. 75, no. 9, pp. 1298–1307, 1993.

[3] A. F. Joaquim, M. C. Makhni, and K. D. Riew, "Evidence-based use of arthroplasty in cervical degenerative disc disease," *International Orthopaedics*, vol. 43, no. 4, pp. 767–775, 2019.

[4] K. Kim, G. Hoffman, H. Bae et al., "Ten-year outcomes of 1- and 2-level cervical disc arthroplasty from the Mobi-C investigational device exemption clinical trial," *Neurosurgery*, vol. 88, no. 3, pp. 497–505, 2021.

[5] X. Hu, H. Liu, B. Wang et al., "Cervical disc arthroplasty versus anterior cervical discectomy and fusion for the treatment of single-level disc degenerative disease with preoperative reversible kyphosis," *Clinical Neurology and Neurosurgery*, vol. 202, Article ID 106493, 2021.

[6] X. Yang, R. H. M. A. Bartels, R. Donk, M. P. Arts, C. M. W. Goedmakers, and C. L. A. Vleggeert-Lankamp, "The association of cervical sagittal alignment with adjacent segment degeneration," *European Spine Journal*, vol. 29, no. 11, pp. 2655–2664, 2020.

[7] J. K. Scheer, J. A. Tang, J. S. Smith et al., "Cervical spine alignment, sagittal deformity, and clinical implications: a review," *Journal of Neurosurgery: Spine*, vol. 19, no. 2, pp. 141–159, 2013.

[8] S. K. Cho and K. D. Riew, "Adjacent segment disease following cervical spine surgery," *Journal of the American Academy of Orthopaedic Surgeons*, vol. 21, no. 1, pp. 3–11, 2013.

[9] A. S. Hilibrand, G. D. Carlson, M. A. Palumbo, P. K. Jones, and H. H. Bohlman, "Radiculopathy and myelopathy at segments adjacent to the site of a previous anterior cervical arthrodesis," *The Journal of Bone and Joint Surgery*, vol. 81, no. 4, pp. 519–528, 1999.

[10] D.-H. Park, P. Ramakrishnan, T.-H. Cho et al., "Effect of lower two-level anterior cervical fusion on the superior adjacent level," *Journal of Neurosurgery: Spine*, vol. 7, no. 3, pp. 336–340, 2007.

[11] C. F. van Eck, C. Regan, W. F. Donaldson, J. D. Kang, and J. Y. Lee, "The revision rate and occurrence of adjacent segment disease after anterior cervical discectomy and fusion: a study of 672 consecutive patients," *Spine*, vol. 39, no. 26, pp. 2143–2147, 2014.

[12] A. A. Gandhi, S. Kode, N. A. DeVries, N. M. Grosland, J. D. Smucker, and D. C. Fredericks, "Biomechanical analysis of cervical disc replacement and fusion using single level, two level, and hybrid constructs," *Spine*, vol. 40, no. 20, pp. 1578–1585, 2015.

[13] J. H. Lee, J. S. Kim, J. H. Lee, E. R. Chung, C. S. Shim, and S.-H. Lee, "Comparison of cervical kinematics between patients with cervical artificial disc replacement and anterior cervical discectomy and fusion for cervical disc herniation," *The Spine Journal*, vol. 14, no. 7, pp. 1199–1204, 2014.

[14] H. Abudouaini, H. Liu, C. Huang et al., "Effect of changes in postoperative intervertebral space height on clinical and radiological outcomes after cervical disc replacement," *World Neurosurgery*, vol. 145, pp. e61–e67, 2021.

[15] X.-F. Wang, Y. Meng, H. Liu, B.-Y. Wang, and Y. Hong, "The impact of different artificial disc heights during total cervical disc replacement: an in vitro biomechanical study," *Journal of Orthopaedic Surgery and Research*, vol. 16, no. 1, p. 12, 2021.

[16] A. MacDowall, N. Canto Moreira, C. Marques et al., "Artificial disc replacement versus fusion in patients with cervical degenerative disc disease and radiculopathy: a randomized controlled trial with 5-year outcomes," *Journal of Neurosurgery: Spine*, vol. 30, no. 3, pp. 323–331, 2019.

[17] R. B. Delamarter and J. Zigler, "Five-year reoperation rates, cervical total disc replacement versus fusion, results of a prospective randomized clinical trial," *Spine (Phila Pa 1976)*, vol. 38, no. 9, pp. 711–717, 2013.

[18] G. M. Ghobrial, W. F. Lavelle, J. E. Florman, K. D. Riew, and A. D. Levi, "Symptomatic adjacent level disease requiring surgery: analysis of 10-year results from a prospective, randomized, clinical trial comparing cervical disc arthroplasty to anterior cervical fusion," *Neurosurgery*, vol. 84, no. 2, pp. 347–354, 2019.

[19] C. W. B. Peng, M. Quirnoa, J. A. Bendo, J. M. Spivak, and J. A. Goldstein, "Effect of intervertebral disc height on

postoperative motion and clinical outcomes after Prodisc-C cervical disc replacement," *The Spine Journal*, vol. 9, no. 7, pp. 551–555, 2009.

[20] V. M. Lu, L. Zhang, D. B. Scherman, P. J. Rao, R. J. Mobbs, and K. Phan, "Treating multi-level cervical disc disease with hybrid surgery compared to anterior cervical discectomy and fusion: a systematic review and meta-analysis," *European Spine Journal*, vol. 26, no. 2, pp. 546–557, 2017.

[21] Z. Jia, Z. Mo, F. Ding, Q. He, Y. Fan, and D. Ruan, "Hybrid surgery for multilevel cervical degenerative disc diseases: a systematic review of biomechanical and clinical evidence," *European Spine Journal*, vol. 23, no. 8, pp. 1619–1632, 2014.

[22] Y.-D. Yang, H. Zhao, Y. Chai et al., "A comparison study between hybrid surgery and anterior cervical discectomy and fusion for the treatment of multilevel cervical spondylosis," *The Bone & Joint Journal*, vol. 102-b, no. 8, pp. 981–996, 2020.

[23] C. V. Maldonado, R. D. Paz, and C. B. Martin, "Adjacent-level degeneration after cervical disc arthroplasty versus fusion," *European Spine Journal*, vol. 20, no. Suppl 3, pp. 403–407, 2011.

[24] A. Di Martino, R. Papalia, E. Albo, L. Cortesi, L. Denaro, and V. Denaro, "Cervical spine alignment in disc arthroplasty: should we change our perspective?" *European Spine Journal*, vol. 24, no. Suppl 7, pp. 810–825, 2015.

[25] X. Wang, Y. Meng, H. Liu, H. Chen, B. Wang, and Y. Hong, "Cervical sagittal alignment after Prestige LP cervical disc replacement: radiological results and clinical impacts from a single-center experience," *BMC Musculoskeletal Disorders*, vol. 22, no. 1, p. 82, 2021.

[26] X. Wang, Y. Meng, H. Liu, H. Chen, B. Wang, and Y. Hong, "Association of cervical sagittal alignment with adjacent segment degeneration and heterotopic ossification following cervical disc replacement with Prestige-LP disc," *Journal of Orthopaedic Surgery (Hong Kong)*, vol. 28, no. 3, 2020.

[27] R. D. Ferch, A. Shad, T. A. Cadoux-Hudson, and P. J. Teddy, "Anterior correction of cervical kyphotic deformity: effects on myelopathy, neck pain, and sagittal alignment," *Journal of Neurosurgery*, vol. 100, no. 1 Suppl Spine, pp. 13–19, 2004.

[28] S. Iyer, V. M. Nemani, J. Nguyen et al., "Impact of cervical sagittal alignment parameters on neck disability," *Spine (Phila Pa 1976)*, vol. 41, no. 5, pp. 371–377, 2016.

[29] X. Gao, Y. Yang, H. Liu et al., "A comparison of cervical disc arthroplasty and anterior cervical discectomy and fusion in patients with two-level cervical degenerative disc disease: 5-year follow-up results," *World Neurosurgery*, vol. 122, pp. e1083–e1089, 2019.

[30] G. D. Schroeder, M. F. Kurd, P. W. Millhouse, A. R. Vaccaro, and A. S. Hilibrand, "Performing an anterior cervical discectomy and fusion," *Clinical Spine Surgery: A Spine Publication*, vol. 29, no. 5, pp. 186–190, 2016.

[31] M. Alhashash, H. Allouch, H. Boehm, and M. Shousha, "Results of four-level anterior cervical discectomy and fusion using stand-alone interbody titanium cages," *Asian Spine Journal*, 2021.

[32] D. Leven, J. Meaike, K. Radcliff, and S. Qureshi, "Cervical disc replacement surgery: indications, technique, and technical pearls," *Current Reviews in Musculoskeletal Medicine*, vol. 10, no. 2, pp. 160–169, 2017.

[33] X. Wang, H. Liu, Y. Meng et al., "Effect of disc height and degree of distraction on heterotopic ossification after cervical disc replacement," *World Neurosurgery*, vol. 145, pp. e100–e107, 2021.

[34] N. Khalil, A. J. Bizdikian, Z. Bakouny et al., "Cervical and postural strategies for maintaining horizontal gaze in asymptomatic adults," *European Spine Journal*, vol. 27, no. 11, pp. 2700–2709, 2018.

[35] B. G. Diebo, V. Challier, J. K. Henry et al., "Predicting cervical alignment required to maintain horizontal gaze based on global spinal alignment," *Spine*, vol. 41, no. 23, pp. 1795–1800, 2016.

[36] J. E. Zigler, R. Delamarter, D. Murrey, J. Spivak, and M. Janssen, "ProDisc-C and anterior cervical discectomy and fusion as surgical treatment for single-level cervical symptomatic degenerative disc disease: five-year results of a Food and Drug Administration study," *Spine*, vol. 38, no. 3, pp. 203–209, 2013.

[37] J. Dejaegher, J. Walraevens, J. van Loon, F. Van Calenbergh, P. Demaerel, and J. Goffin, "10-year follow-up after implantation of the bryan cervical disc prosthesis," *European Spine Journal*, vol. 26, no. 4, pp. 1191–1198, 2017.

[38] M. S. Hisey, J. E. Zigler, R. Jackson et al., "Prospective, randomized comparison of one-level Mobi-C cervical total disc replacement vs. Anterior cervical discectomy and fusion: results at 5-year follow-up," *International Journal of Spine Surgery*, vol. 10, p. 10, 2016.

[39] T. P. Loumeau, B. V. Darden, T. J. Kesman et al., "A RCT comparing 7-year clinical outcomes of one level symptomatic cervical disc disease (SCDD) following ProDisc-C total disc arthroplasty (TDA) versus anterior cervical discectomy and fusion (ACDF)," *European Spine Journal*, vol. 25, no. 7, pp. 2263–2270, 2016.

[40] M. Skeppholm, L. Lindgren, T. Henriques, L. Vavruch, H. Löfgren, and C. Olerud, "The Discover artificial disc replacement versus fusion in cervical radiculopathy-a randomized controlled outcome trial with 2-year follow-up," *The Spine Journal*, vol. 15, no. 6, pp. 1284–1294, 2015.

[41] A. Vaccaro, W. Beutler, W. Peppelman et al., "Clinical outcomes with selectively constrained SECURE-C cervical disc arthroplasty: two-year results from a prospective, randomized, controlled, multicenter investigational device exemption study," *Spine*, vol. 38, no. 26, pp. 2227–2239, 2013.

[42] J. A. Tang, J. K. Scheer, J. S. Smith et al., "The impact of standing regional cervical sagittal alignment on outcomes in posterior cervical fusion surgery," *Neurosurgery*, vol. 76, no. Suppl 1, pp. S14–S21, 2015.

[43] S. W. Kim, J. H. Shin, J. J. Arbatin, M. S. Park, Y. K. Chung, and P. C. McAfee, "Effects of a cervical disc prosthesis on maintaining sagittal alignment of the functional spinal unit and overall sagittal balance of the cervical spine," *European Spine Journal*, vol. 17, no. 1, pp. 20–29, 2008.

[44] S.-H. Lee, E.-S. Son, E.-M. Seo, K.-S. Suk, and K.-T. Kim, "Factors determining cervical spine sagittal balance in asymptomatic adults: correlation with spinopelvic balance and thoracic inlet alignment," *The Spine Journal*, vol. 15, no. 4, pp. 705–712, 2015.

[45] Y. H. Kuo, C. H. Kuo, H. K. Chang et al., "The effect of T1-slope in spinal parameters after cervical disc arthroplasty," *Neurosurgery*, vol. 87, no. 6, pp. 1231–1239, 2020.

[46] P. T. Knott, S. M. Mardjetko, and F. Techy, "The use of the T1 sagittal angle in predicting overall sagittal balance of the spine," *The Spine Journal*, vol. 10, no. 11, pp. 994–998, 2010.

[47] C. Weng, J. Wang, A. Tuchman et al., "Influence of T1 slope on the cervical sagittal balance in degenerative cervical spine: an analysis using kinematic MRI," *Spine*, vol. 41, no. 3, pp. 185–190, 2016.

[48] H. Li, J. Lou, H. Liu, and B. Wang, "Effect of intervertebral disc height on the range of motion and clinical outcomes after single-level implantation of Prestige LP cervical disc

prosthesis," *Clinical Neurology and Neurosurgery*, vol. 148, pp. 1–4, 2016.

[49] B. Godlewski, M. K. Stachura, R. A. Czepko, M. Banach, and R. Czepko, "Analysis of changes in cervical spinal curvature and intervertebral disk space height following ACDF surgery in a group of 100 patients followed up for 12 months," *Journal of Clinical Neuroscience*, vol. 52, pp. 92–99, 2018.

[50] B. Basques, J. M. Khan, M. T. Nolte et al., "262. Do large increases in disc space height have consequences after ACDF?" *The Spine Journal*, vol. 19, no. 9, p. S128, 2019.

Hindawi
Pain Research and Management
Volume 2022, Article ID 2690291, 7 pages
https://doi.org/10.1155/2022/2690291

Research Article

Changes in Paraspinal Muscles and Facet Joints after Minimally Invasive Posterior Lumbar Interbody Fusion Using the Cortical Bone Trajectory Technique: A Prospective Study

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Received 4 November 2021; Revised 19 December 2021; Accepted 3 January 2022; Published 12 January 2022

Academic Editor: Sidong Yang

In this prospective cohort study, we aimed to determine the surgical and adjacent segment changes in paraspinal muscles and facet joints in patients with lumbar spinal stenosis after minimally invasive posterior lumbar interbody fusion (PLIF) using the cortical bone trajectory (CBT) technique. We enrolled 30 consecutive patients who underwent the single-level CBT technique between October 2017 and October 2018. We evaluated preoperative and 1-month, 3-month, 6-month, and 1-year postoperative clinical data including Visual Analogue Scale (VAS) scores and Oswestry Disability Index (ODI). Magnetic resonance imaging (MRI) was performed a year after surgery. The erector spinae (ES) muscle area, volume, and fat infiltration (FI) on the surgical and adjacent segments were evaluated using the thresholding method, and the degree of adjacent facet joint degeneration was calculated using the Weishaupt scale. FI rate was graded using the Kjaer method. All patients underwent a 12-month follow-up. The VAS and ODI scores significantly improved after surgery in all patients. No patient showed degeneration of the adjacent facet joints ($P > 0.05$) during the 1-year follow-up postoperation. There was no significant difference in ES muscle volume, area, and FI on the surgical and adjacent segments ($P > 0.05$). The FI rate of the upper ES muscles increased postoperatively ($P < 0.05$); however, there were no significant changes in FI rate of the lower ES muscles. Patients with lumbar spinal stenosis could obtain satisfactory short-term clinical outcomes via minimally invasive PLIF using the CBT technique. Moreover, this technique may reduce the impact on the paravertebral muscles, especially the ES muscle, and the adjacent facet joints.

1. Introduction

Lumbar spinal stenosis (LSS) is a common spinal condition and the most frequent indication for spinal surgery in elderly people. Posterior lumbar interbody fusion (PLIF) surgery is a widely accepted surgical technique for the treatment of LSS [1]. Paravertebral muscles play an important role in maintaining lumbar spine stability [2]. Paraspinal muscle degeneration may lead to loss of functional muscle support, segmental movement disorders, and increased biomechanical strain, resulting in persistent postoperative low back pain [3]. Three main mechanisms have been proposed for structural changes in back muscles: disuse, denervation, and an active process mediated by a localized muscle inflammatory response [4]. Traditional pedicle screws point lateral to the pars interarticularis, and the operation lacks protection of the paravertebral muscles and requires a relatively wide dissection of the paraspinal muscles [5], which may predispose to injury to the medial and posterior branches of the spinal nerve and causes volume atrophy of the paravertebral muscles [1, 6]. Muscle degeneration is characterized by a decrease in muscle size and/or an increase in the amount of fat infiltration on magnetic resonance imaging (MRI) [7]. Moreover, the violation of the adjacent facet joint surface could lead to adjacent segment degeneration (ASD) [8]. Therefore, traditional PLIF with pedicle

screws may cause paraspinal muscle injury and ASD, eventually leading to chronic low back pain.

In 2009, Santoni et al. introduced a new method for screw insertion called the cortical bone trajectory (CBT) technique [9]. This new trajectory follows caudocephalad and lateral paths in the sagittal and transverse planes, respectively, thereby increasing the purchase of the screw in the pedicle and vertebral body. Since the starting point of the screw is closer to the medial side, the incision and muscle separation lengths are also reduced [10]. Thus, shorter muscle dissection and incision lengths are associated with less parafacial muscle atrophy [11]. Moreover, a unique screw path reduces the violation of adjacent facet joints. In a previous study, the incidence of symptomatic ASD in the traditional PLIF group was approximately twice that in the CBT group [12]. Additionally, the incidence of symptomatic ASD was usually associated with paravertebral muscle injury and facet joint violation [13, 14]. However, few studies have assessed muscle injury and facet joint violation following the CBT technique based on MRI. Therefore, we aimed to investigate the changes in paraspinal muscles and facet joint degeneration after minimally invasive posterior interbody fusion using the CBT technique.

2. Materials and Methods

2.1. Study Design and Participants. We prospectively enrolled 30 consecutive patients with lesions at L4/5 from October 2017 to October 2018. LSS diagnosis was confirmed by MRI or computed tomography (CT). We included LSS patients (1) with severe low back and leg pains persisting after at least 3–6 months of conservative treatment and (2) without an obvious ASD on MRI before surgery. We excluded patients with (1) degenerative scoliosis (Cobb angle $>10^{\circ}$), because scoliosis affects the calculation of muscle volume; (2) infection, trauma, or spondylolisthesis; and (3) severe psychosis who were uncooperative during follow-up.

This study complied with the Declaration of Helsinki and was approved by the Ethics Committee of Beijing Chaoyang Hospital, ID: 2017-KE-103. Participant informed consent was exempted because of the retrospective study design.

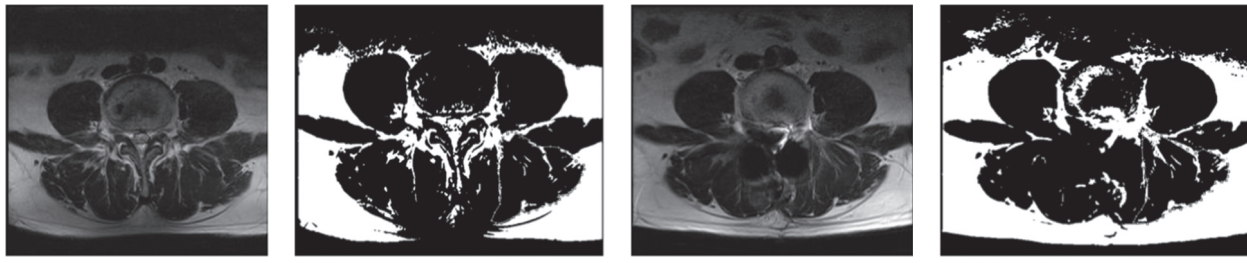
2.2. Surgical Technique. The patient was placed in a prone position, and an approximately 5 cm midline skin incision was made on lumbar. The muscles were separated layer-by-layer to expose the surgical site. Muscle was exposed to the exposed vertebral isthmus. The facet joints were exposed, avoiding the exposure of facet joints adjacent to the fused segment. Decompression was achieved by partial laminectomy and unilateral or bilateral facetectomy. The decompression-resected autogenous bone was made into bone blocks and filled into polyetheretherketone cages. After removing the disc and treating the superior and inferior endplates, the residual particulate bone was inserted into the anterior portion of the disc space, and the cage was subsequently inserted into the disc space. In the CBT technique, surgeons use screws typically measuring 5.5 mm in diameter and ranging from 35 to 40 mm in length. All procedures were performed by the same surgeon and there were no technical differences. All patients returned to normal activities after removal of the drainage tube. After discharge, low back muscle exercises were performed appropriately according to the rehabilitation.

2.3. Assessment Criteria. Pre- and postoperative parameters were assessed, including the degree of upper and lower facet joint ASD, the muscle area and volume, and the fatty infiltration (FI) rate of the adjacent and surgical segments of the erector spinae (ES) muscle.

FI rate was graded using the Kjaer method [7], "normal" for estimates of 0–10% fat within the muscle, "slight" for 10–50% fat, and "severe" for >50% fat. Upper and lower facet joints were assessed using the Weishaupt scale [15]. Grade 0 indicated normal facet joint space (2 ± 4 mm width). Grade 1 indicated narrowing of the facet joint space (<2 mm) and/or small osteophytes and/or mild hypertrophy of the articular process. Grade 2 indicated narrowing of the facet joint space and/or moderate osteophytes and/or moderate hypertrophy of the articular process and/or mild subarticular bone erosions. Grade 3 indicated narrowing of the facet joint space and/or large osteophytes and/or severe hypertrophy of the articular process and/or severe subarticular bone erosions and/or subchondral cysts. All parameters were measured on MRI. Facet joint ASD, at the same level, was expressed as the sum of the left and right facet joint Weishaupt scores.

ES muscle measurements were obtained from T2-weighted images using ImageJ software. The selection method for muscle regions of interest (ROI) was based on the technique proposed by Crawford et al. [16]. Based on fascial plane separation, the facet joint was used as a landmark between the multifidus and erector spinae muscles. A large fat-filled tent between the longissimus and iliocostal muscles was excluded from the ROI. In addition, fat areas lateral to the iliocostal and subfascial planes were excluded in the ROI. MRI was performed using Signa Hdxt 3.0t (Siemens). The slice thickness was 3 mm with a 3 mm gap between each slice, the parameters were set as FoV 200 mm, TR 2870 ms, and TE 87 ms. Patients were placed in the supine position, with their legs straight and the lumbar spine in a neutral position. Axial MRI was parallel to the inferior endplate of the vertebral body. Paraspinal muscle parameters were measured at the midpoint of the intervertebral disc. The surgical and adjacent segments were measured for each patient. Left and right values were summed, from which the average values for ES muscle area, volume, and FI were calculated. The ES muscle area and FI were measured using a thresholding technique (see Figure 1), while the ES muscle volume was estimated by multiplying the muscle area and height in the adjacent upper and lower regions (see Figure 2). The paraspinal muscles were regarded as approximate prisms, and the volume of the paraspinal muscles was calculated from a three-dimensional (3-D) perspective.

Clinical effects were assessed using the Visual Analogue Scale (VAS) score for back pain and the



(a) (b) (c) (d)

Figure 1: A 45-year-old male patient diagnosed with lumbar spinal stenosis. (a) represents L4-L5 vertebral MRI, while (b) is the same image obtained after processing by the ImageJ software. (c) represents L4-L5 vertebral MRI after CBT surgery, while (d) is the same image obtained after processing by the ImageJ software. The area enclosed by the yellow line after image thresholding in the ImageJ software is the ES portion of the paravertebral muscle. ES area and FI obtained by calculation using the ImageJ software.

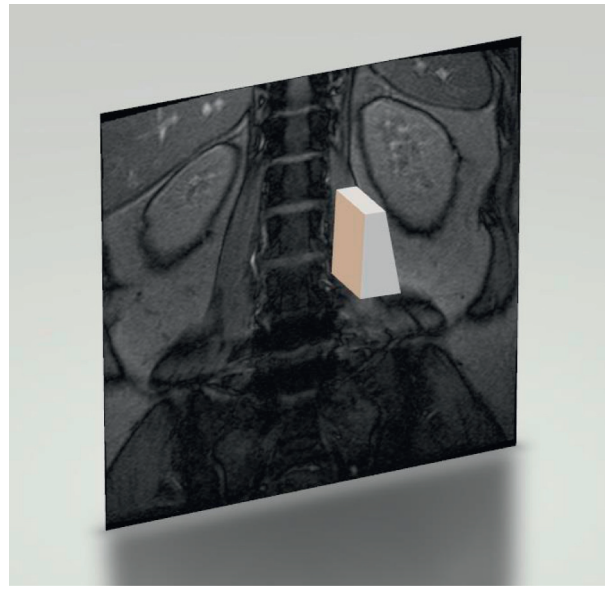


Figure 2: To estimate the volume, the entire ES muscle is considered as a circular table. The areas of the upper and lower segments are A and B, respectively. Using the height h between the upper and lower segments, the volume of the ES is estimated using the formula $V = (1/3)h(S_A + S_B + \sqrt{S_A S_B})$.

Oswestry Disability Index (ODI) evaluated preoperatively and at 1-month, 3-month, 6-month, and 1-year postsurgery. In VAS, pain is divided into 10 points, 2 points indicating no pain, 10 points indicating severe pain, and the middle part indicating varying degrees of pain. The patient was asked to place a mark on the horizontal line according to his/her feeling to indicate the degree of pain, 2–4 points for mild pain, 5–7 points for moderate pain, and 8-9 points for severe pain. The ODI covered 1 item on pain and 9 items on activities of daily living (personal care, lifting, walking, sitting, standing, sleeping, sex life, social life, and traveling). Each item was measured on a 6-point ordinal scale, ranging from the best scenario to the worst scenario.

2.4. Statistical Analysis. SPSS version 21.0 was used to analyze the collected data. All values were expressed as mean ± standard deviation. The Wilcoxon rank-sum test was used for grade data selection such as muscle FI and facet joint degeneration. Student's t-test was used to examine differences between groups of continuous variables such as muscle area, VAS, and ODI. $P < 0.05$ was considered statistically significant.

3. Results

Of the 30 patients enrolled, 16 were men while 14 were women, with an average age of 63.63 ± 9.51 years (range, 45–82 years). Single-level L4/5 PLIF was performed on all patients, respectively. The mean body mass index was 24.54 ± 3.83 kg/m^2 and the average operation time was 153.33 ± 29.87 min. The mean intraoperative blood loss was 183.33 ± 69.89 ml, and the average hospital stay was 7.97 ± 2.20 days (see Table 1).

The mean preoperative and postoperative ODI scores and VAS scores are presented in Table 2, while the upper and lower segment ES muscle areas, surgical segment ES muscle areas, and ES muscle volumes are presented in Table 3. The

Table 1: Characteristics of patients with lumbar disease in this series.

Characteristics	*n*
Sex	
Male	14 (46.7%)
Female	16 (53.3%)
Age	63.63 ± 9.51 years
Body mass index	24.54 ± 3.83 kg/m^2
Operation time	153.33 ± 29.87 min
Intraoperative blood loss	183.33 ± 69.89 ml
Hospital stay	7.97 ± 2.20 days

Table 2: Clinical outcome assessment.

	Preoperative	1-month follow-up	3-month follow-up	6-month follow-up	1-year follow-up
ODI	77.63 ± 5.36	61.85 ± 8.65	50.52 ± 12.37	38.89 ± 10.56	34.70 ± 13.56
VAS	7.70 ± 0.65	5.03 ± 1.35	4.07 ± 1.09	3.23 ± 1.28	2.70 ± 1.21

VAS, Visual Analogue Scale; ODI, Oswestry Disability Index.

Table 3: Preoperative and postoperative paraspinal muscle parameters.

	Preoperative	1-year follow-up	*P*
USES area (mm^2)	3168.14 ± 744.88	3215.08 ± 663.34	0.417
LSES area (mm^2)	2989.21 ± 871.46	2968.72 ± 795.05	0.711
SSES area (mm^2)	3495.66 ± 772.81	3463.48 ± 774.95	0.069
ESV (mm^3)	192480.767 ± 45962.31	189865.65 ± 42912.18	0.384

USES, upper segment erector spinae muscle; LSES, lower segment erector spinae muscle; SSES, surgical segment erector spinae muscle; ESV, erector spinae muscle volume.

VAS and ODI scores significantly improved after surgery in all patients. There was no significant difference between the preoperative and 1-year postoperative ES muscle area and volume ($P > 0.05$) (see Table 2). The median preoperative surgical segment ES muscle FI was 1 and the median 1-year postoperative surgical segment ES muscle FI was 1, the difference was not significant ($Z = -1.41$, $P = 0.16$). The median preoperative upper segment ES muscle FI was 0.5 and the median 1-year postoperative upper segment ES muscle FI was 1, the difference was statistically significant ($Z = -2.00$, $P < 0.05$). The median preoperative lower segment ES muscle FI was 1 and the median 1-year postoperative lower segment ES muscle FI was 1, the difference was not significant ($Z = -1.00$, $P = 0.32$).

There was no significant difference between the preoperative and 1-year postoperative facet joint scores. The median preoperative upper segment facet joint score was 1 and the median 1-year postoperative lower segment facet joint (LSFJ) was 2; however, the difference was not significant ($Z = 2.45$, $P > 0.05$) (see Figure 3). The median preoperative and 1-year postoperative LSFJ scores were both 2; however, the difference was not significant ($Z = 1.89$, $P > 0.05$) (see Figure 4).

4. Discussion

Our study mainly focused on the effect of the CBT technique on the ES muscle, a paravertebral muscle. The results showed that the CBT technique could adequately protect the ES muscle and facet joints during posterior open surgery. Moreover, it effectively relieved the patient's symptoms while protecting the ES muscle from destruction and avoiding the occurrence of persistent lower back pain caused by postoperative paraspinal muscle atrophy and ASD of the facet joints.

Paravertebral muscles play an important role in lumbar motion and maintenance of stability [17]. The paraspinal system mainly includes the multifidus and ES muscles. The ES muscle plays an important role in balancing the vertebral column. Previous studies have focused more on the multifidus muscle relative to the ES muscle. Öztürk et al. [18] found that in patients with low back pain caused by lumbar disc herniation, the ES muscle had more FI than the multifidus muscle. Paraspinal muscle atrophy indicates a reduction in the force generated by the ES muscles to support the basic load of the spine [19]. Some reports have indicated that the reduction in the cross-sectional area (CSA) of paravertebral muscles is associated with chronic low back pain [17, 20]. In the CBT technique, paravertebral muscle dissection is reduced because the entry point is closer to the midline. Therefore, the CBT technique is considered to have unique advantages in terms of reduced postoperative pain because of its smaller incision and less paravertebral muscle dissection. Hung et al. [21] found that patients who underwent CBT surgery had a smaller rate of the superior or inferior adjacent levels multifidus muscle FI than the pedicle screws group. Fan et al. [22] also demonstrated that the CBT techniques involved less paravertebral muscle dissection, less affected the paraspinal muscles, and better improved the postoperative VAS score than the traditional PLIF. This finding was like that of our study. The surgical and adjacent segment ES muscle areas did not change significantly in the 30 patients before and after surgery. Postoperative follow-up showed improvement in pain and quality of life (assessment by VAS and ODI). Thus, the CBT

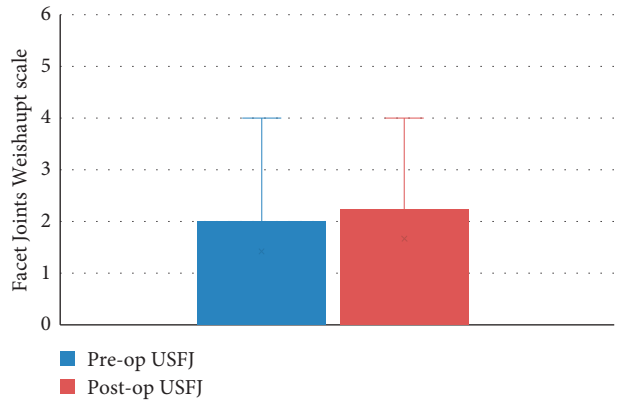


Figure 3: Preoperative and 1-year postoperative Weishaupt scale scores of the upper segment facet joints. USFJ, upper segment facet joints.

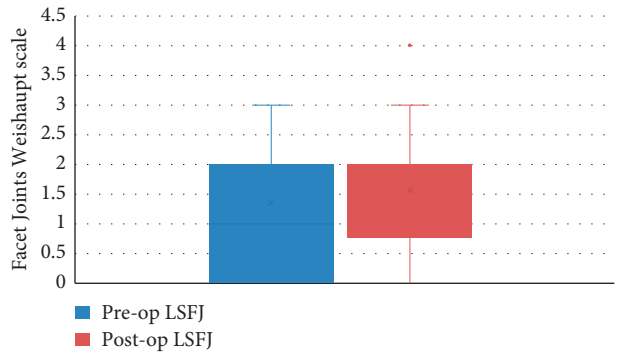


Figure 4: Preoperative and 1-year postoperative Weishaupt scale scores of the lower segment facet joints. LSFJ, lower segment facet joints.

technique reduces interference with the ES muscle, which leads to the improvement of postoperative pain and function.

Previous studies on paraspinal muscles have mostly used two-dimensional (2D) analyses, by calculating the area of the paraspinal muscles. 2D analysis can only provide partial evaluation, whereas three-dimensional (3D) analysis, involving muscle volume calculation, more accurately evaluates the extent of muscle injury [23]. This study innovatively uses a 3D method of muscle volume estimation by measuring the cross-sectional area and the muscle length. This parameter better evaluates the effect of surgery on muscles. In the 30 patients, there was no statistically significant change in ES muscle volume after CBT surgery. No paraspinal muscle atrophy occurred during 1-year follow-up after surgery. This also demonstrates that CBT surgery has less effect on the paraspinal muscles.

In addition, unlike previous studies that assessed paraspinal muscle using CT, we used MRI to investigate the rate of paravertebral muscle FI. The results showed that the FI rate of the surgical and lower segments of the ES muscles did not change significantly after surgery. However, the rate of FI in the upper segment of the ES muscles increased at 1-year follow-up ($P < 0.05$). It has been shown that muscle swelling due to edema may persist for 10 months after surgery [21]. Therefore, to avoid the interference of edema, chronic FI changes should be evaluated more than 10 months after surgery [22]. Skin incisions for CBT surgery are usually small. Moreover, the contraction of the back muscles through this small skin incision increases the intramuscular pressure to a level that impedes local blood flow to the muscle and leads to muscle degeneration [24]. Small surgical incisions exert a greater tension when pulling surrounding tissue. Due to the learning curve relationship, the operation time and peri-incisional muscle traction time will be increased when the surgeon is inexperienced. Studies on the learning curve suggest that a shift in surgical technique and greater efficiency over time decreased the incidence of overall complications in the late cohort [25]. Both the operation time and the greater tension exerted by the small incision relative to pedicle screws can cause prolonged ischemia of the paravertebral muscles, which in turn causes postoperative muscle tissue lipidation. Surgeons in this study have completed more than 100 cases of CBT before performing this study and are proficient in surgical techniques with no impact on the study.

Facet joint violation is much lower in the CBT technique than in traditional techniques because the entry point of the former is near the midline, which is far from the superior facet joint [26, 27]. Facet joint violation has been reported to cause symptomatic adjacent segment disease and may affect the fusion rate after fusion surgery, resulting in low back pain [28]. Degenerative changes of the facet joints are often characterized by cartilage loss, subchondral bone sclerosis, and osteophyte formation. In this study, there was no statistically significant change in the 1-year postoperative facet

joint scores of the 30 patients and no obvious facet joint degeneration was found during follow-up, demonstrating that the CBT technique effectively avoided interference with the upper and lower adjacent facet joints and avoided the occurrence of ASD. However, the follow-up time in this study was 1 year, and a longer follow-up may have different results.

Several limitations of our study should be acknowledged. First, the 1-year follow-up period may be too short to assess the long-term effect of the CBT procedure on pain relief and ASD. Second, our procedure focused only on single-level CBT surgery. The effects of long-segment CBT on the paraspinal muscles and adjacent segments need to be studied. Third, there was no comparison group for analysis. Comparison groups with conventional techniques should be included in subsequent studies for controlled studies to clarify the effects of CBT techniques on the paraspinal muscles. Fourth, postoperative low back muscle exercise is one of the effective measures to relieve postoperative paraspinal muscle fatty infiltration. The effect of surgical rehabilitation exercises on the paraspinal muscles was not focused on this study. Fifth, the learning curve of CBT techniques can also affect the paraspinal muscles. Surgical proficiency varies among surgeons at different stages of the learning curve. Surgeons in this study are already familiar with CBT techniques, but the effects of surgery on paraspinal muscles for different learning curve stages should be further investigated. Lastly, MRI generates incremental cost for the patient. This could cause patients to be lost to follow-up and increase the difficulty of long-term follow-up.

5. Conclusions

Our results showed that patients with lumbar spinal stenosis could obtain satisfactory clinical outcomes via minimally invasive PLIF using the CBT technique in the short run. Moreover, the aforementioned technique may reduce the impact on the paravertebral muscles, especially the ES muscle, and adjacent facet joints.

Data Availability

The datasets generated and/or analyzed during the current study are not publicly available due to the data being confidential; however, they are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Authors' Contributions

Yue Li and Yuxiang Chen are the co-first author.

Acknowledgments

The authors would like to thank Editage (https://www.edihyntage.cn) for English language editing.

References

[1] S. M. Cho, S. H. Kim, S. K. Ha et al., "Paraspinal muscle changes after single-level posterior lumbar fusion: volumetric analyses and literature review," *BMC Musculoskeletal Disorders*, vol. 21, no. 1, p. 73, 2020.

[2] M. D. Freeman, M. A. Woodham, and A. W. Woodham, "The role of the lumbar multifidus in chronic low back pain: a review," *PM&R The Journal of Injury Function and Rehabilitation*, vol. 2, no. 2, pp. 142–146, 2010.

[3] T. Sihvonen, A. Herno, L. Paljärvi, O. Airaksinen, J. Partanen, and A. Tapaninaho, "Local denervation atrophy of paraspinal muscles in postoperative failed back syndrome," *Spine*, vol. 18, no. 5, pp. 575–581, 1993.

[4] X. Chen, P. W. Hodges, G. James, and A. D. Diwan, "Do markers of inflammation and/or muscle regeneration in lumbar multifidus muscle and fat differ between individuals with good or poor outcome following microdiscectomy for lumbar disc herniation?" *Spine*, vol. 46, no. 10, pp. 678–686, 2021.

[5] A. A. Rosinski, A. Mittal, K. Odeh et al., "Alternatives to traditional pedicle screws for posterior fixation of the degenerative lumbar spine," *JBJS Reviews*, vol. 9, no. 7, Article ID e20.00177, 2021.

[6] H. F. Zhu, G. L. Wang, Z. J. Zhou, and S. W. Fan, "Prospective study of long-term effect between multifidus muscle bundle and conventional open approach in one-level posterior lumbar interbody fusion," *Orthopaedic Surgery*, vol. 10, no. 4, 2018.

[7] P. Kjaer, T. Bendix, J. S. Sorensen, L. Korsholm, and C. Leboeuf-Yde, "Are MRI-defined fat infiltrations in the multifidus muscles associated with low back pain?" *BMC Medicine*, vol. 5, no. 1, pp. 1–10, 2007.

[8] G. Keorochana, S. Pairuchvej, W. Trathitephun, A. Arirachakaran, P. Predeeprompan, and J. Kongtharvonskul, "Comparative outcomes of cortical screw trajectory fixation and pedicle screw fixation in lumbar spinal fusion: systematic review and meta-analysis," *World Neurosurgery*, vol. 102, pp. 340–349, 2017.

[9] B. G. Santoni, R. A. Hynes, K. C. Mcgilvray et al., "Cortical bone trajectory for lumbar pedicle screws," *The Spine Journal*, vol. 9, no. 5, pp. 366–373, 2009.

[10] R. J. Mobbs, "The "Medio-Latero-Superior Trajectory Technique": an alternative cortical trajectory for pedicle fixation," *Orthopaedic Surgery*, vol. 5, no. 1, pp. 56–59, 2013.

[11] S. Fan, Z. Hu, F. Zhao, X. Zhao, Y. Huang, and X. Fang, "Multifidus muscle changes and clinical effects of one-level posterior lumbar interbody fusion: minimally invasive procedure versus conventional open approach," *European Spine Journal*, vol. 19, no. 2, pp. 316–324, 2010.

[12] H. Sakaura, T. Miwa, T. Yamashita, Y. Kuroda, and T. Ohwada, "Cortical bone trajectory screw fixation versus traditional pedicle screw fixation for 2-level posterior lumbar interbody fusion: comparison of surgical outcomes for 2-level degenerative lumbar spondylolisthesis," *Journal of Neurosurgery: Spine*, vol. 28, no. 1, pp. 57–62, 2018.

[13] J. Y. Kim, D. S. Ryu, H. K. Paik et al., "Paraspinal muscle, facet joint, and disc problems: risk factors for adjacent segment degeneration after lumbar fusion," *The Spine Journal*, 2016.

[14] H. Wang, L. Ma, D. Yang et al., "Incidence and risk factors of adjacent segment disease following posterior decompression and instrumented fusion for degenerative lumbar disorders," *Medicine*, vol. 96, no. 5, Article ID e6032, 2017.

[15] D. Weishaupt, M. Zanetti, N. Boos, and J. J. S. R. Hodler, "MR imaging and CT in osteoarthritis of the lumbar facet joints," *Skeletal Radiology*, vol. 28, no. 4, pp. 215–219, 1999.

[16] R. J. Crawford, J. Cornwall, R. Abbott, and J. M. Elliott, "Manually defining regions of interest when quantifying paravertebral muscles fatty infiltration from axial magnetic resonance imaging: a proposed method for the lumbar spine with anatomical cross-reference," *BMC Musculoskeletal Disorders*, vol. 18, no. 1, p. 25, 2017.

[17] M. E. Lonnemann, S. V. Paris, and G. C. Gorniak, "A morphological comparison of the human lumbar multifidus by chemical dissection," *Journal of Manual and Manipulative Therapy*, vol. 16, no. 4, pp. 84E–92E, 2008.

[18] P. E. Ztürk and N. Aylan, "Which is the most affected muscle in lumbar back pain - multifidus or erector spinae?" *Polish Journal of Radiology*, vol. 85, pp. e278–e286, 2020.

[19] K. P. Barr, M. Griggs, and T. Cadby, "Lumbar stabilization: core concepts and current literature, part 1," *American Journal of Physical Medicine and Rehabilitation*, vol. 84, no. 6, pp. 473–480, 2005.

[20] J. A. Hides, M. J. Stokes, M. Saide, G. A. Jull, and D. H. Cooper, "Evidence of lumbar multifidus muscle wasting ipsilateral to symptoms in patients with acute/subacute low back pain," *Spine*, vol. 19, p. 165, 1994.

[21] C.-W. Hung, M.-F. Wu, R.-T. Hong, M.-J. Weng, G.-F. Yu, and C.-H. Kao, "Comparison of multifidus muscle atrophy after posterior lumbar interbody fusion with conventional and cortical bone trajectory," *Clinical Neurology and Neurosurgery*, vol. 145, pp. 41–45, 2016.

[22] S.-w. Fan, Z.-j. Hu, X.-q. Fang, F.-d. Zhao, Y. Huang, and H.-j. Yu, "Comparison of paraspinal muscle injury in one-level lumbar posterior inter-body fusion: modified minimally invasive and traditional open approaches," *Orthopedic Surgery*, vol. 2, no. 3, pp. 194–200, 2010.

[23] H. Tonomura, Y. Hatta, Y. Mikami et al., "Magnetic resonance imaging evaluation of the effects of surgical invasiveness on paravertebral muscles after muscle-preserving interlaminar decompression (MILD)," *Clinical Spine Surgery*, vol. 30, no. 2, pp. E76–E82, 2017.

[24] N. Nakajima, T. Maenaka, and H. Kano, "Postoperative low back pain after posterior lumbar interbody fusion surgery using cortical bone trajectory screws," *Asian Spine Journal*, vol. 14, no. 5, pp. 655–662, 2020.

[25] F. Dayani, Y. R. Chen, E. Johnson, S. Deb, and H. Singh, "Minimally invasive lumbar pedicle screw fixation using cortical bone trajectory–screw accuracy, complications, and learning curve in 100 screw placements," *Journal of Clinical Neuroscience*, vol. 61, pp. 106–111, 2018.

[26] H. Sakaura, D. Ikegami, T. Fujimori et al., "Early cephalad adjacent segment degeneration after posterior lumbar interbody fusion: a comparative study between cortical bone trajectory screw fixation and traditional trajectory screw fixation," *Journal of Neurosurgery: Spine*, vol. 32, no. 2, pp. 155–159, 2019.

[27] Q. Zhang, Y.-F. Xu, W. Tian et al., "Comparison of superior-level facet joint violations between robot-assisted percutaneous pedicle screw placement and conventional open fluoroscopic-guided pedicle screw placement," *Orthopaedic Surgery*, vol. 11, no. 5, 2019.

[28] X. Le, W. Tian, Z. Shi et al., "Robot-assisted versus fluoroscopy-assisted cortical bone trajectory screw instrumentation in lumbar spinal surgery: a matched-cohort comparison," *World Neurosurgery*, vol. 120, pp. e745–e751, 2018.

Hindawi
Pain Research and Management
Volume 2021, Article ID 1288246, 7 pages
https://doi.org/10.1155/2021/1288246

Research Article

Posterior Dynamic Stabilization with Limited Rediscectomy for Recurrent Lumbar Disc Herniation

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Received 5 September 2021; Revised 11 December 2021; Accepted 13 December 2021; Published 23 December 2021

Academic Editor: Sidong Yang

Objective. Recurrent lumbar disc herniation (RLDH) is the most common cause of sciatica after primary discectomy. The purpose of this study was to evaluate the efficacy of transpedicular dynamic stabilization (TDS) combined with limited rediscectomy in the treatment of single-level RLDH. *Methods*. We retrospectively evaluated a consecutive series of 24 middle-aged patients who underwent TDS (Dynesys system) combined with limited rediscectomy (i.e., removing only extruded or loose disc fragments) for single-level Carragee type II and type IV RLDH between April 2012 and September 2017. Clinical results were evaluated with visual analog scale (VAS) for leg and low back pain, Oswestry Disability Index (ODI) scores, and complications. Imaging data include lumbar segment motion and intervertebral height. *Results*. The mean follow-up period was 38 months. The VAS and ODI scores were significantly improved at the last follow-up. The average range of motion (ROM) at the stabilized segment was 6.4° before surgery and 4.2° at the last follow-up, with a 78.6% mean preservation ($P < 0.05$). Intervertebral height at the stabilized segment decreased slightly after surgery ($P < 0.05$). However, there was no further decline at the last follow-up. There were no cases of reherniation, screw loosening, or segmental instability. *Conclusions*. TDS combined with limited rediscectomy resulted in an effective procedure in middle-aged patients with Carragee type II and type IV RLDH. It was able to stabilize the operated segment with partial motion preservation. Moreover, it could maintain disc height and decrease the risk of recurrence in patients with a large posterior annular defect.

1. Introduction

Discectomy is considered as the main surgical method in patients with lumbar disc herniation (LDH) without segmental instability [1]. Nevertheless, recurrent lumbar disc herniation (RLDH) is one of the most common complications that can cause severe pain and reoperation after primary discectomy, with reported incidence ranging from 7% to 24% [2]. The definition of RLDH has varied among different authors. In most studies, recurrent lumbar disc herniation was defined as a disc hernia at the same level of a previous discectomy in patients with a pain-free interval of at least 6 months long after surgery, regardless of ipsilateral or contralateral herniation [3]. Numerous factors have been associated with an increased rate of reherniation following primary discectomy. Lumbar instability and increased stress upon the intervertebral disc after discectomy may be the major controllable risk factors for RLDH [4].

Surgical treatment for RLDH is indicated in patients with continuous and severe pain, resistant to conservative treatment or cases with motor deficiency. Traditional surgical options include revision discectomy or discectomy supplemented with instrumented fusion. According to the reports by Buchmann et al. [5] and Hou et al. [6], rediscectomy provided good to excellent pain relief in 55%–96% of the patients. Because of peridural adhesion, extension interlaminar fenestration would be necessary to reduce the risk of dural and nerve root injury. However, excessive laminectomy may result in lumbar instability. In addition, the intervertebral height decreases after rediscectomy, which can lead to the progression of disc degeneration [7]. Therefore, some surgeons advocate the routine use of

instrumented fusion in the treatment of RLDH [8]. Intervertebral fusion can maintain lumbar stability and restore intervertebral height. A recent review by Dower et al. [9] demonstrated that fusion resulted in a statistically significant improvement in back pain compared with discectomy (60.1% vs. 47.2%, respectively). Nonetheless, intervertebral fusion sacrifices the activity of the fixed segment and may accelerate degeneration of adjacent segments [10].

Based on the above deficiencies, transpedicular dynamic stabilization (TDS) was introduced as an alternative to fusion to preserve the activity of the instrumented segments while stabilizing the lumbar spine. Moreover, this technique is targeted to maintain the intervertebral height and reduce the mechanical load upon the disc. It is reported that dynamic stabilization is useful to prevent or diminish recurrent disc herniation after discectomy [11]. Therefore, we proposed TDS combined with limited rediscectomy (i.e., removing only extruded or loose disc fragments) [12] for the treatment of patients with RLDH as an alternative to instrumented fusion. The purpose of this study is to assess the clinical outcomes of TDS with the Dynesys system (Zimmer, USA) for RLDH.

2. Materials and Methods

2.1. Patients. This retrospective study included 24 consecutive patients who underwent Dynesys stabilization combined with limited rediscectomy for single-level RLDH from April 2012 to September 2017. There were 16 men and 8 women with an average age of 47.6 years (range of 32–62 years). This study has been approved by the Ethical Committee of the Third Affiliated Hospital of Chongqing Medical University (SKYW20190316). The study was conducted per the ethical principles that have their origins in the Declaration of Helsinki and its subsequent amendments. Informed consent was obtained from all patients. Inclusion criteria were as follows: (1) age ≥30 years at the time of surgery; (2) patients with symptoms of new onset low back pain and radicular leg pain and/or decreased muscular strength and/or abnormal sensation; (3) diagnosis of single-level RLDH confirmed by MRI (primary surgery included open discectomy or microendoscopic discectomy); (4) Carragee type II (presence of extruded or sequestered fragments with wide annular rupture; rupture **>** 6 mm) or type IV herniation (the width of the basilar part of the herniated disc >6 mm; annulus is intact and without free fragments under the annulus) [13]; (5) failed in at least 6 weeks of conservative treatment (oral medication, physical therapy, and so on); and (6) underwent the operation of TDS (Dynesys, Zimmer Spine) combined with limited rediscectomy. Exclusion criteria included the following: (1) more than 1/2 reduction in intervertebral height; (2) rigid segmental kyphosis; and (3) osteoporosis (T-score ≤−2.5, DEXA).

2.2. Surgical Procedure. The Dynesys system is a pedicle screw-based dynamic stabilization system. In the system, titanium alloy pedicle screws are connected by a polyethylene terephthalate (PET) cord that goes through the center of a hollow cylinder polycarbonate urethane (PCU) spacer instead of the traditional rigid rod (Figure 1). By appropriately tightening the cord and selecting the length of the spacer, dynamic stabilization would be achieved in the instrumented segment [14].

Patients were placed in the prone position under general anesthesia. A midline dorsal incision in the skin, subcutaneous tissue, and lumbodorsal fascia was applied. Extended interlaminar fenestration decompression was performed through the posterior median approach on the symptomatic side. Only extruded or loose disc fragments were removed. Pedicle screws were inserted through the Wiltse approach under imaging control. The entry point was located at the junction of the lateral border of the superior articular process and the basilar part of the transverse process. Then, the patients' position was modified to obtain the appropriate lumbar lordosis. The spacer was cut according to the measured distance between the screws (distraction force of 1.5 N). The central cord and the spacer were then locked within the screw heads. Patients received a soft support lumbar corset for 3 weeks after surgery.

2.3. Clinical and Radiologic Evaluation. Clinical outcomes were assessed with visual analog scale (VAS) for low back and leg pain and Oswestry Disability Index (ODI). Operative time, blood loss, and complications were also documented. Standing plain and dynamic radiographs with flexion and extension views were obtained preoperatively, at 3 months postoperatively, and the last follow-up. The evaluation index included the lordosis at the instrumented segment, the height of the intervertebral disc, and range of motion (ROM) at the instrumented level, the 1st proximal segment, and the lumbar spine (L1-S1). Disc height (DH) was calculated using the anterior intervertebral space height (AH) and posterior intervertebral space height (PH) on the lateral standing lumbar X-ray: (AH + PH)/2. Segmental ROM was calculated as the angle difference value between the inferior surface of the upper vertebrae and the superior surface of the lower vertebrae on the lateral standing lumbar flexion-extension X-ray. Disc degeneration grade was evaluated according to the Pfirrmann classification on T2-weighted sagittal and axial MRI [15].

2.4. Statistical Analysis. Statistical analysis was conducted using SPSS (version 16.0, SPSS Inc.). The clinical and radiologic results were analyzed using two-way ANOVA. Significance was defined as $P < 0.05$.

3. Results

3.1. Perioperative Data and Complications. The mean interval between the primary and revision surgeries was 66.0 ± 53.2 months (range of 6–192 months). The RLDH level was L4/5 in 14 (58.3%) and L5/S1 in 10 (41.7%) patients (Table 1). The mean operative time was 136 minutes (range

Figure 1: The Dynesys system consists of titanium alloy screws, PET cords, and PCU spacers.

of 98–183 minutes), with an average blood loss of 266 ml (range of 100–500 ml). The mean follow-up duration was 38 months (range of 28–63 months). Superficial incision infection was observed in one patient 6 days after surgery. The patient was cured by debridement and antibiotics. One patient developed low back and hip pain 3 weeks after surgery, which was relieved after 10 days of conservative treatment. There were no cases of reherniation, screw loosening, or dural and nerve root injury.

3.2. Clinical Outcome. The mean VAS scores for low back pain decreased from 3.8 ± 0.8 (range of 3–5) preoperatively to 1.3 ± 0.6 (range of 0–2) at 3 months postoperatively and 0.9 ± 0.4 (range of 0–2) at the last follow-up. The VAS scores for low back pain were significantly improved at the final follow-up evaluation compared with the baseline values ($P < 0.05$). Similar to the VAS scores for low back pain, the mean VAS scores for leg pain decreased from 5.5 ± 1.1 (range of 4–8) to 0.9 ± 0.6 (range of 0–2) at 3 months postoperatively and 0.7 ± 0.5 (range of 0-1, $P < 0.05$) at the last follow-up. The mean ODI was $57.9\% \pm 10.6\%$ (range of 40%–76%) preoperatively, $23.2\% \pm 7.8\%$ (range of 6%–40%) at the 3-month follow-up, and $12.8\% \pm 6.2\%$ (range of 0%–24%) at the last follow-up. The changes in VAS_{leg} and ODI scores between the preoperative period and the follow-ups were statistically significant as well ($P < 0.05$) (Table 2).

3.3. Radiologic Outcome. The lordosis at instrumented segment was reduced from 8.0° (range of −5.7° to −13.3°) before surgery to 6.8° (range of 2.3°–10.8°) at the 3 months follow-up ($P < 0.05$) and 7.0° (range of 2.6°–11.3°) at last follow-up ($P > 0.05$). The average disc height decreased slightly from preoperative 10.4 mm (range of 6.8 mm–13.8 mm) to 9.3 mm (range of 6.3 mm–12.6 mm) at 3 months postoperatively ($P < 0.05$). There was no further decline at the last follow-up ($P > 0.05$). The average ROM at instrumented segment was 6.4° (range of 3.1°–17.3°) before surgery, 4.0°(range of 2.6°–5.9°) at 3 months after surgery, and 4.2° (range of 3.0°–5.2°) at last follow-up. Compared with preoperatively, 78.6% (range of 24%–152%) of ROM was preserved at the last follow-up. The ROM at the 1st proximal segment was 9.0° (range of 3.5°–16.0°) before surgery, 9.5° (range of 5.8°–15.7°) at 3 months after surgery, and 9.9° (range of 5.5°–14.9°) at the last follow-up. The differences were not statistically significant ($P > 0.05$). The lumbar motion was reduced from 34.1° (range of 13.2°–60.4°) before surgery to 28.8° (range of 17.2°–40.4°) at 3 months after surgery ($P < 0.05$) and 34.8° (range of 18.7°–63.2°) at last follow-up ($P > 0.05$) (Table 3). MRI was performed in 11 patients during the follow-up period. Of the 11 patients, the disc degeneration grade (Pfirrmann classification) improved at the index level was observed in 6 patients (Figure 2). The other 5 patients demonstrated no visible signal intensity change at the index level. No progressive degeneration was noted at the first proximal segment in the 11 patients.

4. Discussion

The optimal treatment for RLDH remains controversial. Several studies demonstrated that rediscectomy could be able to achieve satisfactory clinical results [3, 6, 16]. However, the chance of segmental lumbar instability increases as rediscectomy often requires more aggressive laminectomy and facetectomy for better exposure of the nerve root canal [17, 18]. Moreover, excessive sagittal activity at the involved segment after discectomy is a risk factor for recurrent lumbar disc herniation [19, 20]. Furthermore, large posterior annular defect is prone to develop recurrent disc herniation. According to the study by Carragee et al., the recurrence rate after discectomy in patients with Carragee type II and IV herniations was 27% and 38%, respectively [13]. Discectomy alone might be insufficient to achieve satisfactory results. Thus, we performed posterior dynamic stabilization with limited rediscectomy for the treatment of Carragee type II and type IV RLDH to stabilize the lumbar spine, reduce excessive intervertebral motion, and decrease the risk of re-recurrent disc herniation.

The Dynesys system is supposed to stabilize the operated segment with partial motion preservation. The biomechanical analysis demonstrated that the Dynesys system reduced the intersegmental motion in flexion, extension, lateral bending, and axial rotation compared with structurally damaged specimens so that it could provide substantial stability in case of lumbar degenerative disease [21, 22]. We investigated the clinical and radiologic results of patients undergoing TDS and limited rediscectomy for RLDH. In general, patients had clinically and statistically significant improvements in $VAS_{back,leg}$ and ODI scores. In addition, flexion/extension radiographs showed significant preservation of ROM at the stabilized segment without lumbar instability or spondylolisthesis. Some studies have also shown that the Dynesys system provides the lumbar spine with sufficient stability in treating degenerative spondylolisthesis [23, 24]. In the long term, there is always a concern of screw loosening in patients treated with dynamic stabilization [25] although the loosened screws appeared to be asymptomatic [26]. In the present study, no cases of screw loosening were found at the last follow-up. The reasons

Table 1: Demographics of dynamic stabilization for recurrent lumbar disc herniation.

Case no.	Sex	Age (years)	Level	Primary surgery	Recurrence time (months)	Follow-up (months)	Complication
1	F	53	L5-S1	OD	120	28	
2	F	62	L4-5	OD	12	49	
3	M	45	L5-S1	OD	60	54	
4	M	34	L4-5	MED	19	33	Superficial wound infection
5	M	41	L4-5	OD	24	42	
6	M	48	L5-S1	OD	120	30	
7	F	48	L5-S1	MED	9	32	
8	F	40	L4-5	OD	84	30	
9	M	35	L5-S1	MED	36	63	
10	M	58	L4-5	OD	108	40	
11	F	34	L4-5	OD	60	37	
12	M	53	L4-5	OD	96	36	
13	M	52	L4-5	OD	24	46	
14	M	47	L4-5	OD	6	32	
15	F	50	L5-S1	OD	192	56	
16	F	61	L4-5	OD	168	30	
17	M	59	L4-5	OD	60	47	
18	F	58	L4-5	OD	96	38	
19	M	46	L4-5	MED	132	34	Transient low back and hip pain
20	F	52	L5-S1	OD	7	32	
21	M	38	L5-S1	OD	72	33	
22	M	43	L5-S1	OD	24	29	
23	M	54	L5-S1	OD	24	33	
24	M	32	L4-5	OD	30	36	

M: male, F: female, OD: open discectomy, and MED: microendoscopic discectomy.

might be the patients with osteoporosis were excluded, and minimal bone resection as well as pedicle screws placement lateral to the facet joints that makes the rotation axis of the Dynesys system close to the rotation axis of the motion segment could reduce the stress on the system.

Disc removal may lead to accelerated disc degeneration at the operative level. Disc height reduction and endplate degeneration may be the most common findings following discectomy [27, 28]. Excessive removal is associated with the progression of disc space narrowing, which may lead to low back pain over time [29]. Conversely, limited nucleus pulposus removal, preserved disc height, and moderate disk degeneration are significant risk factors for RLDH [19, 30, 31]. Therefore, surgical treatment which can both preserve the disc height and decrease the incidence of reherniation may allow for improved outcomes. According to the literature, discectomy with additional transpedicular dynamic stabilization is useful to prevent progression of intervertebral disc degeneration and decrease the risk of recurrence in treating primary lumbar disc herniation [32, 33]. Our results showed that disc height decreased slightly after TDS and limited discectomy, but there was no further decline at the last follow-up. The disc height could be maintained at the last follow-up compared with the postoperative value. The result may indicate that dynamic stabilization can delay or prevent the progression of disc degeneration. Of the 11 patients who underwent MRI examination during the follow-up period, 6 patients demonstrated improved disc degeneration grade at the index level, whereas the other patients showed no visible signal intensity change at the index level. In addition, a second recurrence did not occur in any patients in this study at the last follow-up. This further confirms that the Dynesys system can decelerate the degeneration process. However, its mechanism remains unclear. One possible mechanism is that intradiscal pressure is reduced by axial distraction [34], and moderate dynamic compression or distraction could promote anabolism in nucleus pulposus cells [35, 36], thus allowing the disc to repair itself. Some studies reported disc rehydration at the bridged level after dynamic stabilization [37, 38]. However, severe degeneration of the disc is difficult to reverse. Therefore, patients with a significant reduction in intervertebral disc height were excluded from this study.

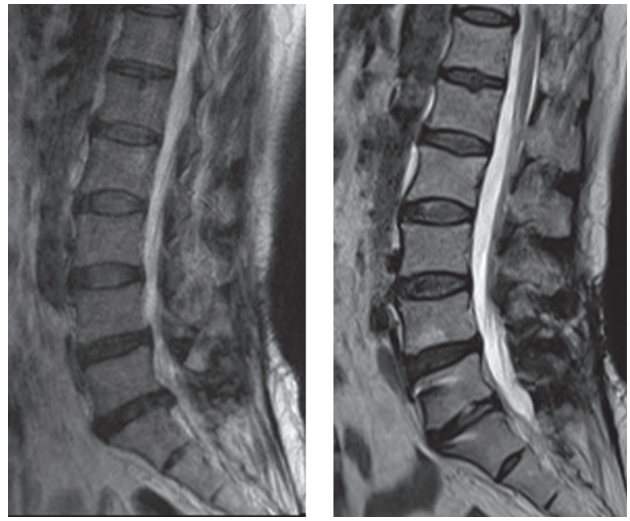
Table 2: Clinical outcomes.

	Preoperative	3 months	Last follow-up	F	P
VAS_{back}	3.8 ± 0.8	1.3 ± 0.6	0.9 ± 0.4	110.49	0.001
VAS_{leg}	5.5 ± 1.1	0.9 ± 0.6	0.7 ± 0.5	525.16	0.001
ODI (%)	57.9 ± 10.6	23.2 ± 7.8	12.8 ± 6.2	171.475	0.001

There were limitations to this study: lack of a control group, limited patient number, and short follow-up period. Nevertheless, these are common issues when evaluating a new surgical technique. Besides, there was no further analysis of the causes of low back pain before the second surgery and the role of dynamic stabilization in alleviating it. In addition, due to the high costs, only 11 patients received MRI at postoperative follow-up in the study. A longer follow-up period and more patients receiving MRI will contribute to better observation of the disc changes after dynamic stabilization.

Table 3: Radiographic outcomes.

	Preoperative	3 months	Last follow-up	F	P
Lordosis at instrumented segment (°)	8.0 ± 4.2	6.8 ± 2.4	7.0 ± 2.6	2.379	0.104
Disc height at instrumented segment (mm)	10.4 ± 1.9	9.3 ± 1.9	9.1 ± 1.8	57.562	0.001
ROM at instrumented segment (°)	6.4 ± 3.2	4.0 ± 0.9	4.2 ± 0.6	12.578	0.001
ROM at the 1st proximal segment (°)	9.0 ± 3.9	9.5 ± 2.8	9.9 ± 2.6	1.969	0.151
ROM at L1-S1 (°)	34.1 ± 13.1	29.2 ± 6.8	34.8 ± 10.5	4.496	0.016



(a) (b)

Figure 2: A case of a 53 years old female patient with RLDH at L5-S1. MRI scans showed rehydration at 22-month follow-up after transpedicular dynamic stabilization.

5. Conclusions

Our results suggest that TDS combined with limited rediscectomy resulted in a safe and effective procedure in middle-aged patients with Carragee type II and type IV RLDH. It was able to stabilize the operated segment with partial motion preservation. Moreover, it could maintain disc height and decrease the risk of recurrence in patients with a large posterior annular defect.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Authors' Contributions

LL and QZ conceived and designed the study. QZ and FL carried out the operation. LL, CZ, PL, and LC L (Lichuan Liang) collected the data. LH L (Liehua Liu) analyzed the data. LL and QZ wrote the manuscript. All authors have read and approved the final manuscript.

Acknowledgments

This study was supported by Postdoctoral Research Start-Up Fund of Chongqing Medical University (R9005).

References

[1] A. Blamoutier, "Surgical discectomy for lumbar disc herniation: surgical techniques," *Orthopaedics & Traumatology, Surgery & Research: OTSR*, vol. 99, no. 1 Suppl, pp. S187–S196, 2013.

[2] J. A. O'Donnell, J. T. Anderson, A. R. Haas et al., "Treatment of recurrent lumbar disc herniation with or without fusion in workers' compensation subjects," *Spine (Phila. Pa. 1976)*, vol. 42, no. 14, pp. E864–E870, 2017.

[3] H. Mashhadinezhad, E. Sarabi, S. Mashhadinezhad, and B. Ganjeifar, "Clinical outcomes after microdiscectomy for recurrent lumbar disk herniation: a single-center study," *The archives of bone and joint surgery*, vol. 6, no. 5, pp. 397–401, 2018.

[4] C. U. Onyia and S. K. Menon, "Impact of comorbidities on outcome following revision of recurrent single-level lumbar disc prolapse between revision microdiscectomy and posterior lumbar interbody fusion: a single-institutional analysis," *Asian Journal of Neurosurgery*, vol. 14, no. 2, pp. 392–398, 2019.

[5] N. Buchmann, A. Preuß, J. Gempt et al., "Outcome after surgical treatment for late recurrent lumbar disc herniations in standard open microsurgery," *World Neurosurgery*, vol. 89, pp. 382–386, 2016.

[6] T. Hou, Q. Zhou, F. Dai et al., "Repeated microendoscopic discectomy for recurrent lumbar disk herniation," *Clinics*, vol. 70, no. 2, pp. 120–125, 2015.

[7] J. P. Jarman, V. E. Arpinar, D. Baruah, A. P. Klein, D. J. Maiman, and L. Tugan Muftuler, "Intervertebral disc height loss demonstrates the threshold of major pathological changes during degeneration," *European Spine Journal*, vol. 24, no. 9, pp. 1944–1950, 2015.

[8] T. E. Mroz, D. Lubelski, S. K. Williams et al., "Differences in the surgical treatment of recurrent lumbar disc herniation among spine surgeons in the United States," *The Spine Journal*, vol. 14, no. 10, pp. 2334–2343, 2014.

[9] A. Dower, R. Chatterji, A. Swart, and M. J. Winder, "Surgical management of recurrent lumbar disc herniation and the role of fusion," *Journal of Clinical Neuroscience*, vol. 23, pp. 44–50, 2016.

[10] S. Okuda, Y. Nagamoto, T. Matsumoto, T. Sugiura, Y. Takahashi, and M. Iwasaki, "Adjacent segment disease after single segment posterior lumbar interbody fusion for degenerative spondylolisthesis: minimum 10 years follow-up," *Spine (Phila. Pa. 1976)*, vol. 43, no. 23, pp. E1384–E1388, 2018.

[11] A. F. Ozer, F. Keskin, T. Oktenoglu et al., "A novel approach to the surgical treatment of lumbar disc herniations: indications of simple discectomy and posterior transpedicular dynamic stabilization based on carragee classification," *Advances in Orthopedics*, vol. 2013, Article ID 270565, 6 pages, 2013.

[12] E. J. Carragee, A. O. Spinnickie, T. F. Alamin, and S. Paragioudakis, "A prospective controlled study of limited versus subtotal posterior discectomy: short-term outcomes in patients with herniated lumbar intervertebral discs and large posterior anular defect," *Spine (Phila. Pa. 1976)*, vol. 31, no. 6, pp. 653–657, 2006.

[13] E. J. Carragee, M. Y. Han, P. W. Suen, and D. Kim, "Clinical outcomes after lumbar discectomy for sciatica," *Journal of Bone and Joint Surgery American Volume*, vol. 85, no. 1, pp. 102–108, 2003.

[14] O. Schwarzenbach and U. Berlemann, "Dynamic posterior stabilization with the pedicle screw system DYNESYS®," *Operative Orthopädie und Traumatologie*, vol. 22, no. 5–6, pp. 545–557, 2010.

[15] C. W. A. Pfirrmann, A. Metzdorf, M. Zanetti, J. Hodler, and N. Boos, "Magnetic resonance classification of lumbar intervertebral disc degeneration," *Spine (Phila. Pa. 1976)*, vol. 26, no. 17, pp. 1873–1878, 2001.

[16] C. Mehren, L. Wanke-Jellinek, and A. Korge, "Revision after failed discectomy," *European Spine Journal*, vol. 29, 2019.

[17] S. Ramhmdani, Y. Xia, R. Xu et al., "Iatrogenic spondylolisthesis following open lumbar laminectomy: case series and review of the literature," *World Neurosurgery*, vol. 113, pp. e383–e390, 2018.

[18] A. Okawa, K. Shinomiya, K. Takakuda, and O. Nakai, "A cadaveric study on the stability of lumbar segment after partial laminotomy and facetectomy with intact posterior ligaments," *Journal of Spinal Disorders*, vol. 9, no. 6, pp. 518–526, 1996.

[19] K.-T. Kim, D.-H. Lee, D.-C. Cho, J.-K. Sung, and Y.-B. Kim, "Preoperative risk factors for recurrent lumbar disk herniation in L5-S1," *Journal of Spinal Disorders & Techniques*, vol. 28, no. 10, pp. E571–E577, 2015.

[20] E.-H. Shin, K.-J. Cho, Y.-T. Kim, and M.-H. Park, "Risk factors for recurrent lumbar disc herniation after discectomy," *International Orthopaedics*, vol. 43, no. 4, pp. 963–967, 2019.

[21] W. Schmoelz, J. F. Huber, T. Nydegger, D. Ing, L. Claes, and H. J. Wilke, "Dynamic stabilization of the lumbar spine and its effects on adjacent segments," *Spine (Phila. Pa. 1976)*, vol. 28, no. 4, pp. 418–423, 2003.

[22] C. A. Niosi, Q. A. Zhu, D. C. Wilson, O. Keynan, D. R. Wilson, and T. R. Oxland, "Biomechanical characterization of the three-dimensional kinematic behaviour of the Dynesys dynamic stabilization system: an in vitro study," *European Spine Journal*, vol. 15, no. 6, pp. 913–922, 2006.

[23] S. W. Yu, S. C. Yang, C. H. Ma, C. H. Wu, C. Y. Yen, and Y. K. Tu, "Comparison of Dynesys posterior stabilization and posterior lumbar interbody fusion for spinal stenosis L4L5," *Acta Orthopaedica Belgica*, vol. 78, no. 2, pp. 230–239, 2012.

[24] C. H. Kuo, P. Y. Chang, J. C. Wu et al., "Dynamic stabilization for L4-5 spondylolisthesis: comparison with minimally invasive transforaminal lumbar interbody fusion with more than 2 years of follow-up," *Neurosurgical Focus*, vol. 40, no. 1, pp. E3–E9, 2016.

[25] M. Prud'homme, C. Barrios, P. Rouch, Y. P. Charles, J.-P. Steib, and W. Skalli, "Clinical outcomes and complications after pedicle-anchored dynamic or hybrid lumbar spine stabilization: a systematic literature review," *Journal of Spinal Disorders & Techniques*, vol. 28, no. 8, pp. E439–E448, 2015.

[26] J. C. Wu, W. C. Huang, H. W. Tsai et al., "Pedicle screw loosening in dynamic stabilization: incidence, risk, and outcome in 126 patients," *Neurosurgical Focus*, vol. 31, no. 4, p. E9, 2011.

[27] M. Barth, M. Diepers, C. Weiss, and C. Thomé, "Two-year outcome after lumbar microdiscectomy versus microscopic sequestrectomy: part 2: radiographic evaluation and correlation with clinical outcome," *Spine (Phila. Pa. 1976)*, vol. 33, no. 3, pp. 273–279, 2008.

[28] B. K. Weiner, M. Vilendecic, D. Ledic et al., "Endplate changes following discectomy: natural history and associations between imaging and clinical data," *European Spine Journal*, vol. 24, no. 11, pp. 2449–2457, 2015.

[29] M. J. DePalma, J. M. Ketchum, T. R. Saullo, and B. L. Laplante, "Is the history of a surgical discectomy related to the source of chronic low back pain?" *Pain Physician*, vol. 15, no. 1, pp. E53–E58, 2012.

[30] M. J. Mcgirt, S. Eustacchio, P. Varga et al., "A prospective cohort study of close interval computed tomography and magnetic resonance imaging after primary lumbar discectomy," *Spine*, vol. 34, no. 19, pp. 2044–2051, 2009.

[31] E. Yorimitsu, K. Chiba, Y. Toyama, and K. Hirabayashi, "Long-term outcomes of standard discectomy for lumbar disc herniation: a follow-up study of more than 10 years," *Spine (Phila. Pa. 1976)*, vol. 26, no. 6, pp. 652–657, 2001.

[32] M. Putzier, S. V. Schneider, J. F. Funk, S. W. Tohtz, and C. Perka, "The surgical treatment of the lumbar disc prolapse: nucleotomy with additional transpedicular dynamic stabilization versus nucleotomy alone," *Spine (Phila. Pa. 1976)*, vol. 30, no. 5, pp. 109–114, 2005.

[33] T. Kaner, M. Sasani, T. Oktenoglu, M. Cosar, and A. F. Ozer, "Clinical outcomes after posterior dynamic transpedicular stabilization with limited lumbar discectomy: Carragee classification system for lumbar disc herniations," *SAS Journal*, vol. 4, no. 3, pp. 92–97, 2010.

[34] C. Schilling, S. Krüger, T. M. Grupp, G. N. Duda, W. Blömer, and A. Rohlmann, "The effect of design parameters of dynamic pedicle screw systems on kinematics and load bearing: an in vitro study," *European Spine Journal*, vol. 20, no. 2, pp. 297–307, 2011.

[35] P. Li, Y. Gan, H. Wang et al., "Dynamic compression effects on immature nucleus pulposus: a study using a novel intelligent and mechanically active bioreactor," *International Journal of Medical Sciences*, vol. 13, no. 3, pp. 225–234, 2016.

[36] M. Kroeber, F. Unglaub, T. Guehring et al., "Effects of controlled dynamic disc distraction on degenerated intervertebral discs: an in vivo study on the rabbit lumbar spine model," *Spine (Phila. Pa. 1976)*, vol. 30, no. 2, pp. 181–187, 2005.

[37] A. Yilmaz, S. Senturk, M. Sasani et al., "Disc rehydration after dynamic stabilization: a report of 59 cases," *Asian Spine Journal*, vol. 11, no. 3, pp. 348–355, 2017.

[38] L.-Y. Fay, J.-C. Wu, T.-Y. Tsai et al., "Intervertebral disc rehydration after lumbar dynamic stabilization: magnetic resonance image evaluation with a mean followup of four years," *Advances in Orthopedics*, vol. 2013, Article ID 437570, 8 pages, 2013.

Hindawi
Pain Research and Management
Volume 2021, Article ID 6894001, 8 pages
https://doi.org/10.1155/2021/6894001

Research Article

Accuracy of Robot-Assisted Percutaneous Pedicle Screw Placement under Regional Anesthesia: A Retrospective Cohort Study

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Received 15 November 2021; Revised 6 December 2021; Accepted 7 December 2021; Published 20 December 2021

Academic Editor: Sidong Yang

Background. Robot-assisted pedicle screw placement is usually performed under general anesthesia to keep the body still. The aim of this study was to compare the accuracy of the robot-assisted technique under regional anesthesia with that of conventional fluoroscopy-guided percutaneous pedicle screw placement under general anesthesia in minimally invasive lumbar fusion surgery. *Methods*. This study recruited patients who underwent robot-assisted percutaneous endoscopic lumbar interbody fusion (PELIF) or fluoroscopy-guided minimally invasive transforaminal lumbar interbody fusion (MIS-TLIF) between December 2017 and February 2020 at a single center. Based on the method of percutaneous pedicle screw placement used, patients were divided into the robot-assisted under regional anesthesia (group RE-RO) and fluoroscopy-guided under general anesthesia (group GE-FLU) groups. The primary outcome measures were screw accuracy and the incidence of facet joint violation (FJV). Secondary outcome measures included X-ray and visual analogue scale (VAS) scores which were used to evaluate the degree of the postoperative pain at 4 hours and on postoperative days 1, 2, and 3. Intraoperative adverse events were also recorded. *Results*. Eighteen patients were included in group RE-RO, and 23 patients were included in group GE-FLU. The percentages of clinically acceptable screws (Gertzbein and Robbins grades A and B) were 94.4% and 91.5%, respectively. There was no significant difference in the percentages of clinically acceptable screws ($p = 0.44$) or overall Gertzbein and Robbins screw accuracy grades ($p = 0.35$). Only the top screws were included in the analysis of FJVs. The percentages of FJV (Babu grades 1, 2, and 3) were 5.6% and 28.3%, respectively. This difference was statistically significant ($p = 0.01$). Overall, the FJV grades in group RE-RO were significantly better than those in group GE-FLU ($p = 0.009$). The mean fluoroscopy time for each screw in group RE-RO was significantly shorter than that in group GE-FLU (group RE-RO: 5.4 ± 1.9 seconds and group GE-FLU: 6.8 ± 2.0 seconds; $p = 0.03$). The postoperative pain between the RE-RO and GE-FLU groups was not statistically significant. The intraoperative adverse events included 1 case of registration failure and 1 case of guide-wire dislodgment in group RE-RO, as well as 2 cases of screw misplacement in group GE-FLU. No complications related to anesthesia were observed. *Conclusion*. Robot-assisted pedicle screw placement under regional anesthesia can be performed effectively and safely. The accuracy is comparable to the conventional technique. Moreover, this technique has the advantage of fewer FJVs and a lower radiation time.

1. Background

Pedicle screw fixation, a rigid surgical technique, has been widely used in spine surgery since the 1970s [1] and has been shown to stabilize the spine in a variety of spinal diseases, such as trauma, tumors, degeneration, and deformities. With the imaging guidance from fluoroscopy, freehand pedicle screw placement has been performed with high levels of accuracy. However, complications related to misplacements, such as nerve and vascular injuries, still persist. In addition, percutaneous pedicle screw implantation is associated with a high incidence of iatrogenic facet joint violation (FJV),

which is an independent risk factor for adjacent segment disease (ASD) [2–4]. In addition to these patient-related disadvantages, the surgeon's intraoperative radiation exposure is becoming increasingly concerning [5–7]. Previous studies have shown that spinal surgical robots may be able to offer solutions to both of these concerns [8, 9].

Robot-assisted pedicle screw placement is usually performed under general anesthesia to keep the body still and improve screw placement accuracy. However, general anesthesia may be associated with high percentages of perioperative complications and medical costs, especially for elderly patients [10, 11]. In addition, some spine surgeons prefer patient feedback to reduce the possibility of nerve injury in some special surgeries, such as percutaneous endoscopic lumbar discectomy (PELD) and percutaneous kyphoplasty [12, 13]. Regional anesthesia has been suggested to be comfortable and safe in some open and minimally invasive spine surgeries [14].

Our medical team found that patients could remain motionless and painless during fluoroscopy-guided percutaneous pedicle screw placement under regional anesthesia in percutaneous endoscopic lumbar interbody fusion (PELIF) surgery. We predict that accurate, robot-assisted placement of pedicle screws in this patient state can be achieved. Therefore, we attempted to use a spine robot instead of fluoroscopy to guide pedicle screw placement. To the best of our knowledge, no previous study has been reported focusing on robot-assisted pedicle screw accuracy under regional anesthesia. This study, therefore, aimed to evaluate the accuracy and safety of robot-assisted pedicle screw placement under regional anesthesia in lumbar fusion surgery.

2. Methods

2.1. Patients. This study was approved by the Ethics Committee of the Hebei General Hospital before data collection and analysis. This retrospective study recruited patients with lumbar degenerative disease who underwent robot-assisted PELIF or fluoroscopy-guided minimally invasive transforaminal lumbar interbody fusion (MIS-TLIF) between December 2017 and February 2020. The diagnoses included lumbar spinal stenosis, lumbar disc herniation, and lumbar spondylolisthesis. The patients were divided into two groups according to the pedicle screw implantation method: robot-assisted under regional anesthesia (group RE-RO) and fluoroscopy-guided under general anesthesia (group GE-FLU).

The inclusion criteria were as follows: (1) scheduled 1- or 2-level PELIF or MIS-TILF surgery with either robot-assisted or fluoroscopy-guided percutaneous pedicle screw placement as the internal fixation technique; and (2) postoperative computed tomography (CT) scans taken before discharge with images meeting the measurement requirements. The exclusion criteria were as follows: (1) patients with a degree of lumbar spondylolisthesis or lumbar spondylolysis of II or higher; (2) patients with infection, tumors, or scoliosis of the spine; and (3) history of previous spinal surgery.

2.2. Surgical Technique

2.2.1. Group RE-RO. All procedures were performed by the same senior spine surgeon who had performed more than 20 cases of robot-assisted surgery. The patients' CT data of the lumbar vertebrae (continuous scanning, ≤1-mm cuts) were copied from the inspection equipment and input into the robotic surgical plan workstation (Mazor Renaissance Surgical Technologies, Caesarea, Israel) for preoperative planning. Before surgery, the patient was told how to cooperate with the surgery, including keeping still and breathing evenly for some special period. During surgery, the patients were placed in a comfortable prone position on the operating table, with oxygen inhalation and ECG and vital sign monitoring. Dexmedetomidine (4 μg/ml) was pumped at a rate of 3–8 ml/h. The administration of epidural anesthesia was performed using the loss-of-resistance technique through the interlaminar space of the operating segments (Figure 1). The anesthetic drug for the injection was a mixture of 0.5% lidocaine and 0.25% ropivacaine. The dose was 10 ml. In this anesthetic state, patients had hypoesthesia rather than loss of sensation in the operative region and lower extremities. The motion of the lower limbs persisted.

The surgical procedure was performed as follows: First, the working platform was installed. The Hover-T frame platform was used for all operations in this group. After local infiltration anesthesia (1% lidocaine), three needles were inserted into the spinous process of the upper lumbar spine and bilateral posterior superior iliac spines to fix the frame (Figure 2(a)). After image acquisition, registration (Figure 2(b)), and robot motion (Figure 2(c)), local infiltration anesthesia was administered to the skin and around the facet joints before incision and drilling (Figure 2(d)). To minimize deviations caused by spine movement, drilling was carried out in a painless state. Otherwise, additional local anesthesia was administered, as pedicle screw insertion could aggravate the patient's pain. It was essential to increase the speed of drug pumping in advance. Details of the robot-assisted procedure have been described in previous articles [8, 15]. After screw (minimally invasive spinal system; WEGORTHO Paedic Device Co., Ltd.; Weihai, China) placement, decompression, and interbody fusion were performed (Figure 3). No drainage system was required. Postoperative MRI and CT were necessary. Patients could walk with waist support on the first day. The protocol has been outlined in Table 1.

2.3. Group GE-FLU. The pedicle screw placement procedures were completed by two senior spine surgeons who had each performed more than 50 cases of fluoroscopy-guided pedicle screw insertion. After general anesthesia, the patient was placed in a prone position. A C-arm was used to locate the targeted vertebral pedicles and plan the screw route. A puncture needle was inserted through a 1.5 cm incision with fluoroscopy guidance. After a final fluoroscopy check on the AP and lateral views, the puncture needle was replaced with a spacer. Screw (minimally

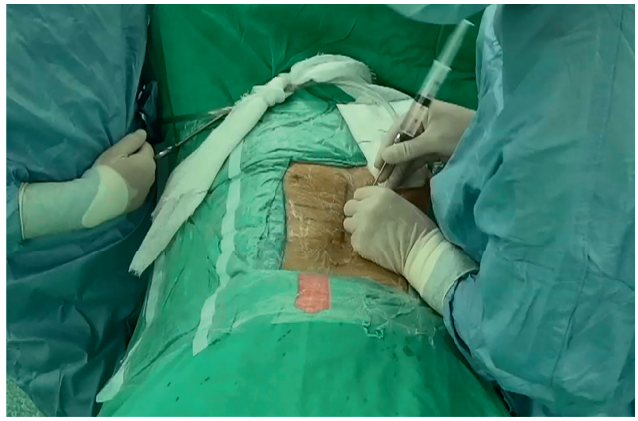


Figure 1: Epidural anesthesia before the operation.

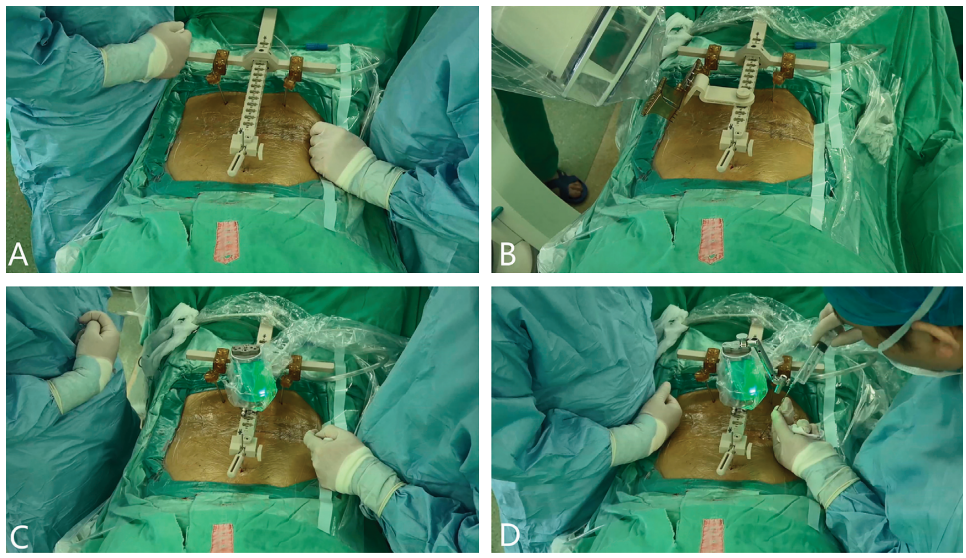


Figure 2: The Hover-T frame platform was fixed on the patient's spine (a); an anteroposterior image and an image 60°oblique to the plane were captured by the C-arm for registration with the preoperative CT (b); the guiding robot moved on the platform according to the preoperative plan (c); local infiltration anesthesia around the facet joints before drilling (d).

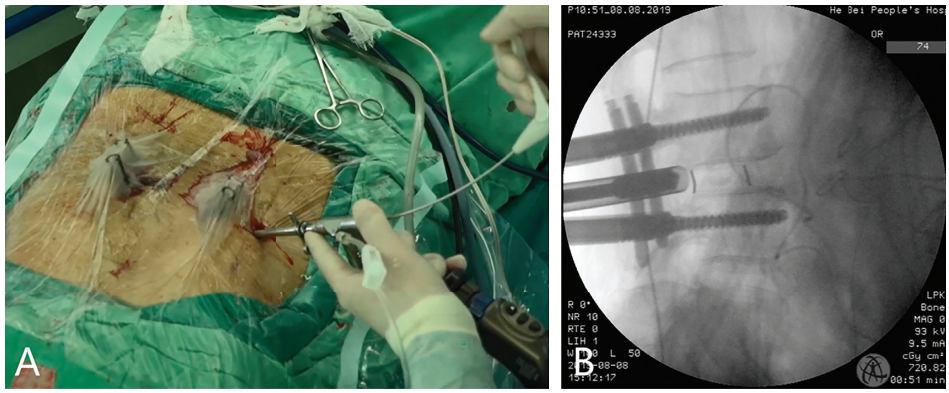


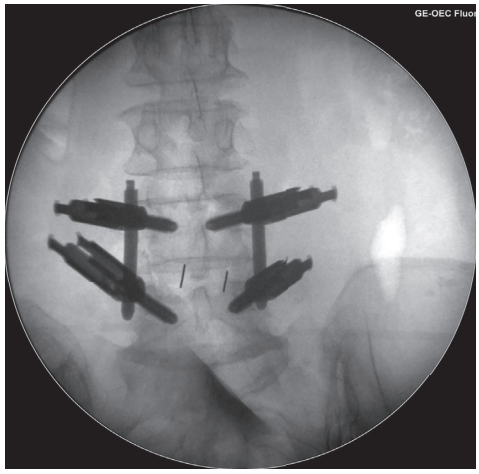
Figure 3: Percutaneous endoscopic lumbar interbody fusion following robot-assisted percutaneous pedicle screw implantation (a); intraoperative fluoroscopy image during the interbody fusion cage placement (b).

invasive spinal system; WEGORTHO Paedic Device Co., Ltd.; Weihai, China) placement was performed after decompression and interbody fusion (Figure 4).

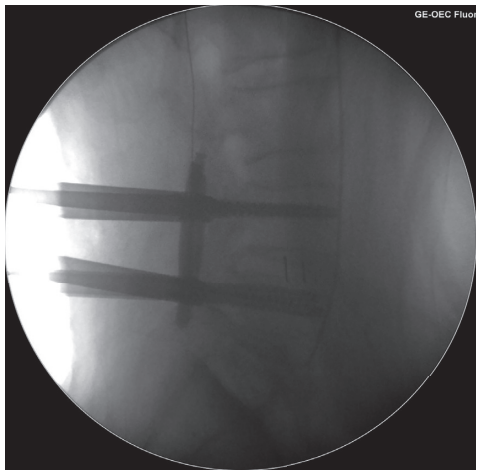
2.4. Outcome Evaluation. The primary outcome measures were screw accuracy and the incidence of FJV. All patients underwent thin-slice CT scans (≤1.2-mm slices) of the

Table 1: The protocol of robot-assisted percutaneous endoscopic lumbar interbody fusion under regional anesthesia.

Key steps of this surgery
(1) Preoperative planning
(2) Patient preparation and education
(3) Monitoring and sedation
(4) Epidural anesthesia
(5) Working platform installed and robot registration
(6) Adequate local anesthesia
(7) Drilling under the guidance of the robot
(8) Pedicle screw inserted
(9) Screw evaluation with fluoroscopy
(10) Decompression and interbody fusion
(11) Postanesthetic care unit observation (1 hour)
(12) Postoperative MRI and CT (1 day after surgery)
(13) Walking with waist support (1 day after surgery)



(a)



(b)

Figure 4: Intraoperative fluoroscopy images in group GE-FLU: AP X-ray image (a) and lateral X-ray image (b).

lumbar spine postoperatively. Screw accuracy was evaluated using the Gertzbein and Robbins criteria [16]: grade A, completely within the pedicle; grade B, < 2 mm cortical breach; grade C, 2–4 mm cortical breach; grade D, 4–6 mm cortical breach; and grade E, >6 mm cortical breach. Screw grades A and B were considered clinically acceptable [17–19]. Differences in the screw accuracy grades between the two groups and the proportions of clinically acceptable screws were assessed as the accuracy comparison parameters. FJV was evaluated only for the upper pedicle screws because of the related clinical significance using the Babu classification system [20]: grade 0, the screw does not violate the facet joint; grade 1, the screw violates the lateral facet; grade 2, the screw penetrates the articular facet by 1 mm; and grade 3, the screw lies within the articular facet surface. Differences in violation grades and the percentages of violating screws (grades 1, 2, and 3) were assessed as the FJV comparison parameters. The data were measured independently by two spinal graduate students using a picture archiving and communication system (PACS) (Neusoft Medical image diagnostic reporting system; Neusoft Co. Ltd., Shenyang, China) who were not aware of the purpose of the study in advance. If there was a discrepancy between the results, the worst result was adopted.

As secondary outcome measures, we compared the X-ray exposure and intraoperative adverse events related to the screw placement procedure as well as to anesthesia. X-ray exposure measurements were determined by the fluoroscopy time for each screw including the robot registration and intraoperative screw evaluation (sum of exposure times of the whole screw implantation and rod connecting procedures/number of screws inserted). A visual analogue scale (VAS) score was used to evaluate the degree of the postoperative pain at 4 hours and on postoperative days 1, 2, and 3.

2.5. Statistical Analysis. Statistical analyses were performed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp, Armonk, NY, USA). Fisher's exact test and Pearson's chi-squared test were used for group comparisons of sex, the distribution of diagnosis and screw location, as well as the percentages of clinically acceptable screws and facet violation screws. Two-sample t tests were used for group comparisons of age, body mass index (BMI), the superior facet joint angle, fluoroscopy time for each screw, and the VAS score at 4 hours and on postoperative days 1, 2, and 3. The Mann–Whitney U tests were used for group comparisons of accuracy and FJV grades. The statistical significance of these parameters was set at $p < 0.05$.

3. Results

Ninety-four consecutive patients were initially included in this study. Because of the requirement of postoperative CT results and other disease-related criteria, only 41 patients (22 women and 19 men) met the inclusion criteria. Eighteen patients (10 women and 8 men) who underwent PELIF were included in group RE-RO. Twenty-three patients (12 women and 11 men) were included in group GE-FLU; 20 patients (9 women and 11 men) underwent MIS-TLIF and 3 women underwent PELIF. The baseline characteristics of age, sex distribution, BMI, the superior facet joint angle, distribution

of diagnosis, and screw location did not differ between the groups RE-RO and GE-FLU (Table 2).

A total of 168 screws were inserted into patients' 4 vertebrae. Among them, 74 were implanted using the robot-assisted technique under regional anesthesia (group RE-RO), and 94 were implanted using the fluoroscopy-guided technique under general anesthesia (group GE-FLU). The incidence of pedicle breach (grades B, C, D, and E) in the two groups was 10.8% (8/74) and 20.2% (19/94), respectively. There was no significant difference in the incidence of clinically acceptable screws (grades A and B), with percentages of 94.4% and 91.5% for groups RE-RO and GE-FLU, respectively ($p = 0.44$). The difference in the Gertzbein and Robbins screw accuracy grades was also not statistically significant ($p = 0.35$). Considering the relationship between FJV and ASD as well as the surgeon's level of concern during insertion in different segments, only the 82 top screws were included in the analysis. In group RE-RO, 5.6% of the 36 screws analyzed violated the facet joint (grades 1, 2, and 3). In group GE-FLU, the incidence of FJV was 28.3%. This difference between these two groups was statistically significant ($p = 0.01$). The FJV grades in group RE-RO were significantly better than those in group GE-FLU ($p = 0.009$). A detailed list of the pedicle screw accuracy grades is presented in Table 3.

The mean fluoroscopy time for each screw in group RE-RO was significantly shorter than that in group GE-FLU (group RE-RO, 5.4 ± 1.9 seconds; group GE-FLU, 6.8 ± 2.0 seconds; $p = 0.03$). The VAS scores at 4 hours and on 1, 2, 3 days after surgery in group RE-RO were 4.7 ± 2.5, 4.7 ± 1.9, 3.9 ± 1.1, and 2.7 ± 1.0, which were lower than those in group GE-FLU at each time point (5.5 ± 2.0, 5.1 ± 1.5, 3.9 ± 1.3, and 2.7 ± 1.1). However, this difference was not statistically significant ($p = 0.26$, $p = 0.44$, $p = 0.94$, and $p = 0.81$). No patients suffered from neurovascular complications postoperatively or underwent revision surgery due to screw misplacement. No cases of cerebrospinal fluid (CSF) leakage or surgical site infection were observed. Other adverse events of the screw placement procedure were as follows:

(1) 1 case of registration failure in group RE-RO. The screws were placed by the fluoroscopy-guided technique instead of the robot-assisted technique.

(2) 1 case of guide wire dislodgment in group RE-RO. It was found during the operation, and the fragment was removed under the guidance of fluoroscopy.

(3) 2 screws in 2 cases of screw misplacement in group GE-FLU. They were revised intraoperatively by the fluoroscopy-guided technique after an X-ray check. There were no complications related to anesthesia in either group.

4. Discussion

In this study, we showed that robot-assisted percutaneous pedicle screw placement under regional anesthesia has a high accuracy of 94.6%. The accuracy reported under general anesthesia is 85%–99% [8, 21–23]. Although the difference was not significant, group RE-RO showed higher percentages in overall grade and clinically acceptable grade compared with group GE-FLU. This outcome is clinically satisfactory. Robot-assisted screw accuracy is closely related to spine movement because of its fundamental mechanism and working principles [24]. Regional anesthesia has proved to be a safe and effective anesthetic technique under which patients can be stable and pain-free. Kang et al. reported on 111 patients who underwent open lumbar spinal decompression, endoscopic decompression, and open posterior fusion surgery under regional anesthesia [14]. The anesthetic effect was satisfactory. Xu et al. revealed an intraoperative mean VAS score of low back pain of 1.25 under epidural anesthesia during PELD surgery [12]. According to our experience, spine movement mainly affects screw accuracy by the movement of the robotic arm and screw passage drilling steps. The first step takes a short time, and cooperative patient immobility is feasible. Additional local infiltration anesthesia around the facet joints can reduce discomfort during the drilling procedure. However, once spine movement is detected, reregistration is required.

In terms of the baseline, there were some differences in the sequence of screw placement and decompression between the two groups. In the RE-RO group, to avoid the accuracy reduction in robot image acquisition and registration procedure after decompression, screw placement was carried out before decompression. In order to prevent the screw tail from affecting the decompression operation, screw placement was carried out after decompression and interbody fusion in the 20 patients who underwent MIS-TLIF. However, the screw path was established and marked with a guide wire before the decompression step. Both groups completed the screw path preparation before decompression. Therefore, we think that different decompression methods have little effect on the accuracy of screws.

In the robot-assisted cohort, the robotic platform was a Hover-T frame, which is designed for minimally invasive surgery. The frame is fixed on the spine and pelvis during the whole insertion procedure. Relative resting of the body and platform can reduce the influence of accidental body motion on screw accuracy. Ringel et al. [22] reported a lower screw accuracy of 85% by using a "bed mount" platform (a platform fixed on the edge of the operating bed) and attributed the inaccuracy to the inappropriate platform choice. The relative movement of the robot to the patient may be slightly larger with this method.

In terms of FJV events, the robot-assisted technique was better than the fluoroscopy-guided technique. This finding is consistent with previous studies [8, 25, 26]. We only analyzed the top two pedicle screws in each patient to measure the incidence of FJV for two reasons. First, only FJV from the top screws is related to ASD and even reoperation. Second, accurate measurement was difficult in the lower segments because facetectomy was performed for decompression. Furthermore, an offset from the operator might exist. To reduce the probability of FJV, surgeons should pay more attention to the entry points of the top screws during preoperative planning or intraoperative localization. Different from the robot's one-time drilling, the fluoroscopy-guided technique requires adjustment of the entry point a

Table 2: Baseline characteristics.

Characteristics	Group EP-RO	Group GE-FLU	Overall	p value
No. of patients*	18	23	41	
Female sex (%)*	55.6	52.2	53.7	0.83
Age (years)†	61.6 ± 7.1	62.4 ± 6.1	62.1 ± 6.5	0.71
Mean BMI (kg/m^2)†	26.0 ± 3.6	25.5 ± 2.9	25.7 ± 3.2	0.58
Superior facet joint angle†	44.1 ± 3.6	43.8 ± 2.1	44.0 ± 3.2	0.56
Diagnoses*				0.88
LDH	4	5	9	
LSS	9	10	19	
Lumbar spondylolisthesis	5	8	13	
Location of screws*				0.98
L3	3	4	7	
L4	14	19	33	
L5	16	20	36	
S1	4	4	8	

*Values are the number or the number (%) of patients. †Values are presented as mean ± SD. BMI indicates body mass index.

Table 3: Comparison of pedicle screw placement accuracy, FJV, and fluoroscopy time.

Characteristics	Group EP-RO	Group GE-FLU	Total	$p$value
No. of screws*	74	94	168	
Accuracy grade*				
(n%)				0.102
Grade A	66 (89.2%)	75 (79.8%)	141 (83.9%)	
Grade B	4 (5.4%)	11 (11.7%)	15 (8.9%)	
Grade C	4 (5.4%)	5 (5.3%)	9 (5.4%)	
Grade D	—	2 (2.1%)	2 (1.2%)	
Grade E	—	1 (1.1%)	1 (0.6%)	
Clinically acceptable*				
(Grade A + B)	70 (94.6%)	86 (91.5%)	156 (92.8%)	0.44
No. of screws for FJV comparison*	36	46	82	
FJV grade*				
(n%)				0.009
Grade 0	34 (94.4%)	33 (71.7%)	67 (81.7%)	
Grade 1	1 (2.8%)	8 (17.4%)	9 (11.0%)	
Grade 2	1 (2.8%)	2 (4.3%)	3 (3.7%)	
Grade 3	—	3 (6.5%)	3 (3.7%)	
Violating screws*				
(Grade 1 + 2+3)	2(5.6%)	13(28.3%)	15(18.3%)	0.01
Fluoroscopy time per screw† (secs)	5.4 ± 1.9	6.8 ± 2.0	6.2 ± 2.0	0.03
Postoperative pain rating † (VAS)				
4 hours after surgery	4.7 ± 2.5	5.5 ± 2.0		0.26
Postoperative day 1	4.7 ± 1.9	5.1 ± 1.5		0.44
Postoperative day 2	3.9 ± 1.1	3.9 ± 1.3		0.94
Postoperative day 3	2.7 ± 1.0	2.7 ± 1.1		0.81

*Values are the number or the number (%) of patients. †Values are presented as the mean ± SD. FJV indicates facet joint violation. VAS indicates visual analogue score.

few times. Joint capsule injury may occur during this step. We deduce that it may aggravate the degeneration of the facet joint and cause ASD. No research has described this phenomenon.

Because of the different decompression methods, we only compared the radiation exposure time during the screw placement procedure. The results showed that the robot performed significantly better in minimizing this time. The advantage of the short radiation exposure time is more remarkable as the number of screws increases, especially in some spinal deformity surgeries. This is because most of the radiation exposure in robotic surgery occurs during the registration and platform process, which only needs to be performed once per operation. Fan et al. [18] compared the radiation dose among robots, novel guided templates, and CT-based navigation in adult degenerative scoliosis. The robot-based surgeries exhibited the lowest intraoperative radiation dose. In our study, we included the exposure time involved in connecting the percutaneous rod. The robot can preoperatively plan a better screw order, which can reduce operation times and radiation exposure. This may be one of the reasons for the low radiation exposure time.

Intraoperative adverse events were equal in the two techniques. However, it seems that the complications in the

robot group are less likely to cause serious consequences. Keric et al. [27] also found no significant differences between robotic-assisted and fluoroscopy-guided screw placement regarding intraoperative complications. The identification of additional adverse events requires studies with larger sample sizes.

The findings of our study provide a new anesthesia method for the clinical application of spine robots. It proves that the spinal robot can be used under regional anesthesia. The accuracy is clinically acceptable. Considering that regional anesthesia has many advantages over general anesthesia [10], we expect that some minimally invasive operations, such as PELD, bone biopsy, and percutaneous kyphoplasty, can be performed under regional anesthesia. Medical costs and recovery periods can be reduced accordingly. There are some limitations in this study. First, this is a single-center retrospective study, so the sample size is small (only 41 patients included). Thus, selection bias may exist. Second, the preoperative and postoperative screw positions were not compared because of technical issues.

5. Conclusion

Robot-assisted pedicle screw placement under regional anesthesia can be performed effectively and safely. The accuracy is comparable to that of the fluoroscopy-guided technique. Moreover, this technique has the advantage of fewer FJVs and a lower radiation time.

Abbreviations

PELIF: Percutaneous endoscopic lumbar interbody fusion
MIS-TLIF: Minimally invasive transforaminal lumbar interbody fusion
RE-RO: Robot-assisted under regional anesthesia
GE-FLU: Fluoroscopy-guided under general anesthesia
FJV: Facet joint violation
ASD: Adjacent segment disease
PELD: Percutaneous endoscopic lumbar discectomy
VAS: Visual analogue scale
CSF: Cerebrospinal fluid.

Data Availability

The data are available upon request to the corresponding author.

Ethical Approval

This study was approved by the Ethics Committee of Hebei General Hospital (no. 202029) and was conducted in accordance with the Declaration of Helsinki.

Consent

Written informed consent was obtained from the participants whose radiological data were selected for publication in the journal.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

Shangju Gao and Wenyi Li carried out study design, statistical analysis, and preparation of the manuscript. Jingchao Wei collected data, conducted the literature search, and prepared the manuscript. Long Zhang collected the data and performed the statistical analysis. Can Cao, Jinshuai Zhai, and Bo Gao collected the data and conducted the literature search. All authors read and approved the final manuscript. Shangju Gao and Jingchao Wei contributed equally to this work.

Acknowledgments

The authors would like to give special thanks to Miss Hua Wan for assistance with the patients' follow-up. The research was supported by the Key Research of Medical Science in Hebei Province, China (grant no. 20180004).

References

[1] R. Roy-Camille, M. Roy-Camille, and C. Demeulenaere, "Osteosynthesis of dorsal, lumbar, and lumbosacral spine with metallic plates screwed into vertebral pedicles and articular apophyses," *La Presse Médicale*, vol. 78, no. 32, pp. 1447-1448, 1970.

[2] J. Y. Patel, V. G. Kundnani, Z. I. Merchant, S. Jain, and N. Kire, "Superior facet joint violations in single level minimally invasive and open transforaminal lumbar interbody fusion: a comparative study," *Asian Spine Journal*, vol. 14, no. 1, pp. 25–32, 2020.

[3] L. Jia, Y. Yu, K. Khan et al., "Superior facet joint violations during single level minimally invasive transforaminal lumbar interbody fusion: a preliminary retrospective clinical study," *BioMed Research International*, vol. 2018, Article ID 6152769, 2018.

[4] C. Herren, M. Reijnen, M. Pishnamaz et al., "Incidence and risk factors for facet joint violation in open versus minimally invasive procedures during pedicle screw placement in patients with trauma," *World Neurosurgery*, vol. 112, pp. e711–e718, 2018.

[5] L. Ricciardi, N. Montano, G. F. D'Onofrio et al., "X-ray exposure in odontoid screwing for Anderson type II fracture: comparison between O-arm and C-arm-assisted procedures," *Acta Neurochirurgica*, vol. 162, no. 3, pp. 713–718, 2020.

[6] A. S. Narain, F. Y. Hijji, K. H. Yom, K. T. Kudaravalli, B. E. Haws, and K. Singh, "Radiation exposure and reduction in the operating room: perspectives and future directions in spine surgery," *World Journal of Orthopedics*, vol. 8, no. 7, pp. 524–530, 2017.

[7] D. S. Mulconrey, "Fluoroscopic radiation exposure in spinal surgery," *Clinical Spine Surgery: A Spine Publication*, vol. 29, no. 7, pp. E331–E335, 2016.

[8] J.-S. Yang, B. He, F. Tian et al., "Accuracy of robot-assisted percutaneous pedicle screw placement for treatment of lumbar spondylolisthesis: a comparative cohort study," *Medical Science Monitor*, vol. 25, pp. 2479–2487, 2019.

[9] N. A. Konovalov, I. N. Shevelev, V. N. Kornienko et al., "Application of robotic assistance in surgical treatment of

degenerative disease of lumbosacral spine," *Zh Vopr Neirokhir Im N N Burdenko*, vol. 34, no. 3, pp. 10–14, 2010.

[10] E. J. Ahn, H. J. Kim, K. W. Kim, H. R. Choi, H. Kang, and S. R. Bang, "Comparison of general anaesthesia and regional anaesthesia in terms of mortality and complications in elderly patients with hip fracture: a nationwide population-based study," *BMJ Open*, vol. 9, no. 9, Article ID e029245, 2019.

[11] J. F. Van der Meulen, M. Y. Bongers, S. F. P. J. Coppus et al., "The (cost) effectiveness of procedural sedation and analgesia versus general anaesthesia for hysteroscopic myomectomy, a multicentre randomised controlled trial: PROSECCO trial, a study protocol," *BMC Women's Health*, vol. 19, no. 1, p. 46, 2019.

[12] T. Xu, R. Tian, P. Qiao, Z. Han, Q. Shen, and Y. Jia, "Application of continuous epidural anesthesia in transforaminal lumbar endoscopic surgery: a prospective randomized controlled trial," *Journal of International Medical Research*, vol. 47, no. 3, pp. 1146–1153, 2019.

[13] L. Liu, H. Wang, J. Wang et al., "A study on the puncture method of extrapedicular infiltration anesthesia applied during lumbar percutaneous vertebroplasty or percutaneous kyphoplasty," *Medicine (Baltimore)*, vol. 98, no. 33, Article ID e16792, 2019.

[14] S. Y. Kang, O. N. Kashlan, R. Singh et al., "Advantages of the combination of conscious sedation epidural anesthesia under fluoroscopy guidance in lumbar spine surgery," *Journal of Pain Research*, vol. 13, pp. 211–219, 2020.

[15] D. P. Devito, L. Kaplan, R. Dietl et al., "Clinical acceptance and accuracy assessment of spinal implants guided with SpineAssist surgical robot: retrospective study," *Spine (Phila Pa 1976*, vol. 35, no. 24, pp. 2109–2115, 2010.

[16] S. D. Gertzbein and S. E. Robbins, "Accuracy of pedicular screw placement in vivo," *Spine*, vol. 15, no. 1, pp. 11–14, 1990.

[17] J. D. Van Dijk, R. P. van den Ende, S. Stramigioli, M. Köchling, and N. Höss, "Clinical pedicle screw accuracy and deviation from planning in robot-guided spine surgery: robot-guided pedicle screw accuracy," *Spine*, vol. 40, no. 17, pp. E986–E991, 2015.

[18] Y. Fan, J. Peng Du, J. J. Liu, J. N. Zhang, S. C. Liu, and D. J. Hao, "Radiological and clinical differences among three assisted technologies in pedicle screw fixation of adult degenerative scoliosis," *Scientific Reports*, vol. 8, no. 1, p. 890, 2018.

[19] V. Solomiichuk, J. Fleischhammer, G. Molliqaj et al., "Robotic versus fluoroscopy-guided pedicle screw insertion for metastatic spinal disease: a matched-cohort comparison," *Neurosurgical Focus*, vol. 42, no. 5, p. E13, 2017.

[20] R. Babu, J. G. Park, A. I. Mehta et al., "Comparison of superior-level facet joint violations during open and percutaneous pedicle screw placement," *Neurosurgery*, vol. 71, no. 5, pp. 962–970, 2012.

[21] G. Molliqaj, B. Schatlo, A. Alaid et al., "Accuracy of robot-guided versus freehand fluoroscopy-assisted pedicle screw insertion in thoracolumbar spinal surgery," *Neurosurgical Focus*, vol. 42, no. 5, p. E14, 2017.

[22] F. Ringel, C. Ster, A. Reinke et al., "Accuracy of robot-assisted placement of lumbar and sacral pedicle screws: a prospective randomized comparison to conventional freehand screw implantation," *Spine*, vol. 37, no. 8, pp. E496–E501, 2012.

[23] F. Roser, M. Tatagiba, and G. Maier, "Spinal robotics: current applications and future perspectives," *Neurosurgery*, vol. 72, no. Suppl 1, pp. 12–18, 2013.

[24] Y. Liu, C. Zeng, M. Fan, L. Hu, C. Ma, and W. Tian, "Assessment of respiration-induced vertebral motion in prone-positioned patients during general anaesthesia," *International Journal of Medical Robotics and Computer Assisted Surgery*, vol. 12, no. 2, pp. 214–218, 2016.

[25] H. J. Kim, W. I. Jung, B. S. Chang, C. K. Lee, K. T. Kang, and J. S. Yeom, "A prospective, randomized, controlled trial of robot-assisted vs. freehand pedicle screw fixation in spine surgery," *The international journal of medical robotics + computer assisted surgery: MRCAS*, vol. 13, no. 3, 2017.

[26] Q. Zhang, Y. F. Xu, W. Tian et al., "Comparison of superior-level facet joint violations between robot-assisted percutaneous pedicle screw placement and conventional open fluoroscopic-guided pedicle screw placement," *Orthopaedic Surgery*, vol. 11, no. 5, pp. 850–856, 2019.

[27] N. Keric, D. J. Eum, F. Afghanyar et al., "Evaluation of surgical strategy of conventional vs. percutaneous robot-assisted spinal trans-pedicular instrumentation in spondylodiscitis," *Journal of Robotic Surgery*, vol. 11, no. 1, pp. 17–25, 2017.

Hindawi
Pain Research and Management
Volume 2021, Article ID 1723471, 8 pages
https://doi.org/10.1155/2021/1723471

Research Article

Analgesic Impact of a Popliteal Plexus Block to Standard Adductor Canal Block in Arthroscopic Anterior Cruciate Ligament Reconstruction: A Randomized Blind Clinical Trial

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Received 17 September 2021; Accepted 25 November 2021; Published 17 December 2021

Academic Editor: Sidong Yang

Background. Damage to the anterior cruciate ligament (ACL) is crippling and often requires an arthroscopic outpatient surgery. Nevertheless, many patients experience severe pain during the first day after ACL reconstruction (ACLR). The adductor canal block (ACB) has yielded conflicting results for post-ACLR pain relief. This research investigated the effect of a supplemental popliteal plexus block on postoperative pain outcomes compared to a sole ACB. *Methods*. Following a randomized design, 60 cases scheduled for knee arthroscopy with ACLR using an ipsilateral hamstring graft were separated into two categories. Subjects in group A ($n = 30$) received an ACB only, while subjects in group B ($n = 30$) received combined ACB and popliteal plexus block (PPB). *Results*. We found significant differences between the two groups. The time of the first analgesic request (TFR) was later for the combined ACB and PPB (median 8 h) compared to the ACB only group (median 0.5 h). Morphine consumption was lower for patients who received combined ACB and PPB (median 12 mg) compared to ACB only (median 30 mg). The number of the requested doses was lower for the combined ACB and PPB group (median 3 doses) compared to the ACB only group (median 7 doses). *Conclusions*. The addition of PPB to ACB was associated with improved analgesia and a reduced need for opioid-based sedatives following ACLR with an ipsilateral hamstring graft (https://clinicaltrials.gov/ct2/show/NCT04020133).

1. Introduction

One of the most common injuries to the knee is an anterior cruciate ligament (ACL) sprain or tear due to trauma [1, 2]. ACL damage is crippling and often requires repair with an arthroscopic method, which is an outpatient surgery. Nevertheless, patients experience severe postoperative pain on the first day after the ACL reconstruction (ACLR) [3, 4]. Efficient postsurgery pain management is an important part of patient recovery that is also crucial for their satisfaction. Psychological factors are important for predicting outcomes of patients who undergo ACLR. There is also a negative association between function and quality of life evaluation [5, 6]. Efforts are ongoing to minimize postoperative muscle weakness and maximize postoperative analgesia [7, 8]. ACLR interventions affect the complex innervation of the affected anatomical parts, including the femoral nerve (including its infrapatellar and saphenous branches), obturator nerve, and tibial and common peroneal branches of the sciatic nerve. The anterolateral (camera), anteromedial (instrumentation), and superomedial ports (fluid channel) used during arthroscopy are innervated by the common peroneal, infrapatellar, and saphenous nerves, respectively [9]. Additional vertical incisions (anteromedial port) may traverse the overspreading nerves like the infrapatellar nerve [10]. Shearing, stripping, and excising forces are applied during hamstring tendon harvesting, while the posteromedial thigh incision at the donor site is innervated by branches of the tibial nerve. Hence, surgery-related parameters like surgery port location and graft origin are of crucial importance for selecting appropriate nerve blocks for multimodal analgesic regimens. Ignoring such factors in the

analgesic plan can cause severe postsurgery pain [11]. The adductor canal block (ACB) is a novel method for postsurgery analgesia after knee operations. It provides good analgesia to the medial and anterior aspect of the knee by blocking sensory branches of the saphenous nerve and the nerve from the vastus medialis to the knee [12]. Concerning postsurgery pain management, its effectiveness is similar to the femoral nerve block (FNB) [13–18]. The major benefit of ACB is maintaining, or minimizing quadriceps strength decline, which accelerates ambulating and recovery following knee operations [18]. However, its use in ACLR has produced contradictory results due to the anatomical reasons mentioned above [4, 11, 19–24]. Adding a tibial nerve block can effectively cover the hamstring tendon graft area, but at the expense of leg weakness, which could increase the risk of falling. There are also logistical challenges and time limitations associated with given several injections while maintaining rapid case turnover for ambulatory ACLR procedures [25, 26].

The popliteal plexus block (PPB) is a novel sensory block to the posterior knee compartment that anesthetizes the sensory tibial genicular postobturator nerve branches with a minimal effect on the ankle musculature. Here, we performed a randomized clinical trial (RCT) that combined PPB with the standard ACB in patients undergoing ACLR. We investigated whether this protocol improved postoperative analgesia without affecting motor function compared to the effects of ACB alone.

2. Methods

This study was performed at Fayoum University Hospital and enrolled 60 adult cases scheduled for ACLR surgery following approval of the Scientific and Ethical Committee of El Fayoum University Hospitals with study number (D 182) in December 2018. This study was registered at ClinicalTrials.gov (identifier: NCT04020133), and written informed consent was obtained from all participants. Patients scheduled for ACL reconstruction with American Society of Anesthesiologist physical status I/II/III, aged >18 years, and body mass index (BMI) $<40\,kg/m^2$ were included in the study. Patients were excluded if they refused to participate, were not cooperative, had a BMI $>40\,kg/m^2$, or were allergic to local anesthetics. We also excluded patients with anticoagulation or bleeding problems, previous nerve dysfunction, swelling or contamination over the injection area(s), and daily morphine consumption >40 mg. Sixty patients were randomly chosen to receive either ACB (group A, $n = 30$) or ACB with PPB (group B, $n = 30$) using random sequence numbers that were hidden in envelopes that were opened in the operating room. Physicians and nurses who were in charge of treating participants and gathering data were not aware of the allocation process. Patient history investigations, routine examinations, and other necessary tests were performed following the local guidelines, including complete blood count, blood glucose, serum urea and creatinine levels, liver function tests, coagulation profile, and electrocardiogram. Before the operation, the visual analogue scale (VAS) was explained to all patients ranging from 0 ("no pain") to 100 ("worst imaginable pain"). In addition, they were informed about the nerve block interventions. All patients fasted for 6 h before surgery. Those in the intervention group received 0.03 mg/kg of intravenous (IV) midazolam and intravenous (IV) 1 g of cefotaxime to prevent infection. Routine monitoring was performed for all cases, including pulse oximetry, electrocardiography, and noninvasive blood pressure monitoring. General anesthesia was used instead of spinal anesthesia, as the latter may affect the primary outcome of the time of the first analgesic request (TFR). It was induced with 1-2 mg/kg of propofol, 1-2 μg/kg of fentanyl, and 0.5 mg/kg of atracurium. All patients were mechanically ventilated via an endotracheal tube. Anesthesia was continued using oxygen and isoflurane 1-2%. In necessary, 10 mg of atracurium was used every 30 min. If heart rate or mean arterial pressure was increased by >20%, 0.5 μg/kg of fentanyl boluses was repeated. To address postoperative nausea and vomiting, 4 mg of IV ondansetron was administered. Nerve blocks were applied following the randomization scheme. The skin was disinfected, and the adductor canal was located via ultrasound. The transducer was placed anteromedially, nearly at the mid-thigh level, and a sterilized high-frequency linear probe 5Y 12 MHz was used (Phillips HD11, Amsterdam, the Netherlands). For cases where the femoral artery was not obvious, color Doppler scanning was used. After identifying the femoral artery, the probe was moved distally to track the artery to the adductor hiatus to become the popliteal artery. The block needle (Stimuplex; Braun Medical, Bethlehem, PA) was administered in the plane of a lateral-to-medial orientation, then advanced toward the femoral artery. After observing the needle tip at the anterior aspect of the artery, local anesthetic (1 to 2 mL) was administered. Needle repositioning was considered in cases when local anesthetics failed. [27] Next, we moved distally with the artery in the adductor canal in order to enter the adductor hiatus, where PPB was given above the artery. [28] Both blocks were performed using bupivacaine 0.5% (1 mg/kg) + epinephrine (0.05 mg). Following ACLR, the VAS score, need for opioid analgesia and sedation level were measured every 4 h for 24 h. For cases with VAS > 4, rescue analgesia was performed (as morphine per a titration protocol of 3 mg morphine sulfate IV as a bolus dose). If necessary, the injection was repeated every 5 minutes (15 mg) for 4 h or 45 mg per 24 h. The morphine titration protocol was suspended with oxygen saturation <95%, respiratory rate <10/min, the development of sedation (Ramsay sedation scale >2), acute adverse effects (e.g., allergy, marked itching, unusual vomiting, and hypotension with systolic blood pressure <20% of baseline values), or reaching a sufficient level of analgesia.

The primary outcome was the TFR, and the secondary outcomes were cumulative opioid consumption, interval in between doses within 24 h after surgery, number of patients requiring postoperative analgesia, and analgesia quality (according to the VAS), which were evaluated every 4 h for 24 h. For all patients, adverse effects such as vomiting, pruritus, and excessive sedation were documented. Sedation

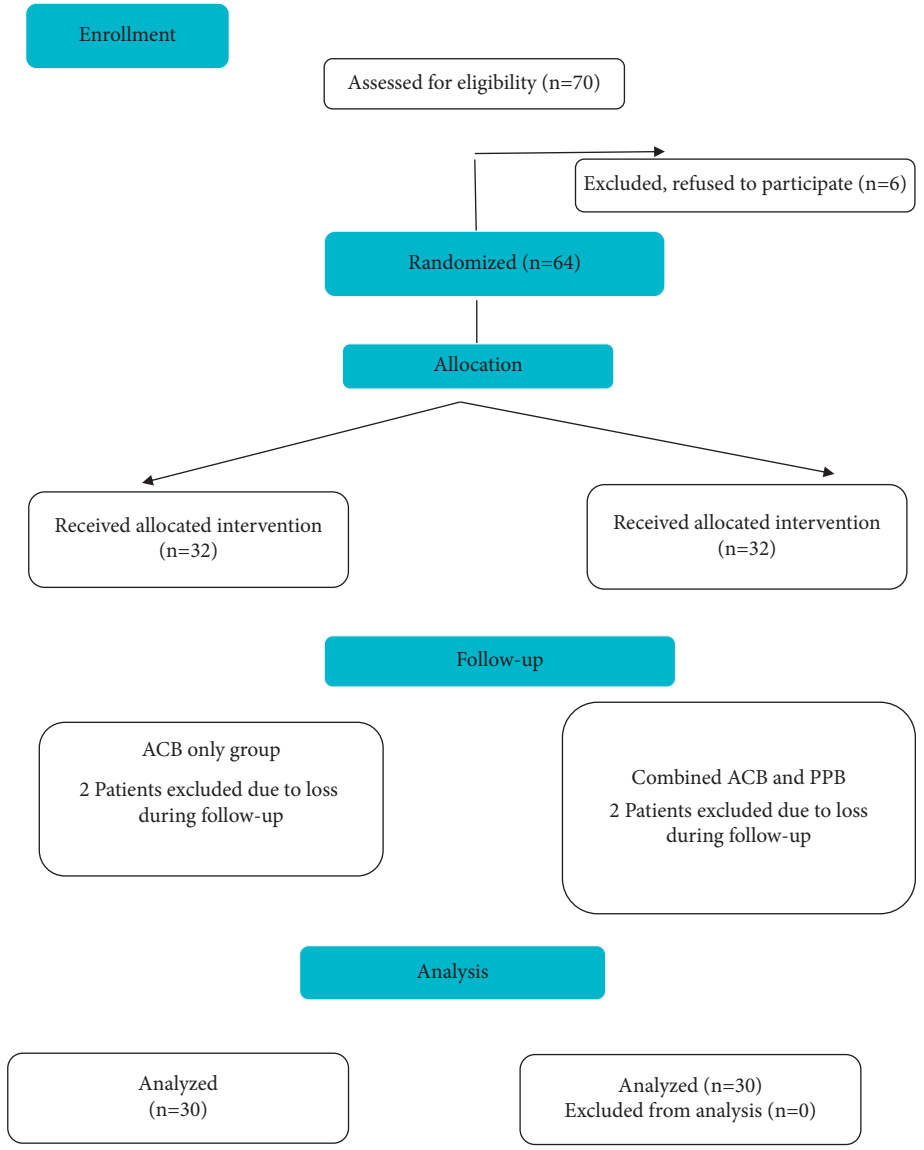

Figure 1: CONSORT flow diagram.

was assessed every 4 h using Ramsay's score, which ranges from 1 ("awake") to 5 ("aroused only by shaking"). Oversedation was considered as a sedation score higher than 4 and a respiratory rate <8 breaths in a minute, and these patients were admitted to the intensive care unit for monitoring. Patients were given 0.15 mg/kg ondansetron for vomiting [29]. At 24 h after surgery, we measured participants' satisfaction with analgesia using a four-point Likert scale, ranging from 0 ("poor") to 3 ("excellent").

2.1. Sample Size Calculation. G power version 3 software was applied to estimate the sample size. The minimal sample size was determined to be 52, with 26 subjects in each group, with a statistical power of 0.80 and alpha level of 0.05. This sample size was sufficient to compare the time for analgesic requests following the intervention between the study groups. The sample size was increased by 15% to account for potential attrition bias.

2.2. Statistical Analyses. Descriptive statistics are presented as mean (SD) for normally distributed numeric variables, median (interquartile range (IQR)) for nonnormally distributed numeric variables, or frequencies and percentages for categorical variables. Group comparisons were carried out with independent sample *t*-tests for normally distributed numeric variables and Mann–Whitney *U* tests for nonnormally distributed numeric variables or ordinal variables. Chi-square and Fisher exact tests were used for categorical variables. SPSS statistics software (version 26; IBM Corp., Armonk, NY) was used for the analyses, and $p < 0.05$ was considered statistically significant.

3. Results

Seventy patients scheduled for ACLR were admitted to the Orthopedic Department of Fayoum University Hospital between January 2019 and January 2021. Six patients rejected

Table 1: Comparison of age, BMI, gender, ASA status, morphine consumption, and TFR between groups.

Variable		ACB only	ACB and PPB	p value
Age[a]	Mean (SD)	24.1 (2)	24.2 (2.8)	0.823
BMI[a]	Mean (SD)	21.2 (2.3)	21.2 (2.1)	0.953
Morphine consumption (mg)[b]	Median (IQR)	**30.0 (14)**	**12 (4)**	**<0.001**
Number of requested doses[b]	Median (IQR)	**7.0 (3)**	**3.0 (1)**	**<0.001**
TFR[b]	Median (IQR)	**0.5 (3.5)**	**8 (12)**	**<0.001**

[a]Comparison with independent sample t-tests. [b]Comparison with Mann–Whitney U tests.

Table 2: Comparison of opioid dose intervals between groups[a].

	ACB only		ACB and PPB		p value
	n	Median (IQR)	n	Median (IQR)	
1st dose interval in hours	**30**	**4 (4)**	**26**	**8 (0)**	**<0.001**
2nd dose interval in hours	**30**	**4 (4)**	**20**	**8 (0)**	**<0.001**
3rd dose interval in hours	30	4 (0)	6	4 (0)	>0.999
4th dose interval in hours	22	4 (0)	0		
5th dose interval in hours	22	4 (0)	0		
6th dose interval in hours	22	4 (0)	0		

[a]Comparison with Mann–Whitney U tests.

Table 3: Comparison of the postoperative pain scores between groups[a].

	VAS score	Postoperative pain score 30 min	Postoperative pain score 4 h	Postoperative pain score 8 h	Post operative pain score 12 h	Postoperative pain score 16 h	Postoperative pain score 20 h	Postoperative pain score 24 h
ACB only group	Postoperative pain score 30 min							
	Postoperative pain score 4 h	0.383						
	Postoperative pain score 8 h	>0.999	>0.999					
	Postoperative pain score 12 h	0.233	>0.999	>0.999				
	Postoperative pain score 16 h	>0.999	>0.999	>0.999	>0.999			
	Postoperative pain score 20 h	0.012	>0.999	0.126	>0.999	>0.999		
	Postoperative pain score 24 h	0.012	>0.999	0.126	>0.999	>0.999	>0.999	
ACB and PPB	Postoperative pain score 30 min							
	Postoperative pain score 4 h	0.021						
	Postoperative pain score 8 h	>0.999	>0.999					
	Postoperative pain score 12 h	0.126	>0.999	>0.999				
	Postoperative pain score 16 h	0.029	>0.999	>0.999	>0.999			
	Postoperative pain score 20 h	<0.001	>0.999	0.137	>0.999	>0.999		
	Postoperative pain score 24 h	0.001	>0.999	0.300	>0.999	>0.999	>0.999	

[a]Friedman's test was used as a repeated measures test to study if there is a change in the VAS score at different time points.

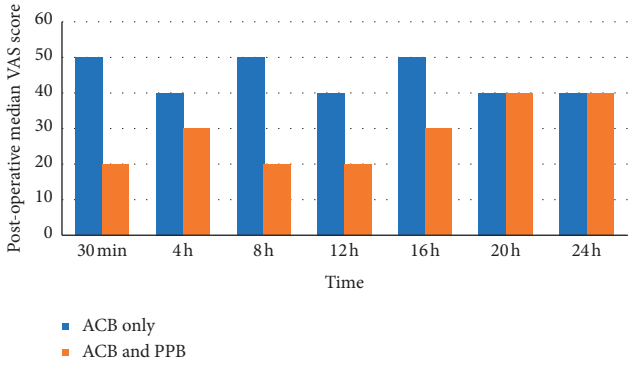

Figure 2: Comparison of postoperative pain scores between groups.

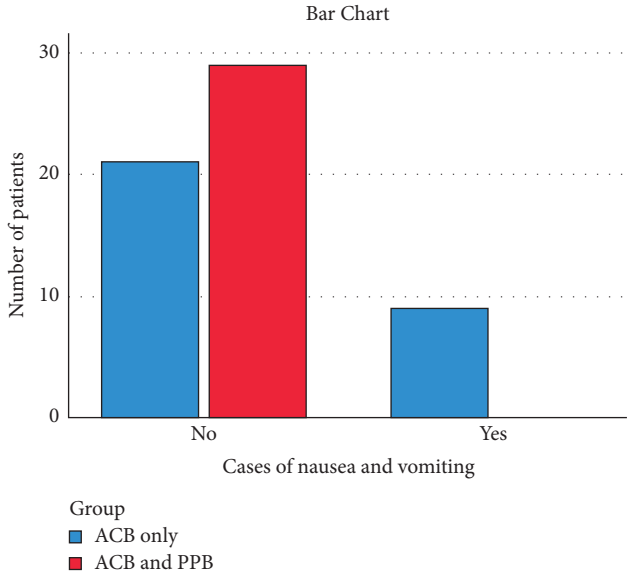

Figure 3: Comparison of postoperative nausea and vomiting.

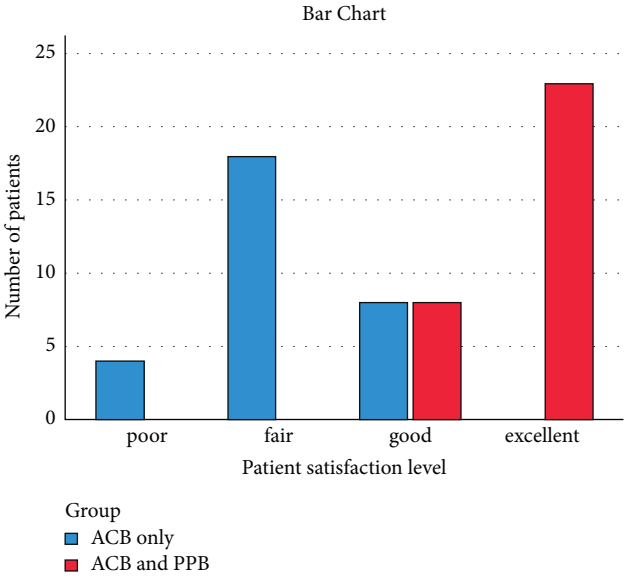

Figure 4: Comparison of postoperative patient satisfaction level.

Table 4: Comparison of Ramsay sedation scores between groups[a].

Ramsey sedation score (h)	Status		ACB only	ACB and PPB
4	Awake	*n*	30	29
		%	0.508	0.492
8	Awake	*n*	30	29
		%	0.508	0.492
12	Awake	*n*	30	29
		%	0.508	0.492
16	Awake	*n*	30	29
		%	0.508	0.492
20	Awake	*n*	30	29
		%	0.508	0.492
24	Awake	*n*	30	29
		%	0.508	0.492

[a]Statistical comparison of Ramsay sedation scores between the two groups was not possible as they did not change over time.

the regional anesthesia method, and the remaining 64 were randomly divided into two groups. Two cases in the ACB only and two in the combined ACB and PPB group were removed due to failed insertion. The study design and final patient cohort are shown in Figure 1. The mean patient age was 24.17 ± 2.28, and the mean BMI was 21.22 ± 2.18 (both $p > 0.05$, Table 1). The TFR, morphine consumption, and number of requested doses were compared. All three variables were significantly different between the study groups (Table 1). TFR was later for the combined ACB and PPB group (median 8 h) compared to the ACB only group (median 0.5 h) (Table 1). Morphine consumption was lower for the combined ACB and PPB group (median 12 mg) compared to the adductor canal block only (median 30 mg) (Table 1). The number of requested doses was significantly lower for the combined block group (median 3 doses) compared to the ACB only group (median 7 doses) ($p < 0.001$) (Table 1). The interval time between analgesic doses was longer in the combined block group compared to the ACB only group ($p < 0.001$) (Table 2). Comparison of the postoperative VAS scores revealed that at each time point from 30 min to 24 h post-ACLR, the median score was lower for the combined block compared to the ACB only ($p < 0.001$) (Table 3, Figure 2). Nausea and vomiting were more common in the ACB only group; only nine cases accounting for 30% of patients had nausea or vomiting compared to none in the combined group, presumably due to higher opioid consumption (Figure 3). Patient satisfaction with analgesia was significantly different between the two groups. All patients in the combined group gave ratings of good or excellent, while no patients in the ACB only group reported excellent satisfaction and only eight cases accounting for 26.7% had good satisfaction (Figure 4). Statistical comparison of the Ramsay sedation scores between groups was not possible, as they did not change (Table 4). No cases of pruritus were observed in either group. As regard, ASA classification in both groups was ASA I in both groups. In regard to gender, in the ACB group, there were was 25 male patients (83%) and 26 male patients in the PPB group (86.6%) with p value = 0.730, which was nonsignificant.

Surgical time, anesthesia time, and tourniquet time ranged between one and half hours to two hours which was nonsignificant.

4. Discussion

The impacted region confirmed in cadaveric studies showed that dye injected in the distal area of the adductor canal stained the tibial genicular nerves, postobturator nerve, and popliteal vessels [28, 30, 31]. Gautier and colleagues used the same technique to inject 20 mL of a solution containing 18 mL of 1% mepivacaine and 2 mL of radio-opaque contrast medium into healthy volunteers prior to computed tomography scans. They reported staining of the popliteal vessels and branches of the sciatic nerves with a minimal effect on the ankle muscles [31].

In their feasibility study, Runge and colleagues used the same approach to evaluate the analgesic impact of adding a PPB to a femoral triangle block (FTB) [32]. They performed unilateral total knee replacement (TKA) in 17 patients with spinal anesthesia using an FTB and evaluated cutaneous sensation and postsurgery pain. The ratio of cases with a numeric rating scale (NRS) score >3 (followed by a decline to <3 after PPB) was defined as the primary outcome. PPB was also administered for 10 (out of 17) cases with a median NRS score of 5.5 (IQR 4–8) following unilateral TKA. For all cases, the NRS was declined to <3 (NRS 1.5 (IQR 0–3)) within a mean time of 8.5 (95% confidence interval 6.8–10.2) minutes. Interestingly, three cases had no pain after receiving PPB. They concluded that PPB was effective in controlling posterior and deep genicular pain after TKA, but the validity of their results was limited by lack of a control group, blinding, and randomization.

Our results are consistent with those of Thobhani and colleagues who used a different approach of local anesthetic infiltration between the popliteal artery and knee capsule (iPACK block) in patients undergoing TKA. They compared a femoral and adductor canal block versus femoral nerve block only. The combined adductor and iPACK block were better than femoral only in terms of adequate control of postoperative pain, especially posterior and deep knee pain. This combination was better than femoral block only in terms of postoperative muscle weakness and length of hospital stay [33]. Similar results were reported by Sankineani and colleagues who concluded that ACB + iPACK is a novel method for improving postoperative analgesia without influencing knee joint motor function, which translated into improved movement compared to ACB alone [34].

The limited efficacy of ACB only in our study was consistent with the results of a meta-analysis by Sehmbi and colleagues [11]. A comparison of ACB to placebo (2 RCTs, 110 cases) revealed that ACB did not increase analgesia following ACLR [4, 19–35]. Nevertheless, a comparison of FNB and ACB (3 RCTs, 308 patients) suggested a potential impact of FNB [13, 36, 37]. It is worth noting that this finding was not confirmed by Mall and Wright [38]. Overall, the low analgesic impact of nerve blocks in ACLR can be attributed to inefficient pain management at graft sites and/or a lack of additional pain relief with multimodal analgesia (MMA) [11]. Ramlogan and colleagues support the routine use of MMA in combination with local infiltration of anesthesia for postoperative analgesia in ACLR and reserve ACB only for patients with opioid contraindications and considering the type of the graft used [22].

Performing combined ACB and PPB with our technique has the advantage that both blocks can be given without changing patient position, saving time in an outpatient setting. It is worth noting the area of pain in the ACB only group moved from a predominantly posterior area to a predominantly anterior or posterior area. However, pain in the combined ACB and PPB group was mainly anterior, reflecting the efficacy of the PPB. Unfortunately, the study was not sufficiently powered to detect changes in the pain site. The second limitation is that we could not evaluate the success of the block as it was done after general anesthesia, but the distribution of the injection was easily seen under ultrasound, which helped us to reduce the incidence of side effects and intravascular injections. The third limitation was short follow-up time. Finally, we did not assess postoperative motor function, as the policy in our institute is to splint patients for 24 h after ACLR. Ultimately, our results are restricted to the study group, procedures, and clinical environments evaluated and cannot be extended to other knee operations, local anesthetic amounts, or analgesic methods.

5. Conclusions

The addition of PPB to ACB significantly decreases pain and the need for opioid-based drugs following ACLR with an ipsilateral hamstring graft.

Abbreviations

abrACB: Adductor canal block
ACL: Anterior cruciate ligament
ACLR: Anterior cruciate ligament reconstruction
FNB: Femoral nerve block
FTB: Femoral triangle block
iPACK: In between popliteal artery and knee capsule block
MMA: Multimodal analgesia
PPB: Popliteal plexus block
TFR: Time of first analgesic requirement
TKA: Total knee arthroscopy.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Ethical Approval

The protocol was approved by the Scientific and Ethical Committee of El Fayoum University Hospitals with study number (D 182) in December 2018.

Consent

Written informed consent was obtained from all participants.

Conflicts of Interest

All authors declare that there are no conflicts of interest.

Authors' Contributions

AM and MM designed the study. AM and MM collected data. SR, MB, JB, and MA wrote the manuscript. All authors discussed the results and commented on the manuscript.

Acknowledgments

The authors acknowledge everyone who played a role in this academic accomplishment. This study was registered prospectively at ClinicalTrials.gov (NCT04020133).

References

[1] B. Akova, "ACL surgery: how to get it right the first time and what to do if it fails," *Journal of Sports Science and Medicine*, vol. 9, no. 3, pp. 527-528, 2010.

[2] S. Barnett, M. M. Murray, S. Liu et al., "Resolution of pain and predictors of postoperative opioid use after bridge-enhanced anterior cruciate ligament repair and anterior cruciate ligament reconstruction," *Arthroscopy, Sports Medicine, and Rehabilitation*, vol. 2, no. 3, pp. e219–e228, 2020.

[3] S. R. Filbay, I. N. Ackerman, T. G. Russell, E. M. Macri, and K. M. Crossley, "Health-related quality of life after anterior cruciate ligament reconstruction," *The American Journal of Sports Medicine*, vol. 42, no. 5, pp. 1247–1255, 2014.

[4] E. S. Secrist, K. B. Freedman, M. G. Ciccotti, D. W. Mazur, and S. Hammoud, "Pain management after outpatient Anterior cruciate ligament reconstruction," *The American Journal of Sports Medicine*, vol. 44, no. 9, pp. 2435–2447, 2016.

[5] G. S. Fanton, M. F. Dillingham, M. S. Wall et al., "Novel drug product to improve joint motion and function and reduce pain after arthroscopic anterior cruciate ligament reconstruction," *Arthroscopy: The Journal of Arthroscopic & Related Surgery*, vol. 24, no. 6, pp. 625–636, 2008.

[6] T. L. Chmielewski, D. Jones, T. Day, S. M. Tillman, T. A. Lentz, and S. Z. George, "The association of pain and fear of movement/reinjury with function during anterior cruciate ligament reconstruction rehabilitation," *Journal of Orthopaedic & Sports Physical Therapy*, vol. 38, no. 12, pp. 746–753, 2008.

[7] A. S. Terkawi, D. Mavridis, D. I. Sessler et al., "Pain management modalities after total knee arthroplasty," *Anesthesiology*, vol. 126, no. 5, pp. 923–937, 2017.

[8] K. R. Okoroha, R. A. Keller, E. K. Jung et al., "Pain assessment after anterior cruciate ligament reconstruction," *Orthopaedic Journal of Sports Medicine*, vol. 4, no. 12, pp. 232596711667492–232596711667496, 2016.

[9] B. D. Ward and J. H. Lubowitz, "Basic knee arthroscopy part 2: surface anatomy and portal placement," *Arthroscopy Techniques*, vol. 2, no. 4, pp. e501–e502, 2013.

[10] C. D. Tifford, L. Spero, T. Luke, and K. D. Plancher, "The relationship of the infrapatellar branches of the saphenous nerve to arthroscopy portals and incisions for anterior cruciate ligament surgery: an anatomic study," *The American Journal of Sports Medicine*, vol. 28, no. 4, pp. 562–567, 2000.

[11] H. Sehmbi, R. Brull, U. J. Shah et al., "Evidence basis for regional anesthesia in ambulatory arthroscopic knee surgery and anterior cruciate ligament reconstruction," *Anesthesia & Analgesia*, vol. 128, no. 2, pp. 223–238, 2019.

[12] D. Burckett-St Laurant, P. Peng, L. Girón Arango et al., "The nerves of the adductor canal and the innervation of the knee," *Regional Anesthesia and Pain Medicine*, vol. 41, no. 3, pp. 321–327, 2016.

[13] F. W. Abdallah, D. B. Whelan, V. W. Chan et al., "Adductor canal block provides noninferior analgesia and superior quadriceps strength compared with femoral nerve block in anterior cruciate ligament reconstruction," *Anesthesiology*, vol. 124, no. 5, pp. 1053–1064, 2016.

[14] M. U. Vora, T. A. Nicholas, C. A. Kassel, and S. A. Grant, "Adductor canal block for knee surgical procedures: review article," *Journal of Clinical Anesthesia*, vol. 35, pp. 295–303, 2016.

[15] S. Kolli and M. F. Malik, "The adductor canal block: a clinical review," *Current Anesthesiology Reports*, vol. 9, no. 3, pp. 291–294, 2019.

[16] A. Mcewen and D. Quemby, "Ultrasound guided adductor canal block (saphenous nerve block) anaesthesia tutorial of the week 301 13th january 2014 Dr daniel quemby, specialist trainee anaesthesia torbay hospital, torquay," *Anaesthesia Tutor Week*, vol. 301, pp. 1–11, 2014.

[17] A. H. Saad, N. A. Gad El-Rab, M. G. Aly, and H. G. Said, "Review article: ultrasound-guided adductor canal block for post-operative analgesia in knee arthroscopy," *The Medical Journal of Cairo University*, vol. 86, no. 9, pp. 2141–2148, 2018.

[18] M. R. Rasouli and E. R. Viscusi, "Adductor canal block for knee surgeries: an emerging analgesic technique," *The archives of bone and joint surgery*, vol. 5, no. 3, pp. 131-132, 2017.

[19] M. Espelund, U. Grevstad, P. Jaeger et al., "Adductor canal blockade for moderate to severe pain after arthroscopic knee surgery: a randomized controlled trial," *Acta Anaesthesiologica Scandinavica*, vol. 58, no. 10, pp. 1220–1227, 2014.

[20] K. Stebler, R. Martin, K. R. Kirkham, J. Lambert, A. De Sede, and E. Albrecht, "Adductor canal block versus local infiltration analgesia for postoperative pain after anterior cruciate ligament reconstruction: a single centre randomised controlled triple-blinded trial," *British Journal of Anaesthesia*, vol. 123, no. 2, pp. e343–e349, 2019.

[21] R. Kejriwal, J. Cooper, A. Legg, J. Stanley, M. P. Rosenfeldt, and S. J. Walsh, "Efficacy of the adductor canal approach to saphenous nerve block for anterior cruciate ligament reconstruction with hamstring autograft: a randomized controlled trial," *Orthopaedic Journal of Sports Medicine*, vol. 6, no. 10, pp. 232596711880094-232596711880095, 2018.

[22] R. Ramlogan, S. Tierney, and C. J. L. McCartney, "Anterior cruciate ligament repair and peripheral nerve blocks: time to change our practice?" *British Journal of Anaesthesia*, vol. 123, no. 2, pp. e186–e188, 2019.

[23] J. F. Sztain, B. Khatibi, A. M. Monahan et al., "Proximal versus distal continuous adductor canal blocks," *Anesthesia & Analgesia*, vol. 127, no. 1, pp. 240–246, 2018.

[24] F. W. Abdallah, J. Mejia, G. A. Prasad et al., "Opioid- and motor-sparing with proximal, mid-, and distal locations for adductor canal block in anterior cruciate ligament reconstruction," *Anesthesiology*, vol. 131, no. 3, pp. 619–629, 2019.

[25] D. F. Johnston, R. V. Sondekoppam, V. Uppal, R. Litchfield, R. Giffin, and S. Ganapathy, "Effect of combining perihamstring injection or anterior obturator nerve block on the analgesic efficacy of adductor canal block for anterior cruciate ligament reconstruction: a randomised controlled trial," *British Journal of Anaesthesia*, vol. 124, no. 3, pp. 299–307, 2020.

[26] A. Zorrilla-Vaca and J. Li, "The role of sciatic nerve block to complement femoral nerve block in total knee arthroplasty: a meta-analysis of randomized controlled trials," *Journal of Anesthesia*, vol. 32, no. 3, pp. 341–350, 2018.

[27] B. Manickam, A. Perlas, E. Duggan, R. Brull, V. W. S. Chan, and R. Ramlogan, "Feasibility and efficacy of ultrasound-guided block of the saphenous nerve in the adductor canal," *Regional Anesthesia and Pain Medicine*, vol. 34, no. 6, pp. 578–580, 2009.

[28] C. Runge, B. Moriggl, J. Børglum, and T. F. Bendtsen, "The spread of ultrasound-guided injectate from the adductor canal to the genicular branch of the posterior obturator nerve and the popliteal plexus," *Regional Anesthesia and Pain Medicine*, vol. 42, no. 6, pp. 725–730, 2017.

[29] C. N. Sessler, M. J. Grap, and M. A. Ramsay, "Evaluating and monitoring analgesia and sedation in the intensive care unit," *Critical Care*, vol. 12, no. 3, p. S2, 2008.

[30] P. Goffin, J.-P. Lecoq, V. Ninane et al., "Interfascial spread of injectate after adductor canal injection in fresh human cadavers," *Anesthesia & Analgesia*, vol. 123, no. 2, pp. 501–503, 2016.

[31] P. E. Gautier, A. Hadzic, J.-P. Lecoq, J. F. Brichant, M. M. Kuroda, and C. Vandepitte, "Distribution of injectate and sensory-motor blockade after adductor canal block," *Anesthesia & Analgesia*, vol. 122, no. 1, pp. 279–282, 2016.

[32] C. Runge, S. Bjørn, J. M. Jensen et al., "The analgesic effect of a popliteal plexus blockade after total knee arthroplasty: a feasibility study," *Acta Anaesthesiologica Scandinavica*, vol. 62, no. 8, pp. 1127–1132, 2018.

[33] S. Thobhani, L. Scalercio, C. E. Elliott et al., "Novel regional techniques for total knee arthroplasty promote reduced hospital length of stay: an analysis of 106 patients," *The Ochsner Journal*, vol. 17, no. 3, pp. 233–238, 2017.

[34] S. R. Sankineani, A. R. C. Reddy, K. K. Eachempati, A. Jangale, and A. V. Gurava Reddy, "Comparison of adductor canal block and IPACK block (interspace between the popliteal artery and the capsule of the posterior knee) with adductor canal block alone after total knee arthroplasty: a prospective control trial on pain and knee function in immediate postoperative period," *European Journal of Orthopaedic Surgery and Traumatology*, vol. 28, no. 7, pp. 1391–1395, 2018.

[35] M. Lundblad, M. Forssblad, S. Eksborg, and P.-A. Lönnqvist, "Ultrasound-guided infrapatellar nerve block for anterior cruciate ligament repair: a prospective, randomised, double-blind, placebo-controlled clinical trial," *European Journal of Anaesthesiology*, vol. 28, no. 7, pp. 511–518, 2011.

[36] M. F. Chisholm, H. Bang, D. B. Maalouf et al., "Postoperative analgesia with saphenous block appears equivalent to femoral nerve block in ACL reconstruction," *HSS Journal*, vol. 10, no. 3, pp. 245–251, 2014.

[37] M. El Ahl, "Femoral nerve block versus adductor canal block for postoperative pain control after anterior cruciate ligament reconstruction: a randomized controlled double blind study," *Saudi Journal of Anaesthesia*, vol. 9, no. 3, pp. 279–282, 2015.

[38] N. A. Mall and R. W. Wright, "Femoral nerve block use in anterior cruciate ligament reconstruction surgery," *Arthroscopy: The Journal of Arthroscopic & Related Surgery*, vol. 26, no. 3, pp. 404–416, 2010.

Hindawi
Pain Research and Management
Volume 2021, Article ID 3960553, 15 pages
https://doi.org/10.1155/2021/3960553

Review Article

Anterior Cervical Discectomy and Fusion Using Zero-P System for Treatment of Cervical Spondylosis: A Meta-Analysis

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Received 26 September 2021; Accepted 17 November 2021; Published 16 December 2021

Academic Editor: Sidong Yang

Objective. The current study aimed to explore the efficacy of Zero profile intervertebral fusion system (Zero-P) and traditional anterior plate cage system (PC) in the treatment of cervical spondylotic myelopathy (CSM). Further, the present study evaluated effects of the treatments on medical security, height of intervertebral disc, adjacent-level ossification development (ALOD), and adjacent segmentation disease (ASD) through a systematic retrospective analysis. *Methods*. Studies on Zero-P system and traditional anterior plate cage system for ACDF in the treatment of CSM were searched in PubMed, Web of Science, Ovid, Embase, and Cochrane Library databases. Two independent researchers screened articles, extracted data, and evaluated the quality of the articles based on the inclusion and exclusion criteria of the current study. RevMan5.3 software was used for meta-analysis following the guidelines of Cochrane collaboration network. Cervical curvature, interbody fusion rate, preoperative and postoperative disc height index (DHI), fusion cage sinking rate, postoperative dysphagia, ASD, ALOD, and loosening of screw were compared between the two groups. *Results*. A total of 17 literatures were included in the present study, including 6 randomized controlled trials and 11 observational studies. The studies comprised a total of 1204 patients with CSM, including 605 patients in the Zero-P system group (Zero-P group) and 599 patients in the traditional animal plate cage group (PC group). Results of this meta-analysis showed that postoperative dysphagia [OR = 0.40, CI (0.28, 95% 0.58), $P < 0.00001$], ALOD [OR = 0.09, CI (0.02, 95% 0.39), $P = 0.001$], ASD [OR = 0.42, CI (0.20, 95% 0.86), $P = 0.02$], and screw loosening [OR = 0.20, CI (0.08, 95% 0.52), $P = 0.0009$] of the Zero-P group were significantly lower compared with the PC group. On the other hand, preoperative cervical curvature [WMD = −0.23, CI (−1.38, 95% 0.92), $P = 0.69$], postoperative cervical curvature [WMD = −0.38, CI (−1.77, 95% 1.01), $P = 0.59$], cage sinking rate [OR = 1.41, CI [0.52, 95% 3.82], $P = 0.50$], intervertebral fusion rate [OR = 0.76, CI (0.27, 95% 2.48), $P = 0.38$], preoperative DHI [WMD = −0.04, CI (−0.14, 95% 0.22), $P = 0.65$], and postoperative DHI [WMD = 0.06, CI (−0.22, 95% 0.34), $P = 0.675$] were not significantly different between the two groups. *Conclusion*. It was evident that the Zero-P system used in ACDF is superior compared with the traditional anterior plate cage system in postoperative dysphagia, avoiding ALOD, ASD, and screw loosening.

1. Introduction

Incidence of degenerative diseases is annually increasing due to the increase in the number of elderly population. Therefore, previous studies have also shown an increase in the incidence of cervical spondylotic myelopathy (CSM) which is a common cause of spinal cord dysfunction. Currently, the onset of CSM occurs at an early age and the condition is becoming more complicated. Several studies have explored methods for effective alleviation of spinal cord compression in patients with CSM and restoration of the spinal cord function. When conservative methods are ineffective or in the case of worsening symptoms, active surgical treatment is recommended for patients with CSM to release nerve compression for timely restoration of normal spinal cord function [1, 2]. The commonly used cervical

spine anterior approaches for surgical treatment of cervical spine diseases are cervical spine posterior approach, combined anterior, and posterior surgery as well as the various minimally invasive techniques.

Anterior cervical surgery was first reported as a safe and effective method for treatment of the degenerative cervical spondylosis by Cloard, Smith, and Robinson in 1958. Anterior cervical discectomy and fusion (ACDF) surgery is one of the most advanced cervical spine surgery approaches which play an important role in treatment of cervical disease [3–5]. Anterior cervical discectomy and fusion (ACDF) is conventionally fixed with anterior interbody fusion cage and steel plate. This fixing system has several advantages but is also associated with potential disadvantages. The most common shortcomings of these techniques include fracture or loosening of plates and screws, tracheal-esophageal interference and influence, and difficulties in postoperative swallowing [6, 7].

Recent studies have explored a lower, more smoothly contoured Zero-P system that reduces incidence of dysphagia after ACDF. Notably, the system can be fully implanted in the intervertebral space, providing sufficient stability and avoiding contact between the implant and the prevertebral soft tissue [8, 9]. Therefore, the zero-notch interbody fusion and internal fixation system is widely used in ACDF to reduce occurrence of these complications.

Currently, it is not clear whether the Zero-P system significantly reduces the incidence of postoperative ALOD, ASD, and screw loosening compared with the traditional anterior plate cage system. Therefore, the aim of the current meta-analysis was to summarize the available evidence from high-quality relevant studies and explore the effects of using Zero-P system as well as traditional anterior plate cage system. The findings of this study can help in clinical decision-making.

2. Materials and Methods

2.1. Search Strategy. English articles were retrieved for this study from PubMed, Web of Science, Ovid, Embase, and Cochrane Library databases. Literature search was carried out based on the search terms determined by the PICOS principle. The present study included English articles about studies on the use of Zero-P and titanium plate combined with cage for ACDF surgery from the time of inception of the databases to December, 2020. Clinical studies on efficacy of treatment degenerative cervical spondylosis were selected using the following keywords and phrases: "Zero-P," "Zero Profile," "anterior cervical discectomy and fusion," and "ACDF" as search terms. The keywords were searched independently and all synonyms as well as variants of the keywords were searched by combining free words and subject words concurrently. Free words and subject words of each keyword were searched by the logical connection word "OR," and the logical connection word "AND." The search group segment was connected and the search results were retrieved.

2.2. Literature Screening and Data Extraction. Inclusion criteria for the present study were as follows: (1) research type: randomized controlled trial and observational study; (2) research object: cervical spondylotic myelopathy; (3) intervention measures: the experimental group represents the Zero-P group, and the control group was the titanium plate cage group (PC Group); (4) follow-up time: 12 months or more; (5) comparative data: ① imaging parameters including preoperative and postoperative follow-up cervical spine curvature, degree of intervertebral fusion, and preoperative intervertebral height index (DHI); ② complications including postoperative dysphagia, cage sinking, and adjacent segment ossification (ALOD); adjacent segment disease (ASD); and screw migration (screw migration), and the literature should have at least one outcome indicator.

Exclusion criteria for this study included the following: ① only studies on Zero-P or titanium plate cage; ② reviews, conference papers, abstracts, or unpublished documents; ③ incomplete data or documents with errors that may affect results; ④ repeated papers; ⑤ research design for self-comparison before and after or without a control group; ⑥ studies with trial design which is not rigorous or inappropriate statistical methods; ⑦ other types of zero-notch interbody fusion internal fixation systems, such as PREVALIL; and ⑧ follow-up time less than 12 months.

Titles and abstracts of the articles retrieved based on inclusion and exclusion criteria were read. Articles that did not meet the inclusion criteria were excluded after reading the title and abstract. Full texts of the documents that met the inclusion criteria were then read to further explore whether they met the inclusion criteria. The original author was contacted whenever the original data was found to be unclear. Two reviewers carried out independent data extraction for articles that met the including criteria. The two reviewers jointly developed a standard data extraction table and, after data extraction, each reviewer cross-checked the data for their partner. Any disagreement between the reviewers was resolved by a third reviewer.

2.3. Methodological Quality Evaluation. Randomized controls were compared from seven aspects including random sequence generation, allocation hiding, double blinding of participants and staff, blinding of result evaluation, data completeness, selective outcome reports, and other sources of bias following the evaluation criteria of the Cochrane Evaluation Manual. The quality of included observational studies was evaluated using Newcastle-Ottawa Scale (NOS). Evaluation was independently conducted and cross-checked by two researchers. However, any case of disagreement was resolved through a third evaluator.

2.4. Statistical Analysis. Statistical analysis of the data obtained in the present study was performed using Review Manager 5.3 (RevMan5.3) software which was developed by Cochrane collaboration network. Analysis of continuous variables in the current study including cervical vertebra Cobb angle, preoperative, and postoperative DHI was carried out using weighted mean difference (WMD) at 95%

confidence interval (95% CI). Odds ratio (OR) and 95% CI were used for analysis of association between the continuous variables of the current study and adjacent segmental ossification rate, adjacent segmental disease incidence, dysphagia incidence, interbody fusion rate, fusion cage sinking rate, and screw loosening rate. Statistically significant difference was set at $P < 0.05$.

Chi-square and I^2 tests were used to evaluate the heterogeneity of the included studies. A $P > 0.1$ for the chi-square test and $I^2 < 50\%$ implied that the heterogeneity was low. Fixed effect model was used for determining the combined effect. When the heterogeneity was high, individual studies were singly eliminated for sensitivity analysis to find the source of heterogeneity. Funnel charts were generated to determine the publication bias for studies comprising more than ten articles (Figure 1).

3. Results

3.1. Search Results. A total of 536 studies were obtained from the databases following an independent search conducted by two scholars. The search was conducted according to the predesigned retrieval strategy. A total of 480 articles were obtained after eliminating cross-documents and repeated published documents. Among the 480 articles, a total of 72 articles were obtained after excluding documents that did not meet the inclusion criteria. A total of 55 abstracts and full papers were then excluded based on the inclusion and exclusion criteria. Finally, it was found that 17 studies met the inclusion criteria and were hence included in the current study (Figure 2 and Table 1).

3.2. Quality Evaluation. Six of the 17 original studies included in the present study [10–15] were randomized controlled trials whereas 11 studies were observational studies [16–26]. Randomized controlled studies were evaluated based on the evaluation criteria of the Cochrane evaluation manual including 7 items (Figure 3). Newcastle-Ottawa Scale was used to evaluate the quality of observational studies. Further, 9, 6, and 2 studies were allocated 7, 8, and 9 stars, respectively, implying that the studies were of high quality (Figure 3 and Table 2).

3.3. Meta-Analysis

3.3.1. Imaging Parameters

(1) Cervical Curvature. It was found that a total of 5 studies including 1 randomized controlled trial and 4 non-randomized retrospective studies [15, 17, 22, 25, 26] reported C2-C7 cervical spine curvature before and after surgery (Table 3).

A total of 321 patients were included based on preoperative cervical curvature as the evaluation index. Out of the 321 patients, 150 of them were in the Zero-P group whereas 171 patients were in the PC group. All the studies passed the heterogeneity test ($P = 0.72$, $I^2 = 0\%$ for each). Analysis results of this study showed that there was no heterogeneity between the original studies. In addition, the fixed effects model was used for analysis of combined effect size of the preoperative C2-C7 cervical spine curvature between the two groups (WMD = −0.23, 95% CI [−1.38, 0.92], $P = 0.69$). The finding of this study showed that the difference was not statistically significant (Figure 4).

A total of 321 patients were included in the present study, out of which 150 patients were in the Zero-P group whereas 171 patients were in the PC group for evaluation based on postoperative cervical curvature. Moreover, the studies passed the heterogeneity test ($P = 0.85$, $I^2 = 0\%$; each). These findings evidently show that there was no heterogeneity between the original studies. The fixed effect model was used for analysis of combined effect size of C2-C7 cervical spine curvature and the findings showed that there was no significant difference between the two groups (WMD = −0.38, 95% CI[−1.77, 1.01], $P = 0.59$, Figure 4).

(2) Intervertebral Fusion Rate. A total of 6 original studies including 2 randomized controlled trials and 4 non-randomized retrospective studies [13, 14, 17, 18, 22, 25] reported fusion rate and provided valid data. A total of 383 patients were included in these studies, including 184 and 199 patients in the Zero-P group and PC groups, respectively.

Results of heterogeneity analysis showed that there was no heterogeneity between the original studies ($P = 0.97$, $I^2 = 0\%$). Further, the analysis of combined effect size using fixed-effects model showed that the difference between the two groups was not statistically significant (OR = 0.76, 95% CI [0.27, 2.48], $P = 0.38$, Figure 5).

(3) Disc Height Index (DHI). It was found that a total of 5 original studies [18–20, 22, 25] reported the intervertebral height index and provided valid data. All the 5 studies were nonrandomized retrospective studies. A total of 380 cases including 181 and 199 in the Zero-P group and PC groups, respectively, were included based on preoperative intervertebral height index. The results of heterogeneity analysis showed no heterogeneity between the original studies ($P = 0.66$, $I^2 = 0\%$). Further, the analysis of the combined effect size using fixed-effect model showed no statistically significant difference in preoperative intervertebral height index between the two groups (WMD = −0.04, 95% CI [−0.14, 0.22], $P = 0.65$; Figure 6).

A total of 380 cases including 181 and 199 in the Zero-P group and PC groups, respectively, were selected based on the postoperative intervertebral height index. Results of heterogeneity analysis in the current study showed a high heterogeneity between the original studies ($P = 0.03$, $I^2 = 63\%$). Analysis of the combined effect using the random effects model showed no significant difference in intervertebral height index between the two groups (WMD = 0.06, 95% CI [−0.22, 0.34], $P = 0.675$; Figure 7(a)). Sensitivity analysis was carried out by eliminating individual studies one by one.

Removal of a study by Liu (2016) significantly decreased heterogeneity ($P = 0.21$, $I^2 = 33\%$). Further, the results of the analysis of the combined effect using the fixed effects model

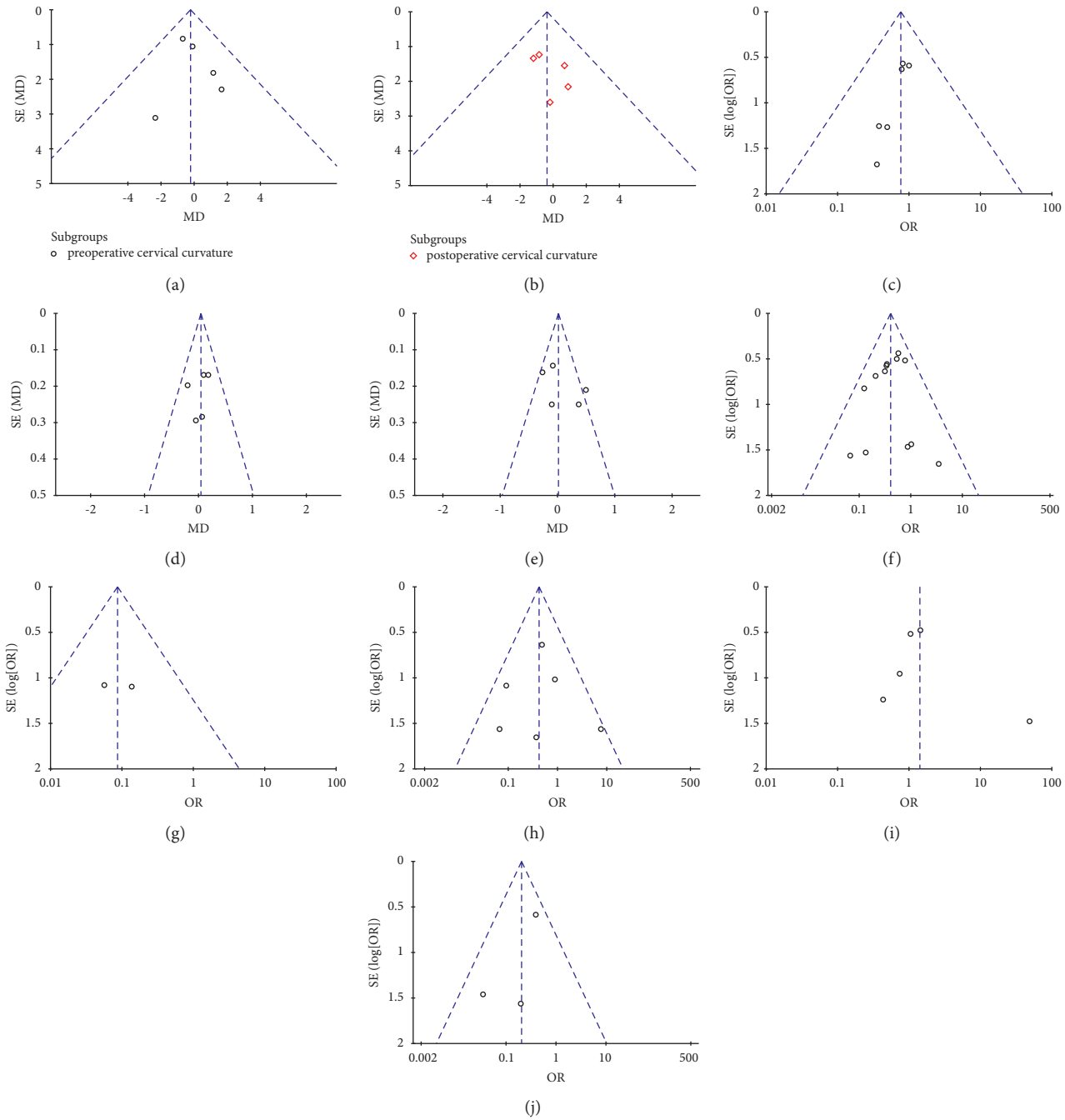


Figure 1: (a) Preoperative cervical curvature funnel diagram; (b) postoperative cervical curvature funnel diagram; (c) funnel diagram for interbody fusion rate; (d) preoperative DHI funnel diagram; (e) postoperative DHI funnel diagram; (f) postoperative dysphagia funnel diagram; (g) ALOD funnel diagram; (h) ASD funnel diagram; (i) postoperative sinking rate funnel diagram of fusion cage; (j) screw loosening funnel diagram (IV) evaluation of publication bias.

showed that the difference between the two groups was not statistically significant (WMD = −0.08, 95% CI [−0.26, 0.10], $P = 0.38$, Figure 7(b)).

3.3.2. Postoperative Complications

(1) Dysphagia. It was found that a total of 13 original studies [10–16, 18, 20, 22, 23, 25, 26] reported dysphagia and provided valid data. Out of the 13 studies, 6 of them were randomized controlled trials whereas 7 were non-randomized retrospective studies.

A total of 904 cases were included including 458 and 446 patients in the Zero-P group and PC groups, respectively, based on incidence of postoperative dysphagia as the evaluation criteria. Results of heterogeneity analysis showed no heterogeneity between the original studies ($P = 0.62$, $I^2 = 0\%$). On the other hand, the results of analysis of combined effect using the fixed-effect model showed a significant difference between the two groups (OR = 0.40,

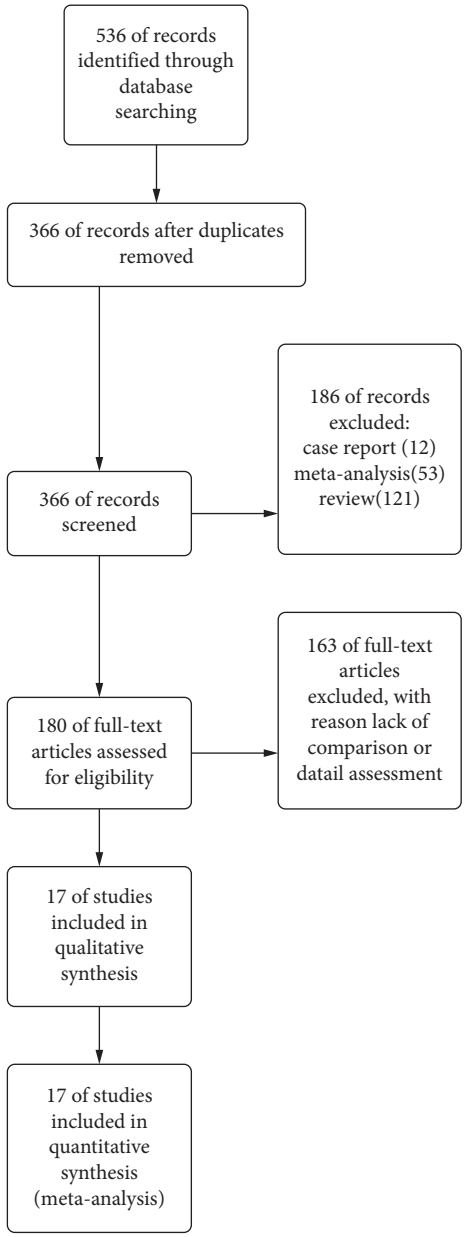


Figure 2: Flowchart of literature screening.

95% CI [0.28, 0.58], $P < 0.00001$). The incidence of dysphagia in the Zero-P group (13.97%) was significantly lower compared with that in the PC group (26.01%; Figure 8).

(2) Adjacent-Level Ossification Development (ALOD). A total of 2 original studies, including 1 randomized controlled trial and 1 nonrandomized retrospective study [10, 24], reported ALOD findings and provided valid data. Further, a total of 133 cases were included, including 63 and 70 patients in the Zero-P group and PC groups, respectively. Heterogeneity was analyzed and the result showed no heterogeneity between the original studies ($P = 0.57$, $I^2 = 0\%$). Analysis results of the combined effect using fixed-effects model showed that the incidence of ALOD in the Zero-P group (3.17%) was significantly lower compared with that in the PC group (27.14%) (OR = 0.09, 95% CI [0.02, 0.39], $P = 0.001$; Figure 9).

(3) Adjacent Segment Disease (ASD). It was found that a total of 6 original studies including 2 randomized controlled trials and 4 nonrandomized retrospective studies [12, 13, 18, 19, 21, 22] reported ASD and provided valid data. A total of 440 cases were included in the present meta-analysis, including 219 and 221 patients in the Zero-P group and pc groups, respectively. Results of the heterogeneity analysis showed insignificant heterogeneity between the original studies ($P = 0.20$, $I^2 = 32\%$). Analysis results for the combined effect using the fixed-effect model showed that the incidence of ASD in the Zero-P Group (4.57%) was significantly lower compared with that in the PC group (11.31%) (OR = 0.42, 95% CI [0.20, 0.86], $P = 0.02$; Figure 10)

(4) Sinking Rate of the Cage. A total of 4 original studies [18, 20, 22, 25] reported the sinking rate of the cage and provided valid data. All the 4 studies were nonrandomized retrospective studies. Notably, a total of 448 cases were based on postoperative fusion cage sinking rate including 221 and 227 patients in the Zero-P and PC groups respectively. Results of heterogeneity analysis showed a high heterogeneity among the original studies ($P = 0.09$, $I^2 = 51\%$). The results of the combined effect analysis using the random effects model showed that the difference between the two groups was not statistically significant from each other (OR = 1.41, 95% CI [0.52, 3.82], $P = 0.50$; Figure 11(a)).

Sensitivity analysis was carried out by eliminating individual studies one by one. It was found that the removal of a study by Sun (2020) significantly reduced the heterogeneity ($P = 0.78$, $I^2 = 0\%$). It was also found that the combined effect analysis using the fixed effects model showed no statistical difference between the two groups (OR = 1.10, 95% CI [0.59, 2.03], $P = 0.77$; Figure 11(b)).

(5) Screw Loosening. Results of the present study show that a total of 3 original studies [18, 19, 21] had screw loosening and provided valid data. Further, all the 3 studies were nonrandomized retrospective studies.

A total of 326 patients were included based on postoperative screw loosening, including 164 of them in the Zero-P group and 162 patients in the PC group. Heterogeneity analysis showed low heterogeneity between the original studies ($P = 0.25$, $I^2 = 28\%$). The results of combined effect analysis of the fixed-effect model showed significant difference between the two groups (OR = 0.20, 95% CI [0.08, 0.52], $P = 0.0009$). Incidence of screw loosening in the Zero-P group (3.66%) was significantly lower compared with that in the PC group (15.43%) (Figure 12).

4. Discussion

Anterior cervical discectomy and bone graft fusion (ACDF) is a safe and an effective surgical method for the treatment of degenerative cervical spine diseases [27]. Anterior titanium plate cage is used in ACDF and has become a conventional surgical method for treatment of degenerative cervical spondylosis [28]. It significantly restores the height of intervertebral disc of spine, ensures high bone graft fusion rate, preserves segmental lordosis, and has strong corner ability [28–30].

Table 1: Quality evaluation of RCT.

First author and author (year of publication)	Country	Type of study	Surgical segment	Sample size		Gender (M/F)		Age ($x \pm s$, years)		Follow-up time ($x \pm s$)	
				Zero-P	PC	Zero-P	PC	Zero-P	PC	Zero-P	PC
Li et al. (2015) [12]	China	Randomized controlled trial	1	12	11	7/5	5/6	50.3 ± 8.8	51.1 ± 6.7	24	24
He et al. (2018) [11]	China	Randomized controlled trial	2	52	52	28/24	27/25	55.4 ± 12.4	59.5 ± 12.6	24	24
Yan and Nie (2018) [15]	China	Randomized controlled trial	1	49	49	29/20	29/20	43.1 ± 5.3	43.3 ± 5.2	12	12
Chen et al. (2016) [10]	China	Randomized controlled trial	3	34	38	21/13	25/13	56.9 ± 5.9	56.2 ± 5.7	12	12
Qizhi et al. (2016) [13]	China	Randomized controlled trial	2	16	14	11/5	9/5	48.13 ± 5.98	46.79 ± 5.15	32.4	32.4
Scholz et al. (2020) [14]	Germany	Randomized controlled trial	1	21	20	13/8	11/9	58	58	24	24
Alimi et al. (2016) [16]	United States	Nonrandomized retrospective study	1, 2, 3	69	35	35/34	18/17	58.2 ± 1.45	51.5 ± 1.95	15.7 ± 1.23	14.8 ± 2.13
Li et al. (2017) [18]	China	Nonrandomized retrospective study	1, 2, 3, 4	68	70	41/27	45/25	50.6 ± 7.5	51.3 ± 7.9	29.7 ± 6.5	30.8 ± 6.6
Liu et al. (2016) [19]	China	Nonrandomized retrospective study	3, 4	28	32	10/18	12/20	56.6 ± 9.7	57.5 ± 9.5	23.3 ± 6.9	24.2 ± 6.4
Cho et al. (2015) [17]	Korea	Nonrandomized retrospective study	1	21	29	12/9	19/10	56.1 ± 12	55.2 ± 10.4	24	24
Shi et al. (2016) [21]	China	Nonrandomized retrospective study	1	68	60	33/35	24/36	47.4 ± 7.0	46.5 ± 6.8	48	48
Sun et al. (2020) [22]	China	Nonrandomized retrospective study	3	27	34	15/12	25/9	54.7 ± 7.6	56.4 ± 7.5	60	60
Wang et al. (2014) [23]	China	Nonrandomized retrospective study	1, 2	30	33	18/12	14/19	56.8 ± 11.0	54.0 ± 10.0	24.1 ± 7.8	23.8 ± 8.2
Yang et al. (2015) [24]	China	Nonrandomized retrospective study	1, 2, 3	30	32	20/10	22/10	44.1 ± 5.8	42.8 ± 6.1	30.6 ± 2.4	33.1 ± 3.0
Shen et al. (2018) [20]	China	Nonrandomized retrospective study	1, 2, 3	27	31	16/11	14/17	52.3 ± 9.2	54.7 ± 9.2	37.2 ± 22.8	46.8 ± 21.6
Yun et al. (2016) [25]	Korea	Nonrandomized retrospective study	3	31	32	29/3	22/9	53.29 ± 7.55	54.18 ± 9.87	12.77 ± 7.85	13.62 ± 9.21
Zhang et al. (2016) [26]	China	Nonrandomized retrospective study	1, 2	22	27	11/12	13/14	48.6 ± 8.1	52.7 ± 8.3	24	24

However, the titanium plate is associated with several limitations, such as screw loosening, titanium plate displacement, soft tissue injury, adjacent segment disease, adjacent segment ossification, and increased incidence of dysphagia [8, 31, 32].

Therefore, Zero-P interbody fusion cage was developed to circumvent limitations of the titanium plate. It is a cervical fusion system that can be independently used in single-segment or multisegment anterior degenerative cervical spondylosis [33]. Several previous studies have reported that Zero-P interbody fusion cage significantly limits the potential risks of dysphagia after fixed surgery of cervical vertebrae, which is in agreement with the findings of the current study [34]. However, there has been no systematic review and analysis conducted to compare the effects of the two techniques on cervical spine curvature, intervertebral height, ALOD, and ASD.

4.1. Zero-P Significantly Reduces Incidence of Long-Term ASD Compared with Traditional Anterior Steel Plates. Anterior cervical discectomy and fusion method is associated with high incidence of ASD. In addition, the traditional fixation methods cause ASD, which may eventually require additional treatment [35–37]. The exact pathophysiological mechanism of ASD has not been fully explored [35–41]. It may be derived from the existing lesions in adjacent segments and changes in biomechanical forces near the previous fusion site and this may increase the risk of degenerative changes [42]. Previous studies have shown that the biomechanical changes of adjacent vertebral bodies after spinal fusion are the major causes of ASD.

Cunningham et al. [43] used a specially designed pressure needle transducer to quantify the intradiscal pressure changes at the level of 3 adjacent intervertebral discs in 11 patients. The findings of that study showed that the proximal disc pressure increased by 45% in case of instability and internal fixation of the fusion zone. It was also found that the presence of steel plates may increase risk of degenerative changes in adjacent segments. Several previous studies have also reported the range of motion and intradiscal pressure increase in untreated segments adjacent to the fused segment [37, 40, 41, 44, 45]. According to

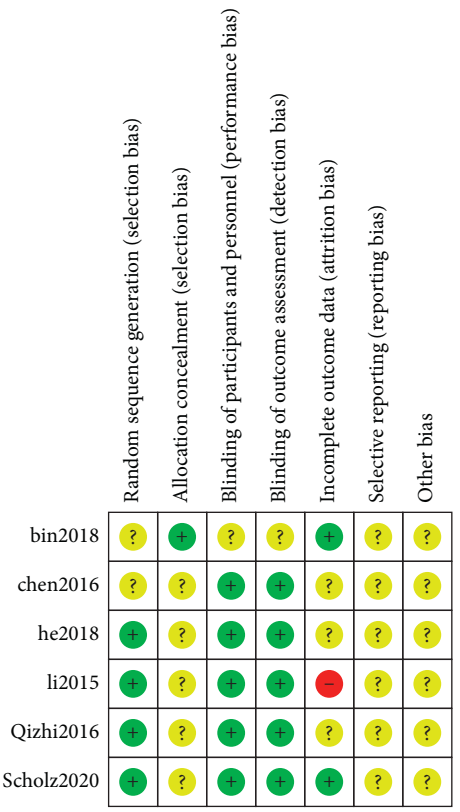


Figure 3: Literature quality evaluation chart of RCT.

Table 2: Newcastle-Ottawa Scale evaluation of observational studies.

Methodological quality assessment for inclusion in observational studies (score)									
Research	Study population selection				Intergroup comparison (2 points)	Measurement of exposure factors			Total (9 points)
	A (1 point)	B (1 point)	C (1 point)	D (1 point)		E (1 point)	F (1 point)	G (1 point)	
Alimi, 2016	1	1	1	0	2	1	1	0	7
Li, 2017	1	1	1	0	2	0	1	0	6
Liu, 2016	1	1	1	0	2	1	1	0	7
Cho, 2015	1	1	1	1	2	1	1	1	9
Shi, 2016	1	1	1	1	2	0	1	0	7
Sun, 2020	1	1	1	1	2	1	1	0	8
Wang, 2014	1	1	1	1	2	1	1	0	8
Yang, 2015	1	1	1	0	2	0	1	0	6
Yong, 2018	1	1	1	0	2	1	1	1	8
Yun, 2016	1	1	1	0	2	0	1	0	6
Zhang, 2016	1	1	1	1	2	1	0	0	7

A, case determination being appropriate; B, case representation; C, selection of control; D, determination of control; E, determination of exposure factors; F, determination of case and control exposure factors being the same; G, response rate.

Hilibrand and Robbins [44] approximately 25% of patients who used traditional steel plates for single-segment ACDF treatment developed ASD within 10 years.

Previous studies on the effect of Zero-P internal fixation system in reducing occurrence of long-term ASD reported inconsistent findings. A study conducted on 71 patients by Chen et al. [46] reported that there was no significant difference in incidence of degenerative diseases in the adjacent segments after treatment with Zero-P and plate cage. In addition, in a separate study, a total of 79 patients with cervical spondylopathy were also treated with anterior cervical fusion and internal fixation. Out of the 79 patients, 41 of them were in the Zero-P group whereas 38 patients were in the steel cage internal fixation group. Incidence of ASD in the two groups was 14.63 and 26.31%, respectively. These findings show that the Zero-P device was more

Table 3: Meta-analysis results of included studies.

Research projects		Number of studies	Sample size			Results			Heterogeneity P-values (I^2)	Statistical methodology
			Total	Zero-P	PC	P-value	OR/ WMD	CI 95 per cent		
Cervical curvature	Preoperative	5	321	150	171	0.69	−0.23	−1.38, 0.92	0.72 (0%)	WMD (IV, fixed)
	Postoperative	5	321	150	171	0.59	−0.38	−1.77, 1.01	0.85(0%)	WMD (IV, fixed)
Intervertebral fusion rate		6	383	184	199	0.38	0.76	0.27, 2.48	0.97(0%)	OR (M-H, fixed)
DHI	Preoperative	5	380	181	199	0.65	−0.04	−0.14, 0.22	0.66(0%)	WMD (IV, fixed)
	Postoperative	5	380	181	199	0.675	0.06	−0.22, 0.34	0.03(63%)	WMD (IV, random)
Dysphagia		13	904	458	446	<0.00001	0.40	0.28, 0.58	0.62(0%)	OR (M-H, fixed)
ALOD		2	133	63	70	0.001	0.09	0.02, 0.39	0.57(0%)	OR (M-H, fixed)
ASD		6	440	219	221	0.02	0.42	0.20, 0.86	0.20(32%)	OR (M-H, fixed)
Sinking rate of the cage		5	448	221	227	0.50	1.41	0.52, 3.82	0.09(51%)	OR (M-H, random)
Screw loosening		3	326	164	162	0.0009	0.20	0.08, 0.52	0.25(28%)	OR (M-H, fixed)

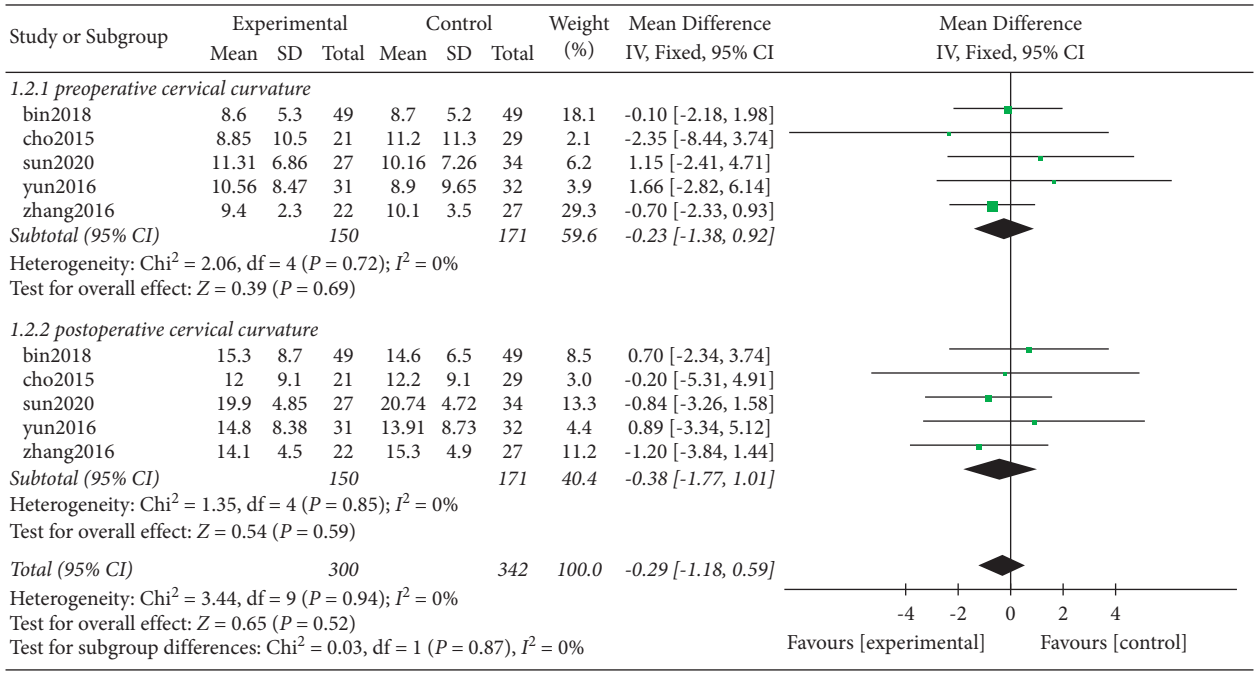


Figure 4: Cervical curvature before and after surgery.

effective in reducing degeneration of adjacent segments after degenerative cervical disease compared with the plate cage internal fixation system. However, it was found that the difference between the two groups was not statistically significant. It is, hence, not clear whether the use of Zero-P system treatment reduces incidence of postoperative ASD.

In the current study, the total number of patients with cervical spondylopathy included was 440, with 219 and 221 of them in the Zero-P and PC groups, respectively. The findings of this study showed that the incidence of ASD in the Zero-P group (4.57%) was significantly lower compared with that in the PC group (11.31%). Higher efficacy may be because Zero-P fixes the intervertebral disc space away from the adjacent segment, thus reducing the impact on the biomechanics of the adjacent segment. Therefore, it is evident that Zero-P minimizes the risk of degeneration of adjacent intervertebral discs.

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight (%)	Odds Ratio M-H, Fixed, 95% CI
cho2015	13	21	18	29	24.4	0.99 [0.31, 3.16]
li2017	62	68	65	70	23.9	0.79 [0.23, 2.74]
Qizhi2016	15	16	14	14	5.7	0.36 [0.01, 9.47]
Scholz2020	19	21	19	20	7.8	0.50 [0.04, 5.99]
sun2020	25	27	33	34	9.2	0.38 [0.03, 4.42]
yun2016	22	31	24	32	29.0	0.81 [0.27, 2.48]
Total (95% CI)		*184*		*199*	*100.0*	*0.76 [0.41, 1.40]*
Total events	156		173			

Heterogeneity: Chi^2 = 0.85, df = 5 (P = 0.97); I^2 = 0%
Test for overall effect: Z = 0.87 (P = 0.38)

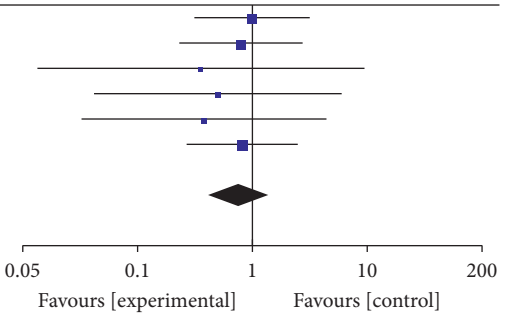


Figure 5: Intervertebral fusion rate.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight (%)	Mean Difference IV, Fixed, 95% CI
li2017	6.13	1.75	68	6.06	1.58	70	10.4	0.07 [-0.49, 0.63]
liu2016	4.6	0.7	28	4.5	0.6	32	29.1	0.10 [-0.23, 0.43]
sun2020	5.46	0.66	27	5.28	0.65	34	29.3	0.18 [-0.15, 0.51]
yong2018	5	0.7	27	5.2	0.8	31	21.6	-0.20 [-0.59, 0.19]
yun2016	4.53	1.14	31	4.58	1.19	32	9.7	-0.05 [-0.63, 0.53]
Total (95% CI)			*181*			*199*	*100.0*	*0.04 [-0.14, 0.22]*

Heterogeneity: Chi^2 = 2.40, df = 4 (P = 0.66); I^2 = 0%
Test for overall effect: Z = 0.45 (P = 0.65)

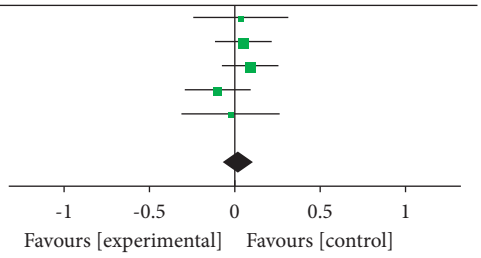
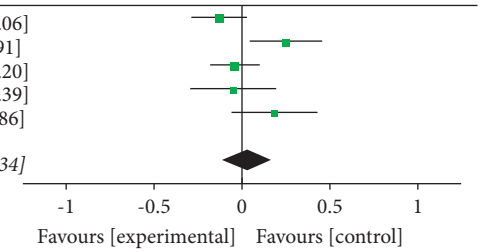


Figure 6: Preoperative DHI.

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight (%)	Mean Difference IV, Random, 95% CI
li2017	6.85	0.85	68	7.11	1.04	70	23.1	-0.26 [-0.58, 0.06]
liu2016	6.5	0.9	28	6	0.7	32	19.3	0.50 [0.09, 0.91]
sun2020	6.96	0.55	27	7.04	0.57	34	24.6	-0.08 [-0.36, 0.20]
yong2018	6.5	0.9	27	6.6	1	31	16.5	-0.10 [-0.59, 0.39]
yun2016	7.66	1	31	7.29	0.98	32	16.5	0.37 [-0.12, 0.86]
Total (95% CI)			*181*			*199*	*100.0*	*0.06 [-0.22, 0.34]*

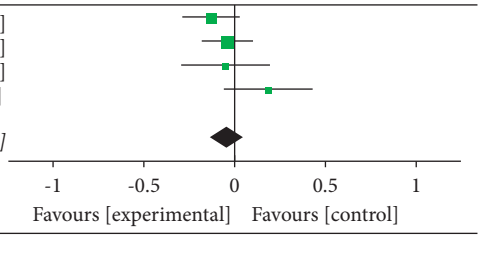
Heterogeneity: Tau^2 = 0.06; Chi^2 = 10.89, df = 4 (P = 0.03); I^2 = 63%
Test for overall effect: Z = 0.42 (P = 0.67)



(a)

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Weight (%)	Mean Difference IV, Fixed, 95% CI
li2017	6.85	0.85	68	7.11	1.04	70	32.3	-0.26 [-0.58, 0.06]
sun2020	6.96	0.55	27	7.04	0.57	34	40.6	-0.08 [-0.36, 0.20]
yong2018	6.5	0.9	27	6.6	1	31	13.5	-0.10 [-0.59, 0.39]
yun2016	7.66	1	31	7.29	0.98	32	13.5	0.37 [-0.12, 0.86]
Total (95% CI)			*153*			*167*	*100.0*	*-0.08 [-0.26, 0.10]*

Heterogeneity: Chi^2 = 4.50, df = 3 (P = 0.21); I^2 = 33%
Test for overall effect: Z = 0.87 (P = 0.38)



(b)

Figure 7: (a) Postoperative DHI and (b) sensitivity analysis on postoperative DHI.

4.2. Zero-P Reduces Incidence of Long-Term ALOD Compared with Traditional Anterior Steel Plates. Adjacent-level ossification development (ALOD) is a common complication of ACDF which occurs as early as 3 months after surgery [47]. Previous studies have shown that cervical spine plate is associated with increased risk of ALOD. According to Garrido et al. [48], the incidence of ALOD in cervical disc replacement during two-year and four-year follow-up was

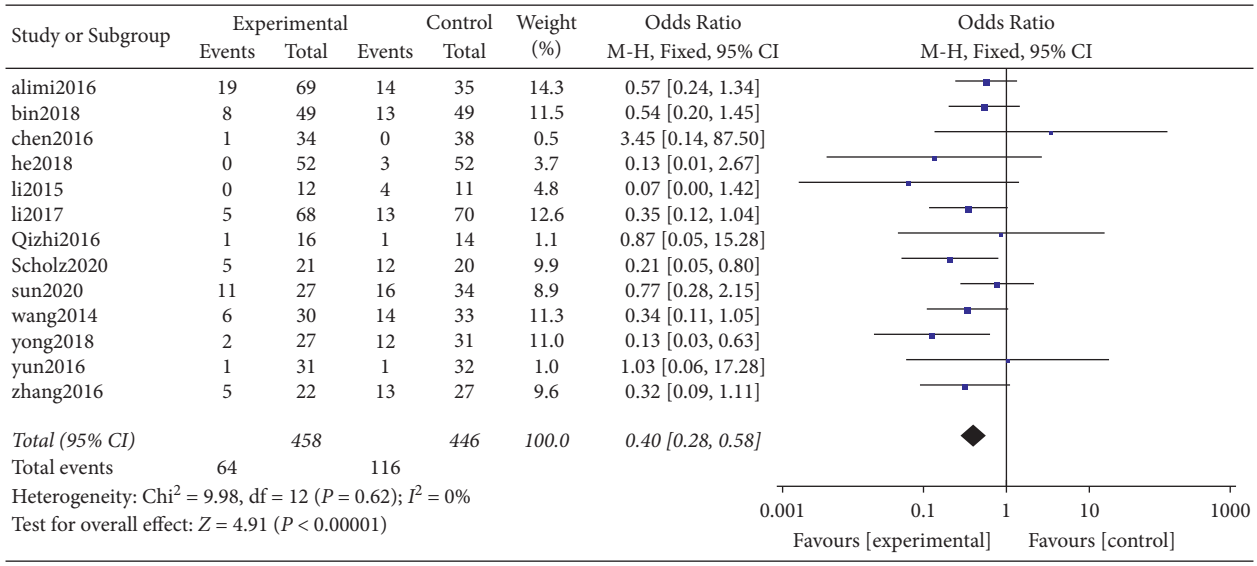


Figure 8: Postoperative dysphagia.

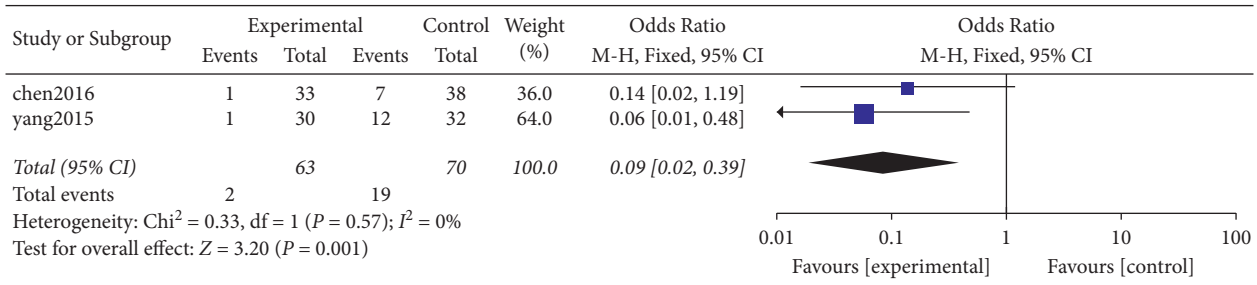


Figure 9: Postoperative ALOD.

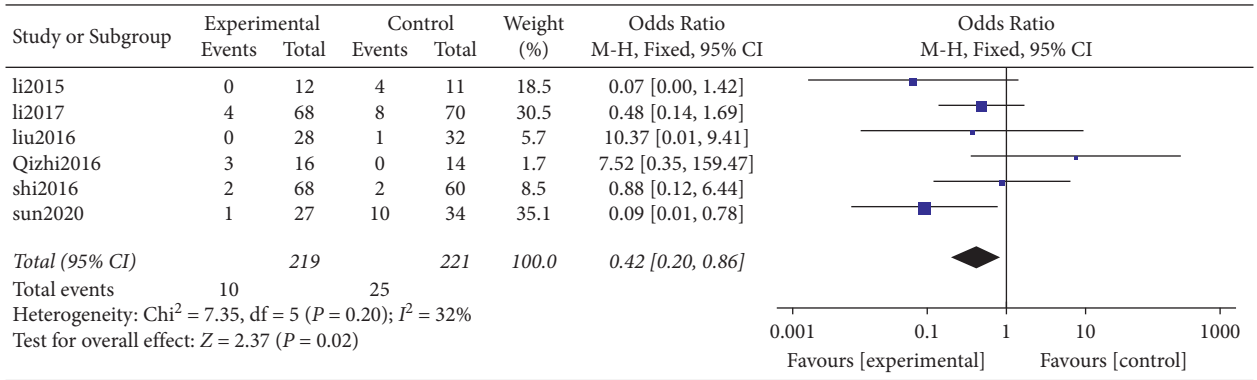


Figure 10: Postoperative ASD.

significantly lower compared with that of plate fixation. In a separate study, Yang et al. [24] performed a retrospective study and reported that Zero-P was associated with lower incidence of ALOD. In addition, the length of the steel plate was associated with the incidence of ALOD. Further, Park et al. [35] explored the incidence of ALOD after internal fixation of the anterior cervical plate. The findings of the study showed that the incidence of ALOD was higher when the distance between the tip of the plate and the adjacent intervertebral disc was less than 5 mm. According to Lee et al. [49] and Park et al. [50], the use of short plates with inclined screw tracks reduces occurrence of ALOD.

Findings of the current study showed that the incidence of ALOD in the Zero-P group (3.17%) was significantly lower compared with that of the PC group (27.14%), which were in agreement with findings from previous studies. Although the anterior longitudinal ligament was injured by a spreader or an electric knife in the two groups of patients, it was evident that the plate promoted formation of osteophytes during repair of the anterior longitudinal ligament.

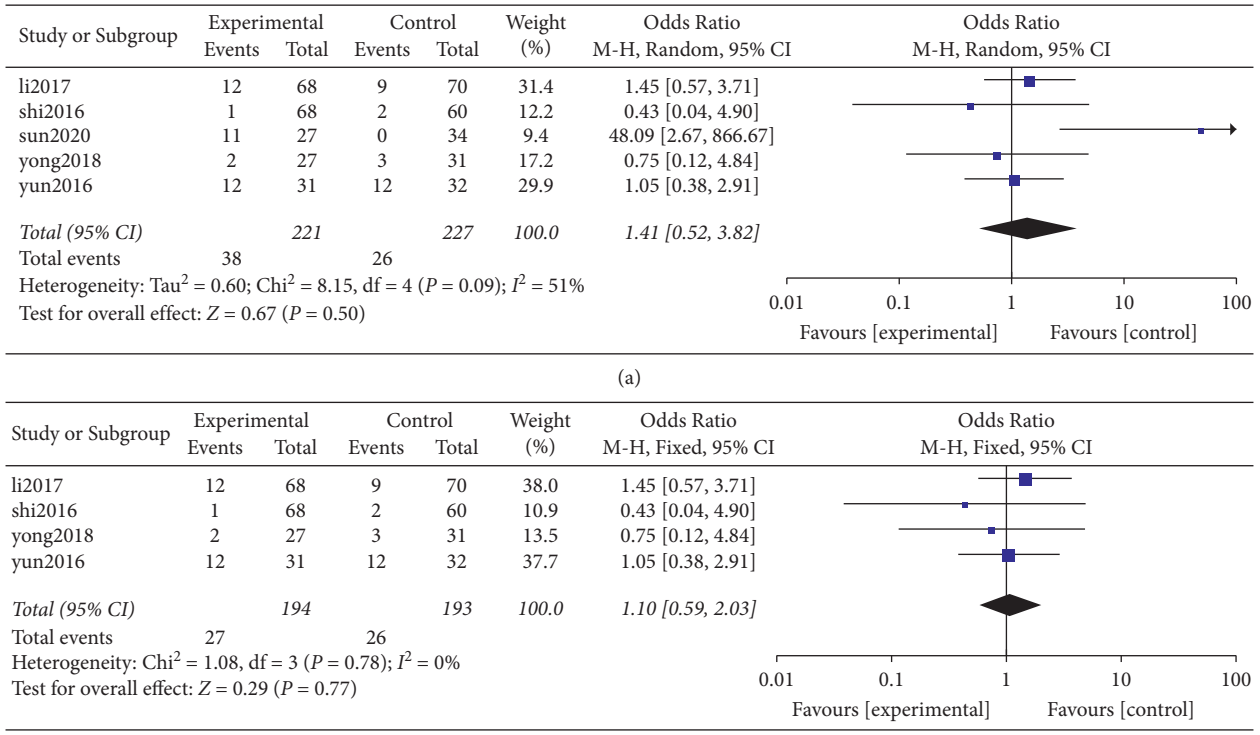


Figure 11: (a) Fusion sinking rate after surgery. (b) Sensitivity analysis of fusion sinking rate after operation.

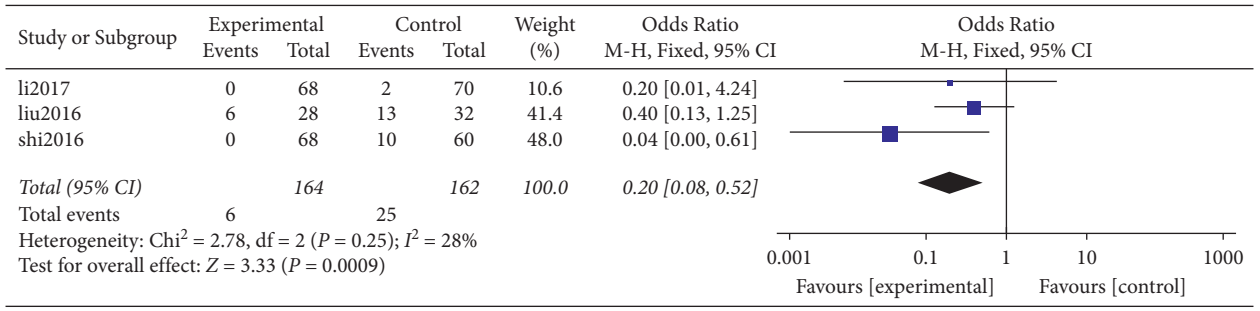


Figure 12: Screw loosening after operation.

On the other hand, the Zero-P group had no plate internal fixation and no mechanical stimulation; hence, the incidence of ALOD was relatively low.

4.3. Zero-P Reduces Incidence of Dysphagia Compared with Traditional Anterior Plates. Dysphagia is a complication of ACDF after using additional anterior plate. Previous studies have reported that the incidence of postoperative dysphagia is as high as 71%. Incidence of persistent dysphagia can reach 35.1% after 7.2 years of anterior cervical plate fixation, but most symptoms of dysphagia decrease within a month. However, between 12 and 14% of patients presented with difficulties in swallowing 1 year after surgery [51]. Possible causes of dysphagia include postoperative soft tissue edema, esophageal injury, postoperative hematoma, and adhesions around the implanted cervical spine plate. Moreover, the anterior cervical plate is placed directly behind the esophagus, which may affect or irritate the esophagus. Previous studies have reported that the design and thickness of the anterior locking plate are correlated with postoperative dysphagia. According to Lee et al. [34], a correlation between plate thickness and incidence of dysphagia was reported, and thus the use of thinner plates can reduce incidence of dysphagia. Another possible mechanism of dysphagia after ACDF anterior plate surgery may be the need for additional traction to place the anterior locking plate. During the process of anterior plate implantation, it has been reported that an increase in esophageal pressure may cause dysphagia in patients with ACDF anterior plate. Furthermore, the Zero-P cervical fusion cage does not straddle the anterior vertebral body and can be completely contained in the decompressed intervertebral space. Therefore, there is a reduced mechanical stimulation of esophagus and other prevertebral soft tissues, and it retains as much normal anatomy as possible. This explains the lower incidence of postoperative dysphagia in the Zero-P group.

4.4. Zero-P and Traditional Anterior Plate Show No Significant Difference in Maintenance of Cervical Spine Curvature and Intervertebral Height. The curvature of the cervical spine plays an important role in maintaining efficacy of surgery. Poor cervical spine curvature increases stress distribution of the internal fixation device and adjacent segments, thus increasing the incidence of internal fixation failure and ASD. It has been reported that insufficient recovery of cervical spine curvature after ACDF significantly affects cervical spine instability and postoperative axial pain and may also affect the recovery of nerve function [52]. However, the role of Zero-P in maintaining postoperative cervical spine curvature is controversial. According to Shi et al. [53], the loss of cervical spine curvature in the Zero-P group was significantly higher compared with that in the PC group after a 30-month follow-up.

A study by Chen et al. [46] reported that the average C2-C7 Cobb angle of the traditional steel plate group was significantly greater compared with that of the Zero-P group. Use of steel plate can also reconstruct the ideal sagittal position balance with the spine compared with Zero-P fixation. A separate study by Lan et al. [54] reported that the cervical spine Cobb angle was significantly corrected after the operation in the Zero-P group and the traditional plate group with no statistical difference, which is in consonance with the findings of the current study. The findings of the current meta-analysis study showed that there was no statistical difference between the two groups; however, postoperative cervical spine curvature was significantly improved as compared to preoperative cervical spine curvature.

Furthermore, a drop in intervertebral height caused by sinking of the cage is a common postoperative complication of ACDF [25]. It is defined as the loss of more than 2 mm of disc height in two measurements [6]. Previous studies have shown that sinking of the fusion cage is associated with several factors including preoperative cervical spine curvature, size of the plate, contact area with the endplate, age, and the titanium plate as well as the distance between the implant and the anterior edge of the vertebral body [33, 55–57].

The findings of a study by Wu et al. [58] showed that a decrease in the height of the intervertebral disc was related to sinking of the intervertebral fusion cage. Notably, Zero-P interbody fusion cage can effectively restore the physiological structure of the cervical spine and maintain the height of the intervertebral space more effectively compared with traditional steel plates. Results of a different study by Lee et al. [59] revealed that the sinking rate of the Zero-P device (21.7%) was higher compared with that of the front steel plate (11.1%). On the other hand, Scholz et al. [60] reported that during the 6-month follow-up, the patients treated with the Zero-P device did not present sinking of the intervertebral fusion cage. According to Noh and Zhang [61] the settlement rate of Zero-P group (25%) was slightly higher at the last follow-up, compared with that of the plate cage group (21%). However, the difference between the two groups was not statistically significant from each other. In the current meta-analysis, it was found that the sinking rate of the Zero-P group was 17.19%, whereas that of the PC group was 11.45%. Although the results were not statistically different, it was evident that the sinking rate of the fusion cage in the Zero-P group was higher compared with that of the PC Group, which is consistent with the findings of a study by Noh and Zhang [61].

The findings of the present meta-analysis show that both methods can effectively maintain intervertebral height. During the operation, a distractor was used to open the intervertebral space and a Zero-P intervertebral fusion cage or a traditional steel plate cage was implanted. Therefore, the height of the intervertebral space was significantly increased compared with the space before the operation and hence restoring the intervertebral height.

4.5. Zero-P Reduces Incidence of Screw Loosening Compared with Traditional Front Steel Plates. According to a study by Vaccaro et al., the incidence of traditional anterior cervical fixation of plate screws and plate loosening was 15.4%, whereas the fracture rates of screws and plates were as high as 13.3 and 6.7%, respectively. Notably, plates and bone grafts were displaced (with or without transplantation). The incidence of bone fracture was high (21.4%) whereas the incidence of implant failure for long-segment plates (intervertebral screws and plates of unfused segments) ranged from 0 to 12.5%.

The design of the implant has different screw fixation mechanisms and loosening of the implant screw may be related to the design of the fixed plate-screw interface. It has been found that the "zero notch" design of the Zero-P intervertebral fusion cage has more advantages compared with the traditional plate cage system. The intervertebral screw of the Zero-P system is a self-tapping screw, which can strengthen the thread and the screw during screwing. Further, the bite force of the bone between the vertebral bodies increases the immediate stability between the vertebral bodies. Moreover, the angle of the screw and that of the cervical spine biological force line are larger compared with those for the traditional steel plate, and the pullout resistance is stronger. Therefore, the findings of the current study revealed that the incidence of screw loosening in the Zero-P group (3.66%) was significantly lower compared with that in the PC group (15.43%), which can be attributed to the described reasons.

5. Limitations

This study had some limitations. ① Although random effects models and sensitivity analysis were used to eliminate statistical heterogeneity, they may have led to a certain degree of measurement error. ② Although most effect sizes are sensitive, after sensitivity analysis, heterogeneity was eliminated or reduced; however, there was still some heterogeneity after the merging of individual effect data and some results could not be reliable. ③ At present, the application of Zero-P is in the early stage, the clinical practice has not been fully carried out, and the corresponding high-quality clinical research requires further long-term follow-up.

6. Conclusion

In conclusion, it was evident that the use of Zero-P system during anterior cervical discectomy and fusion reduces the risk of ALOD, ASD, and screw loosening and reduces the operation time, intraoperative blood loss, and the incidence of postoperative dysphagia compared with the traditional anterior plate cage system.

Data Availability

The data used in this study are all included in this paper and open to all readers.

Disclosure

Zhaoyang Guo and Xiaolin Wu are co-first authors.

Conflicts of Interest

The authors declare no potential conflicts of interest.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (82172478, 81802190, and 81772412); the Young Taishan Scholars Program (tsqn201909190); Postdoctoral Science Foundation of China (2021M701813); National Key Research and Development Project (2019YFC0121404); Shandong Provincial Science Foundation, China (ZR2019BH084); Qingdao Postdoctoral Applied Research Project (2020); and Innovation Fund of National Orthopedics and Sports Rehabilitation Clinical Medicine Research Center (2021-NCRC-CXJJ-ZH-02). The authors would like to acknowledge the translation support of Home for Researchers (http://www.home-for-researchers.com) for this paper.

References

[1] A. Iyer, T. D. Azad, and S. Tharin, "Cervical spondylotic myelopathy," *Clinical Spine Surgery: A Spine Publication*, vol. 29, no. 10, pp. 408–414, 2016.

[2] P. Vanek, O. Bradac, P. DeLacy, K. Saur, T. Belsan, and V. Benes, "Comparison of 3 fusion techniques in the treatment of the degenerative cervical spine disease. Is stand-alone autograft really the "gold standard?"," *Spine*, vol. 37, no. 19, pp. 1645–1651, 2012.

[3] M. Korinth, "Treatment of cervical degenerative disc disease-current status and trends," *Zentralblatt für Neurochirurgie-Central European Neurosurgery*, vol. 69, no. 3, pp. 113–124, 2008.

[4] H. Le, I. Thongtrangan, and D. H. Kim, "Historical review of cervical arthroplasty," *Neurosurgical Focus*, vol. 17, no. 3, pp. 1–9, 2004.

[5] P. G. Matz, T. C. Ryken, M. W. Groff et al., "Techniques for anterior cervical decompression for radiculopathy," *Journal of Neurosurgery: Spine*, vol. 11, no. 2, pp. 183–197, 2009.

[6] E. Gercek, V. Arlet, J. Delisle, and D. Marchesi, "Subsidence of stand-alone cervical cages in anterior interbody fusion: warning," *European Spine Journal: Official Publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*, vol. 12, no. 5, pp. 513–516, 2003.

[7] K. Schmieder, M. Wolzik-Grossmann, I. Pechlivanis, M. Engelhardt, M. Scholz, and A. Harders, "Subsidence of the wing titanium cage after anterior cervical interbody fusion: 2-year follow-up study," *Journal of Neurosurgery: Spine*, vol. 4, no. 6, pp. 447–453, 2006.

[8] W.-M. Yue, W. Brodner, and T. R. Highland, "Persistent swallowing and voice problems after anterior cervical discectomy and fusion with allograft and plating: a 5- to 11-year follow-up study," *European Spine Journal, and the European Section of the Cervical Spine Research Society*, vol. 14, no. 7, pp. 677–682, 2005.

[9] K. N. Fountas, E. Z. Kapsalaki, L. G. Nikolakakos et al., "Anterior cervical discectomy and fusion associated complications," *Spine*, vol. 32, no. 21, pp. 2310–2317, 2007.

[10] Y. Chen, H. Chen, X. Wu, X. Wang, W. Lin, and W. Yuan, "Comparative analysis of clinical outcomes between zero-profile implant and cages with plate fixation in treating multilevel cervical spondilotic myelopathy: a three-year follow-up," *Clinical Neurology and Neurosurgery*, vol. 144, pp. 72–76, 2016.

[11] S. He, H. Feng, Z. Lan et al., "A randomized trial comparing clinical outcomes between zero-profile and traditional multilevel anterior cervical discectomy and fusion surgery for cervical myelopathy," *Spine*, vol. 43, no. 5, pp. E259–e266, 2018.

[12] Y. Li, D. Hao, B. He, X. Wang, and L. Yan, "The efficiency of zero-profile implant in anterior cervical discectomy fusion," *Journal of Spinal Disorders & Techniques*, vol. 28, no. 10, pp. 398–403, 2015.

[13] S. Qizhi, S. Lei, L. Peijia et al., "A comparison of zero-profile devices and artificial cervical disks in patients with 2 non-contiguous levels of cervical spondylosis," *Clinical Spine Surgery: A Spine Publication*, vol. 29, no. 2, pp. E61–E66, 2016.

[14] M. Scholz, B. Onal, P. Schleicher, A. Pingel, C. Hoffmann, and F. Kandziora, "Two-level ACDF with a zero-profile stand-alone spacer compared to conventional plating: a prospective randomized single-center study," *European Spine Journal*, vol. 29, no. 11, pp. 2814–2822, 2020.

[15] B. Yan and L. Nie, "Clinical comparison of Zero-profile interbody fusion device and anterior cervical plate interbody fusion in treating cervical spondylosis," *International Journal of Clinical and Experimental Medicine*, vol. 8, no. 8, pp. 13854–13858, 2015.

[16] M. Alimi, I. Njoku, C. P. Hofstetter et al., "Anterior cervical discectomy and fusion (ACDF): comparison between zero profile implants and anterior cervical plate and spacer," *Cureus*, vol. 8, no. 4, p. e573, 2016.

[17] H.-J. Cho, J. W. Hur, J.-B. Lee, J.-S. Han, T.-H. Cho, and J.-Y. Park, "Cervical stand-alone polyetheretherketone cage versus zero-profile anchored spacer in single-level anterior cervical discectomy and fusion: minimum 2-year assessment of radiographic and clinical outcome," *Journal of Korean Neurosurgical Society*, vol. 58, no. 2, pp. 119–124, 2015.

[18] Z. Li, Y. Zhao, J. Tang et al., "A comparison of a new zero-profile, stand-alone Fidji cervical cage and anterior cervical plate for single and multilevel ACDF: a minimum 2-year follow-up study," *European Spine Journal, and the European Section of the Cervical Spine Research Society*, vol. 26, no. 4, pp. 1129–1139, 2017.

[19] Y. Liu, H. Wang, X. Li et al., "Comparison of a zero-profile anchored spacer (ROI-C) and the polyetheretherketone (PEEK) cages with an anterior plate in anterior cervical

discectomy and fusion for multilevel cervical spondylotic myelopathy," *European Spine Journal: official Publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*, vol. 25, no. 6, pp. 1881–1890, 2016.

[20] Y. Shen, W. Du, L.-F. Wang, Z. Dong, and F. Wang, "Comparison of zero-profile device versus plate-and-cage implant in the treatment of symptomatic adjacent segment disease after anterior cervical discectomy and fusion: a minimum 2-year follow-up study," *World Neurosurgery*, vol. 115, pp. e226–e232, 2018.

[21] S. Shi, S. Zheng, X.-F. Li, L.-L. Yang, Z.-D. Liu, and W. Yuan, "Comparison of 2 zero-profile implants in the treatment of single-level cervical spondylotic myelopathy: a preliminary clinical study of cervical disc arthroplasty versus fusion," *PLoS One*, vol. 11, no. 7, Article ID e0159761, 2016.

[22] B. Sun, C. Shi, H. Wu et al., "Application of zero-profile spacer in the treatment of three-level cervical spondylotic myelopathy," *Spine*, vol. 45, no. 8, pp. 504–511, 2020.

[23] Z. Wang, W. Jiang, X. Li et al., "The application of zero-profile anchored spacer in anterior cervical discectomy and fusion," *European Spine Journal: Official Publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*, vol. 24, no. 1, pp. 148–154, 2015.

[24] H. Yang, D. Chen, X. Wang, L. Yang, H. He, and W. Yuan, "Zero-profile integrated plate and spacer device reduces rate of adjacent-level ossification development and dysphagia compared to ACDF with plating and cage system," *Archives of Orthopaedic and Trauma Surgery*, vol. 135, no. 6, pp. 781–787, 2015.

[25] D.-J. Yun, S.-J. Lee, S.-J. Park et al., "Use of a zero-profile device for contiguous 2-level anterior cervical diskectomy and fusion: comparison with cage with plate construct," *World Neurosurgery*, vol. 97, pp. 189–198, 2017.

[26] L. Zhang, J. Wang, Y. Tao, X. Feng, J. Yang, and S. Zhang, "Outcome evaluation of zero-profile implant compared with an anterior plate and cage used in anterior cervical discectomy and fusion: a two-year follow-up study," *Turkish Neurosurgery*, vol. 26, no. 3, pp. 416–422, 2014.

[27] Y. Liu, Y. Hou, L. Yang et al., "Comparison of 3 reconstructive techniques in the surgical management of multilevel cervical spondylotic myelopathy," *Spine*, vol. 37, no. 23, pp. E1450–E1458, 2012.

[28] K.-J. Song, C. E. Taghavi, K.-B. Lee, J.-H. Song, and J.-P. Eun, "The efficacy of plate construct augmentation versus cage alone in anterior cervical fusion," *Spine*, vol. 34, no. 26, pp. 2886–2892, 2009.

[29] S. Fujibayashi, M. Neo, and T. Nakamura, "Stand-alone interbody cage versus anterior cervical plate for treatment of cervical disc herniation: sequential changes in cage subsidence," *Journal of Clinical Neuroscience*, vol. 15, no. 9, pp. 1017–1022, 2008.

[30] C.-J. Lee, M.-H. Lee, J.-Y. Lee, J. H. Song, H. S. Lee, and Y.-Y. Cho, "RSK2-induced stress tolerance enhances cell survival signals mediated by inhibition of GSK3β activity," *Biochemical and Biophysical Research Communications*, vol. 440, no. 1, pp. 112–118, 2013.

[31] R. L. Sahjpaul, "Esophageal perforation from anterior cervical screw migration," *Surgical Neurology*, vol. 68, no. 2, pp. 205–209, 2007.

[32] A. L. Rhyne III, L. R. Spector, G. L. Schmidt et al., "Anatomic mapping and evaluation of the esophagus in relation to the cervical vertebral body," *European Spine Journal: Official Publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*, vol. 16, no. 8, pp. 1267–1272, 2007.

[33] P. Barsa and P. Suchomel, "Factors affecting sagittal malalignment due to cage subsidence in standalone cage assisted anterior cervical fusion," *European Spine Journal: Official Publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*, vol. 16, no. 9, pp. 1395–1400, 2007.

[34] M. J. Lee, R. Bazaz, C. G. Furey, and J. Yoo, "Influence of anterior cervical plate design on dysphagia," *Journal of Spinal Disorders & Techniques*, vol. 18, no. 5, pp. 406–409, 2005.

[35] J.-B. Park, Y.-S. Cho, and K. D. Riew, "Development of adjacent-level ossification in patients with an anterior cervical plate," *The Journal of Bone and Joint Surgery*, vol. 87, no. 3, pp. 558–563, 2005.

[36] J.-Y. Yang, H.-S. Song, M. Lee, H. H. Bohlman, and K. D. Riew, "Adjacent level ossification development after anterior cervical fusion without plate fixation," *Spine*, vol. 34, no. 1, pp. 30–33, 2009.

[37] J.-Y. Chung, S.-K. Kim, S.-T. Jung, and K.-B. Lee, "Clinical adjacent-segment pathology after anterior cervical discectomy and fusion: results after a minimum of 10-year follow-up," *The Spine Journal*, vol. 14, no. 10, pp. 2290–2298, 2014.

[38] K.-J. Song, B.-W. Choi, T.-S. Jeon, K.-B. Lee, and H. Chang, "Adjacent segment degenerative disease: is it due to disease progression or a fusion-associated phenomenon? Comparison between segments adjacent to the fused and non-fused segments," *European Spine Journal, and the European Section of the Cervical Spine Research Society*, vol. 20, no. 11, pp. 1940–1945, 2011.

[39] R. J. Mobbs, P. Rao, and N. K. Chandran, "Anterior cervical discectomy and fusion: analysis of surgical outcome with and without plating," *Journal of Clinical Neuroscience*, vol. 14, no. 7, pp. 639–642, 2007.

[40] X.-P. Xia, H.-L. Chen, and H.-B. Cheng, "Prevalence of adjacent segment degeneration after spine surgery," *Spine*, vol. 38, no. 7, pp. 597–608, 2013.

[41] S. Litrico, N. Lonjon, G. Riouallon et al., "Adjacent segment disease after anterior cervical interbody fusion. A multicenter retrospective study of 288 patients with long-term follow-up," *Orthopaedics and Traumatology: Surgery & Research*, vol. 100, no. 6, pp. S305–S309, 2014.

[42] D. G. Tobert, V. Antoci, S. P. Patel, E. Saadat, and C. M. Bono, "Adjacent segment disease in the cervical and lumbar spine," *Clinical Spine Surgery: A Spine Publication*, vol. 30, no. 3, pp. 94–101, 2017.

[43] B. W. Cunningham, Y. Kotani, P. S. McNulty, A. Cappuccino, and P. C. McAfee, "The effect of spinal destabilization and instrumentation on lumbar intradiscal pressure," *Spine*, vol. 22, no. 22, pp. 2655–2663, 1997.

[44] A. S. Hilibrand and M. Robbins, "Adjacent segment degeneration and adjacent segment disease: the consequences of spinal fusion?" *The Spine Journal*, vol. 4, no. 6, pp. S190–S194, 2004.

[45] M. Hussain, R. N. Natarajan, A. H. Fayyazi, B. R. Braaksma, G. B. J. Andersson, and H. S. An, "Screw angulation affects bone-screw stresses and bone graft load sharing in anterior cervical corpectomy fusion with a rigid screw-plate construct: a finite element model study," *The Spine Journal*, vol. 9, no. 12, pp. 1016–1023, 2009.

[46] Y. Chen, Y. Liu, H. Chen, P. Cao, and W. Yuan, "Comparison of curvature between the zero-P spacer and traditional cage and plate After 3-level anterior cervical discectomy and

fusion," *Clinical Spine Surgery: A Spine Publication*, vol. 30, no. 8, pp. E1111–e1116, 2017.

[47] J.-B. Park, T. Watthanaaphisit, and K. D. Riew, "Timing of development of adjacent-level ossification after anterior cervical arthrodesis with plates," *The Spine Journal*, vol. 7, no. 6, pp. 633–636, 2007.

[48] B. J. Garrido, J. Wilhite, M. Nakano et al., "Adjacent-level cervical ossification after Bryan cervical disc arthroplasty compared with anterior cervical discectomy and fusion," *Journal of Bone and Joint Surgery*, vol. 93, no. 13, pp. 1185–1189, 2011.

[49] D.-H. Lee, J.-S. Lee, J.-S. Yi, W. Cho, L. P. Zebala, and K. D. Riew, "Anterior cervical plating technique to prevent adjacent-level ossification development," *The Spine Journal*, vol. 13, no. 7, pp. 823–829, 2013.

[50] J.-H. Park, S.-J. Hyun, C.-H. Lee et al., "Efficacy of a short plate with an oblique screw trajectory for anterior cervical plating," *Clinical Spine Surgery: A Spine Publication*, vol. 29, no. 1, pp. E43–E48, 2016.

[51] S. K. Cho, Y. Lu, and D.-H. Lee, "Dysphagia following anterior cervical spinal surgery," *The Bone & Joint Journal*, vol. 95-b, no. 7, pp. 868–873, 2013.

[52] S. Yang, Y. Yu, X. Liu et al., "Clinical and radiological results comparison of allograft and polyetheretherketone cage for one to two-level anterior cervical discectomy and fusion," *Medicine (Baltimore)*, vol. 98, no. 45, Article ID e17935, 2019.

[53] S. Shi, Z.-D. Liu, X.-F. Li, L. Qian, G.-B. Zhong, and F.-J. Chen, "Comparison of plate-cage construct and stand-alone anchored spacer in the surgical treatment of three-level cervical spondylotic myelopathy: a preliminary clinical study," *The Spine Journal*, vol. 15, no. 9, pp. 1973–1980, 2015.

[54] T. Lan, J.-Z. Lin, S.-Y. Hu, X.-J. Yang, and Y. Chen, "Comparison between zero-profile spacer and plate with cage in the treatment of single level cervical spondylosis," *Journal of Back and Musculoskeletal Rehabilitation*, vol. 31, no. 2, pp. 299–304, 2018.

[55] O. Nemoto, A. Kitada, S. Naitou, A. Tachibana, Y. Ito, and A. Fujikawa, "Stand-alone anchored cage versus cage with plating for single-level anterior cervical discectomy and fusion: a prospective, randomized, controlled study with a 2-year follow-up," *European Journal of Orthopaedic Surgery and Traumatology*, vol. 25, no. S1, pp. 127–134, 2015.

[56] C. H. Kim, C. K. Chung, T.-A. Jahng, S. B. Park, S. Sohn, and S. Lee, "Segmental kyphosis after cervical interbody fusion with stand-alone polyetheretherketone (PEEK) cages," *Journal of Spinal Disorders & Techniques*, vol. 28, no. 1, pp. E17–E24, 2015.

[57] Y.-S. Lee, Y.-B. Kim, and S.-W. Park, "Risk factors for postoperative subsidence of single-level anterior cervical discectomy and fusion," *Spine*, vol. 39, no. 16, pp. 1280–1287, 2014.

[58] W.-J. Wu, L.-S. Jiang, Y. Liang, and L.-Y. Dai, "Cage subsidence does not, but cervical lordosis improvement does affect the long-term results of anterior cervical fusion with stand-alone cage for degenerative cervical disc disease: a retrospective study," *European Spine Journal, and the European Section of the Cervical Spine Research Society*, vol. 21, no. 7, pp. 1374–1382, 2012.

[59] Y.-S. Lee, Y.-B. Kim, and S.-W. Park, "Does a zero-profile anchored cage offer additional stabilization as anterior cervical plate?" *Spine*, vol. 40, no. 10, pp. E563–E570, 2015.

[60] M. Scholz, K. J. Schnake, A. Pingel, R. Hoffmann, and F. Kandziora, "A new zero-profile implant for stand-alone anterior cervical interbody fusion," *Clinical Orthopaedics and Related Research*, vol. 469, no. 3, pp. 666–673, 2011.

[61] S. H. Noh and H. Y. Zhang, "Comparison among perfect-C, zero-P, and plates with a cage in single-level cervical degenerative disc disease," *BMC Musculoskeletal Disorders*, vol. 19, no. 1, p. 33, 2018.

Hindawi
Pain Research and Management
Volume 2021, Article ID 3716696, 6 pages
https://doi.org/10.1155/2021/3716696

Research Article

The Effect of Lower-Limb Exercise on Pain Management of the Patients Undergoing Posterior Lumbar Fusion Surgery: A Retrospective Case-Control Study

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Received 23 October 2021; Accepted 19 November 2021; Published 3 December 2021

Academic Editor: Sidong Yang

Purpose. The purpose of this study is to investigate the clinical effect of lower-limb exercise, when combined with celecoxib, on pain management of patients undergoing posterior lumbar fusion surgeries. *Methods*. The patients undergoing posterior lumbar fusion surgeries between 01/2018 and 06/2021 were retrospectively identified, with their data collected. After surgery, some patients took celecoxib for analgesia (celecoxib group, 200 mg/day) while the others took celecoxib together with lower-limb exercise (combined group, celecoxib-200 mg/day). On postoperative days (POD) 1, 3, 7, and 14, data were collected and analyzed regarding the following items: patient satisfaction, lower-limb muscle force, lumbar JOA score (29 points), Oswestry Disability Index (ODI), and visual analog scale (VAS) score. *Results*. A total of 225 participants were included in this study. Specifically, 120 cases were admitted into in the celecoxib group and 105 were included in the combined group. Comparisons of baseline data did not indicate any difference between the combined group and the celecoxib group. Data analysis showed that patient satisfaction in the combined group was significantly higher than the celecoxib group on POD 3, 7, and 14, respectively (all $p < 0.001$). Moreover, the combined group had less VAS score compared with the celecoxib group on POD 3, 7, and 14, respectively (all $p < 0.01$). In addition, lower-limb muscle force in the combined group was significantly stronger than that in the celecoxib group on POD 3 and POD 7, respectively (both $p < 0.01$). Furthermore, the combined group achieved less ODI score than the celecoxib group on POD 3, 7, and 14, respectively (all $p < 0.05$). Comparisons of the lumbar JOA score did not suggest any statistical difference during the whole follow-up period. *Conclusions*. In conclusion, postoperative lower-limb rehabilitation exercise can help to release pain after lumbar fusion surgeries. Additionally, postoperative lower-limb exercise can facilitate the recovery of lower-limb muscle force, as well as improving patient satisfaction.

1. Introduction

In clinical scenarios, lower back pain (LBP) mainly derives from intervertebral disc degeneration (IVDD) [1–3]. IVDD-related diseases, such as lumbar disc herniation, can lead to severe symptoms including LBP and lower-limb radicular pain. In such a situation, the patients usually need to undergo surgeries to remove the protruded disc and decompress the nerve root and spinal canal. To date, posterior lumbar interbody fusion surgery has been a widely used surgical procedure for treating IVDD-derived diseases, in particular, lumbar spinal diseases [4–6]. However, it has been reported by previous studies that postoperative patients may experience prolonged LBP and low quality of life [7–10], that is one of the key reasons that some patients would seek physical therapy after lumbar fusion surgery, for a purpose of speeding up their rehabilitation.

As suggested by previous studies, postoperative rehabilitation procedures can help pain management after spinal surgeries, even decreasing the disability events [11–13]. In the past few years, accumulative studies have indicated that postoperative lower-limb exercise can facilitate rehabilitation and help relieve pain after orthopedic surgery [14] and lumbar spine surgery [15, 16]. Clinically, celecoxib, one of nonsteroidal anti-inflammatory drugs (NSAIDS), has been commonly administered to the patients for pain relief, the regular oral dose of celecoxib being 200 mg daily [17–19]. However, it remains unclear whether postoperative lower-limb exercise can increase pain relief when administered together with celecoxib for the patients undergoing spine surgery.

Thus, the purpose of this study is to investigate the effect of lower-limb exercise, when combined with celecoxib, on pain management of the patients who undergo posterior lumbar fusion surgeries.

2. Patients and Methods

2.1. Ethics. Prior to the commencement of this study, the medical ethics has been approved by Medical Ethics Council of Nantong Tongzhou People's Hospital. All informed consent was signed by the patients (or their lawful guardians) before undergoing lumbar fusion surgeries.

2.2. Patients. The patients undergoing posterior lumbar fusion surgeries (Figure 1) between 01/2018 and 06/2021 were retrospectively identified and screened. All participants were diagnosed with lumbar disc herniation or lumbar spinal stenosis. The related data were then collected, including the data followed up with different time points on postoperative days (POD) 1, 3, 7, and 14. After surgery, some of these patients took celecoxib for analgesia (celecoxib group, celecoxib-200 mg/day), while the others took celecoxib together with lower-limb exercise (combined group, celecoxib-200 mg/day). Both in the celecoxib group and the combined group, celecoxib was administrated to the patients 200 mg/time/day, administrated in the evening. During the perioperation period, all the participants underwent the same routine medical care regardless of treatment groups. Postoperatively, the patients in the combined group did rehabilitation exercise by following the lower-limb rehabilitation procedures as previously reported [14–16] and maintained for up to 14 days.

2.3. Assessment. Data were collected and analyzed regarding the following items: patient satisfaction, lower-limb muscle force, lumbar JOA score (29 points), Oswestry Disability Index (ODI), and visual analog scale (VAS) score. The grading of lower-limb muscle force was based on the classification criteria which British Medical Research Council applies. In addition, the patient satisfaction rate was scored to three levels: very satisfied, satisfied, and dissatisfied.

2.4. Statistical Analyses. Statistical analysis in this study was performed using the software SPSS for Windows 18.0 (SPSS Inc., USA). The data of ODI, JOA score, and VAS score are presented as mean ± standard deviation (SD). The data of age are presented as median (range). Multiple comparisons were carried out with analysis of variance (ANOVA) if homogeneity and normality of variance were assumed, subsequently followed by Student–Newman–Keuls t-tests used to identify the difference between two groups. Moreover, chi-square tests were conducted to analyze the categorical data (gender, patient satisfaction, and muscle force). A p value of 0.05 was set as the significance level.

3. Results

3.1. Baseline Data of Participants. After the identification of all patients, a total of 225 participants were included in this case-control study. Specifically, 120 cases were admitted into the celecoxib group and 105 cases were included in the combined group. The combined group consists of 48 males and 57 females, while the celecoxib group consists of 54 males and 66 females. The median age of the combined group is 54 years (range 21–67), while the median age of the celecoxib group is 56 years (range 23–70). Comparisons of those baseline data did not suggest any difference between the combined group and the celecoxib group (all $p > 0.05$).

3.2. Patient Satisfaction. As given in Table 1, the patient satisfaction was categorized to three grades: very satisfied, satisfied, and dissatisfied. Most of the patients were very satisfied and satisfied about their treatment regardless of the treatment groups or postoperative time points. Data analysis showed that patient satisfaction in the combined group was significantly higher than the celecoxib group on POD 3, 7, and 14, respectively (all $p < 0.001$). There was no difference regarding the patient satisfaction on POD 1 between the combined group and the celecoxib group ($p > 0.05$).

3.3. VAS Score. As given in Table 2, the combined group obtained less VAS score compared with the celecoxib group on POD 3 (2.6 ± 1.2 vs. 3.5 ± 1.1), POD 7 (1.5 ± 1.2 vs. 2.3 ± 1.1), and POD 14 (1.1 ± 0.3 vs. 1.2 ± 0.2), respectively (all $p < 0.01$). No significant difference of VAS score was indicated on POD 1 between the combined group and the celecoxib group ($p > 0.05$).

3.4. Lower-Limb Muscle Strength Grading. As given in Table 3, most grading of the preoperative lower-limb muscle strength was grade III and grade IV in both the combined group and the celecoxib group. Grade IV and grade V (as a whole) took the majority after surgery, and grade V increased continuously during the postoperative follow-up period regardless of the groups. As compared with the preoperative grading, the muscle strength got improved in both the combined group and the celecoxib group. Lower-limb muscle force in the combined group was significantly stronger than that in the celecoxib group on POD 3 and POD 7, respectively (both $p < 0.01$). There was no significant difference found between the combined group and the celecoxib group on POD 1 or POD 14.

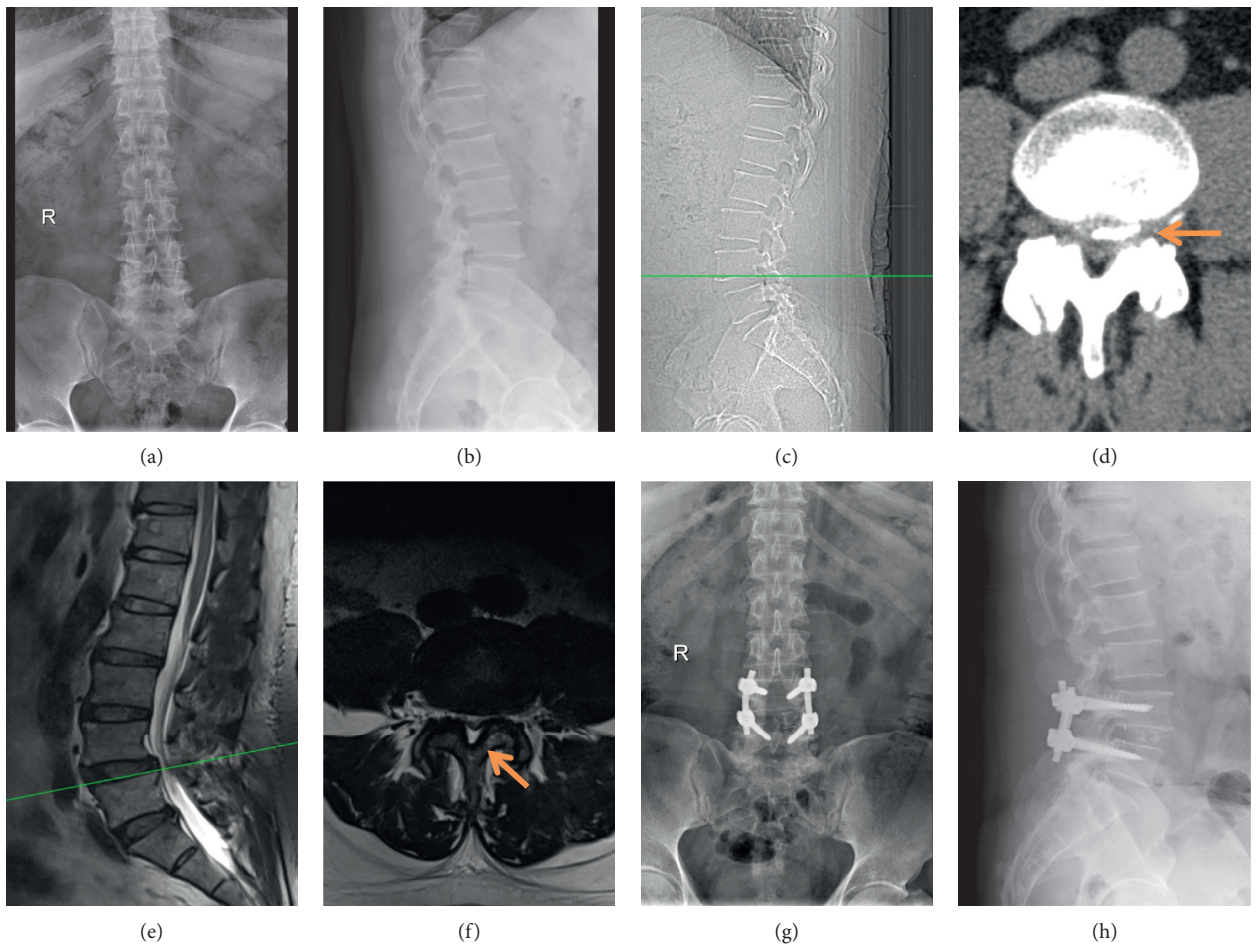

Figure 1: A representative case of posterior fusion surgery. (a)-(b) Preoperative X-ray radiographs. (c)-(d) Preoperative CT scan. (e)-(f) Preoperative MRI scan. (g)-(h) Postoperative X-ray radiographs. The arrows indicate the herniation of nucleus pulposus in the intervertebral disc.

Table 1: Patient satisfaction at discharge.

After surgery	Combined group ($n = 105$) Very satisfied/satisfied/dissatisfied	Celecoxib group ($n = 120$) Very satisfied/satisfied/dissatisfied	Chi-square tests	
			χ^2	P value
POD 1	30 cases/60 cases/15 cases	32 cases/69 cases/19 cases	0.164	0.921
POD 3	72 cases/30 cases/3 cases	40 cases/64 cases/16 cases	**29.47**	**<0.001**
POD 7	92 cases/12 cases/1 cases	52 cases/58 cases/10 cases	**47.92**	**<0.001**
POD 14	101 cases/4 cases/0 case	78 cases/37 cases/5 cases	**33.67**	**<0.001**

All values with $P < 0.05$ are presented in bold, which indicate statistical significance. Combined group, celecoxib and lower-limb rehabilitation exercise; POD, postoperative day.

Table 2: Assessment of VAS score.

Group	Pre-op	POD 1	POD 3	POD 7	POD 14
Celecoxib ($n = 120$)	6.8 ± 1.7	5.7 ± 1.4	3.5 ± 1.1	2.3 ± 1.1	1.2 ± 0.2
Combined ($n = 105$)	6.6 ± 2.1	5.4 ± 1.6	2.6 ± 1.2	1.5 ± 1.2	1.1 ± 0.3
P value	0.431	0.135	**<0.001**	**<0.001**	**0.003**

All values with $P < 0.05$ are presented in bold, which indicate statistical significance.VAS, visual analog scale; combined group, celecoxib and lower-limb rehabilitation exercise; POD, postoperative day; Pre-op, preoperation.

3.5. ODI Score. As given in Table 4, preoperatively, there was no significant difference regarding the ODI score between the combined group and the celecoxib group ($p > 0.05$). Postoperatively, both of the combined group and the celecoxib group achieved significant improvement of the ODI score, compared to their preoperative data, respectively. The combined group scored less ODI than the celecoxib group on POD 3, 7, and 14, respectively (all ($p < 0.05$)). There was no statistical difference between the combined group and the celecoxib group on POD 1 ($p > 0.01$).

Table 3: Lower-limb muscle force.

Group	Pre-op			POD 1			POD 3			POD 7			POD 14		
Grade	III	IV	V	III	IV	V	III	IV	V	III	IV	V	III	IV	V
Celecoxib ($n = 120$)	34	68	18	31	77	12	28	75	17	25	64	31	12	24	84
Combined ($n = 105$)	27	63	15	23	72	10	18	52	35	12	43	50	8	18	79
χ^2	0.268			0.537			11.622			12.200			0.814		
P value	$P = 0.875$			$P = 0.764$			$P = 0.003$			$P = 0.002$			$P = 0.666$		

$P < 0.001$, in terms of muscle force comparison between the celecoxib group and the combined group. POD, postoperative day; combined group, celecoxib and lower-limb rehabilitation exercise; Pre-op, preoperation.

Table 4: ODI assessment and comparisons.

Groups	Pre-op	POD 1	POD 3	POD 7	POD 14
Celecoxib ($n = 120$)	48 ± 22	41 ± 20	33 ± 16	21 ± 11	13 ± 4
Combined ($n = 105$)	46 ± 23	40 ± 19	27 ± 15	18 ± 9	11 ± 4
P value	0.506	0.702	**0.0042**	**0.027**	**<0.001**

All values with $P < 0.05$ are presented in bold, which indicate statistical significance.ODI, Oswestry Disability Index; combined group, celecoxib and lower-limb rehabilitation exercise; POD, postoperative day; Pre-op, preoperation.

Table 5: JOA score (lumbar, 29 points) assessment and comparisons.

Groups	Pre-op	POD 1	POD 3	POD 7	POD 14
Celecoxib ($n = 120$)	7.5 ± 1.3	10.5 ± 1.5	14.7 ± 2.2	19.8 ± 6.1	22.1 ± 6.6
Combined ($n = 105$)	7.8 ± 1.2	10.2 ± 1.7	15.1 ± 2.4	20.3 ± 6.3	22.3 ± 6.5
P value	0.075	0.161	0.194	0.546	0.820

JOA, Japanese Orthopedic Association; combined group, celecoxib and lower-limb rehabilitation exercise; POD, postoperative day; Pre-op, preoperation.

3.6. Lumbar JOA Score. As given in Table 5, preoperatively, there was no significant difference regarding the lumbar JOA score between the combined group and the celecoxib group ($p > 0.05$). Postoperatively, comparisons of the lumbar JOA score did not suggest any statistical differences between the combined group and the celecoxib group during the whole follow-up period ($p > 0.05$).

4. Discussion

In our department, as a routine procedure for the prophylaxis of potential postoperative complications (such as deep vein thrombosis), the patients are required to do lower-limb rehabilitation exercise postoperatively; the exercise procedures are given in previous studies [14–16]. All participants are asked to do the same intensity rehabilitation for up to two weeks. The pain relief effect of lower-limb rehabilitation exercise on the patients after orthopedic surgery and spinal surgery has already been documented in those previous studies [14–16]. In this study, the patients in the combined group kept doing rehabilitation exercise for up to 14 days. That was because many patients can walk well and start to do some normal exercise, other than the lower-limb rehabilitation procedures, after 14 days after surgery. Thus, 14-day exercise with the lower-limb rehabilitation procedures after surgery was considered as an endpoint of our study on the postoperative pain management.

Celecoxib, a selective cyclooxygenase-2 inhibitor and an NSAID, has been routinely used by the patients after spinal surgery for pain relief, with its advantage of minimizing the gastrointestinal adverse effects [17]. Considering the pain relief effects of celecoxib and lower-limb exercise, it would be possible for them to have synergistic effects on pain relief. However, thus far, it has been unclear whether postoperative lower-limb exercise can increase pain relief when administered together with celecoxib for the patients undergoing spine surgery. Thus, this study was designed to investigate the effect of lower-limb exercise, when combined with celecoxib, on pain management of the patients who underwent posterior lumbar fusion surgery in our department.

As a result, a total of 225 cases were included in our study. Baseline data (age and gender) were well matched between the combined group and the celecoxib group. Compared with preoperative situations, the combined group and the celecoxib group have significantly improved in terms of the patient satisfaction, VAS score, lower-limb muscle force, lumbar JOA score, and ODI score. Also, it was found that the combined group achieved better results than the celecoxib group, in terms of the patient satisfaction, VAS score, lower-limb muscle force, and ODI score. These findings in this study stay consistent with the reports from previous studies [14–16] which indicate that lower-limb exercise can effectively increase postoperative pain relief, accelerate functional recovery, and decrease complications (such as deep vein thrombosis).

It is noticeable in this study that the postoperative lumbar JOA score is not significantly different between the combined group and the celecoxib group during the whole follow-up period (up to 14 days). This result of the JOA score is inconsistent with previous reports indicating that postoperative lower-limb exercise can improve the JOA score. One possible reason for this result is that our follow-up period is too short, only 14 days postsurgery. By contrast, the maximum follow-up period in the previous studies are up to 3 months [14–16]. Another reason could be the different study designs between this study and other studies. In this study, the combined group was designed to compare with the celecoxib group, while the lower-limb exercise group was compared with the control group (settings unknown) in those previous studies.

Up to now, there is no consensus regarding whether postoperative rehabilitation can effectively promote the

recovery of patients undergoing spinal surgery. In terms of pain relief, functional improvement, and patient satisfaction, the positive effects of postoperative rehabilitation procedures have been declared in some studies [12, 14, 16, 20, 21], while some others are negative towards postoperative rehabilitation [4, 22, 23]. Apparently, the findings in the current study support the former, with increased pain relief, great functional improvement, and higher patient satisfaction in the rehabilitation group, compared to the non-rehabilitation group postoperatively.

This study has some limitations that might have restricted the interpretation of the data. First, this is a single-center, retrospective, case-control study, making the participants included lack for extensive representativeness and the data accuracy decreases to a certain extent. In addition, the patient sample is not large, just a total of 225 participants were included in this study. It would make the results and conclusions more robust if the patient sample size is greater. Moreover, the follow-up period in this study is not long enough (just 14 days), which can potentially influence the results and conclusions. Therefore, a better future study needs to resolve all of the shortcomings listed above. It can be designed to be multicenter, prospective, blinded, and randomly controlled; the sample size should be big enough.

5. Conclusions

In summary, postoperative lower-limb rehabilitation exercise can synergistically work with celecoxib, increasing pain relief for the patients undergoing lumbar fusion surgeries. In addition, postoperative lower-limb exercise can facilitate functional recovery and increase patient satisfaction.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

References

[1] Y. Huo, D. Yang, L. Ma, H. Wang, W. Ding, and S. Yang, "Oblique lumbar interbody fusion with stand-alone cages for the treatment of degenerative lumbar spondylolisthesis: a retrospective study with 1-year follow-up," *Pain Research and Management*, vol. 2020, Article ID 9016219, 6 pages, 2020.

[2] S. Yang, F. Zhang, J. Ma, and W. Ding, "Intervertebral disc ageing and degeneration: the antiapoptotic effect of oestrogen," *Ageing Research Reviews*, vol. 57, Article ID 100978, 2020.

[3] H. Wang, Z. Li, Y. Huo et al., "17β-Estradiol alleviates intervertebral disc degeneration by inhibiting NF-κB signal pathway," *Life Sciences*, vol. 284, Article ID 119874, 2021.

[4] T. J. Aalto, V. Leinonen, A. Herno et al., "Postoperative rehabilitation does not improve functional outcome in lumbar spinal stenosis: a prospective study with 2-year postoperative follow-up," *European Spine Journal, and the European Section of the Cervical Spine Research Society*, vol. 20, no. 8, pp. 1331–1340, 2011.

[5] A. F. Mannion, R. Denzler, J. Dvorak, M. Müntener, and D. Grob, "A randomised controlled trial of post-operative rehabilitation after surgical decompression of the lumbar spine," *European Spine Journal*, vol. 16, no. 8, pp. 1101–1117, 2007.

[6] R. M. A. van Erp, J. Jelsma, I. P. J. Huijnen, M. Lundberg, P. C. Willems, and R. J. E. M. Smeets, "Spinal surgeons' opinions on pre- and postoperative rehabilitation in patients undergoing lumbar spinal fusion surgery," *Spine*, vol. 43, no. 10, pp. 713–719, 2018.

[7] K.-å. Jansson, G. Németh, F. Granath, B. Jönsson, and P. Blomqvist, "Health-related quality of life (EQ-5D) before and one year after surgery for lumbar spinal stenosis," *Journal of Bone and Joint Surgery British Volume*, vol. 91-B, no. 2, pp. 210–216, 2009.

[8] K.-å. Jansson, G. Németh, F. Granath, B. Jönsson, and P. Blomqvist, "Health-related quality of life in patients before and after surgery for a herniated lumbar disc," *Journal of Bone and Joint Surgery British Volume*, vol. 87-B, no. 7, pp. 959–964, 2005.

[9] A. F. Mannion, R. Denzler, J. Dvorak, and D. Grob, "Five-year outcome of surgical decompression of the lumbar spine without fusion," *European Spine Journal*, vol. 19, no. 11, pp. 1883–1891, 2010.

[10] B. I. Martin, S. K. Mirza, B. A. Comstock, D. T. Gray, W. Kreuter, and R. A. Deyo, "Reoperation rates following lumbar spine surgery and the influence of spinal fusion procedures," *Spine*, vol. 32, no. 3, pp. 382–387, 2007.

[11] T. Oosterhuis, L. O. Costa, C. G. Maher, H. C. de Vet, M. W. van Tulder, and R. W. Ostelo, "Rehabilitation after lumbar disc surgery," *Cochrane Database of Systematic Reviews*, vol. 2014, no. 3, Article ID CD003007, 2014.

[12] R. W. J. G. Ostelo, L. O. Pena Costa, C. G. Maher, H. C. W. de Vet, and M. W. van Tulder, "Rehabilitation after lumbar disc surgery," *Spine*, vol. 34, no. 17, pp. 1839–1848, 2009.

[13] R. W. Ostelo, L. O. P. Costa, C. G. Maher, H. C. de Vet, and M. W. van Tulder, "Rehabilitation after lumbar disc surgery," *Cochrane Database of Systematic Reviews*, vol. 8, no. 4, Article ID CD003007, 2008.

[14] S.-D. Yang, S.-H. Ning, L.-H. Zhang, Y.-Z. Zhang, W.-Y. Ding, and D.-L. Yang, "The effect of lower limb rehabilitation gymnastics on postoperative rehabilitation in elderly patients with femoral shaft fracture," *Medicine*, vol. 95, no. 33, Article ID e4548, 2016.

[15] S.-K. Liu, Y.-L. Song, W.-Y. Ding, D.-L. Yang, L. Ma, and S.-D. Yang, "The effect of systematic lower-limb rehabilitation training in elderly patients undergoing lumbar fusion surgery: a retrospective study," *Oncotarget*, vol. 8, no. 68, pp. 112720–112726, 2017.

[16] H. Wang, Y. Huo, Y. Zhao et al., "Clinical rehabilitation effect of postoperative lower-limb training on the patients undergoing OLIF surgery: a retrospective study," *Pain Research and Management*, vol. 2020, Article ID 1065202, 6 pages, 2020.

[17] M. S. Park, C.-N. Kang, W.-S. Lee et al., "A comparative study of the efficacy of NAXOZOL compared to celecoxib in patients with osteoarthritis," *PLoS One*, vol. 15, no. 1, Article ID e0226184, 2020.

[18] H. Yuan, Q.-Y. Chang, J. Chen et al., "A retrospective analysis of the effects of different analgesics on the pain of patients with traumatic thoracolumbar fractures in the peri-treatment period," *Journal of Orthopaedic Surgery and Research*, vol. 16, no. 1, Article ID 268, 2021.

[19] M. Haffner, A. M. Saiz Jr., R. Nathe et al., "Preoperative multimodal analgesia decreases 24-hour postoperative narcotic consumption in elective spinal fusion patients," *The Spine Journal*, vol. 19, no. 11, pp. 1753–1763, 2019.

[20] P. R. Nielsen, L. D. Jørgensen, B. Dahl, T. Pedersen, and H. Tønnesen, "Prehabilitation and early rehabilitation after spinal surgery: randomized clinical trial," *Clinical Rehabilitation*, vol. 24, no. 2, pp. 137–148, 2010.

[21] N. Canbulat, M. Sasani, Y. Ataker et al., "A rehabilitation protocol for patients with lumbar degenerative disk disease treated with lumbar total disk replacement," *Archives of Physical Medicine and Rehabilitation*, vol. 92, no. 4, pp. 670–676, 2011.

[22] A. H. McGregor, C. J. Doré, T. P. Morris, S. Morris, and K. Jamrozik, "ISSLS prize winner," *Spine*, vol. 36, no. 21, pp. 1711–1720, 2011.

[23] O. Ilves, A. Häkkinen, J. Dekker et al., "Quality of life and disability: can they be improved by active postoperative rehabilitation after spinal fusion surgery in patients with spondylolisthesis? a randomised controlled trial with 12-month follow-up," *European Spine Journal*, vol. 26, no. 3, pp. 777–784, 2017.

Hindawi
Pain Research and Management
Volume 2021, Article ID 3573460, 9 pages
https://doi.org/10.1155/2021/3573460

Research Article

Enhanced Recovery after Surgery Protocol Accelerates Recovery of Lumbar Disc Herniation among Elderly Patients Undergoing Discectomy via Promoting Gastrointestinal Function

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Received 7 October 2021; Revised 31 October 2021; Accepted 5 November 2021; Published 22 November 2021

Academic Editor: Sidong Yang

This study aimed to analyze the effect of the enhanced recovery after surgery (ERAS) protocol on the recovery of gastrointestinal function in patients with lumbar disc herniation after discectomy. A total of 179 patients with lumbar disc herniation were randomly divided into the ERAS and non-ERAS groups. The non-ERAS group received routine nursing, and the ERAS group received ERAS strategy. The two groups were compared for general recovery indicators such as postoperative hemoglobin and prealbumin, satisfaction, and length of hospital stay. Gastrointestinal function was also evaluated, such as postoperative feeding time, intestinal chirping recovery time, intestinal exhaust gas recovery time, and complications such as ileus, nausea, and vomiting. The satisfaction of patients in the ERAS group (86.15 ± 2.43) was significantly higher than that in the non-ERAS group (77.19 ± 3.32), and the difference was statistically significant ($P < 0.05$). The average time of eating in the ERAS group was 2.27 h after surgery. In addition, the amount of eating in the ERAS group was significantly better than that in the non-ERAS group, and the difference was statistically significant. In the ERAS group, intestinal chirping recovery time recovered to normal time, and exhaust recovery time and average defecation time were significantly shorter than those in the non-ERAS group. In the ERAS group, the average amount of hemoglobin and prealbumin decreased 3 days after operation, which was significantly lower than that in the non-ERAS group. To sum up, ERAS has an evident effect on the recovery of gastrointestinal function after discectomy of disc herniation, which can promote the recovery of patients.

1. Introduction

Lumbar disc herniation in the elderly population may cause significant neural compression, leading to increased pain and poor quality of life of patients. Therefore, identifying effective interventions that could improve the quality of life of elderly patients with lumbar spinal disorders is important [1]. Discectomy has been recognized as a primary treatment of degenerative lumbar spine disorders; however, the surgical stress response, such as immunosuppression, increased catabolism, hypercoagulable states, and free radical production, is associated with major surgery [2]. These physiologic alterations are associated with organ function, which may result in undesirable postoperative complications, pain, and extended convalescence [3].

Postoperative paralytic ileus is a frequent complication after lumbar spinal surgery, with an incidence ranging between 2.6% and 12%, depending on the invasiveness of the complication and approach of the surgery [4]. It leads to increased postoperative morbidity, longer hospital stays, and increased medical costs. Several mechanisms are thought to play a role in postoperative ileus, including sympathetic

reflexes, effects of local and systemic inflammatory mediators, and changes of hormone transmitters. Numerous potential treatment options for postoperative ileus have been reported; however, their efficacy is usually limited [5]. In previous reports, lumbar spinal surgery in the aging population has increased [6]. Elderly patients are often complicated with chronic constipation [7]; thus, they may suffer from a higher risk of postoperative ileus after orthopedic surgery than younger patients [8, 9]. Therefore, finding effective measures to prevent postoperative paralytic ileus in the elderly after lumbar spinal surgery is of great significance. Many therapies, including early enteral nutrition, early removal of the nasogastric tube, gastrointestinal motility drugs, and physical therapy, have been suggested and applied in clinical work to prevent postoperative paralytic ileus [10, 11]. However, these therapies cannot be routinely or widely used because of either low compliance or limited clinical efficacy [12].

Enhanced recovery after surgery (ERAS) reduces the surgical stress response, minimizes postoperative complications, and increases readmission rates [2], which are important for vulnerable patients, who often suffer from comorbidities, and the elderly [13]. ERAS can also improve the gastrointestinal function of postoperative orthopedic patients, such as decreasing postoperative ileus, nausea, and vomiting, among which postoperative ileus is a common complication of discectomy and is estimated to occur in a considerable proportion of patients undergoing surgery [14]. Livingston and Passaro defined ileus as "the functional inhibition of propulsive bowel activity, irrespective of pathogenetic mechanism." [15] The pathogenesis of ileus is multifactorial with immobility, opioids, and anesthesia, which affect bowel function [16]. Studies have demonstrated that postoperative ileus can increase the length of hospital stay (LOS) and costs significantly [17]. This study aimed to evaluate the impact of ERAS on gastrointestinal function among elderly patients with spinal disorders undergoing surgery.

2. Methods

2.1. Inclusion and Exclusion Criteria. This is a retrospective cohort study. The study protocol was approved by the Ethics Committee for Human Subjects of the People's Hospital of Jiulongpo District. Written informed consent was obtained from each patient. Patient data were anonymized in this study. Altogether, 179 patients with lumbar disk herniation over the age of 65 who underwent posterior lumbar discectomy at two or lower levels from January 2019 to December 2020 were assigned to the non-ERAS group ($n = 95$) and the ERAS group ($n = 84$). Details of the enrolled patients could be found in Supplementary table. All the treatments were conducted by the same surgical team. Patients in the non-ERAS group were treated under traditional perioperative protocols. Diagnosis of lumbar disk herniation was conducted by at least two spinal orthopedic specialists based on MRI images of the lumbar spine and clinical symptoms, and the responsibility segments were identified. Patients who had typical spinal stenosis symptoms and did not respond to conservative treatments were indicated for surgery. Individuals who had neoplasm, cauda equina injury, trauma, and infectious disease were excluded from this study. All data were collected from the electronic medical record. Demographic data included gender, age, and body mass index (BMI). Comorbidities included hypertension, heart disease, diabetes, osteoporosis, stomach problem, bowel or intestinal problem, and psychological symptoms. Other indices included the American Society of Anesthesiologists (ASA) physical status score, preoperative Japanese Orthopaedic Association (JOA) Score, Oswestry Disability Index (ODI), and visual analogue scale (VAS) for the back and leg. Operative records used for analysis included the number of fusion levels, operative time, and intraoperative blood loss. The primary outcome data included complications, postoperative pain scores, LOS, and 30-day readmission rates.

2.2. ERAS Interventions. In this study, we followed the methods of Wang et al. [18]. The ERAS program was proposed and planned by a core group of anesthesiologists, nutritionists, spine surgeons, physicians, physical therapists, nurses, and geriatricians after literature review and experience exchange [19–21]. With the approval of the Ethical Committee for Human Subjects of the People's Hospital of the Jiulongpo District, the implementation of the ERAS program began in June 2019. ERAS interventions were divided into preoperative, intraoperative, and postoperative, including the following administration: (1) patient education and counseling, (2) antibiosis before surgery, (3) preoperative fasting (without drinks 2 h and food 4 h before surgery), (4) multimodal analgesia, (5) standard anesthetic protocol, (6) gastrointestinal management, (7) early feeding after surgery, (8) early mobilization medical, (9) early removal of the bladder catheter, and (10) antithrombotic prophylaxis. Details of ERAS are displayed in Figure 1.

2.3. Statistical Analysis. Statistical analyses were performed by GraphPad software (version 8.0). Student's t-test and χ^2 test were used to compare comorbidity data, patient demographics, clinical results, and baseline health indicators among the groups. We also used multivariate linear regression analysis and multivariable logistic regression to assess the association among the risk factors of ERAS elements and ileus rate. Differences were considered significant at a level of P value less than 0.05.

3. Results

3.1. Demographics. A total of 179 patients (Figure 2) were included, with 84 patients in the ERAS group (46 men and 38 women, mean age: 71.31 ± 9.17 years, mean BMI: 24.17 ± 2.96) and 95 patients in the non-ERAS group (51 men and 44 women, mean age: 71.63 ± 9.01 years, mean BMI: 24.75 ± 3.67). All surgeries were performed by a senior surgeon (Figure 3). Preoperative characteristics were similar between the two groups (Table 1). Demographic data were compared, and no statistically significant differences were

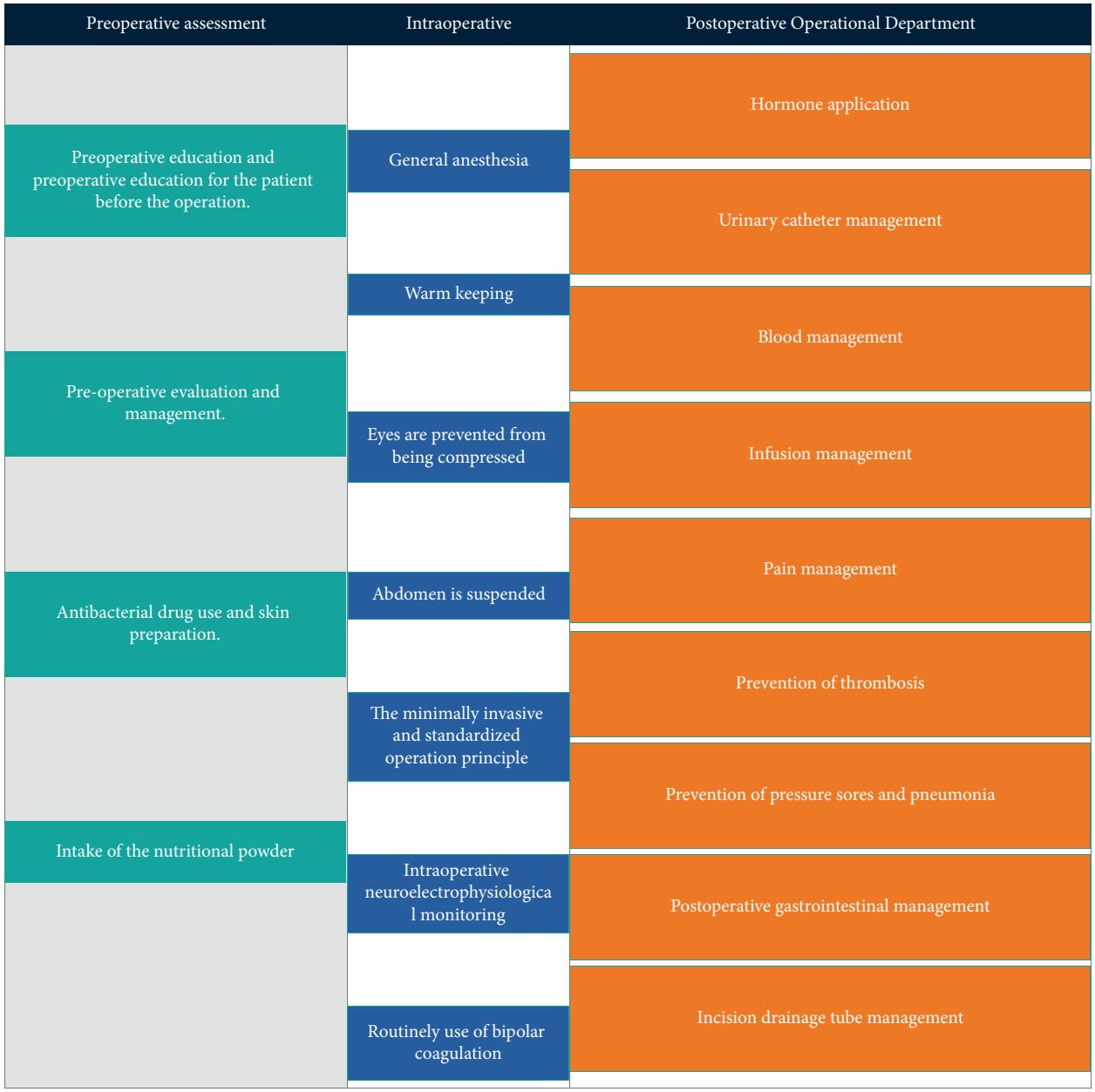

Figure 1: Summary of conducted perioperative topics for ERAS with discectomy.

observed between the two groups. In addition, no significant differences were noted in comorbidities, ASA grade, or the number of fusion levels between both groups. The mean operative time and intraoperative blood loss in the ERAS and non-ERAS groups showed no significant difference. Moreover, the mean preoperative JOA, VAS for the back and legs, and ODI score showed no significant difference (Table 1).

3.2. Compliance with the ERAS Protocol. Our ERAS protocol included 14 pathways, and the overall pathway compliance was 96.4% (Table 2). Patient education and counseling, no prolonged fasting, antimicrobial prophylaxis, and all intraoperative ERAS interventions were performed in all patients of the ERAS group. The pathway with the lowest compliance was early oral feeding (Table 2).

3.3. Outcomes. The main clinical outcomes are shown in Table 3. After the implementation of ERAS, no significant difference in 30-day readmission and mortality was found between the ERAS group and the non-ERAS group. Furthermore, the mean postoperative VAS for the back and legs showed no significant difference at 30-day follow-up as complete data were available for 83% of patients at this early time point. However, we observed a statistically significant decrease in LOS in the ERAS group (11.27 ± 4.07 days in the ERAS group versus 14.60 ± 2.13 days in the non-ERAS group, $P < 0.05$). The patient satisfaction rate of the ERAS

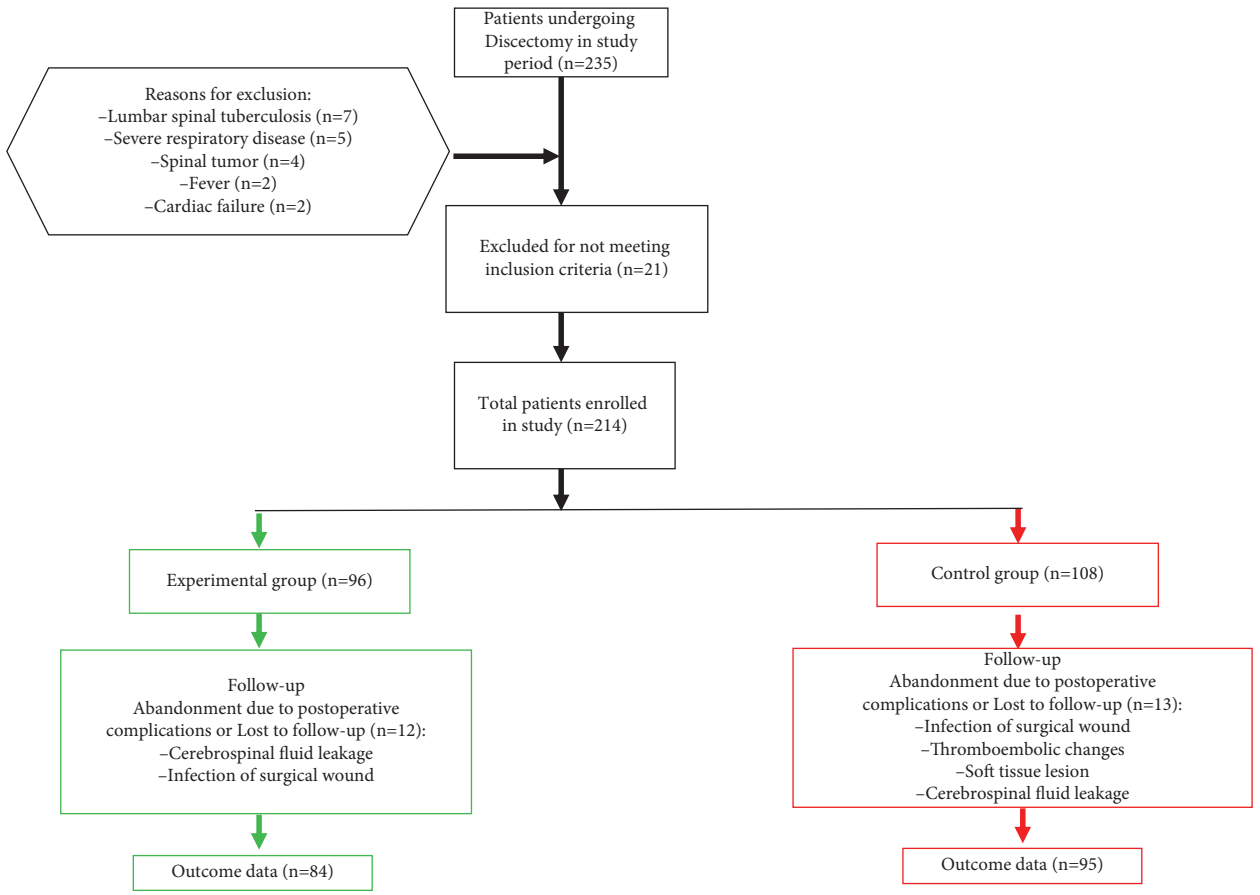

Figure 2: Flow of patients through the study.

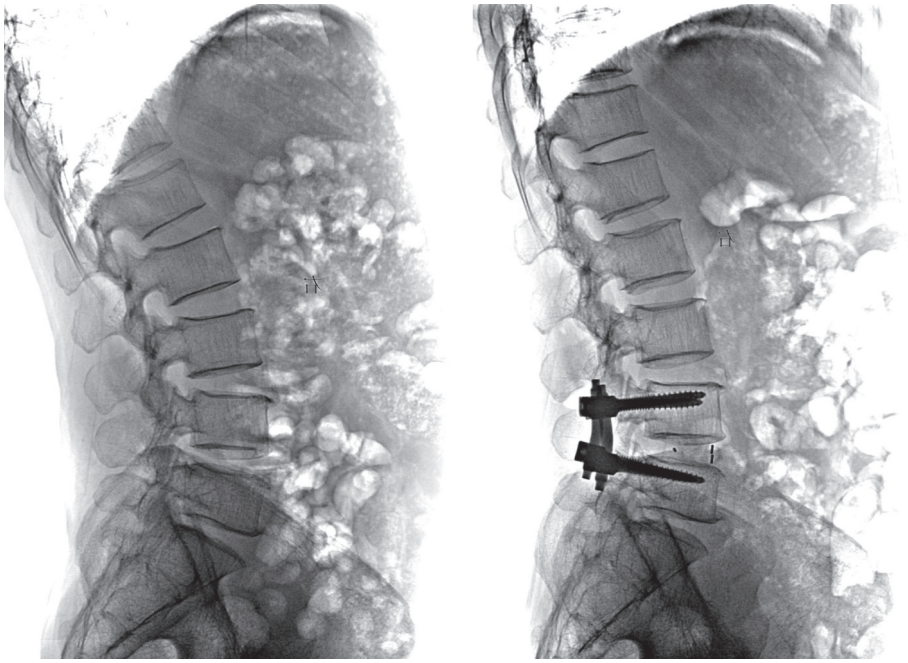

Figure 3: Representative case of a patient with an L4-5 LDH. Preoperative (a) and postoperative (b) radiographs were obtained by ERAS during the operation.

Table 1: Patient demographics.

Patient demographics	ERAS	Non-ERAS	P
Sample size	84	95	
Age (years)	71.31 ± 9.17	71.63 ± 9.01	0.50
Male/female	46/38	51/44	1
Body mass index	24.17 ± 2.96	24.75 ± 3.67	0.86
Smoker	6	7	1
Comorbidities			
Hypertension	53	49	0.13
Heart disease	17	15	0.56
Chronic lung disease	1	2	1
Diabetes	16	13	0.42
Osteoporosis	11	9	0.48
Gastrointestinal	6	7	1
Psychological symptoms	1	0	0.47
Preoperative JOA	7.30 ± 3.07	6.99 ± 2.97	0.49
Preoperative ODI, %	60.88 ± 8.31	61.63 ± 9.27	0.57
Preoperative VAS (back)	6.48 ± 1.21	6.75 ± 1.01	0.11
Preoperative VAS (leg)	6.19 ± 1.76	6.34 ± 1.88	0.58
ASA grade			
I	11	11	
II	60	60	
III	13	13	
IV	0	0	
No. of fusion levels			
1	62	67	0.74
2	22	28	0.74
Operative time (min)	163.88 ± 49.23	168.43 ± 51.62	0.55
Intraoperative blood loss (ml)	283.63 ± 169.64	243.63 ± 188.64	0.14

Table 2: ERAS pathway compliance.

Compliance with the ERAS program	
Variable	n (%)
Preoperative ERAS items	
Patient education and counseling	84 (100)
No prolonged fasting	84 (100)
Fluid and carbohydrate loading	84 (100)
Antithrombotic stockings	84 (100)
Antimicrobial prophylaxis	84 (100)
Intraoperative ERAS items	
Tranexamic acid	84 (100)
Maintenance of normothermia	84 (100)
Local infiltration analgesia	84 (100)
Fluid balance	84 (100)
Postoperative ERAS items	
Early ambulation	77 (91.7)
Early removal of the bladder catheter	67 (79.8)
Early oral feeding	63 (75)
Chewing gum	80 (95.2)
Intermittent pneumatic compression	82 (97.6)
Overall compliance (rate)	81 (96.4)

group was 92.00%, and the difference was statistically significant ($P < 0.05$). In the ERAS group, the average time of eating was 2.27 h after surgery, and patients consumed much more food than those of the non-ERAS group. Moreover, the time for bowel sounds to return to normal (3–5 times/min) was 5.63 h; the recovery time of exhaust gas was 8.14 ± 6.52 h, and the average time of defecation was 1.02 days, which were both significantly less than those of the non-ERAS group. The rate of nausea, vomiting, and flatulence complications in the ERAS group was 2.39%, which was less than that of the non-ERAS group, but the difference was not significant. The average amount of hemoglobin in the ERAS group 3 days after operation was 8.14 g, and the average decreased amount of prealbumin was 5.28 g, with statistical significance ($P < 0.05$).

Multivariable linear regression showed that comorbidities ($P = 0.021$), dose of sufentanil ($P = 0.042$), operative time ($P = 0.041$), and implementation of the ERAS program ($P = 0.036$) were significantly correlated with postoperative ileus. On the contrary, age, gender, BMI, smoking history, ASA ≥3, fusion number, blood loss, preoperative VAS for the back, and preoperative VAS for the leg were not related to postoperative ileus. Multivariable logistic regression showed that no characteristics were associated with postoperative ileus (Table 4).

4. Discussion

Disk herniation and the loss of disk height are largely associated with aging, which places extra loads on adjacent segments and facet joints, leading to low back pain (LBP). LBP and sciatica can significantly impair patients' psychosocial function, leading to depressive symptoms and sleep disorders. Furthermore, LBP and sciatica are correlated with coronary heart disease in elderly people [22]. However, comorbidities and poor physical function can cause high rates of perioperative complications, such as inpatient morbidity, during lumbar spinal surgery in elderly patients [23, 24]. It is reported that thoracic epidural anesthetics can reduce the duration of postoperative ileus by blocking the nerve reflex of the spinal cord and reducing the use of postoperative anesthesia in patients. Nonsteroidal anti-inflammatory drugs can also accelerate the recovery of intestinal function by inhibiting intestinal inflammation and reducing the use of opioids. Thus, a multimodal treatment approach that combines multiple therapies may be a logical approach [9]. As proposed by Henrik Kehle, a Danish surgeon, ERAS is a multidisciplinary and multiprofessional approach for postoperative patients to obtain a relatively rapid recovery [25]. To date, the basic principles of ERAS have been adopted by surgical specialties in multiple fields [26, 27]. This protocol has been shown to be beneficial particularly for elderly people who have comorbidities or a higher risk of surgical complications. The ERAS protocol is specifically designed for patients in adapting to surgical stresses such as immobility, dehydration, and inflammation by all-encompassing approaches, which focuses on various aspects of perioperative care, including changes in mobilization, fasting, early postoperative oral intake, goal-directed fluids, and multimodal analgesia [28, 29]. In our study, the ileus rate in the cohort of patients in the ERAS group was significantly decreased. In addition, the patients in the ERAS group had a shorter hospital stay and decreased readmission rate.

Shortening the time of fasting and feeding is an important preoperative aspect in our ERAS program [30].

Table 3: Postoperative outcomes.

Outcome measure	ERAS	Non-ERAS	P
LOS***	11.27 ± 4.07	14.60 ± 2.13	0
30-day readmission	1	2	0.47
30-day mortality	0	0	1
Decreased amount of hemoglobin (g/L)***	8.14 ± 2.06	12.37 ± 2.21	0
Decreased amount of prealbumin (g)***	5.28 ± 1.07	8.32 ± 1.40	0
Postoperative time (days)***	6.14 ± 1.24	8.14 ± 2.38	0
Satisfaction***	86.15 ± 2.43	77.19 ± 3.32	0
Preoperative VAS (back)	7.09 ± 0.83	7.04 ± 0.67	0.66
Preoperative VAS (legs)	7.32 ± 0.72	7.44 ± 0.23	0.13
Gastrointestinal indicators			
Ileus rate***	5.89	31.89	0
Postoperative feeding time (h)***	2.27 ± 1.50	4.14 ± 3.92	0
Food intake (h)***	5.58 ± 2.57	3.52 ± 2.43	0
Borborygmus recovery time (h)***	5.63 ± 2.54	6.02 ± 3.51	0.04
Intestinal exhaust gas recovery time (h)	8.14 ± 6.52	10.21 ± 7.16	0.05
Postoperative defecation time (d)***	1.02 ± 1.28	2.31 ± 2.10	0
Postoperative nausea and vomiting	2.39	9.53	0.06
General complications			
Cerebrovascular accident	0	1	1
Surgical site infection	1	3	0.62
Spinal fluid leakage	2	3	1
Neurological	1	2	1
Deep vein thrombosis	0	1	1
Cardiac arrest	0	0	1

*P value less than 0.05; **P value less than 0.01; ***P value less than 0.001.

Table 4: Multivariable analyses for LOS and complications.

Characteristics	Multivariable linear regression for LOS		Multivariable logistic regression for any complications	
	Coefficient (95% CI)	P value	OR (95% CI)	P value
Age	0.25 (−0.12 to 0.27)	0.35	1.09 (0.87–1.28)	0.49
Female	1.12 (−0.47 to 1.22)	0.10	1.09 (0.93–1.17)	0.24
BMI	−0.023 (−0.33 to 0.11)	0.74	0.94 (0.89–1.02)	0.07
Smoker	0.78 (−0.19 to 1.20)	0.15	2.21 (0.84–3.12)	0.14
Comorbidities	1.24 (0.23 to 1.63)	0.02	1.46 (0.87–2.21)	0.06
Fusion number	2.21 (−1.19 to 2.97)	0.18	1.99 (0.98–2.38)	0.11
Estimated blood loss	1.21 (−1.96 to 3.75)	0.07	1.74 (0.35–2.06)	0.88
Intraoperative fluids	0.78 (0.01 to 1.17)	0.65	2.11 (0.85–2.21)	0.10
Dose of sufentanil*	0.98 (0.53 to 1.71)	0.04	1.62 (0.99–1.72)	0.05
Operative time*	0.41 (−0.02 to 0.91)	0.04	0.93 (0.87–3.26)	0.13
ERAS*	0.94 (0.73 to 1.13)	0.04	1.23 (0.79–1.88)	0.06
Preoperative VAS (back)	0.29 (−0.56 to 0.98)	0.36	0.71 (0.65–1.46)	0.22
Preoperative VAS (leg)	0.75 (−0.60 to 2.11)	0.75	1.22 (0.91–2.13)	0.34
Preoperative ODI (%)	−0.01 (−0.08 to 0.21)	0.38	1.26 (0.64–2.48)	0.31

*P value less than 0.05; **P value less than 0.01; ***P value less than 0.001.

Traditional preoperative fasting time lasting for at least 8 h and oral feeding on postoperative day 1 may cause metabolic stress and insulin resistance caused by inflammatory cytokine release and lipid product accumulation in skeletal muscles and then increase the rate of postoperative complications [31–33]. Therefore, shortening the time of preoperative fasting and postoperative eating can decrease insulin resistance and improve patient comfort [34]. However, research concerning the shortening of postoperative eating time and preoperative fasting time among elderly patients with lumbar surgery is lacking, although studies have indicated that this approach is effective and safe [35]. Our studies have illustrated that oral carbohydrate drink 1.5 h before anesthesia induction and early feeding 5 h after surgery are safe and are not associated with the increasing risk of complications in elderly patients.

At present, the treatment for postoperative ileus is primarily divided into four parts: perioperative prevention, traditional treatment, drug intervention, and surgical treatment [36]. Traditional treatments, including nasogastric decompression, electrolyte replacement, and early bed movement, have poor patient compliance and efficacy [37].

Pharmacological interventions are commonly applied for the prevention of ileus after abdominal surgery, such as motility agents and antiemetics, μ-receptor antagonists, and neostigmine; however, efficacy of these interventions is also unsatisfactory [38, 39]. Surgical treatment is only suitable for severe complications caused by intestinal obstruction, such as ischemia or bowel perforation. Therefore, postoperative prevention is crucial in the management of postoperative ileus.

ERAS protocol decreases postoperative ileus rate through multiple mechanisms. Preoperatively, patients are allowed to drink clear fluids prior to surgery up to 2 h in this protocol, which prevents prior-surgery dehydration and allows the intake of preoperative carbohydrate. As reported by Varadhan and Lobo, fluid overload is related to increased bowel edema rates, which leads to ileus [31]. However, maintaining adequate tissue perfusion and intravascular volume is necessary [40]. Thus, fluid administration protocol ERAS aims to maintain intravascular volume and mitigate risks. In our cohort, a significant decrease of intraoperative intravenous fluid (IVF) administration was found in ERAS patients compared with controls. Moreover, the standard hourly volume of IVFs in ERAS patients was decreased drastically. Intraoperatively, we have discovered that the use of sufentanil is associated with the increasing rates of ileus [35]. Sufentanil is known for its inhibitory effects on peristalsis of the gastrointestinal smooth muscle and intestinal motility in rats. In addition, narcotics could activate μ-opioid receptors and cause gut motility inhibition, leading to increased ileus rates. Thus, decreasing the use of narcotics plays a vital role in reducing ileus rates. As shown in considerable research, chewing gum is an efficient way to reduce postoperative ileus in the postoperative stage [32]. In our study, the patients in the ERAS group were allowed to chew gums after surgery, which is considered a crucial factor for the significantly decreased rate of ileus in ERAS patients. In the ERAS regimen, chewing gum is a form of sham feeding that can stimulate human intestinal motility [41]. Several possible physiological mechanisms are identified: first, chewing gum stimulates the oropharyngeal chemical mechanoreceptors, activates the cephalovagal pathway, and increases the secretion of gastrointestinal hormones such as motilin, gastric acid, gastrin, and pepsinogen, thus promoting gastrointestinal motility [42, 43]. Second, mastication can stimulate the vagus pathway and increase the release of acetylcholine transmitters, which then bind to nicotine receptors of inflammatory cells, thereby reducing the release of proinflammatory factors and promoting the recovery of gastrointestinal motility [44].

Our results suggest that the ERAS regimen promotes recovery of intestinal function after lumbar surgery in elderly patients, with a significantly accelerated time of first flatus and first defecation. Compared with abdominal surgery, patients in both groups showed significantly better bowel movement. These findings can be explained as follows: first, the operative time of lumbar fusion is relatively short (less than 3 h). Second, the intestinal tract is almost uninterfered during posterior lumbar surgery.

5. Conclusions

This study shows the potential application of a practical ERAS protocol in elderly patients after discectomy, which has been proven to decrease LOS and postoperative ileus rate in elderly patients. Further studies with modified approaches are required to improve adherence to the outcomes.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Disclosure

Xiaohai Zuo and Linbang Wang are the co-first authors.

Conflicts of Interest

The authors declare no conflicts of interest.

Authors' Contributions

Xiaohai Zuo and Linbang Wang contributed equally to this study.

Supplementary Materials

Supplementary table: the detailed data of the enrolled patients. (*Supplementary Materials*)

References

[1] J. A. Rihn, A. S. Hilibrand, W. Zhao et al., "Effectiveness of surgery for lumbar stenosis and degenerative spondylolisthesis in the octogenarian population," *Journal of Bone and Joint Surgery American Volume*, vol. 97, no. 3, pp. 177–185, 2015.

[2] N. Dietz, M. Sharma, S. Adams et al., "Enhanced recovery after surgery (ERAS) for spine surgery: a systematic review," *World Neurosurgery*, vol. 130, pp. 415–426, 2019.

[3] J. Gerhardt, S. Bette, I. Janssen, J. Gempt, B. Meyer, and Y.-M. Ryang, "Is eighty the new sixty? Outcomes and complications after lumbar decompression surgery in elderly patients over 80 Years of age," *World Neurosurgery*, vol. 112, pp. e555–e560, 2018.

[4] S. J. Fineberg, S. V. Nandyala, M. F. Kurd et al., "Incidence and risk factors for postoperative ileus following anterior, posterior, and circumferential lumbar fusion," *The Spine Journal*, vol. 14, no. 8, pp. 1680–1685, 2014.

[5] S. C. Park, S. Y. Chang, S. Mok, H. Kim, B.-S. Chang, and C.-K. Lee, "Risk factors for postoperative ileus after oblique lateral interbody fusion: a multivariate analysis," *The Spine Journal*, vol. 21, no. 3, pp. 438–445, 2021.

[6] Y. Li, S. Zheng, Y. Wu et al., "Trends of surgical treatment for spinal degenerative disease in China: a cohort of 37,897 inpatients from 2003 to 2016," *Clinical Interventions in Aging*, vol. 14, pp. 361–366, 2019.

[7] M. Vazquez Roque and E. P. Bouras, "Epidemiology and management of chronic constipation in elderly patients," *Clinical Interventions in Aging*, vol. 10, pp. 919–930, 2015.

[8] T. H. Lee, J. S. Lee, S. J. Hong et al., "Risk factors for postoperative ileus following orthopedic surgery: the role of

chronic constipation," *Journal of Neurogastroenterology and Motility*, vol. 21, no. 1, pp. 121–125, 2015.

[9] B. Behm and N. Stollman, "Postoperative ileus: etiologies and interventions," *Clinical Gastroenterology and Hepatology*, vol. 1, no. 2, pp. 71–80, 2003.

[10] Y. Toyomasu, E. Mochiki, H. Morita et al., "Mosapride citrate improves postoperative ileus of patients with colectomy," *Journal of Gastrointestinal Surgery*, vol. 15, no. 8, pp. 1361–1367, 2011.

[11] S. S. M. Ng, W. W. Leung, T. W. C. Mak et al., "Electro-acupuncture reduces duration of postoperative ileus after laparoscopic surgery for colorectal cancer," *Gastroenterology*, vol. 144, no. 2, pp. 307–313, 2013.

[12] T. J. Saclarides, "Current choices--good or bad--for the proactive management of postoperative ileus: a surgeon's view," *Journal of Perianesthesia Nursing: Official Journal of the American Society of PeriAnesthesia Nurses*, vol. 21, no. 2A Suppl, pp. S7–S15, 2006.

[13] O. Ljungqvist and M. Hubner, "Enhanced recovery after surgery-ERAS-principles, practice and feasibility in the elderly," *Aging Clinical and Experimental Research*, vol. 30, no. 3, pp. 249–252, 2018.

[14] J. N. Bakkum-Gamez, C. L. Langstraat, J. R. Martin et al., "Incidence of and risk factors for postoperative ileus in women undergoing primary staging and debulking for epithelial ovarian carcinoma," *Gynecologic Oncology*, vol. 125, no. 3, pp. 614–620, 2012.

[15] R. Vather, G. O'Grady, I. P. Bissett, and P. G. Dinning, "Postoperative ileus: mechanisms and future directions for research," *Clinical and Experimental Pharmacology and Physiology*, vol. 41, no. 5, pp. 358–370, 2014.

[16] E. H. Livingston and E. P. Passaro Jr., "Postoperative ileus," *Digestive Diseases and Sciences*, vol. 35, no. 1, pp. 121–132, 1990.

[17] S. Iyer, W. B. Saunders, and S. Stemkowski, "Economic burden of postoperative ileus associated with colectomy in the United States," *Journal of Managed Care Pharmacy*, vol. 15, no. 6, pp. 485–494, 2009.

[18] P. Wang, Q. Wang, C. Kong et al., "Enhanced recovery after surgery (ERAS) program for elderly patients with short-level lumbar fusion," *Journal of Orthopaedic Surgery and Research*, vol. 15, no. 1, p. 299, 2020.

[19] S. The Group of minimally invasive spinal, S. Enhanced recovery professional committee of orthopedic, and T. Enhanced recovery association of China rehabilitation technology and promotion, "Expert consensus on the implementation of enhanced recovery after surgery in percutaneous endoscopic interlaminar lumbar decompression/discectomy," *Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi*, vol. 34, no. 12, pp. 1497–1506, 2020.

[20] M. Y. Wang, P. Y. Chang, and J. Grossman, "Development of an Enhanced Recovery after Surgery (ERAS) approach for lumbar spinal fusion," *Journal of Neurosurgery: Spine*, vol. 26, no. 4, pp. 411–418, 2017.

[21] T. W. Wainwright, T. Immins, and R. G. Middleton, "Enhanced recovery after surgery (ERAS) and its applicability for major spine surgery," *Best Practice & Research Clinical Anaesthesiology*, vol. 30, no. 1, pp. 91–102, 2016.

[22] J. M. Cloyd, F. L. Acosta Jr., and C. P. Ames, "Complications and outcomes of lumbar spine surgery in elderly people: a review of the literature," *Journal of the American Geriatrics Society*, vol. 56, no. 7, pp. 1318–1327, 2008.

[23] D. Drazin, L. Al-Khouja, C. Lagman et al., "Scoliosis surgery in the elderly: complications, readmissions, reoperations and mortality," *Journal of Clinical Neuroscience*, vol. 34, pp. 158–161, 2016.

[24] N. Worley, B. Marascalchi, C. M. Jalai et al., "Predictors of inpatient morbidity and mortality in adult spinal deformity surgery," *European Spine Journal*, vol. 25, no. 3, pp. 819–827, 2016.

[25] L. Bardram, P. Funch-Jensen, P. Jensen, M. E. Crawford, and H. Kehlet, "Recovery after laparoscopic colonic surgery with epidural analgesia, and early oral nutrition and mobilisation," *The Lancet*, vol. 345, no. 8952, pp. 763-764, 1995.

[26] D. S. Keil, L. D. Schiff, E. T. Carey et al., "Predictors of admission after the implementation of an enhanced recovery after surgery pathway for minimally invasive gynecologic surgery," *Anesthesia & Analgesia*, vol. 129, no. 3, pp. 776–783, 2019.

[27] M. J. Stein, S. G. Frank, A. Lui, T. Zhang, and J. Zhang, "Ambulatory latissimus dorsi flap breast reconstruction: a prospective cohort study of an enhanced recovery after surgery (ERAS) protocol," *Journal of Plastic, Reconstructive & Aesthetic Surgery*, vol. 72, no. 12, pp. 1950–1955, 2019.

[28] J. P. Desborough, "The stress response to trauma and surgery," *British Journal of Anaesthesia*, vol. 85, no. 1, pp. 109–117, 2000.

[29] U. O. Gustafsson, M. J. Scott, M. Hubner et al., "Guidelines for perioperative care in elective colorectal surgery: enhanced recovery after surgery (ERAS) society recommendations: 2018," *World Journal of Surgery*, vol. 43, no. 3, pp. 659–695, 2019.

[30] B. Debono, M. V. Corniola, R. Pietton, P. Sabatier, O. Hamel, and E. Tessitore, "Benefits of Enhanced Recovery after Surgery for fusion in degenerative spine surgery: impact on outcome, length of stay, and patient satisfaction," *Neurosurgical Focus*, vol. 46, no. 4, p. E6, 2019.

[31] K. K. Varadhan and D. N. Lobo, "A meta-analysis of randomised controlled trials of intravenous fluid therapy in major elective open abdominal surgery: getting the balance right," *Proceedings of the Nutrition Society*, vol. 69, no. 4, pp. 488–498, 2010.

[32] I. E. Ertas, K. Gungorduk, A. Ozdemir, U. Solmaz, A. Dogan, and Y. Yildirim, "Influence of gum chewing on postoperative bowel activity after complete staging surgery for gynecological malignancies: a randomized controlled trial," *Gynecologic Oncology*, vol. 131, no. 1, pp. 118–122, 2013.

[33] Z. Hamilton, W. Parker, J. Griffin et al., "Alvimopan in an enhanced recovery program following radical cystectomy," *Bladder Cancer*, vol. 1, no. 2, pp. 137–142, 2015.

[34] B. G. Wolff, J. L. Weese, K. A. Ludwig et al., "Postoperative ileus-related morbidity profile in patients treated with alvimopan after bowel resection," *Journal of the American College of Surgeons*, vol. 204, no. 4, pp. 609–616, 2007.

[35] A. Kurz and D. I. Sessler, "Opioid-induced bowel dysfunction," *Drugs*, vol. 63, no. 7, pp. 649–671, 2003.

[36] M. Thompson and B. Magnuson, "Management of postoperative ileus," *Orthopedics*, vol. 35, no. 3, pp. 213–217, 2012.

[37] A. Jain and H. D. Vargas, "Advances and challenges in the management of acute colonic pseudo-obstruction (ogilvie syndrome)," *Clinics in Colon and Rectal Surgery*, vol. 25, no. 1, pp. 37–45, 2012.

[38] M. D. Kraft, "Emerging pharmacologic options for treating postoperative ileus," *American Journal of Health-System Pharmacy: AJHP: official journal of the American Society of Health-System Pharmacists*, vol. 64, no. 20 Suppl, pp. S13–S20, 2007.

[39] C. H. Oh, G. Y. Ji, S. H. Yoon, D. Hyun, H.-c. Park, and Y. J. Kim, "Paralytic ileus and prophylactic gastrointestinal

motility medication after spinal operation," *Yonsei Medical Journal*, vol. 56, no. 6, pp. 1627–1631, 2015.

[40] M. J. Scott, G. Baldini, K. C. H. Fearon et al., "Enhanced Recovery after Surgery (ERAS) for gastrointestinal surgery, part 1: pathophysiological considerations," *Acta Anaesthesiologica Scandinavica*, vol. 59, no. 10, pp. 1212–1231, 2015.

[41] Y. M. Ho, S. R. Smith, P. Pockney, P. Lim, and J. Attia, "A meta-analysis on the effect of sham feeding following colectomy," *Diseases of the Colon & Rectum*, vol. 57, no. 1, pp. 115–126, 2014.

[42] R. M. Stern, H. E. Crawford, W. R. Stewart, M. W. Vasey, and K. L. Koch, "Sham feeding," *Digestive Diseases and Sciences*, vol. 34, no. 4, pp. 521–527, 1989.

[43] J. A. Lunding, L. M. nordström, a.-o. Haukelid, O. H. Gilja, A. Berstad, and T. Hausken, "Vagal activation by sham feeding improves gastric motility in functional dyspepsia," *Neuro-Gastroenterology and Motility*, vol. 20, no. 6, pp. 618–624, 2008.

[44] I. Mennella, R. Ferracane, F. Zucco, V. Fogliano, and P. Vitaglione, "Food liking enhances the plasma response of 2-arachidonoylglycerol and of pancreatic polypeptide upon modified sham feeding in humans," *Journal of Nutrition*, vol. 145, no. 9, pp. 2169–2175, 2015.

Hindawi
Pain Research and Management
Volume 2021, Article ID 6880956, 11 pages
https://doi.org/10.1155/2021/6880956

Research Article

A Novel Capsule Lumbar Interbody Fusion (CLIF) in Treating Foot Drop due to Lumbar Degenerative Diseases: a Prospective, Observational Study

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Received 9 September 2021; Accepted 28 October 2021; Published 12 November 2021

Academic Editor: Sidong Yang

Objective. This present study aimed to explore the clinical effects of a novel capsule lumbar interbody fusion (CLIF) on foot drop due to lumbar degenerative diseases. *Methods*. Between June 2018 and January 2019, a total of 27 patients admitted to our department with lumbar degenerative diseases with associated foot drop were prospectively enrolled. Given the selection of surgical technique, patients were divided into traditional TLIF group and CLIF group. We assessed patients' neurological status using JOA and VAS score, tibialis anterior muscle strength using MMT score, diameter and hemodynamic parameters of the L5 nerve root using intraoperative ultrasonography (IoUS), and related radiological parameters of the lumbar spine. Operation time, blood loss, and surgery-associated complications were also recorded. *Results*. The median duration of follow-up was 150 (6–1460) months. At the final follow-up, all patients acquired satisfactory improvement of neurological function. However, patients in the CLIF group showed better early recovery of foot drop three months after operation than those in the TLIF group, with 75% excellent rate. In addition, IoUS suggested that the diameter and hemodynamic parameters of the L5 nerve root were improved better in the CLIF group, which may suggest the correlation between the recovery of foot drop and the status of L5 nerve root. No severe complications were encountered with CLIF. *Conclusions*. Our preliminary study revealed that the axial tension of L5 nerve root may be involved in the pathological mechanism of foot drop. The novel technique of CLIF can shorten the lumbar spine and can be effective and safe for the treatment of foot drop due to lumbar degeneration-related diseases.

1. Introduction

Foot drop has typically been denoted as a condition with paralyzed or weak tibialis anterior (TA) muscles and even dysfunctional motor function. Patients with foot drop frequently experience stumble or even fall during walking [1]. In fact, foot drop resulting from spinal diseases is not rare in spine-related clinical practice [2]. However, among the massive spinal causes for foot drop, lumbar degenerative diseases (LDD) are the most common [3]. In addition, those patients frequently exhibit lumbar disc herniation (LDH) and lumbar spinal stenosis (LSS), with the L4/5 spinal level being the most affected [4].

LDD-mediated foot drop is an entity significantly different from that of peripheral neuropathy. Although previous studies have described the manifestations of foot drop and its clinical treatments, the clinical recovery of foot drop caused by LDD remains unsatisfactory [5]. Previous studies focused too much on the effects of factors such as duration of palsy and preoperative TA muscle strength on the recovery of foot drop [4–6]. However, disputation still exists. Our previous study found that impairment caused by axial traction of the lumbar nerve root may be another major contributor to symptoms including pain, numbness, and weakness of low extremities in patients with LDD and recommended that the decompression of the lumbar spine should not only include the management of the surrounding compression (herniated disc or narrow intervertebral foramina) of the neural elements but also include the release of the axial tension of the nerve root [7, 8]. However, whether

the release of the lumbar nerve root is effective to the recovery of foot drop remains unknown.

Hence, in this present study, the technique of CLIF was designed to reduce of the axial tension of the neural elements in the lumbar spine, which essentially means rod compression before inserting the interbody fusion cage combined with spine shortening. This present study aimed to investigate the effects of CLIF on the recovery of foot drop caused by LDD.

2. Methods and Materials

2.1. Patients' Population. We conducted a single-centered, prospective, observational study with patients who had LDD, associated with foot drop, from June 2018 to January 2019 in the Spine Center of Changzheng Hospital, Shanghai, China. All the enrolled patients had complete medical records, including X-ray and magnetic resonance imaging (MRI).

All patients were indicated for surgery due to severe LSS with/without LDH. Patients would be excluded if they had concomitant other diseases causing foot drop such as tumor [9], trauma [2], disc herniation at cervical or thoracic spine [2, 10], or inflammation-related diseases such as multiple sclerosis [11]; if they had peripheral neuropathy (peroneal neuropathy) due to external compression, nerve entrapment, iatrogenic factors, weight loss, and diabetes [12, 13]; if they had previous spine surgery; or if they had incomplete medical data during the follow-up. In addition, considering the major contribution of L5 nerve to foot drop, all patients enrolled in this study had surgery levels including L4/5 level.

This study was performed in accordance with the principles of the Declaration of Helsinki and was also approved by the Ethics Committee of our hospital.

2.2. Selection of Surgical Technique. We designed a prospective, observational study enrolling patients with diagnosis of foot drop due to lumbar degenerative diseases. The study period was determined from June 2018 to January 2019. All the patients with foot drop resulting from LDD referred to our clinic during this period would be recruited, and a total of 27 patients were finally enrolled. All patients enrolled would be informed of the benefits and potential risks of these two techniques before operation and came to a consensus to participate in this study. Subsequently, patients would be divided into TLIF group and CLIF group based on the patients' acceptance and doctors' experience. The duration of follow-up lasts for at least 12 months.

2.3. Surgical Technique. The TLIF surgery has been described in detail in previous studies [14, 15]. Here, we presented a case who required lumbar surgery at L4/5 level to illustrate the procedure of CLIF. Briefly, under general endotracheal anesthesia, the patient was placed in a prone position. Firstly, the surgical segments would be confirmed (Figure 1(a)). Subsequently, the pedicle screws were inserted bilaterally in L4-L5 segments. Intraoperative fluoroscopy was used to confirm the good position of screws. Next, the interspinous ligaments between L4 and L5 were resected, with the preservation of the spinous process for later spine compression. The necessary facetectomy on the symptomatic side was performed to achieve adequate decompression of the stenosis, and the superior articular process in the lower vertebra and the inferior articular process in the upper vertebra on both sides were resected with the pedicle preserved to achieve the decompression of the ipsilateral dural sac and nerve roots and intraoperative ultrasound examination. In addition, the contralateral facet joint was managed according to this procedure. Then, the ligamentum flavum was removed bilaterally.

However, different from traditional TLIF, the fixation and tightening of the rods (Figures 1(b) and 1(c)) were performed prior to the placement of the cage followed by necessary discectomy and removal of the cartilage endplate (Figure 1(d)). Notably, slow compression to the operated segment was also performed prior to the insertion of the cage but after the fixation of the rods (Figure 1(e)). Then, a nerve probe was used to evaluate the tension of the nerve root followed by the insertion of the cage (Figure 1(f)). With regard to cage size, a test module would be used prior to cage being implanted into the L4/5 intervertebral space. The surgeon must make sure that the spinous process gap and intervertebral space were appropriately shortened, and the nerve root was loosened. The whole concept of CLIF is illustrated in Figure 1 (Figures 1(g)–1(i)). An intraoperative ultrasound was used to evaluate the condition of the nerve root before and after spine shortening. Patients were suggested to wear a waist support for 12 weeks after surgery.

2.4. Clinical and Radiological Examination. The neurological function of patients was assessed using the Japanese Orthopaedic Association (JOA) score, and the pain symptoms were assessed by the visual analogue scale (VAS score). Other parameters including operation duration time, intraoperative blood loss, and surgery-associated complications were also recorded.

All patients accepted X-rays, MRI, and/or CT before operation. Considering the surgical levels of all patients with foot drop in this study involved L4/5, we chose the height of intervertebral space (HIS), foraminal height (FH), foraminal area (FA), and segmental lordosis (SL) at the level as the research parameters (Figure 2) [8].

The HIS was defined as the distance between the midpoints of cephalic and caudal endplate of the intervertebral space, which was used to evaluate the effect of spine shortening [16]. FH denoted the maximum distance between the lower margin of the superior pedicle and upper margin of the inferior pedicle [8]. FA was determined as illustrated in Figure 2. These two parameters were used to evaluate the potential compression of spine shortening on the nerve root at intervertebral foramina. SL was defined as the angle between the lines parallel to the inferior endplate and the superior endplate of the index disc, which was used to assess the lumbar alignment [8].

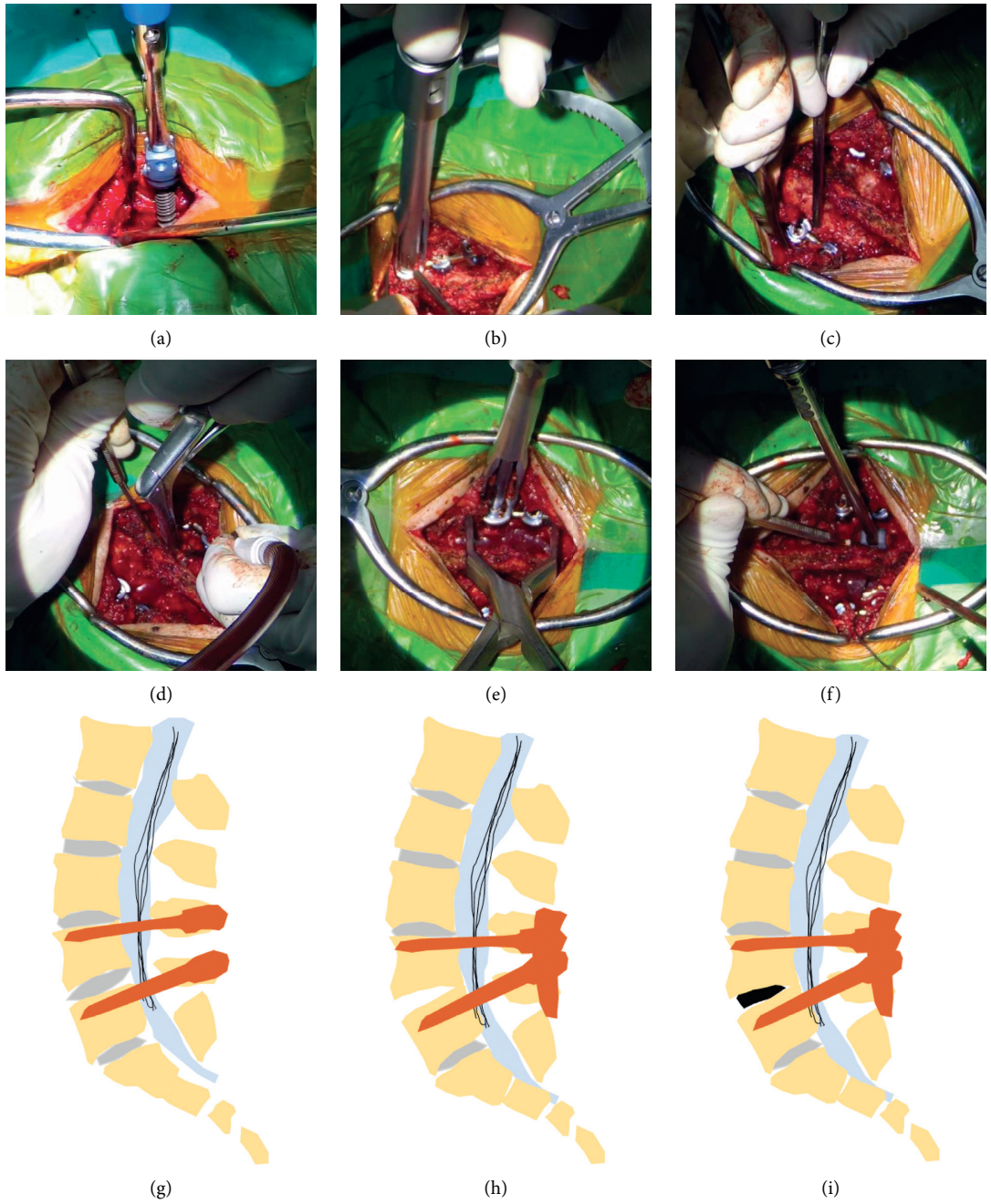


Figure 1: Representative intraoperative images of CLIF: (a) position of surgical segment; (b) insertion of ipsilateral pedicle screws and rods; (c) insertion of contralateral pedicle screws and rods; (d) removal of the disc tissue and partial cartilage endplate; (e) slow axial compression of the operated segment; (f) insertion of the intervertebral cage; (g) insertion of the pedicle screws; (h) installation of the rods prior to the placement of cages; and (i) axial compression of the segment after insertion of the cage. CLIF: transforaminal lumbar interbody fusion with spine shortening.

2.5. Evaluation of Nerve Root Using Intraoperative Ultrasonography (IoUS). IoUS has been previously used in spine surgery, including disc herniations, spinal stenosis, and pedicle screw instrumentation, due to its clear definition of normal structures and pathologic lesions [17, 18]. As reported previously, when the nerve root was pulled axially, the diameter and blood flow volume would decrease [19]. Therefore, IoUS was firstly used to evaluate the effect of CLIF with spine shortening on the axial tension of neural elements via changes of the diameter and blood flow volume of the L5 nerve root in this present study.

Figure 3 shows the details of IoUS measurement before and after shortening. Briefly, IoUS was performed using a water-path imaging technique to investigate the hemodynamic parameters of the L5 nerve root using a digital echo camera (APL10 300 TUS-A300, Prosound a10; TOSHIBA Medical Co., Tokyo, Japan) after resection of the spinous process, lamina, and ligamentum flavum and a 3.5–11 MHz

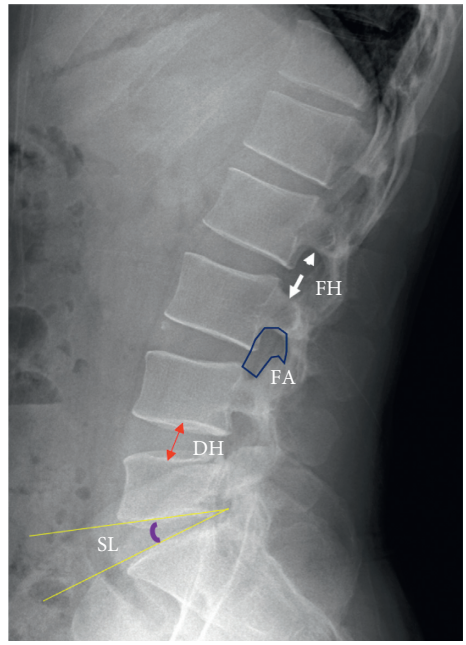


Figure 2: Illustration of the radiological measurement based on X-rays. FH: foraminal height; DH: disc height; FA: foraminal area; SL: segmental lordosis.

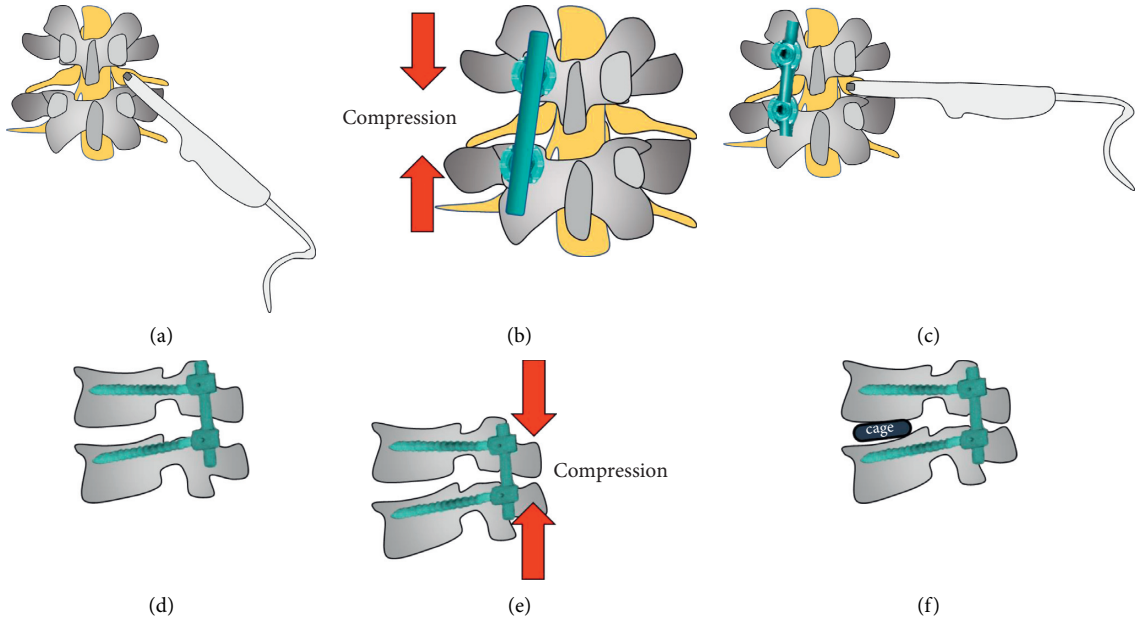


Figure 3: Illustration of the utility of IoUS during operation: (a) measurement of the condition of L5 nerve root before spine shortening; (b) slow spine compression; (c) measurement of the condition of L5 nerve root after spine shortening; (d) sagittal view of the affected segment before compression; (e) sagittal view of slow spine compression; and (f) sagittal view of cage insertion.

linear array transducer before spine shortening (Figure 3(a)). The ultrasound transducer was directed perpendicular to the horizontal plane as much as possible to obtain an accurate axial section of the exiting part of L5 nerve root and was stabilized for several seconds to prevent motion blur in the video (Figure 3(a)). After spine shortening, the dynamics of the L5 nerve root was measured again (Figures 3(b) and 3(c)), and the hemodynamic parameters of the L5 nerve root would be acquired before and after spine shortening. The sagittal view is shown in Figure 3 (Figures 3(d)–3(f)). In addition, to obtain the blood volume of L5 nerve root, a radiocontrast agent (sulfur hexafluoride) was used. After injection of sulfur hexafluoride, the timer would be initiated. Subsequently, the time duration

and the slope ratio of time curve before the radiocontrast agent reached the peak, as well as the value of the peak would be recorded before and after spine shortening, respectively. The curve indicated the concentration changes of the radiocontrast agent over time, and the faster the curve increased, the more the blood flow volume.

2.6. Diagnosis and Evaluation of Foot Drop. The foot drop was diagnosed mainly based on the tibialis anterior (TA) strength and medical history, and the manual muscle test (MMT) was utilized to assess the muscle strength of TA [2]. In this study, foot drop would be diagnosed when muscle strength of TA was below or equal to 3 (out of 5) [2]. The symptoms duration of foot drop was defined as a period from onset of stumbling or weakness of ankle dorsiflexion to surgery. The previous study has indicated that the optimal time for improving foot drop after surgical intervention was 6 weeks, and thus in this study, we evaluated the patients' recovery at preoperation, six weeks after operation, and one year after operation [19].

The recovery grade of foot drop ranged from "excellent" to "poor" based on the postoperative MMT score of TA [2]. Excellent denotes that the MMT score was grade 4 or 5; good denotes grade 3; fair denotes improvement but still below 3; and poor indicates no any recovery until the last follow-up [2]. We also evaluated the recovery rate of TA muscle strength: (grade at the last follow-up − grade before operation)/(5 − grade before operation) × 100% [2]. Grade 3 was considered grade 2.5 in this study.

2.7. Statistics Analysis. Statistical analysis was carried out using GraphPad Prism 9 (GraphPad Software Inc, La Jolla, CA). Data in this present study were presented as the median value. The Mann–Whitney U test was used to detect the statistical differences of demographic parameters (patients' age, symptoms duration, intraoperative blood loss, and operation time), radiological outcomes (HIS, FH, FA, and SL), IoUS parameters, and clinical scores (JOA score and VAS score) between the two groups, and intragroup comparison was conducted via the Wilcoxon signed rank test. Fisher's exact test was used to compare the gender, clinical tests, surgical segments, and comorbidities between the two groups. To further explore the relationship between foot drop and L5 nerve root, we performed the correlation analysis. Values that were less than 0.05 ($p < 0.05$) were considered statistical significance.

3. Results

There were 15 patients in the TLIF group (3 females and 12 males) and 12 in the CLIF group (3 females and 9 males) ($p > 0.999$). The median age of patients in the TLIF group was 43 (27–60) years, not statistically different from those in the CLIF group, 46 (26–69) years ($p = 0.895$). There were no statistical differences between these two groups with regard to duration of symptoms/foot drop, surgical segments, intraoperative blood loss, and operation time (all $p > 0.05$) (Table 1).

Table 2 shows the clinical scores of patients in the TLIF group and CLIF group. No significant differences were observed regarding patients scores, including JOA score and VAS score at preoperation, three months after operation, and the final follow-up (all $p > 0.05$). At the final follow-up, all patients in this present study acquired satisfactory recovery regarding VAS and JOA scores (both $p < 0.05$). In terms of the MMT score, all patients acquired improvement after operation. However, patients in the CLIF group exhibited better early recovery of foot drop, as indicated by the MMT score and its recovery rate at three months after operation ($p = 0.025$). At the final follow-up of one year, almost all patients reported satisfactory recovery of MMT score, without statistical difference between the two groups ($p = 0.065$). No surgery-related complications were observed perioperatively.

In order to investigate the effects of spine shortening, we firstly analyzed the radiological changes at surgical segment. Considering the major contribution of L5 nerve to foot drop, the surgical levels at L4/5 were chosen. We evaluated the changes of HIS, FH, FA, and SL at this level. As shown in Table 3, the HIS of L4/5 for patients in the CLIF group was decreased in comparison with preoperation and that of patients in the TLIF group postoperatively (both $p < 0.05$), which indicated the surgical segment was shortened after operation, and we believed this was the major reason for the satisfactory recovery of foot drop in this present study. We further evaluated the changes of morphology of intervertebral foramina at L4/5 and found that the FH and FA in the CLIF group were slightly lower compared with the TLIF group but without statistical differences (both $p > 0.05$). In fact, during CLIF or TLIF, the bilateral intervertebral foramina decompression was frequently carried out in order to avoid the stenosed foramina after operation, which may result in this result. In addition, no statistical difference was detected regarding SL between the two groups before ($p > 0.999$) and after operation ($p = 0.952$).

In addition, we evaluated the condition of the L5 nerve root using IoUS. As shown in Table 4, the median diameter of L5 nerve root after decompression in two groups was both improved compared with preoperation (both $p < 0.05$). However, patients in the CLIF group had a higher increase of diameter than those in the TLIF group ($p < 0.05$). We further analyzed blood flow volume of the focal L5 nerve root at surgical level and found that the postoperative time interval before peaking in the CLIF group was significantly shorter than that of the TLIF group (20.8 vs. 27.8) ($p = 0.019$). In addition, the postoperative peak value of L5 nerve root in the TILIF-SS group was higher than that in the TLIF group (4.8×10^{-5} vs. 3.7×10^{-5}) ($p = 0.002$).

Correlation analysis showed that both the preoperative time interval before peaking ($r = -0.8712$, $p < 0.001$) and the peak value ($r = 0.9304$, $p < 0.001$) were negatively and positively related with the preoperative MMT score, respectively, which indicated the potential contribution of L5 nerve root injury to foot drop (Figures 4(a) and 4(b)). In addition, the recovery rate of MMT score at three months after operation also correlated positively with the changes of time

Table 1: Clinical characteristics of patients in the TLIF group and CLIF group.

Parameters	Total	TLIF	CLIF	p
Age (years, median (range))	46 (26–69)	43 (27–60)	46 (26–69)	0.895
Gender (N, female/male)	6/21	3/12	3/9	>0.999
Duration of symptoms (months, median (range))	12 (0.3–120)	12 (0.3–120)	10 (0.3–120)	0.837
Duration of foot drop (days, median (range))	150 (6–1460)	182 (6–365)	105 (7–1460)	0.761
Intraoperative parameters				
Operation time, (mins, median (range))	120 (75–260)	120 (75–230)	155 (100–260)	0.390
Blood loss (ml, median (range))	200 (50–1000)	100 (50–1000)	200 (50–600)	0.397
Surgical segments				
1 level	16	9	7	
2 levels	9	5	4	
4 levels	2	1	1	
Duration of follow-up (months, median (range))	19 (13–28)	19 (13–27)	19.5 (14–28)	0.513

Table 2: Clinical evaluation of patients in the TLIF group and CLIF group.

Parameters (median (range))	Total	TLIF	CLIF	p value
Pre				
VAS	3 (0–5)	3 (0–5)	3 (0–5)	0.511
JOA	16 (15–21)	16 (15–21)	15.5 (15–18)	0.211
3 months after operation				
VAS	1 (0–3)*	1 (0–3)*	1.5 (0–3)	0.799
JOA	20 (18–23)*	20 (18–23)*	20 (18–21)*	0.530
Final follow-up				
VAS	0 (0–1)*	0 (0–1)*	0 (0–2)*	0.281
JOA	24 (20–26)*	25 (20–26)*	24 (22–26)*	0.448
Muscle strength of TA				
Pre. muscle	2 (0–3)	2 (0–3)	2 (0–3)	0.989
3 months after operation	4 (1–5)*	3 (1–4)*	4 (3–5)*	0.025
Recovery rate (%)	50 (20–75)	33 (20–60)	55 (33–100)	0.008
Final follow-up	5 (3–5)*	4 (3–5)*	5 (4–5)*	0.065
Recovery rate (%)	100 (50–100)	75 (50–100)	100 (50–100)	0.058

*indicates a statistical difference of the parameter at different time points after surgery compared with that at preoperation. JOA: Japanese Orthopaedic Association; VAS: visual analogue scale.

Table 3: Radiological results of patients in the TLIF group and CLIF group.

Parameters (median (range))		TLIF	CLIF	p value
HIS (mm)	Pre	9.3 (7.6–10.3)	9.5 (8.9–11.5)	0.315
	Post	9.8 (8.6–10.8)	7.4 (6.6–9.2)	<0.001
	Change	1.0 (0.3–1.7)	1.9 (1.4–2.3)	0.249
FH (mm)	Pre	18.6 (11.6–23.7)	19.8 (13.5–22.9)	0.508
	Post	19.8 (12.5–24.6)	17.7 (12.4–19.4)	0.051
	Change	0.9 (0.2–1.2)	2 (1.1–3.5)	0.585
FA (mm^2)	Pre	149.4 (134.2–160.2)	150.1 (139.2–161.4)	0.581
	Post	190.6 (179.5–205.7)	187.1 (179.1–198.2)	0.057
	Change	43.4 (32.0–55.8)	37.2 (27.9–47.8)	0.004
SL (°)	Pre	7.5 (0.9–9.3)	7.1 (1.2–9.1)	>0.999
	Post	7.8 (2.5–10.3)	8.0 (2.4–9.4)	0.952
	Change	0.7 (0.1–1.6)	0.6 (0.08–1.2)	0.523

HIS: height of intervertebral space; FH: foraminal height; FA: foraminal area; SL: segmental lordosis.

Table 4: IoUS parameters of L5 nerve root before and after surgery in the TLIF group and CLIF group.

Parameters (median (range))		TLIF	CLIF	p value
Diameter of L5 nerve root, mm	Pre	1.5 (1.3–1.6)	1.4 (1.3–1.6)	0.933
	Post	1.6 (1.5–2.0)*	2.0 (1.9–2.2)*	<0.001
	Change	0.2 (0.1–0.7))	0.6 (0.5–0.7)	<0.001
Time interval before peaking (s)	Pre	37.1 (30.3–41.9)	37.5 (28.7–43.4)	>0.999
	Post	27.8 (20.9–34.8)*	20.8 (14.9–30.2)*	0.019
	Change	8.6 (2.6–16.1)	12.7 (7.3–21.9)	0.038
Peak value of L5 nerve root ($\times 10^{-5}$)	Pre	3.1 (1.6–3.5)	2.7 (1.5–3.6)	0.492
	Post	3.7 (1.9–4.7)*	4.8 (3.5–5.9)*	0.002
	Change	0.5 (0.1–1.9)	2.0 (1.0–3.3)	<0.001

*indicates a statistical difference of the parameter at different time points after surgery compared with that at preoperation. IoUS: intraoperative ultrasonography.

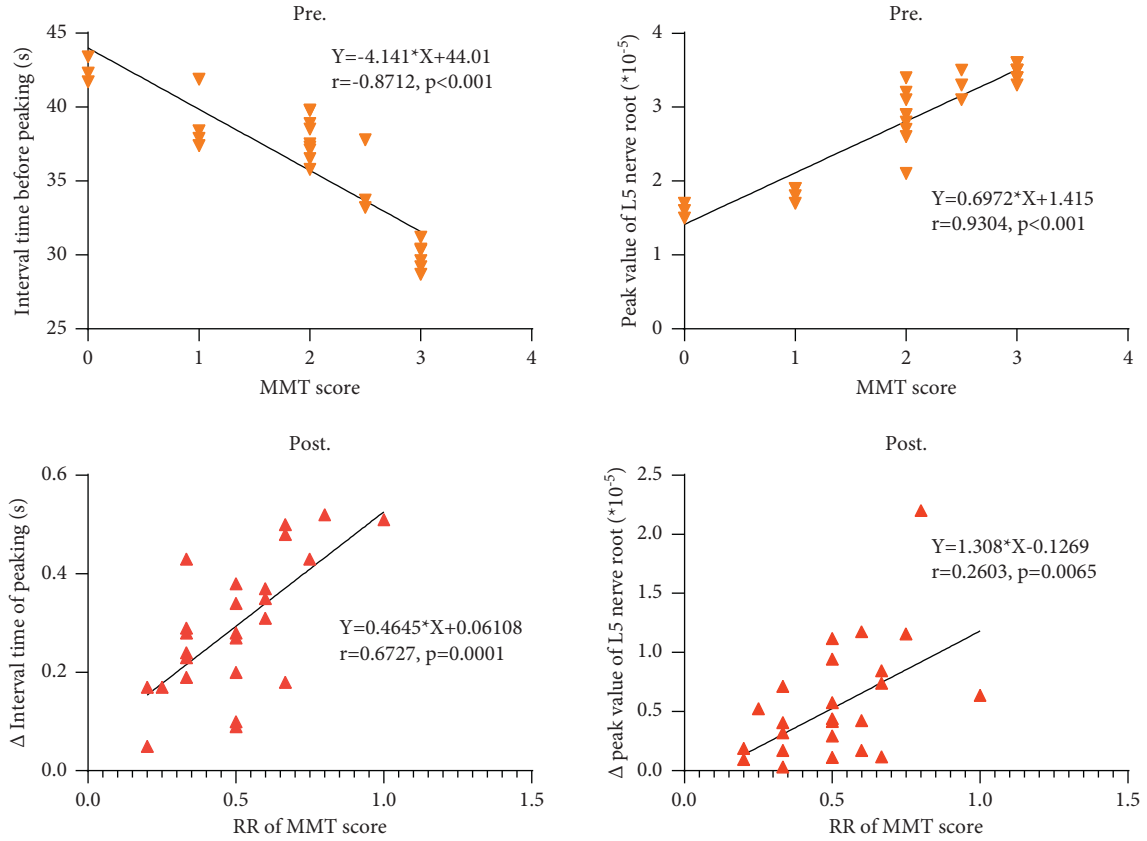
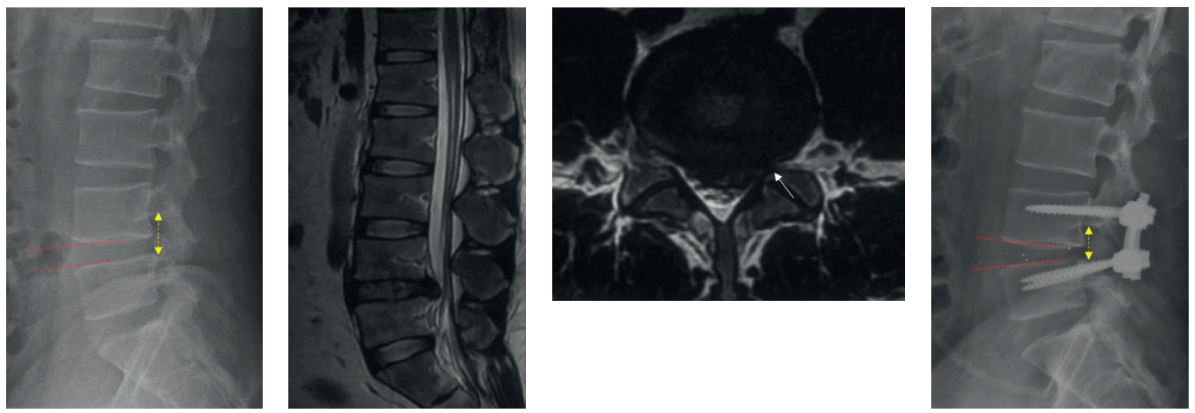


Figure 4: Correlations of the MMT score and IoUS parameters (a) before and (b) after operation.

interval before peaking ($r = 6727$, $p = 0.0001$) and the peak value ($r = 0.2603$, $p = 0.0065$) (Figures 4(c) and 4(d)).

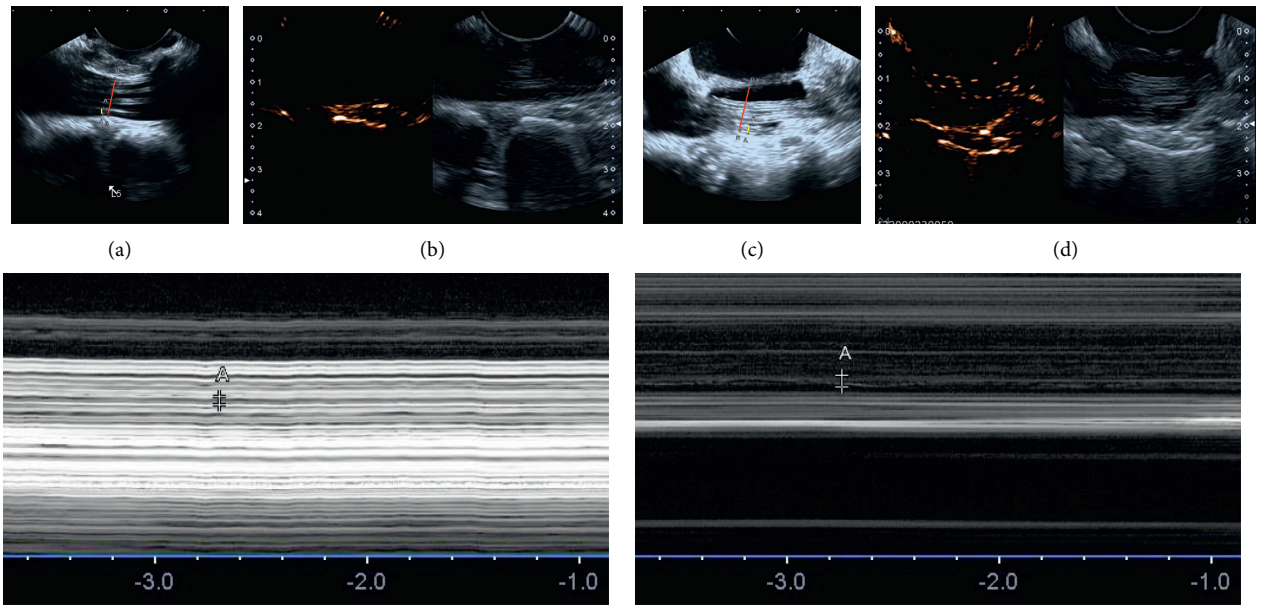
3.1. Case Presentation. A 34-year-old female patient with numbness and pain at her left lower extremity and foot drop for nearly four months was admitted to our institution. Physical examination showed she had positive Lasegue sign of 45°. The MMT score of her left tibialis anterior (TA) was 3 and 5 in her right. Preoperative images indicated that there was a herniated disc compressing neural elements at her L4/5 segment, with the loss of lumbar lordosis (Figures 5(a)–5(c)). A single-level CLIF at L4/5 was given (Figure 5(d)). Six months after operation, the patient had significant improvement regarding neurological function with better lumbar lordosis. More importantly, her dropped foot had satisfactory recovery, with the MMT score of 5.

Figure 4 shows the IoUS of the patients before and after spine shortening. Before we compressed the lumber spine, the diameter of the nerve root and dura mater was 1.5 mm and 10.1 mm, respectively (Figures 6(a) and 6(b)). The blood perfusion of the L5 nerve root was also improved significantly compared with the poor perfusion before spine shortening (Figures 6(c) and 6(d), white arrow). In addition, the amplitude of L5 nerve root was also increased from 1.1 mm before spine shortening to 1.6 mm after shortening (Figures 6(e) and 6(f)). These improved IoUS parameters suggested the patient's nerve root tension acquired satisfactory axial release via spine shortening.



(a) (b) (c) (d)

Figure 5: Images of the case: (a) preoperative lateral X-rays; (b) preoperative sagittal MRI; (c) preoperative axial MRI; and (d) postoperative lateral X-rays.



(a) (b) (c) (d)

(e) (f)

Figure 6: Intraoperative ultrasonography (IoUS) of the case: (a) preoperative diameter of the L5 nerve root (yellow line) and dura mater (red line); (b) preoperative blood perfusion of the L5 nerve root (white arrow); (c) postoperative diameter of the L5 nerve root (yellow line) and dura mater (red line); (d) postoperative blood perfusion of the L5 nerve root (white arrow); (e) preoperative amplitude of the L5 nerve root; and (f) postoperative amplitude of the L5 nerve root.

4. Discussion

Foot drop resulting from LDD has been a hot topic of interest among spine surgeons. Although previous studies have been investigating the mechanism of LDD-derived foot drop and related treatments, the results are still disputed. Anatomically, the TA muscle and extensor hallucis longus were mainly innervated by the L5 nerve root [5]. Aono et al. reported that an impairment at the L5 nerve root was the main contributor to foot drop [1]. In this present study, to minimize the effects of other potential risk factors, all patients enrolled presented with lesion involving the L4/5 level. In addition, to evaluate the changes of the L5 nerve root on the recovery of foot drop, we firstly introduced IoUS during operation. Interestingly, the results of this present study suggested that the severity of foot drop before operation correlated with the blood volume of L5 nerve root. Additionally, the recovery of foot drop was also associated with the changes of the blood volume of L5 nerve root. Therefore, we in this present study confirmed the vital role of the function of L5 nerve root in foot drop. However, McCulloch and Waddell found that except the L5 nerve root, L4 and S1 nerves also innervated certain part of TA based on electrical stimulation [20]. A study by Iizuka et al. also showed that L4

or S1 was also affected in most of the patients with LDH-induced foot drop, and they attributed it to a transitional vertebra, namely lumbarized S1 or sacralized L5 [5]. McCulloch and Waddell ever suggested that the functional L5 root came from the most caudal lumbosacral segments [20]. Therefore, we deduced that the function of S1 root may become more like that of L5 root when there is lumbarization of S1, and that the function of L4 root may become more like that of L5 root when there is sacralization of L5. However, it was reported that a lesion in the thoracolumbar spine (T11-L2) could also cause foot drop, and that foot drop lesion was located at the epiconus [2]. Therefore, foot drop may be a multifactorial disease, and our present study only showed the role of L5 nerve root in foot drop. Further study is needed to explore the exact mechanism of LDD-derived foot drop.

Previous studies have investigated the clinical outcomes of patients with foot drop. However, patients did not acquire satisfactory recovery in spite of sufficient decompression. Eysel et al. performed a study of 240 patients with LDH and found that the postoperative recovery rate was only 40% for patients with grade 2 paresis [21]. Aono et al. reported that only 61% patients had various degrees of functional recovery after lumbar operation, and that 28% had no improvement [1]. Ghahreman et al. reported that only 41% patients who underwent surgical decompression acquired full recovery, with 21% unchanged [22]. A study of Iizuka et al. showed patients with LDH acquired better recovery than those with LSS, and the overall recovery rate was 40% [5]. However, previous studies mainly focused on the routine surgical decompression [1, 5, 21, 22]. Our previous study found another ignored impairment caused by axial traction of the lumbar nerve root may be another major contributor to lumbar symptoms in patients with LDD [8]. Hence, in this present study, the technique of CLIF was designed to reduce the axial tension of the nerve root in the lumbar spine and the surgical outcomes of CLIF were comparable with those of TLIF. As shown in the results, despite the improvement of foot drop in all patients after operation, patients in CLIF acquired better early recovery compared with those in the TLIF group, with 75% patients had excellent recovery at three months after operation. Based on the results above, we deduced that TLIF with spine shortening may facilitate to early recovery of foot drop. In fact, early recovery frequently affects patients' final recovery. As reported by Ghahreman et al., the most significant improvement of ankle weakness occurs within the first 6 weeks, without substantial improvement after that [21]. Therefore, promoting early recovery of foot drop is significantly important to patients' long-term prognosis. Notably, no statistical difference was observed regarding the MMT score at the final follow-up between the two groups, whereas patients in the CLIF group seemed to have higher MMT scores, which we deduced may correlate with the small sample in this present study.

To further confirm the favorable recovery of foot drop in the CLIF group, we focused on the effect of surgical techniques on the L5 nerve root. The diameter and blood flow volume of the L5 nerve root were evaluated. As shown in this study, patients in the CLIF group had a more increased diameter of L5 nerve root, compared with those in the TLIF group. In terms of blood flow volume of L5 nerve root, the time interval before peaking decreased more significantly in the CLIF group than the TLIF group. In addition, the peak value of blood flow volume in the CLIF group was also higher than that in the TLIF group. Collectively, the technique of CLIF resulted in better function recovery of the L5 nerve root. Furthermore, we also evaluated the changes of radiological parameters between the two groups and found that the HIS in the CLIF group was decreased. However, the procedure of spine shortening did not obviously stenosed the intervertebral foramina, as indicated by FA and FH. In fact, during operation, the bilateral decompression was frequently carried out unconsciously to avoid the stenosed foramina after operation. Therefore, the technique of CLIF was feasible and safe.

The prognostic factors for the recovery of foot drop due to LDD have been reported in several studies, with most risk factors being symptoms duration and preoperative TA muscle strength [22, 23]. In this present study, due to the limitation of sample, we did not make further risk analysis. However, patients with worse preoperative muscle strength of TA and longer symptoms duration had relatively bad recovery, consistent with previous studies [23, 24]. Taken together, timely treatment facilitates better recovery. However, it is notable that foot drop is frequently considered a sign for symptom severity of underlying LDD in clinical practice, and almost all the published cases received operation. Therefore, sound and comprehensive evidence in the selection of surgical or conservative treatments for foot drop are imperatively required. However, a RCT study demonstrated the absence of superiority of surgery over conservative therapy in treating LDD-derived foot drop [25]. Resultantly, the selection of surgery should include comprehensive evaluation of the LDD and not solely foot drop. Other clinical examinations, such as neurogenic claudication, might be also required in selection of conservative of surgical treatment.

Based on the results above, we deduced that the spine shortening led to decreased axial tension of the L5 nerve root and added the decompressive effect from an axial aspect to traditional decompression via only elimination of the compressed lesion, which may be the reason of the more satisfactory recovery of foot drop in the CLIF group. However, IoUS parameters were still indirect indicators to evaluate the tension of nerve root; the direct relationship between axial hypertension of nerve root and foot drop remains to be studied. An auxiliary instrument which can directly quantify the axial tension is required.

However, several limitations should be acknowledged here. First, this present study used both radiological and intraoperative ultrasonography results in order to reveal the spine shortening effects of CLIF. In addition, IoUS was firstly used to evaluate the condition of nerve root in this present study, which was a preliminary attempt. Therefore, we did not overstate the cases in regard to the ultrasonic findings at this time. However, our future study will further focus on the relationship between intraoperative ultrasonography and the function of nerve root during spine surgery and validate

the effectiveness of this method, which may extend the application of intraoperative ultrasonography. Second, foot drop is a multifactorial disease, and there may be other types of stretching of the traversing L5 nerves, rather than axial stretching only. In fact, this preliminary study was designed based on the concept that axial stretching of the L5 nerve root may be another pathogenic factor to evaluate the effect of axial decompression of nerve root on the recovery of foot drop, and the encouraging results indicated that CLIF can be effective and safe for the treatment of foot drop due to lumbar degenerative diseases. However, our present study mainly focused on the axial decompression, and more studies are still required to explore the exact pathogenesis of foot drop. Third, although we conducted this study prospectively, this present study was inconsistent with the requirements of the RCT trial, and high-quality studies, such as RCT trial, will be carried out in the future to validate the outcomes of this study.

5. Conclusion

Axial hypertension of L5 nerve root may be involved in the pathological mechanism of foot drop, and transforaminal lumbar interbody fusion with spine shortening (TLIF-SS) can be effective and safe for the treatment of foot drop due to lumbar degenerative diseases. However, further studies with more cases will be required to validate its generalizability and safety.

Data Availability

Data will be available when required.

Ethical Approval

This study was performed in accordance with the principles of the Declaration of Helsinki and was also approved by the Ethics Committee of Changzheng Hospital. This present study was not a clinical trial, and therefore, the authors did not make the corresponding registration in a public trial registry.

Consent

All the patients in this study provided the informed consent and agreed to participate in this study.

Disclosure

Kaiqiang Sun, Feng Lin, and Jialin Jiang are co-first authors.

Conflicts of Interest

The authors declare no conflicts of interest.

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Authors' Contributions

Kaiqiang Sun, Feng Lin, and Jialin Jiang contributed equally to this study . Study design was developed by Jiangang Shi and Jingchuan Sun. Data collection was performed by Kaiqiang Sun, Feng Lin, and Jialin Jiang. Statistical analysis was done by Kaiqiang Sun. Data interpretation was by Jiangang Shi and Jingchuan Sun. Manuscript preparation was done by Kaiqiang Sun. Literature search was carried out by Feng Lin and Jialin Jiang. Funds collection was done by Jiangang Shi and Jingchuan Sun.

Acknowledgments

The authors acknowledge the support by National Natural Science Foundation of China (Nos. 81871828 and 81802218) and the Cultivation Project of Changzheng Hospital (2020YCGPZ-106).

References

[1] H. Aono, M. Iwasaki, T. Ohwada et al., "Surgical outcome of drop foot caused by degenerative lumbar diseases," *Spine*, vol. 32, no. 8, pp. E262–E266, 2007.

[2] T. Miwa, M. Iwasaki, A. Miyauchi, S. Okuda, and T. Oda, "Foot drop caused by a lesion in the thoracolumbar spine," *Journal of Spinal Disorders & Techniques*, vol. 24, no. 3, pp. E21–E25, 2011.

[3] M. Macki, S. Lim, J. Elmenini, M. Fakih, and V. Chang, "Clinching the cause: a review of foot drop secondary to lumbar degenerative diseases," *Journal of the Neurological Sciences*, vol. 395, pp. 126–130, 2018.

[4] K. Liu, W. Zhu, J. Shi et al., "Foot drop caused by lumbar degenerative disease: clinical features, prognostic factors of surgical outcome and clinical stage," *PLoS One*, vol. 8, no. 11, Article ID e80375, 2013.

[5] Y. Iizuka, H. Iizuka, S. Tsutsumi et al., "Foot drop due to lumbar degenerative conditions: mechanism and prognostic factors in herniated nucleus pulposus and lumbar spinal stenosis," *Journal of Neurosurgery: Spine*, vol. 10, no. 3, pp. 260–264, 2009.

[6] A. Nv, S. Rajasekaran, S. V. A. Ks, R. M. Kanna, and A. P. Shetty, "Factors that influence neurological deficit and recovery in lumbar disc prolapse-a narrative review," *International Orthopaedics*, vol. 43, no. 4, pp. 947–955, 2019.

[7] J.-G. Shi, X.-M. Xu, J.-C. Sun, Y. Wang, Q.-J. Kong, and G.-D. Shi, "Theory of bowstring disease: diagnosis and treatment bowstring disease," *Orthopaedic Surgery*, vol. 11, no. 1, pp. 3–9, 2019.

[8] K. Sun, X. Sun, L. Huan et al., "A modified procedure of single-level transforaminal lumbar interbody fusion reduces immediate post-operative symptoms: a prospective case-controlled study based on two hundred and four cases," *International Orthopaedics*, vol. 44, no. 5, pp. 935–945, 2020.

[9] F. D. Westhout, L. S. Pare, and M. E. Linskey, "Central causes of foot drop: rare and underappreciated differential diagnoses," *The journal of spinal cord medicine*, vol. 30, no. 1, pp. 62–66, 2007.

[10] A. Papapostolou, G. Tsivgoulis, M. Papadopoulou, N. Karandreas, T. Zambelis, and K. Spengos, "Bilateral drop foot due to thoracic disc herniation," *European Journal of Neurology*, vol. 14, no. 2, p. e5, 2007.

[11] S. M. Bhagia, E. S. Siegelman, R. V. Gilchrist, and C. W. Slipman, "Compression fracture: identify the diagnosis," *Pain Physician*, vol. 5, no. 4, pp. 401–404, 2002.

[12] M. B. Katirji and A. J. Wilbourn, "Common peroneal mononeuropathy: a clinical and electrophysiologic study of 116 lesions," *Neurology*, vol. 38, no. 11, p. 1723, 1988.
[13] A. Cruz-Martinez, J. Arpa, and F. Palau, "Peroneal neuropathy after weight loss," *Journal of the Peripheral Nervous System*, vol. 5, no. 2, pp. 101–105, 2000.
[14] D. H. Ge, N. D. Stekas, C. G. Varlotta et al., "Comparative analysis of two transforaminal lumbar interbody fusion techniques," *Spine*, vol. 44, no. 9, pp. E555–E560, 2019.
[15] H. E.-B. Abd El-Kader, "Transforaminal lumbar interbody fusion for management of recurrent lumbar disc herniation," *Asian Spine Journal*, vol. 10, no. 1, pp. 52–58, 2016.
[16] K. Sun, J. Sun, S. Wang et al., "Placement of titanium mesh in hybrid decompression surgery to avoid graft subsidence in treatment of three-level cervical spondylotic myelopathy: cephalad or caudal?" *Medical Science Monitor*, vol. 24, pp. 9479–9487, 2018.
[17] P. G. Cho, S. H. Park, K. N. Kim, Y. Ha, D. H. Yoon, and D. A. Shin, "A morphometric analysis of contralateral neural foramen in TLIF," *European Spine Journal, and the European Section of the Cervical Spine Research Society*, vol. 24, no. 4, pp. 783–790, 2015.
[18] A. Kimura, A. Seichi, H. Inoue et al., "Ultrasonographic quantification of spinal cord and dural pulsations during cervical laminoplasty in patients with compressive myelopathy," *European Spine Journal*, vol. 21, no. 12, pp. 2450–2455, 2012.
[19] M. Bilgilisoy Filiz, Z. Kiliç, A. Uçkun, T. Çakir, Ş. Koldaş Doğan, and N. F. Toraman, "Mechanical traction for lumbar radicular pain," *American Journal of Physical Medicine & Rehabilitation*, vol. 97, no. 6, pp. 433–439, 2018.
[20] J. McCulloch and G. Waddell, "Variation of the lumbosacral myotomes with bony segmental anomalies," *Journal of Bone and Joint Surgery British Volume*, vol. 62-B, no. 4, pp. 475–480, 1980.
[21] P. Eysel, J. D. Rompe, and C. Hopf, "Prognostic criteria of discogenic paresis," *European Spine Journal*, vol. 3, no. 4, pp. 214–218, 1994.
[22] A. Ghahreman, R. D. Ferch, P. Rao, N. Chandran, and B. Shadbolt, "Recovery of ankle dorsiflexion weakness following lumbar decompressive surgery," *Journal of Clinical Neuroscience*, vol. 16, no. 8, pp. 1024–1027, 2009.
[23] M. Macki, S. Syeda, P. Kerezoudis, Z. L. Gokaslan, A. Bydon, and M. Bydon, "Preoperative motor strength and time to surgery are the most important predictors of improvement in foot drop due to degenerative lumbar disease," *Journal of the Neurological Sciences*, vol. 361, pp. 133–136, 2016.
[24] F. Saeed, S. Mukherjee, K. Chaudhuri, J. Kerry, S. Ahuja, and D. Pal, "Prognostic indicators of surgical outcome in painful foot drop: a systematic review and meta-analysis," *European Spine Journal*, vol. 30, no. 11, pp. 3278–3288, 2021.
[25] H. Österman, S. Seitsalo, J. Karppinen, and A. Malmivaara, "Effectiveness of microdiscectomy for lumbar disc herniation," *Spine*, vol. 31, no. 21, pp. 2409–2414, 2006.
[26] H. Tian, A. Wu, M. Guo et al., "Adequate restoration of disc height and segmental lordosis by lumbar interbody fusion decreases adjacent segment degeneration," *World neurosurgery*, vol. 118, pp. e856–e864, 2018.

Hindawi
Pain Research and Management
Volume 2021, Article ID 6454760, 8 pages
https://doi.org/10.1155/2021/6454760

Research Article

Full-Endoscopic Transforaminal Ventral Decompression for Symptomatic Thoracic Disc Herniation with or without Calcification: Technical Notes and Case Series

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Received 5 September 2021; Accepted 18 October 2021; Published 3 November 2021

Academic Editor: Sidong Yang

Background. Symptomatic thoracic disc herniation is a challenge in spinal surgery, especially for cases with calcification. Traditional open operation has a high complication rate. The authors introduced a modified full-endoscopic transforaminal ventral decompression technique in this study and evaluated its imaging and clinical outcomes. *Materials and Methods*. Eleven patients with symptomatic thoracic disc herniation who underwent full-endoscopic transforaminal ventral decompression in a single medical center were enrolled. The surgical technique was performed as described in detail. Dilator sliding punching, endoscope-monitored foraminoplasty, and base cutting through the "safe triangle zone" are the key points of the technique. Clinical outcomes were assessed by the modified Japanese Orthopedic Association (mJOA) score for neurological improvement and the visual analogy score (VAS) for thoracic and leg pain. The operation time, hospital stay, and complications were also analyzed. *Results*. Postoperative magnetic resonance imaging (MRI) revealed good decompression of the spinal cord. The mJOA improved from 7.4 (range: 5–10) to 10.2 (range: 9–11). Axial thoracic pain improved in 8 of 9 patients. Leg pain and thoracic radicular pain improved in all patients. No complications were observed. The average operation time was 136 minutes (range: 70–180 minutes). The average length of hospital stay was 5.3 days (range: 2–8 days). *Conclusion*. Minimally invasive full-endoscopic transforaminal ventral decompression for the treatment of symptomatic thoracic disc herniation with or without calcification is feasible and may be another option for this challenging spine disease.

1. Introduction

Symptomatic thoracic disc herniation (TDH) is a relatively uncommon entity, constituting less than 1% of all disc herniations [1]. TDHs often occur in the 4–6th decade of life and may present with radiculopathy and/or myelopathy. The symptoms range from slight back pain to severe intercostal neuralgia, weakness of the lower extremities, and even bowel and urine abnormalities [2, 3]. Surgery is reserved for those patients who are nonresponsive to conservative treatment.

Surgical treatment of TDHs is quite challenging. A variety of surgical approaches have been developed to treat TDHs, including transfacet pedicle-sparing [4], transpedicular [5], costotransversectomy [6], and lateral extracavitary [7]. However, each of these approaches has its own disadvantages and complications [8].

More recently, percutaneous transforaminal endoscopic discectomy (PTED) has been developed and achieved excellent clinical outcomes in the treatment of not only soft lumbar disc herniations (LDH) [9, 10] but also of calcified type of lumbar disc herniation [11–13]. However, there are few reports about endoscopic transforaminal thoracic discectomy to treat TDH.

In the present study, we introduced a posterolateral full-endoscopic transforaminal ventral decompression technique for thoracic disc herniation with or without calcification. This surgical technique is a modification of PTED for lumbar disc disease. We used this modified PTED technique to treat

thoracic disc herniation and achieved good clinical outcomes.

2. Materials and Methods

This study was approved by the Ethics Committee of the Hebei General Hospital before data collection and analysis. It was a retrospective study. The diameter of the endoscope system was 4.3 mm, with a view angle of 30° and 181 mm working length through a working channel with an inside diameter of 6.9 mm (SPINENDOS GmbH, Munich, Germany).

2.1. Clinical Data. Between January 2018 and December 2019, eleven patients with thoracic disc herniation underwent full-endoscopic transforaminal ventral decompression in a single medical center. Seven were male and four were female, aged 25–72 years (mean: 53 years). Patients with a history of fracture, infection, or tumors were excluded. Pathological changes were only or mainly located in the ventral side of the spinal cord, which was clinically recognized as the main cause of the symptoms. As confirmed by the MRI and CT scan, the pathological changes included soft disc herniation (2 cases) and calcified disc herniation (9 cases). Two was located at T9-T10, 3 at T10-T11, 5 at T11-T12, and 1 at T12-L1. The presenting symptoms were classified as axial thoracic pain, thoracic radicular pain, leg pain, and myelopathy (6). The mean symptom duration was 8.6 months (range 2–18 months). The clinical characteristics of the patients are given in Table 1.

2.2. Surgical Technique

2.2.1. Preoperative Preparation and Anesthesia. CT, MRI, and X-ray examinations were performed before the operation. The patients needed to simulate the operation position under the care of the medical staff. There were two advantages: first, the patients could adapt to the position of the operation in advance to avoid anxiety during the operation. Second, whether there were neurological deficits in a specific position could be identified preoperatively. For the operation, the patient was positioned in a comfortable prone position. Some soft cushions were used to keep the patients in a comfortable position and relieve their neurological symptoms. The anesthesia regime was local anesthesia combined with conscious sedation. During this, an electrocardiograph, blood pressure, respiration, and finger pulse oxygen saturation were monitored. Dexmedetomidine hydrochloride was pumped at a rate of 0.1–0.5 μg/kg/hour. The speed of the pump was adjusted according to the patient's surgical tolerance, so that the patient was maintained in a sober yet sedated state. Anesthesiologists took care of the patients throughout the operation. The local anesthetic was a mixture of 0.5% lidocaine and 0.25% ropivacaine. The anesthesia area included the skin, deep fascia, dorsolateral articular process, and intervertebral foramen. No anesthetic was given directly into the spinal canal. This can prevent the spinal cord from being anesthetized, resulting in serious complications.

2.2.2. Working Port Establishment. First, we located the puncture trajectory under X-ray fluoroscopy. The puncture trajectory was consistent with the direction of the intervertebral space. The entry point was located on the medial side of the highest point of the posterior rib. The distance to the spinous process was approximately 6–8 cm. A 16G spinal needle was used for the anesthesia of the skin and the deep fascia. After making an incision, a hollow dilator with a diameter of 6.5 mm was used for the following puncture process. A dilator with a blunt tip could reduce the risk of pleura and spinal cord injury. The punching target was the lateral side of the articular process. The pinhole in the dilator can be used to inject anesthetics along the puncture path. After AP and lateral view were checked by X-ray, the dilator was slid into the lower part of the intervertebral foramen (Figures 1 and 2). The working sheath could be introduced along the dilator. Foraminoplasty and spinal cord decompression were performed subsequently under the endoscopic view.

2.2.3. Endoscopic Operation. After the soft tissue in the foramen was removed, the bony anatomical structure of the intervertebral foramen could be clearly exposed to view. Foraminoplasty was performed with a high-speed diamond burr or a Kerrison rongeur (Figure 3). In the foraminoplasty, the excised bony structure included not only the ventral side of the superior articular process but also part of the posterior edge of the vertebral body, even the upper part of the pedicle. The key point of the foramen foraminoplasty is to increase the range of motion of the working channel. This modified foraminoplasty could not only preserve the stable structure of the spine as much as possible but also expose the ventral pathology clearly. When the space of the intervertebral foramen area was ample enough, the working sheath could be further deepened. There was no extra pressure on the spinal canal during this process. Forced entry of the working sheath was forbidden.

After entering the lateral spinal canal, for a soft disc herniation, discectomy was performed by the "out-in-out" technique. The fibrous ring was exposed and cut open. The soft nucleus pulposus in the intervertebral space could be cleaned. When the space was large enough, the endoscope and surgical instruments would be inserted. The disc herniated into the spinal canal could be seen at 12 o'clock in the field of vision. Discectomy can be achieved by the 30-degree visual field angle of the endoscope and variable angle forceps. Central spinal canal decompression can be achieved by a broad foraminoplasty and working channel pressed down. However, this technique was only suitable for soft lesions. In some cases, the pathogenic factor was a calcified disc, osteophytes, or both. First, the soft disc was removed as described, and a tough shell remained. Bony decompression began at the cranial and caudal edge of the vertebrae, which was the base of the hypertrophic fibrous ring and osteophyte. We can see the spinal cord was jacked

Table 1: Summary of the clinical and imaging characteristics of the 8 cases who underwent full-endoscopic transforaminal ventral decompression surgery.

No. of patients	Gender	Age (years)	Location	Primary symptoms and duration (months)	Soft/calcified
1	Male	59	T11-T12	Axial thoracic pain (12), thoracic radicular pain (7)	Soft
2	Male	65	T10-T11	Axial thoracic pain (6), myelopathy (4)	Calcified
3	Female	25	T11-T12	Axial thoracic pain (12), thoracic radicular pain (7)	Calcified
4	Female	72	T9-T10	Thoracic radicular pain (8), myelopathy (8)	Calcified
5	Male	28	T11-T12	Leg pain (6), myelopathy (3)	Calcified
6	Female	63	T11-T12	Axial thoracic pain (18), leg pain (4), myelopathy (2)	Calcified
7	Male	39	T12-L1	Myelopathy (2)	Calcified
8	Male	55	T10-T11	Axial thoracic pain (9), leg pain (2), myelopathy (2)	Calcified
9	Male	68	T11-T12	Axial thoracic pain (14), myelopathy (3)	Calcified
10	Female	71	T9-T10	Axial thoracic pain (6), thoracic radicular pain (1)	Calcified
11	Male	42	T10-T11	Myelopathy (2)	Soft

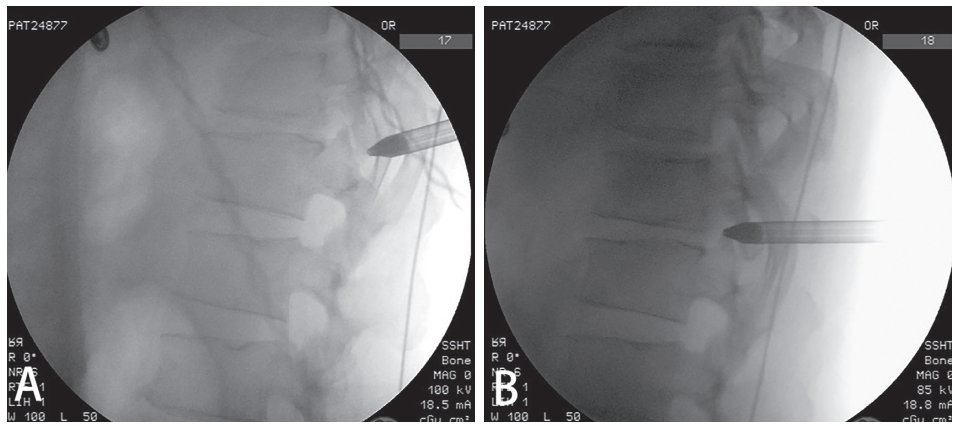
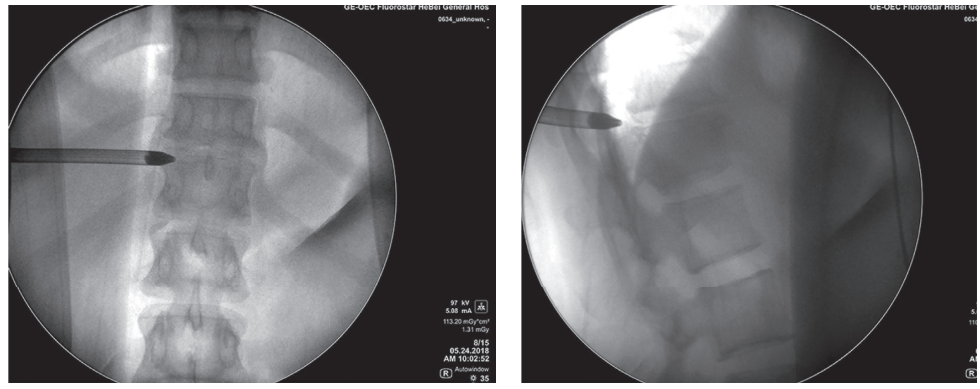


Figure 1: Images of X-ray fluoroscopy showing the dilator punching procedure: a dilator with blunt tip located on the lateral side of the articular process (a). The dilator slid into the lower part of the intervertebral foramen (b).



(a) (b)

Figure 2: The dilator is located at the lower part of the intervertebral foramen, as can be checked on the lateral X-ray fluoroscopy (a) and anteroposterior X-ray fluoroscopy (b).

up at the distal side of the calcification. Epidural fat is filled in this area. After exposure and hemostasis, we could say a space between the spinal cord and calcification. The space was safe for manipulation, and it was named the "safe triangle zone" by our team (Figure 4). The three sides of the triangle were calcification, spinal cord, and posterior wall of the vertebral body. The tools could operate in this area without touching the spinal cord. After the base was disrupted by the high-speed diamond burr, the hump could be cut off piece by piece. Whether the posterior longitudinal ligament needed to be removed was dependent on the rate of dural sac relaxation. Adequate decompression should be the first aim of the surgery (Figure 5). The operation is over after careful hemostasis. No drainage system was applied. Patient feedback is essential throughout the entire operation.

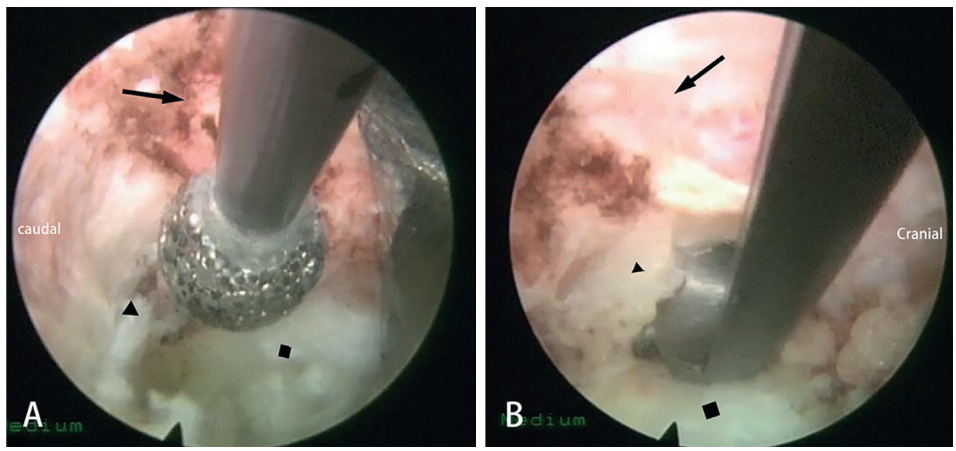


Figure 3: Endoscopic foraminoplasty by the high-speed diamond burr (a) and Kerrison rongeur (b). ⟶ The articular process, ▲ the ligamentum flavum, and the ■ thoracic disc.

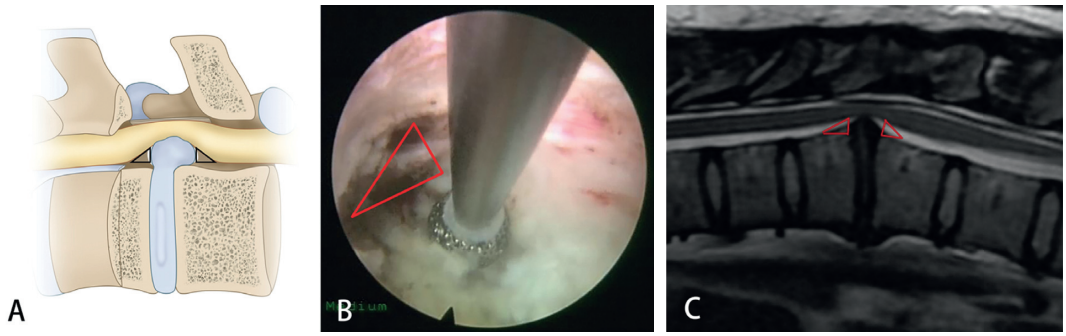
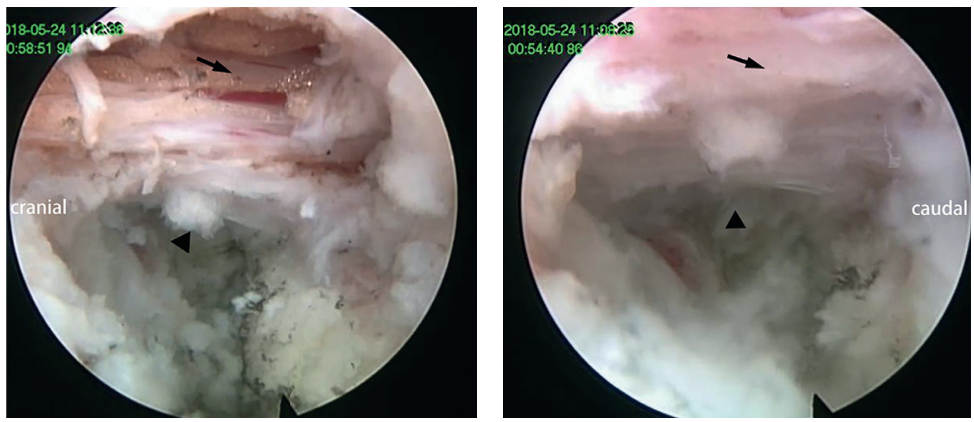


Figure 4: The "safe triangle zone" described by a diagram (a), endoscopic view (b), and MRI.



(a) (b)

Figure 5: The decompressed central spinal canal (a) and lateral spinal canal under endoscopic view (b) ⟶ showing the spinal cord and ▲ intervertebral space.

2.2.4. Postoperative Outcome Evaluation. MRI was used as the radiological assessment, which was performed within 2 days after the operation as well as during the follow-up if necessary (Figure 6). The neurological outcome was assessed using the modified Japanese Orthopedic Association (mJOA) score (11 points) [14]. The degree of axial/radicular thoracic and leg pain was assessed using the visual analogy score (VAS). The operation time and the length of hospital stay were also recorded. The operation time was defined as the time from puncture to suturing. It did not include the time of the operative positioning or the operation target locating. The hospital stay for rehabilitation and physical therapy for patients with myelopathy was not reckoned in the length of hospital stay.

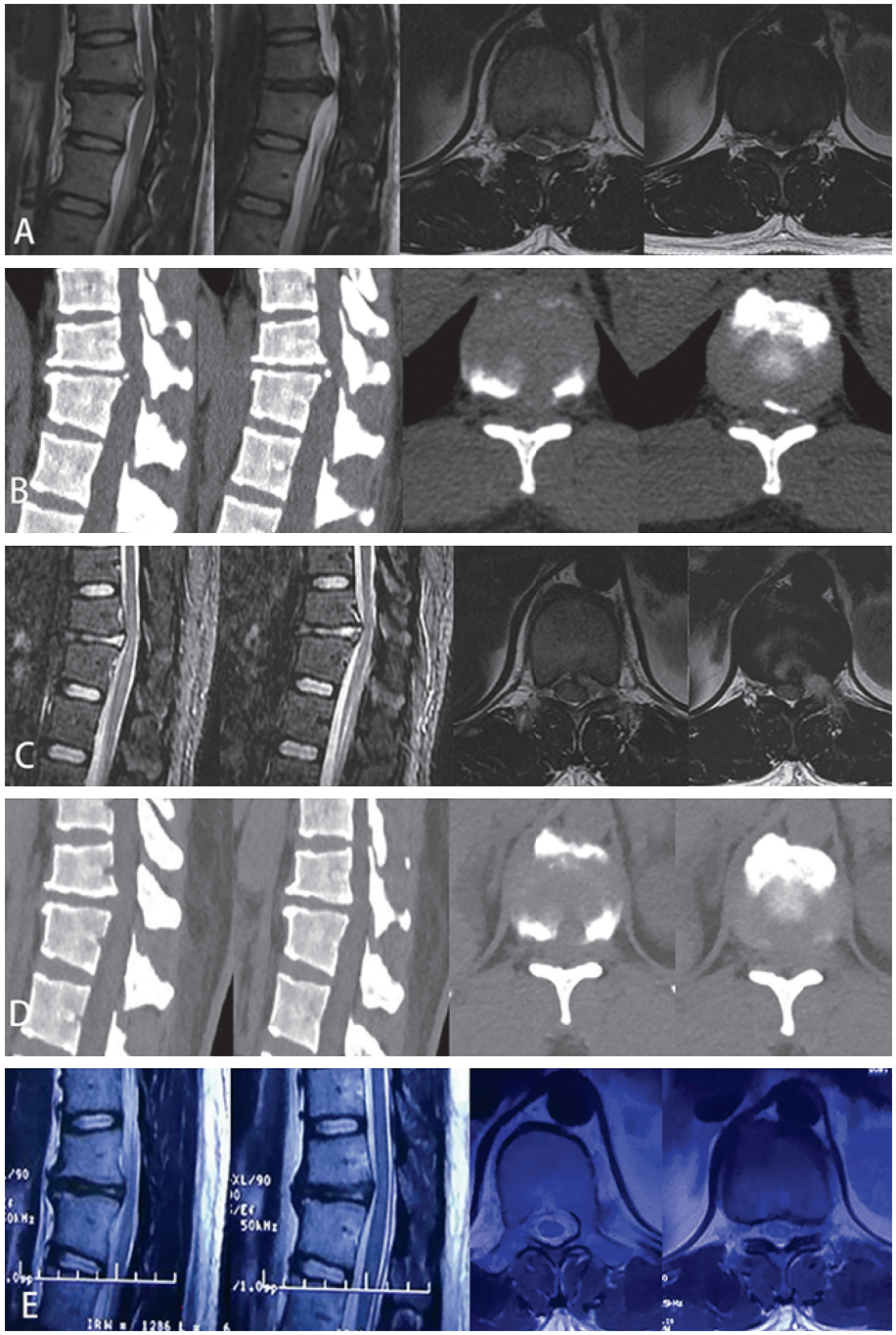


Figure 6: Preoperative MRI (a) and CT (b) scan showing spinal cord compression by calcified disc herniation and posterior vertebral osteophyte at T11-T12 (case 3). Postoperative MRI (c) and CT scan (d) showing sufficient decompression of the spinal cord and the calcified disc was cut off clearly. MRI at the 3-month follow-up (e) showing the spinal cord surrounded by cerebrospinal fluid.

3. Results

All patients in this study successfully underwent surgery as described. Follow-up was available for all of the patients, and it ranged from 13 months to 24 months (average: 15 months). Postoperative MRI imaging revealed good decompression of the spinal cord in all 11 patients.

Intraoperative blood loss was not measured due to continuous fluid irrigation. However, no patient required any intra or postoperative blood transfusion. There were no serious complications such as nerve injury, infection, or hematoma. The average operation time was 136 minutes (range: 70–180 minutes). The average length of hospital stay was 5.3 days (range: 2–8 days). The mJOA improved from 7.4

Table 2: Operative data, length of hospital stay, and pre and postoperative mJOA and VAS assessed at the last follow-up.

No. of patients	Operation time (mins)	Hospital stay (days)	mJOA		Axial VAS		Leg or thoracic radicular VAS	
			Pre-op	Post-op	Pre-op	Post-op	Pre-op	Post-op
1	70	7	10	11	4	1	6	0
2	160	5	6	10	3	1	0	0
3	120	7	9	11	3	3	6	2
4	95	7	6	9	0	2	3	0
5	180	8	8	10	0	0	5	0
6	180	8	5	9	2	2	3	1
7	80	4	7	9	0	0	0	0
8	170	4	9	11	3	2	2	0
9	160	3	6	10	4	1	3	2
10	130	2	8	11	2	0	3	0
11	150	3	7	11	2	0	3	0

(range 5–10) preoperatively to 10.2 (range 9–11) at the last follow-up. Axial thoracic pain improved in 8 of 9 patients with this symptom. Leg pain and thoracic radicular pain improved in all of the patients with this symptom (Table 2).

4. Discussion

Because of the underlying anatomy, ventral decompression of the thoracic spinal canal is a technical challenge. Open decompression inflicts great trauma, has a high rate of complications, and possibly requires additional internal fixation [4, 7, 8]. With the improvement of minimally invasive surgery, video-assisted thoracoscopic surgery, microendoscopic surgery, and full-endoscopic surgery have achieved satisfactory clinical outcomes and fewer complications in the treatment of TDH [15–17]. In this retrospective clinical study, we introduced a modified full-endoscopic ventral decompression technique for TDH. The imaging and clinical results were satisfactory. Postoperative MRI imaging in all cases showed sufficient decompression of the spinal cord. MRI also showed the presence of cerebrospinal fluid between the spinal cord and the dura. mJOA and VAS were improved in all cases except 1 case of axial thoracic pain. Similar surgical techniques and findings have been presented in some previous reports [18–22].

We have made some modifications to the previously reported transforaminal endoscopic ventral decompression techniques. In the punching procedure, we used a dilator downward sliding technology instead of the needle targeting puncture technique to avoid neurovascular injury and pleural injury. Pulmonary complications are one of the troublesome complications of thoracic spine surgeries. Entering the thoracic cavity is the immediate cause, which is more likely to occur in the anterior approach [23, 24]. Although no such complication has been reported for transforaminal endoscopic surgery, we believe that this potential risk exists.

In the foraminoplasty procedure, we used a high-speed diamond burr and a Kerrison rongeur under an endoscopic view instead of a circular saw or bone drill under fluoroscopy to avoid spinal cord injury and to preserve the stability of the spinal posterior column as much as possible. Hua et al. applied this similar technique in lumbar surgery. The neurological complication rate was 1.4%, which is much lower than for traditional PTED surgery (12.4%) [25]. In the establishment of the working channel procedure, we used the "step-by-step" technique instead of the "one-step" technique [19, 21] to avoid any iatrogenic pressure on the spinal canal during the working channel insertion. Wagner et al. applied this working channel establishing technique to a 31-year-old female with T8-9 disc herniation. The imaging and clinical outcomes were excellent [20]. We also reported the sequence applied for endoscopic decompression. Rutten et al. reported a similar technique called "box-shaped" [26]. However, there are some differences. First, for central calcified discs, it is difficult to resect the base directly with the burr because of the obstruction of the spinal cord. A strong pair of forceps needs to reach the safe triangle zone to complete the bone resection. Second, clear exposure of the safe triangle zone before bone resection can help us accurately judge the boundary of resection and the distance from the spinal cord. As far as we know, this is the first time anyone has described the concept of the "safe triangle zone."

The clinical outcomes in this trial are similar to those in previous reports. Guo et al. reported 6 cases of symptomatic TDH. The mJOA improved from 4.4 preoperatively to 6.6 one year after surgery [19]. Choi et al. presented a mean VAS improvement from 6.5 to 3.0 for back pain and 5.8 to 2.5 for leg pain. However, only patients with soft disc herniations were included [27]. Rutten et al. reported a 20% (5/25) rate of complications including 1 dural tear, 1 epidural hematoma, 2 transient intercostal neuralgias, and 1 deterioration of myelopathy [28]. In our previous research on the endoscopic surgery for thoracic OLF, we found complications such as neck pain and dural tear [29]. However, no complication was observed in this study or in Choi and Guo's. This may be due to the small sample size.

Because of the low incidence rate of TDH, this study is limited by its small sample size. It is not sufficient to show that this method is a safe and effective surgical technique. Larger controlled studies are warranted. Long-term follow-up and analysis will be required in the future.

5. Conclusion

Full-endoscopic transforaminal ventral decompression for the treatment of symptomatic thoracic disc herniation with or without calcification is feasible and may be another option for this challenging spine disease.

Abbreviations

mJOA: Modified Japanese Orthopedic Association
MRI: Magnetic resonance imaging
VAS: Visual analogue scale
LDH: Lumbar disc herniation
OLF: Ossification of the ligamentum flavum
PTED: Percutaneous transforaminal endoscopic lumbar discectomy.

Data Availability

The data generated or analyzed during this study are included in the article.

Disclosure

This study was performed at Hebei General Hospital.

Conflicts of Interest

The authors declared no potential conflicts of interest for the research, authorship, and publication of this article.

Authors' Contributions

Shangju Gao and Jingchao Wei contributed equally to this work. All authors reviewed the original study data, reviewed the data analysis, and approved the final paper, and all authors are responsible for archiving the study files.

Acknowledgments

The authors thank Miss Hua Wan for assistance with the patients' follow-up. The research was supported by the Key Researches of Medical Science in Hebei Province and the Fundamental Researches of Medical Science in Hebei Province (20180004).

References

[1] H. Yoshihara, "Surgical treatment for thoracic disc herniation: an update," *Spine*, vol. 39, no. 6, pp. E406–E412, 2014.
[2] J. R. Dimar, K. R. Bratcher, S. D. Glassman, J. M. Howard, and L. Y. Carreon, "Identification and surgical treatment of primary thoracic spinal stenosis," *American Journal of Orthopedics (Belle Mead, N.J.)*, vol. 37, no. 11, pp. 564–568, 2008.
[3] J.-W. Hur, J.-S. Kim, and J.-H. Seung, "Full-endoscopic interlaminar discectomy for the treatment of a dorsal migrated thoracic disc herniati on: case report," *Medicine*, vol. 98, no. 22, Article ID e15541, 2019.
[4] R. Bransford, F. Zhang, C. Bellabarba, M. Konodi, and J. R. Chapman, "Early experience treating thoracic disc herniations using a modified transfacet pedicle-sparing decompression and fusion," *Journal of Neurosurgery: Spine*, vol. 12, no. 2, pp. 221–231, 2010.
[5] P. D. Le Roux, M. M. Haglund, and A. B. Harris, "Thoracic disc disease: experience with the transpedicular approach in twenty consecutive patients," *Neurosurgery*, vol. 33, no. 1, pp. 58–66, 1993.
[6] J. M. Simpson, C. P. Silveri, F. A. Simeone, R. A. Balderston, and H. S. An, "Thoracic disc herniation. re-evaluation of the posterior approach using a modified costotransversectomy," *Spine*, vol. 18, no. 13, pp. 1872–1877, 1993.
[7] D. J. Maiman, S. J. Larson, E. Luck, and A. El-Ghatit, "Lateral extracavitary approach tothe spine for thoracic disc herniation: report of 23 cases," *Neurosurgery*, vol. 14, no. 2, pp. 178–182, 1984.
[8] A. G. Brotis, A. Tasiou, K. Paterakis, C. Tzerefos, and K. N. Fountas, "Complications associated with surgery for thoracic disc herniation: a systematic review and network meta-analysis," *World Neurosurgery*, vol. 132, pp. 334–342, 2019.
[9] J. Xu, Y. Li, B. Wang et al., "Percutaneous endoscopic lumbar discectomy for lumbar disc herniation with modic changes via a transforaminal approach: a retrospective study," *Pain Physician*, vol. 22, no. 6, pp. E601–E608, 2019.
[10] T. Nakamae, Y. Fujimoto, K. Yamada et al., "Transforaminal percutaneous endoscopic discectomy for lumbar disc herniation in athletes under the local anesthesia," *Journal of Orthopaedic Science*, vol. 24, no. 6, pp. 1015–1019, 2019.
[11] Y. Chen, J.-X. Wang, B. Sun et al., "Percutaneous endoscopic lumbar discectomy in treating calcified lumbar intervertebral disc herniation," *World Neurosurgery*, vol. 122, pp. e1449–e1456, 2019.
[12] H. S. Kim, B. Paudel, J. S. Jang, K. Lee, S. H. Oh, and I. T. Jang, "Percutaneous endoscopic lumbar discectomy for all types of lumbar disc herniations (LDH) including severely difficult and extremely difficult LDH cases," *Pain Physician*, vol. 21, no. 4, pp. E401–E408, 2018.
[13] X. Dabo, C. Ziqiang, Z. Yinchuan et al., "The clinical results of percutaneous endoscopic interlaminar discectomy (PEID) in the treatment of calcified lumbar disc herniation: a case-control study," *Pain Physician*, vol. 19, no. 2, pp. 69–76, 2016.
[14] J. Zhang, L. Wang, J. Li, P. Yang, and Y. Shen, "Predictors of surgical outcome in thoracic ossification of the ligamentum flavum: focusing on the quantitative signal intensity," *Scientific Reports*, vol. 6, no. 1, p. 23019, 2016.
[15] İ. Yüce, O. Kahyaoğlu, H. A. Çavuşoğlu, H. Çavuşoğlu, and Y. Aydın, "Midterm outcome of thoracic disc herniations that were treated by microdiscectomy with bilateral decompression via unilateral approach," *Journal of Clinical Neuroscience*, vol. 58, pp. 94–99, 2018.
[16] G. Bordon and S. Burguet Girona, "Experience in the treatment of thoracic herniated disc using image-guided thoracoscopy," *Revista Española de Cirugía Ortopédica y Traumatología*, vol. 61, no. 2, pp. 124–129, 2017.
[17] M. Bydon and Z. Gokaslan, "Minimally invasive approaches in the treatment of thoracic disk herniation," *World Neurosurgery*, vol. 81, no. 5-6, pp. 717-718, 2014.
[18] W. Liu, L. Yao, X. Li et al., "Percutaneous endoscopic thoracic discectomy via posterolateral approach: a case report of migrated thoracic disc herniation," *Medicine*, vol. 98, no. 41, Article ID e17579, 2019.
[19] C. Guo, D. Zhu, Q. Kong et al., "Transforaminal percutaneous endoscopic decompression for lower thoracic spinal stenosis," *World Neurosurgery*, vol. 128, pp. e504–e512, 2019.

[20] R. Wagner, A. E. Telfeian, M. Iprenburg et al., "Transforaminal endoscopic foraminoplasty and discectomy for the treatment of a thoracic disc herniation," *World Neurosurgery*, vol. 90, pp. 194–198, 2016.

[21] Z. Xiaobing, L. Xingchen, Z. Honggang et al., ""U" route transforaminal percutaneous endoscopic thoracic discectomy as a new treatment for thoracic spinal stenosis," *International Orthopaedics*, vol. 43, no. 4, pp. 825–832, 2019.

[22] S. Paolini, S. Tola, P. Missori, V. Esposito, and G. Cantore, "Endoscope-assisted resection of calcified thoracic disc herniations," *European Spine Journal*, vol. 25, no. 1, pp. 200–206, 2016.

[23] E. T. Hurley, A. B. Maye, M. Timlin, and F. G. Lyons, "Anterior versus posterior thoracic discectomy: a systematic review," *Spine*, vol. 42, no. 24, pp. E1437–E1445, 2017.

[24] H. Yoshihara and D. Yoneoka, "Comparison of in-hospital morbidity and mortality rates between anterior and non-anterior approach procedures for thoracic disc herniation," *Spine*, vol. 39, no. 12, pp. E728–E733, 2014.

[25] W. Hua, Y. Zhang, X. Wu et al., "Full-endoscopic visualized foraminoplasty and discectomy under general anesthesia in the treatment of L4-L5 and L5-S1 disc herniation," *Spine*, vol. 44, no. 16, pp. E984–E991, 2019.

[26] S. Ruetten, P. Hahn, S. Oezdemir, X. Baraliakos, G. Godolias, and M. Komp, "Operation of soft or calcified thoracic disc herniations in the full-endoscopic uniportal extraforaminal technique," *Pain Physician*, vol. 21, no. 4, pp. E331–E340, 2018.

[27] K. Y. Choi, S. S. Eun, S. H. Lee, and H. Y. Lee, "Percutaneous endoscopic thoracic discectomy; transforaminal approach," *Minimally Invasive Neurosurgery*, vol. 53, no. 1, pp. 25–28, 2010.

[28] S. Ruetten, P. Hahn, S. Oezdemir et al., "Full-endoscopic uniportal decompression in disc herniations and stenosis of the thoracic spine using the interlaminar, extraforaminal, or transthoracic retropleural approach," *Journal of Neurosurgery: Spine*, vol. 29, no. 2, pp. 157–168, 2018.

[29] W. Li, S. Gao, L. Zhang, C. Cao, and J. Wei, "Full-endoscopic decompression for thoracic ossification of ligamentum flavum: surgical techniques and clinical outcomes: a retrospective clinical study," *Medicine*, vol. 99, no. 44, Article ID e22997, 2020.

Hindawi
Pain Research and Management
Volume 2021, Article ID 2142964, 9 pages
https://doi.org/10.1155/2021/2142964

Review Article

Surgical Procedures Used for Correction of Scheuermann's Kyphosis: A Meta-Analysis

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Received 15 September 2021; Accepted 9 October 2021; Published 23 October 2021

Academic Editor: Sidong Yang

Objectives. Scheuermann's kyphosis can cause severe back pain and cosmetic disorders to patients. Previous studies on surgical procedure selection for correction of Scheuermann's kyphosis have drawn controversial conclusions. Here, a meta-analysis was performed to figure out a better way between anterior-posterior (AP) combined procedures and posterior-only (PO) procedures. *Methods*. We searched PubMed database and Ovid database, as well as Cochrane Library (between January 2009 and December 2020, around recent ten years), for studies reporting Scheuermann's kyphosis correction in an anterior way or a posterior way. Random effects meta-analysis regarding correction degrees and incidence of proximal junctional kyphosis (PJK) was performed. *Results*. Finally, 13 unique studies including 586 patients (AP: 300; PO: 286) were identified and included for this meta-analysis. Overall, 6 AP cohorts and 10 PO cohorts were pooled regarding the correction degrees of kyphosis in the analysis, respectively. Pooled correction degrees in AP cohorts were 33.31 (95% CI: 27.48–39.15; $I^2 = 86\%$, $P < 0.001$) and in PO cohorts were 31.16 (95% CI: 26.97–35.35; $I^2 = 81.1\%$, $P < 0.001$). Comparison of correction between AP and PO cohorts did not indicate any significant difference. Likewise, postoperative PJK incidence showed no difference. Back pain can be caused by both AP and PO procedures, but which causes less pain remains to be conclusive. The PO approach showed less blood loss and shorter surgical duration as compared to the AP approach. *Conclusions*. In summary, this meta-analysis shows similar treatment effects between AP and PO procedures in correcting Scheuermann's kyphosis, suggesting the advantage of PO procedures due to less blood loss and surgical duration. However, the postoperative complications PJK and distal junctional kyphosis (DJK) cannot be well concluded due to the limitation of existing data.

1. Introduction

Scheuermann's kyphosis (SK) is a rigid developmental thoracic kyphosis, which can cause severe back pain and cosmetic disorders to patients [1, 2]. Although conservative treatment measures are initially applied, surgical treatment is indicated for kyphosis that is over 70–75 degrees, with significant pain that has not responded to conservative management, and/or respiratory problems due to severe kyphosis, and neurological issues [3–5]. The surgical treatment consists of two different ways; one is the combined anterior-posterior approach (AP) and the other is a posterior-only way (PO), with various types of anchors [6, 7].

However, previous studies on surgical procedure selection for correction of SK have drawn contradictory conclusions. It was reported that a sufficient correction can be achieved by the PO approach, but the AP approach was more likely to get into a satisfying correction [8]. By contrast, a comparative study reported that the PO approach was more successful with a lower incidence of complications, as compared to the AP approach [9]. Interestingly, Koller et al. [10] found that both approaches achieved similar degrees of correction with higher fusion level in the PO group, after comparing the AP with PO procedures in correcting kyphosis.

Considering the controversy stated above, in this study, a meta-analysis was performed in order to figure out a better way between AP and PO procedures in treating SK patients.

2. Materials and Methods

2.1. Ethical Statement. The ethical approval was waived because all analyses were based on previously published studies.

2.2. Literature Search. We searched PubMed database and Ovid database, as well as Cochrane Library (between January 2009 and December 2020, around recent ten years), for studies reporting SK correction in an anterior way or a posterior way. Articles should be written and published in English. Literature search for studies of interest should include the following terms: (1) Scheuermann's kyphosis AND posterior fusion or (2) Scheuermann's kyphosis AND anterior fusion.

2.3. Inclusion Criteria. All included studies should have at least reported the outcome of kyphosis correction, recruiting a cohort of Scheuermann's disease patients who underwent AP surgery or PO surgery, regardless of comparative or noncomparative studies. Here, we focus on studies of surgical procedure selection for correction of SK based on the effect of kyphosis correction.

2.4. Data Extraction. First, all related article titles and abstracts were screened and only original research was included. Second, full-length relevant articles were intensively read and checked in detail. At last, baseline information was extracted, as well as the raw data regarding follow-up time, patient age, sex distribution, sample size, Cobb angle, correction degrees, correction rate, blood loss, surgical duration, and postoperative complications including proximal junctional kyphosis (PJK) and distal junctional kyphosis (DJK).

2.5. Quality Assessment of Included Studies. All included studies in this meta-analysis were retrospective case-control studies or observational cohort studies. Thus, Newcastle–Ottawa quality assessment scale (9 points) was suitable for quality assessment and used to evaluate the quality of included studies [11].

2.6. Measures of Treatment Effect. Both continuous and dichotomous outcomes were generated in this study. Weighted mean difference (WMD) and 95% confidence interval (CI) were generated for continuous outcomes. Also, the odds ratio (OR) and 95% CI were calculated for dichotomous outcomes.

2.7. Assessment of Heterogeneity. Distributed as χ^2 statistics, Q statistics was used to evaluate heterogeneity, with its P values revealed by the forest plot. The heterogeneity test was considered statistically significant when $P < 0.10$. Simultaneously, I^2 was used to estimate the size of the heterogeneity. $I^2 > 50\%$ indicated considerable heterogeneity among the included studies, and then a random effects analysis should be performed in meta-analysis.

2.8. Test for Risk of Publication Bias. Funnel plot was not performed to determine risk of publication bias due to the small number of included studies. Begg's and Egger's tests were used to assess the publication bias.

2.9. Statistical Analysis. All data analyses were conducted with software STATA 12.0 (Stata Corporation, College Station, TX, USA). Random effects meta-analysis regarding correction degrees and incidence of PJK was performed. Heterogeneity was assessed by I^2 statistic. P values were set at 0.10 as significant in assessment of heterogeneity, Begg's test, and Egger's test [12, 13]. In the rest of all, $P < 0.05$ was regarded as statistically significant. All P values were presented as two-tailed.

3. Results

3.1. Literature Search. As presented in Figure 1, after database search, there were 95 relevant papers included in the first-round literature selection. After study selection, 13 unique studies [4, 6, 10, 14–22] including 586 patients (AP: 300; PO: 286) were identified and included for this meta-analysis. Overall, 6 AP cohorts and 10 PO cohorts were pooled regarding the correction degrees of kyphosis in the analysis, respectively. Three reports were excluded due to unavailability of raw data [23–25].

3.2. Quality Assessment of Included Studies. A summary of quality assessment for each included study is shown in Table 1. Overall, three studies scored 7 points, eight scored 8 points, and two scored 9 points. The methodological quality of all included studies was found to be relatively high.

3.3. Characteristics of Included Studies. As shown in Tables 2–4, we extracted baseline information and relevant raw data regarding follow-up time, patient age, sex distribution, sample size, Cobb angle, correction degrees, correction rate, blood loss, surgical duration, and postoperative complications including PJK and DJK. All studies were retrospective in design. Follow-up time ranged from 22.8 months to 216 months. Patient age was between 11 and 44 ± 8 years. Also, most patients were males.

3.4. Pooled Analysis of Kyphosis Correction. As shown in Figure 2, six studies [6, 10, 16, 19, 21, 22] reported the correction effect by AP and were pooled into the meta-analysis. As a result, pooled correction degrees in AP cohorts were 33.31 (95% CI: 27.48–39.15; $I^2 = 86\%$, $P < 0.001$). Because the study (Koller et al. [10]) might have recruited in the AP cohort 46 patients that were included in another study (Koller et al. [19]), we have revised the pooled analysis of AP group with the study (Koller et al. [10]) excluded; then the pooled correction degrees in AP cohorts were 33.45 (95% CI: 25.97–40.92; $I^2 = 88.8\%$, $P < 0.001$).

As shown in Figure 3, nine studies [5, 6, 10, 14, 17, 21, 22] reported the correction effect by PO, and one [14] of the included studies reported two PO cohorts. Thus, totally ten PO cohorts were pooled into the meta-analysis. Pooled correction degrees in PO cohorts were 31.16 (95% CI: 26.97–35.35; $I^2 = 81.1\%$, $P < 0.001$).

As shown in Figure 4, only two studies [10, 21] compared the correction effect between AP and PO cohorts, and when

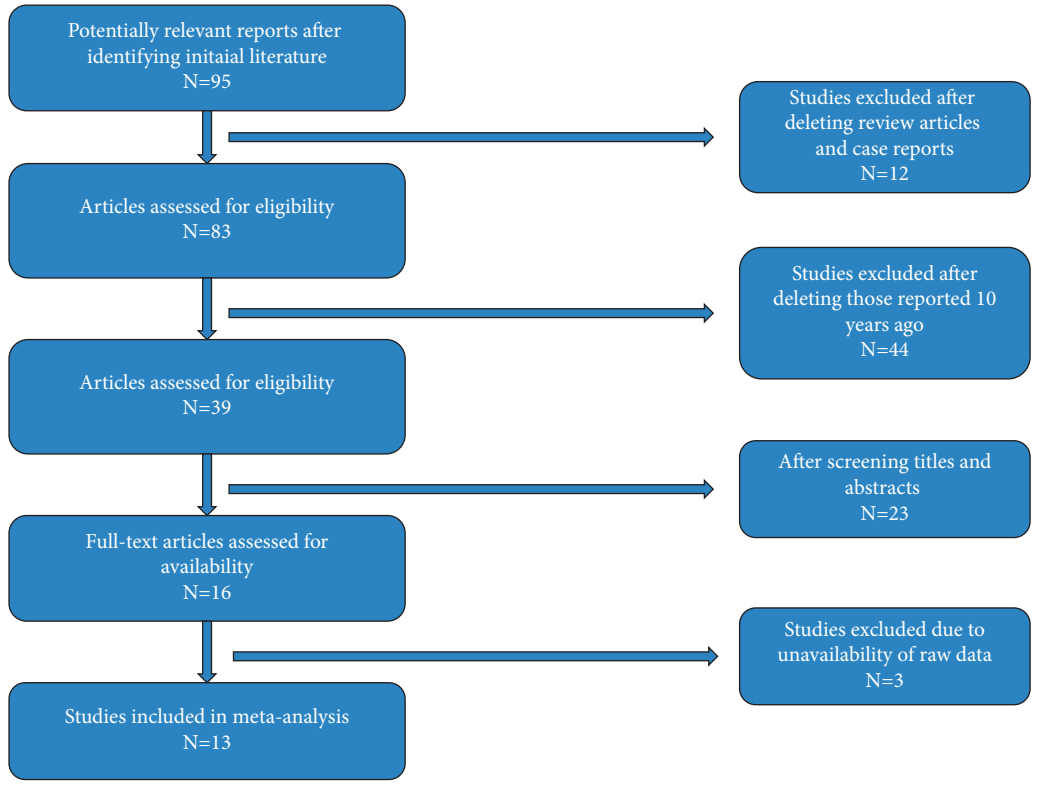


Figure 1: Flow diagram for study selection.

Table 1: Quality assessment of included studies by Newcastle–Ottawa Quality Assessment Scale.

Study	Selection	Comparability	Exposure	Total score
Dikici et al. [5]	3	2	3	8
Riouallon et al. [6]	3	2	3	8
Cobden et al. [4]	2	2	3	7
Graat et al. [18]	3	2	3	8
Etemadifar et al. [16]	4	2	3	9
Faldini et al. [17]	3	2	2	7
Koller et al. [10]	3	2	3	8
Koller et al. [19]	3	2	3	8
Behrbalk et al. [14]	2	2	3	7
Temponi et al. [21]	3	2	3	8
Tsutsui et al. [22]	3	2	3	8
Dasilvaherrero et al. [15]	3	2	3	8
Koptan et al. [20]	4	2	3	9

pooled together for further analysis, the comparison did not indicate any significant difference ($P > 0.05$).

Likewise, only two studies [16, 18] compared postoperative PJK incidence between AP and PO cohorts, and pooled analysis of PJK incidence showed no difference, as shown in Figure 5. Four studies [4, 5, 15, 18] have reported incidence of distal junctional kyphosis (DJK), but no studies compared the incidence of postoperative DJK between AP and PO cohorts. The PJK incidence was reported to range from 0% to 31%. Also, only two studies [16, 20] have reported the surgical data (blood loss and surgical duration), and clearly, the PO approach showed less blood loss and shorter surgical duration as compared to the AP approach.

3.5. Assessment of Pain. As some patients with kyphosis deformity suffer from back pain, we here also incorporated the pain assessment based on the available data. Among all studies included, 4 studies have assessed pain status change and recorded as visual analogue scale (VAS) score [6, 18, 20, 21]. Riouallon et al. [6] performed a comparative study including 131 patients, 79% cases undergoing correction surgeries because of severe back pain and 21% due to cosmetic disorders. They followed up 85 patients for more than one year after surgeries and found that most patients (81%) did not suffer postoperative back pain but 19% patients still suffered back pain of different degrees. Graat et al. [18] performed a long-term follow-up of 28

Table 2: Characteristics of included studies.

Study	Country	Study design	Follow-up (months)		Age (yrs)		Sex		No. of patients	
			AP	PO	AP	PO	M	F	AP	PO
Dikici et al. [5]	Turkey	Retrospective	—	36	—	18.6 ± 3.4	20	19	—	39
Riouallon et al. [6]	France	Retrospective	57	57	Overall: 23 ± 10		81	50	64	67
Cobden et al. [4]	Turkey	Retrospective	—	41	—	19 (15–36)	18	2	—	20
Graat et al. [18]	Netherlands	Cohort study	216	216	Overall: 44 ± 8		—	—	16	13
Etemadifar et al. [16]	Iran	Prospective	69.6	45.6	20.9 ± 5.3	19.3 ± 2.7	20	10	16	14
Faldini et al. [17]	Italy	Retrospective	—	25.2	—	19.6 (13–24)	—	—	—	20
Koller et al. [10]	Germany/US	Matched-pair study	—	—	23.6 ± 11.4	20.7 ± 10.4	—	—	46	46
Koller et al. [19]	Germany	Retrospective	24	—	23.6 ± 10.8	—	74	37	111	—
Behrbalk et al. [14]	UK	Retrospective	—	≥24	—	22 ± 8	8	2	—	10
Behrbalk et al. [14]	UK	Retrospective	—	≥24	—	19 ± 6	10	1	—	11
Temponi et al. [21]	Brazil	Case-control	37.5	22.8	19	27.3	22	6	19	9
Tsutsui et al. [22]	US	Retrospective	—	—	15.1 (13–17)	14.8 (11–19)	13	9	11	11
Dasilvaherrero et al. [15]	Brazil	Retrospective	—	65.8 ± 39.92	—	16.8 ± 2.89	7	3	—	10
Koptan et al. [20]	Egypt	Retrospective	≥24	≥24	16 ± 0.7	15 ± 0.6	12	21	17	16

AP, combined anterior-posterior approach; PO, posterior-only approach; OP, operation; M, male; F, female.

Table 3: Kyphosis correction of the patients included in all studies.

Study	Cobb angle (pre-op)		Cobb angle (post-op)		Correction (degree)		Correction rate	
	AP	PO	AP	PO	AP	PO	AP	PO
Dikici et al. [5]	—	73.3 ± 7.9	—	39 ± 8.7	—	—	—	46% ± 13
Riouallon et al. [6]	76 ± 23	78 ± 13	57 ± 21	61 ± 14	—	—	—	—
Cobden et al. [4]	—	79.8	—	44.9	—	—	—	—
Graat et al. [18]	85	79	62.1	65.6	—	—	27%	17%
Etemadifar et al. [16]	83.7 ± 8.1	81.9 ± 9.4	43 ± 7.5	43.2 ± 9.8	42.2	41.8	50.5%	51%
Faldini et al. [17]	—	78.6 ± 11.2	—	45.8 ± 4.4	—	—	—	—
Koller et al. [10]	75.9 ± 9.6	78.7 ± 10.1	43.4 ± 12.3	47.1 ± 11.7	33.7 ± 14.7	30.6 ± 12.4	—	—
Koller et al. [19]	67.2 ± 12.2	—	38.5 ± 14.8	—	28.9 ± 13.4	—	—	—
Behrbalk et al. [14] [1]	—	72 ± 7	—	43 ± 9	—	29 ± 9	—	—
Behrbalk et al. [14] [2]	—	78 ± 9	—	44 ± 8	—	34 ± 6	—	—
Temponi et al. [21]	77.6 ± 10.4	72.9 ± 12.0	35.8 ± 8.0	44.3 ± 9.8	41.7 ± 12	28.6 ± 6	53.2 ± 11.9	39.3 ± 7.8
Tsutsui et al. [22]	84.9 ± 10.2	82.7 ± 6.4	48.6 ± 5.7	47.9 ± 5.4	—	—	—	—
Dasilvaherrero et al. [15]	—	78.8 ± 7.59	—	47.5 ± 12.54	—	33.9 ± 9.53	—	43.25% ± 12.56%
Koptan et al. [20]	79.8 (65–98)	85.5 (69–102)	—	—	38.8 (37–45)	45.1 (40–49)	48.7%	52.2%

AP, combined anterior-posterior approach; PO, posterior-only approach; op, operation.

Table 4: Other information of the patients in all included studies.

Study	Blood loss (mL)		Surgical duration		PJK (case)		DJK (case)	
	AP	PO	AP	PO	AP	PO	AP	PO
Dikici et al. [5]	—	—	—	—	—	—	—	12 (31%)
Riouallon et al. [6]	—	—	—	—	—	—	—	—
Cobden et al. [4]	—	—	—	—	—	3 (15%)	—	3 (15%)
Graat et al. [18]	—	—	—	—	9	6	0	0
Etemadifar et al. [16]	1380	760	545.3 min	263.5 min	1	1	—	—
Faldini et al. [17]	—	—	—	—	—	—	—	—
Koller et al. [10]	—	—	—	—	—	—	—	—
Koller et al. [19]	—	—	—	—	—	—	—	—
Behrbalk et al. [14]	—	—	—	—	—	—	—	—
Temponi et al. [21]	—	—	—	—	—	—	—	—
Tsutsui et al. [22]	—	—	—	—	—	—	—	—
Dasilvaherrero et al. [15]	—	—	—	—	—	1	—	0
Koptan et al. [20]	910	620	315 min	215 min	—	—	—	—

AP, combined anterior-posterior approach; PO, posterior-only approach; op, operation; PJK, proximal junctional kyphosis; DJK, distal junctional kyphosis.

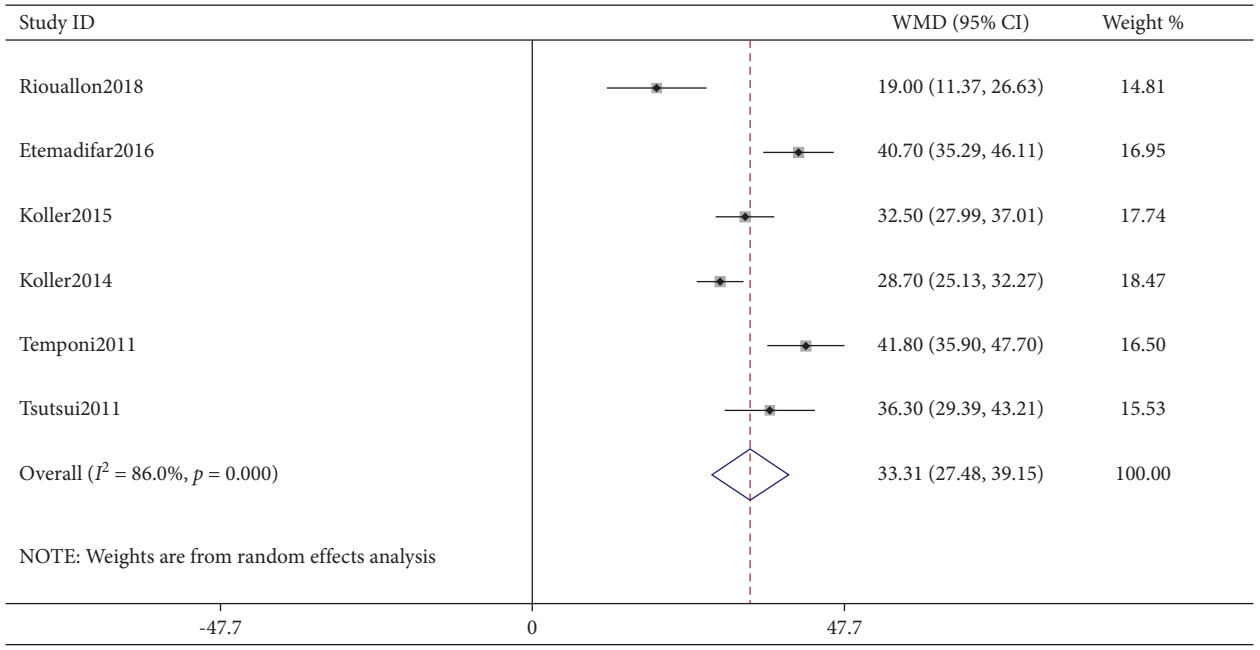


Figure 2: Forest plot of kyphosis correction by the combined anterior-posterior approach.

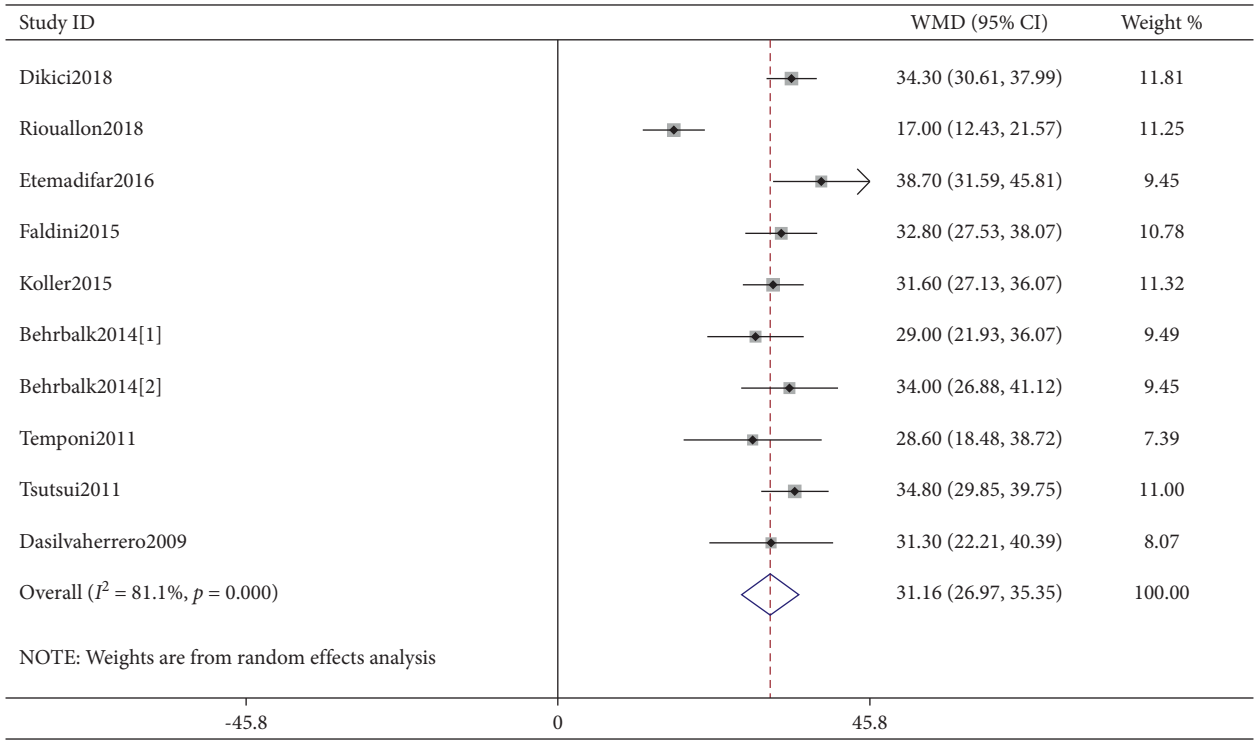


Figure 3: Forest plot of kyphosis correction by the posterior-only approach.

patients postsurgery and compared them regarding back pain; it was found that the AP group suffered less pain than the PO group, while Temponi et al. [21] reported the opposite result to that. Koptan et al. [20] reported that all patients complained of pain preoperatively but did not give further information.

3.6. Publication Bias Assessment. As shown in Figure 6, no publication bias was found relevant to correction of kyphosis in AP cohorts by Begg's rank correlation test and Egger's linear regression test (both $P > 0.10$). Likewise, Figure 7 showed no publication bias with regard to correction of kyphosis in PO cohorts (both $P > 0.10$).

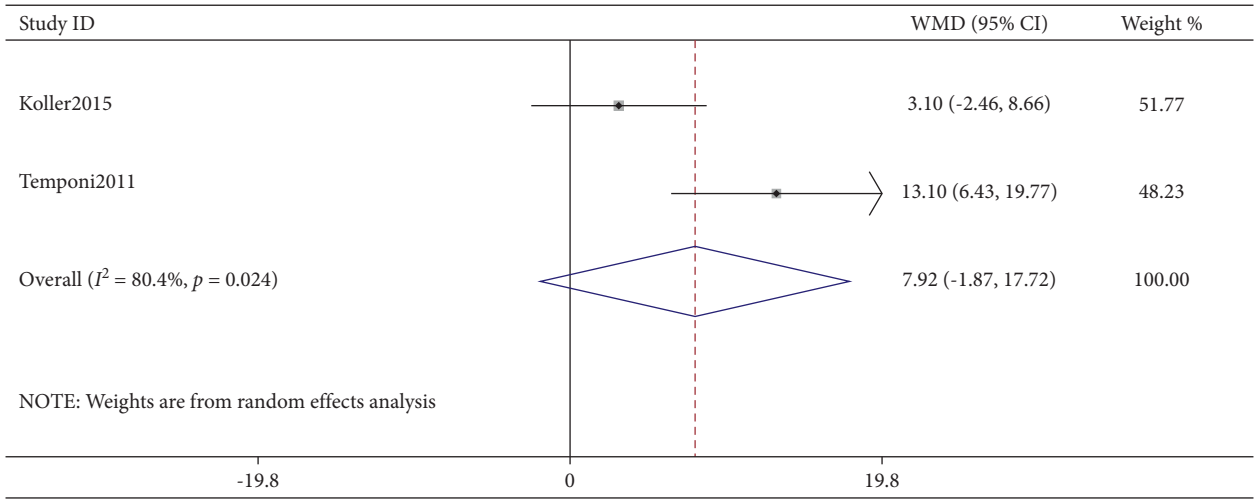


Figure 4: Comparison of kyphosis correction between the combined anterior-posterior approach and the posterior-only approach.

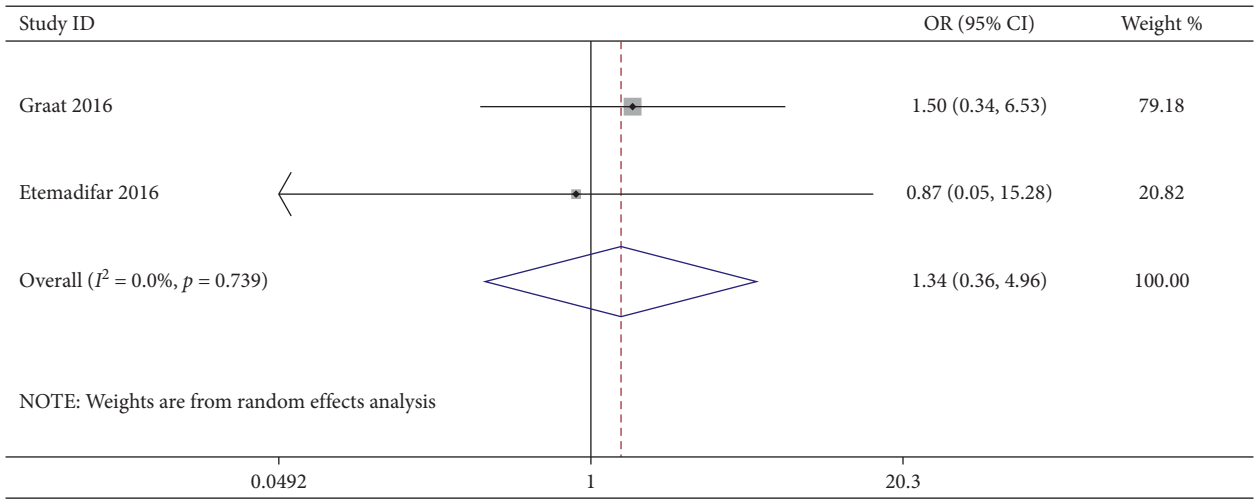
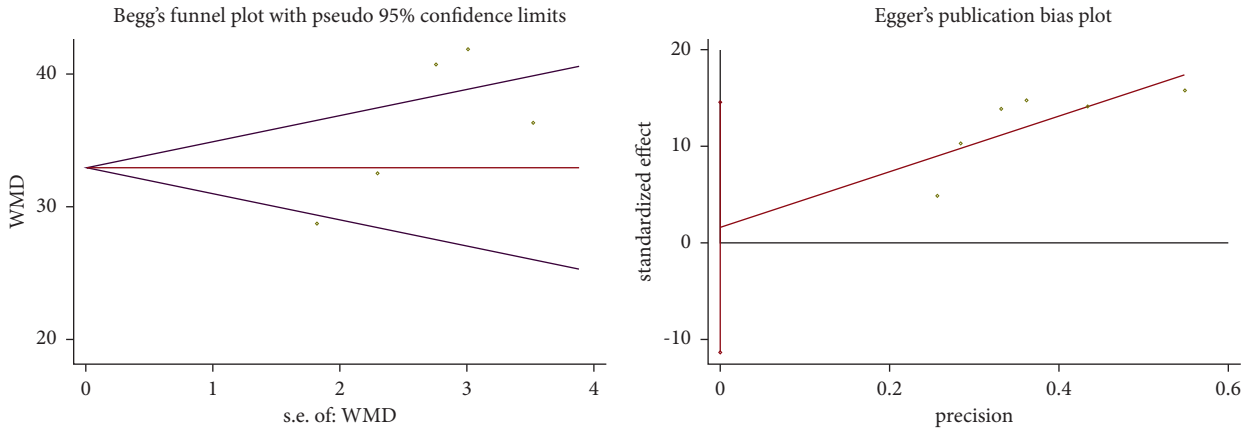


Figure 5: Comparison of proximal junctional kyphosis (PJK) incidence between the combined anterior-posterior approach and the posterior-only approach.

4. Discussion

To the best of our knowledge, the PO approach was the first surgical technique introduced to correct SK deformity and was first performed by Bradford in 1975 [4, 26]. Many clinical and radiological results have reported that PO fusion is an efficient technique for the treatment of SK [4, 6, 10, 14, 16, 17, 21]. Different methods have been introduced over the past few years, and combined AP fusion has been recommended more suitable for rigid and major deformities for many years [10, 19], but complication rates, operation time, and blood loss were significantly higher in AP procedures [16]. Nowadays, debates continue regarding surgical strategy selection between AP and PO fusion for the surgical management of SK [27].

In this study, we performed a meta-analysis in an effort to identify a better approach from AP and PO fusion procedures for correcting SK deformity. The research focus was on the correction effect reflected by achieving more correction degrees, and postoperative complications including PJK were also compared between the two groups, although DJK cannot be compared due to the lack of reports. In our study, six studies reported the correction effect by AP and were pooled into the meta-analysis. As a result, pooled correction effect in AP cohorts was 33.31 degrees (WMD, 95% CI: 27.48–39.15). In addition, nine studies reported the correction effect by PO, and one of them reported two PO cohorts. Thus, totally ten PO cohorts were pooled into the meta-analysis. Also, pooled correction effect in PO cohorts was 31.16 degrees (WMD, 95% CI: 26.97–35.35). Comparing the correction effect between the AP approach and the PO approach, there was no significant difference found although only two studies compared AP cohorts to PO cohorts ($P > 0.05$). Likewise, only two studies compared postoperative PJK incidence between AP and PO cohorts, and pooled analysis of PJK incidence showed no difference.



Tests for Publication Bias

Begg's Test

adj. Kendall's Score (P-Q) = 1
Std. Dev. of score = 5.32
Number of Studies = 6
z = 0.19
Pr > |z| = 0.851
z = 0.00 (continuity corrected)
Pr > |z| = 1.000 (continuity corrected)

Egger's test

Std_Eff	Coef.	Std. Err.	t	p>|t|	[95% Conf.	Interval]
slope	28.81027	12.22735	2.36	0.078	−5.138296	62.75883
bias	1.628813	4.679757	0.35	0.745	−11.36428	14.6219

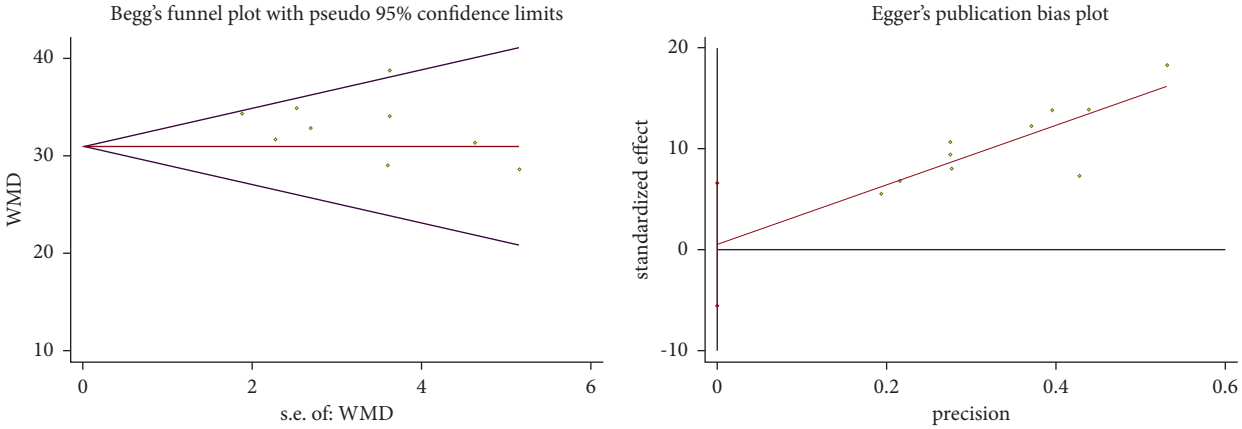
Figure 6: Publication bias analysis by Begg's and Egger's tests regarding the combined anterior-posterior approach.

Unfortunately, there were no studies having compared the incidence of postoperative DJK between AP and PO cohorts, though four studies have demonstrated DJK incidence ranging from 0% to 31%. Also, only two studies have reported the surgical data (blood loss and surgical duration), and apparently, the PO approach showed less blood loss and shorter surgical duration.

A previous meta-analysis [7] has revealed that the pooled correction loss of Cobb angle for the AP group was 4.1 (95% CI: 3.4–4.8), and for the PO group, it was 3.8 (95% CI: 3.3–4.4), without any significant difference indicated by the results. This report is consistent with our meta-analysis results that there was no difference with regard to the change of Cobb angle before and after surgery between the AP group and the PO group. Moreover, it was reported that the PO group showed advantages in blood loss, surgery time, and junctional kyphosis [7]. It was in line with our results that the PO group showed less blood loss and shorter surgery duration. Our analytical results, however, did not indicate any difference regarding the postoperative PJK incidence due to the lack of raw data that were available. That meta-analysis has included a wide range of studies that were published between 1964 and 2012, and those studies varied too much, especially considering that the surgical techniques are ongoing in progress. To overcome the shortcomings, we only included eligible studies published between 2009 and 2020, within around recent ten years. Seven new published articles [4, 6, 10, 16–18] have been included in our meta-analysis, which is a helpful update to that previous meta-analysis [7]. Recently, another meta-analysis showed that PO surgery and AP surgery achieved comparable treatment effects of SK disease, which is consistent with our results [28]. However, that study goes with the limitations that most of the studies included were published ten years ago, and thus that meta-analysis missed some important up-to-date literature.

As to publication bias assessment in this study, there were no publication bias found relating to correction of kyphosis in AP cohorts by Begg's rank correlation test and Egger's linear regression test (both $P > 0.10$). Likewise, it also showed no publication bias with regard to the correction of kyphosis in PO cohorts (both $P > 0.10$). Thus, this meta-analysis is in a good quality in terms of publication bias.

However, we have to demonstrate some potential limitations that may exist in this work. To start with, only English-written studies were selected and included in this meta-analysis, potentially excluding some relevant reports written in other languages, due to a language limitation. Additionally, the number of patients included in both groups was relatively small (AP: 300 vs. PO: 286), which cannot be neglected in the interpretation of findings in this meta-analysis. At last, all included studies in the pooled



Tests for Publication Bias

Begg's Test

adj. Kendall's Score (P-Q) = −7
Std. Dev. of Score = 11.18
Number of Studies = 10
z = −0.63
Pr > |z| = 0.531
z = 0.54 (continuity corrected)
Pr > |z| = 0.592 (continuity corrected)

Egger's test

Std_Eff	Coef.	Std. Err.	t	p>|t|	[95% Conf.	Interval]
slope	29.52363	7.41756	3.98	0.004	12.4187	46.62855
bias	.5211755	2.639498	0.20	0.848	−5.565518	6.607869

Figure 7: Publication bias analysis by Begg's and Egger's tests regarding the posterior-only approach.

analysis were retrospective in design and most are non-comparative studies, thus might reduce the power of this work.

5. Conclusions

In summary, this meta-analysis shows similar treatment effects between AP and PO procedures in correcting Scheuermann's kyphosis, suggesting the advantage of PO procedures due to less blood loss and surgical duration. However, the postoperative complications PJK and DJK cannot be well concluded due to the limitation of existing reports.

Abbreviations

AP: Anterior-posterior
CI: Confidence interval
DJK: Distal junctional kyphosis
OR: Odds ratio
PJK: Proximal junctional kyphosis
PO: Posterior-only
SK: Scheuermann's kyphosis
WMD: Weighted mean difference.

Data Availability

The data used in this study are all included within this article and open to all readers.

Conflicts of Interest

All authors declare no conflicts of interest regarding this study.

References

[1] S. Wang, L. Xu, and M. Wang, "Contribution of postoperative vertebral remodeling to reversal of vertebral wedging and prevention of correction loss in patients with adolescent Scheuermann's kyphosis," *Journal of Neurosurgery. Spine*, vol. 2021, pp. 1–9, 2021.

[2] L. Vital, B. Nunes, S. A. Santos, V. Veludo, F. Serdoura, and A. Pinho, "Sagittal plane alignment and functional outcomes following surgery for scheuermann kyphosis," *Revista brasileira de ortopedia*, vol. 56, no. 4, pp. 446–452, 2021.

[3] V. Arlet and D. Schlenzka, "Scheuermann's kyphosis: surgical management," *European Spine Journal: Official Publication of the European Spine Society*, vol. 14, no. 9, pp. 817–827, 2005.

[4] A. Cobden, A. Albayrak, Y. Camurcu, H. Sofu, T. Tacal, and M. A. Kaygusuz, "Posterior-only approach with pedicle screws for the correction of Scheuermann's kyphosis," *Asian spine journal*, vol. 11, no. 4, pp. 513–519, 2017.

[5] F. Dikici, T. Akgul, and K. Sariyilmaz, "Selection of distal fusion level in terms of distal junctional kyphosis in Scheuermann kyphosis. A comparison of 3 methods," *Acta Orthopaedica et Traumatologica Turcica*, vol. 52, no. 1, pp. 7–11, 2018.

[6] G. Riouallon, C. Morin, and Y. P. Charles, "Posterior-only versus combined anterior/posterior fusion in Scheuermann disease: a large retrospective study," *European Spine Journal*, vol. 27, no. 9, pp. 2322–2330, 2018.

[7] C. Yun and C. L. Shen, "Anterior release for Scheuermann's disease: a systematic literature review and meta-analysis," *European Spine Journal*, vol. 26, no. 3, pp. 921–927, 2017.

[8] D. S. Bradford, K. B. Ahmed, J. H. Moe, R. B. Winter, and J. E. Lonstein, "The surgical management of patients with Scheuermann's disease: a review of twenty-four cases managed by combined anterior and posterior spine fusion," *The Journal of Bone and Joint Surgery*, vol. 62, no. 5, pp. 705–712, 1980.

[9] S. S. Lee, L. G. Lenke, and T. R. Kuklo, "Comparison of Scheuermann kyphosis correction by posterior-only thoracic pedicle screw fixation versus combined anterior/posterior fusion," *Spine*, vol. 31, no. 20, pp. 2316–2321, 2006.

[10] H. Koller, L. G. Lenke, and O. Meier, "Comparison of anteroposterior to posterior-only correction of Scheuermann's kyphosis: a matched-pair radiographic analysis of 92 patients," *Spine deformity*, vol. 3, no. 2, pp. 192–198, 2015.

[11] F. Y. Liu, S. D. Yang, L. S. Huo, T. Wang, D. L. Yang, and W. Y. Ding, "Laminoplasty versus laminectomy and fusion for multilevel cervical compressive myelopathy: a meta-analysis," *Medicine*, vol. 95, no. 23, p. e3588, 2016.

[12] J. Yang, X. Hu, Q. Zhang, H. Cao, J. Wang, and B. Liu, "Homocysteine level and risk of fracture: a meta-analysis and systematic review," *Bone*, vol. 51, no. 3, pp. 376–382, 2012.

[13] S. D. Yang, Q. Chen, and H. K. Wei, "Bone fracture and the interaction between bisphosphonates and proton pump inhibitors: a meta-analysis," *International Journal of Clinical and Experimental Medicine*, vol. 8, no. 4, pp. 4899–4910, 2015.

[14] E. Behrbalk, O. Uri, R. M. Parks, M. P. Grevitt, M. Rickert, and B. M. Boszczyk, "Posterior-only correction of Scheuermann kyphosis using pedicle screws: economical optimization through screw density reduction," *European Spine Journal*, vol. 23, no. 10, pp. 2203–2210, 2014.

[15] C. F. da Silva Herrero, M. A. Porto, M. H. Barbosa, and H. L. Defino, "Multiple segmental osteotomies to the KYPHOSIS correction," *Revista Brasileira de Ortopedia*, vol. 44, no. 6, pp. 513–518, 2009.

[16] M. Etemadifar, A. Ebrahimzadeh, A. Hadi, and M. Feizi, "Comparison of Scheuermann's kyphosis correction by combined anterior-posterior fusion versus posterior-only procedure," *European Spine Journal*, vol. 25, no. 8, pp. 2580–2586, 2016.

[17] C. Faldini, F. Traina, F. Perna, R. Borghi, K. Martikos, and T. Greggi, "Does surgery for Scheuermann kyphosis influence sagittal spinopelvic parameters," *European Spine Journal*, vol. 24, pp. 893–897, 2015.

[18] H. C. Graat, J. J. Schimmel, R. J. Hoogendoorn, L. van Hessem, A. Hosman, and M. de Kleuver, "Poor radiological and good functional long-term outcome of surgically treated scheuermann patients," *Spine*, vol. 41, no. 14, pp. E869–E878, 2016.

[19] H. Koller, Z. Juliane, M. Umstaetter, O. Meier, R. Schmidt, and W. Hitzl, "Surgical treatment of Scheuermann's kyphosis using a combined antero-posterior strategy and pedicle screw constructs: efficacy, radiographic and clinical outcomes in 111 cases," *European Spine Journal*, vol. 23, no. 1, pp. 180–191, 2014.

[20] W. M. Koptan, Y. H. Elmiligui, and H. B. Elsebaie, "All pedicle screw instrumentation for Scheuermann's kyphosis correction: is it worth it," *The Spine Journal: Official Journal of the North American Spine Society*, vol. 9, no. 4, pp. 296–302, 2009.

[21] E. F. Temponi, R. D. de Macedo, L. O. Pedrosa, and B. P. Fontes, "SCHEUERMAN'S KYPHOSIS: comparison between the posterior approach associated with smith-petersen osteotomy and combined anterior-posterior FUSION," *Revista brasileira de ortopedia*, vol. 46, no. 6, pp. 709–717, 2011.

[22] S. Tsutsui, J. B. Pawelek, T. P. Bastrom, S. A. Shah, and P. O. Newton, "Do discs "open" anteriorly with posterior-only correction of Scheuermann's kyphosis," *Spine*, vol. 36, no. 16, pp. E1086–E1092, 2011.

[23] A. Ashraf, A. Noelle Larson, D. W. Polly, G. Ferski, K. J. Guidera, and C. H. Mielke, "Change in sagittal plane alignment following surgery for Scheuermann's kyphosis," *Spine deformity*, vol. 2, no. 5, pp. 404–409, 2014.

[24] J. D. Coe, J. S. Smith, and S. Berven, "Complications of spinal fusion for scheuermann kyphosis: a report of the scoliosis research society morbidity and mortality committee," *Spine*, vol. 35, no. 1, pp. 99–103, 2010.

[25] A. Jain, P. D. Sponseller, K. M. Kebaish, and A. Mesfin, "National trends in spinal fusion surgery for scheuermann kyphosis," *Spine deformity*, vol. 3, no. 1, pp. 52–56, 2015.

[26] C. Palazzo, F. Sailhan, and M. Revel, "Scheuermann's disease: an update," *Joint Bone Spine: revue du rhumatisme*, vol. 81, no. 3, pp. 209–214, 2014.

[27] A. I. Tsirikos and A. K. Jain, "Scheuermann's kyphosis; current controversies," *Journal of Bone and Joint Surgery British Volume*, vol. 93, no. 7, pp. 857–864, 2011.

[28] C. H. Lee, Y. I. Won, and Y. San Ko, "Posterior-only versus combined anterior-posterior fusion in Scheuermann disease: a systematic review and meta-analysis," *Journal of Neurosurgery, Spine*, vol. 25, pp. 1–9, 2020.

Hindawi
Pain Research and Management
Volume 2021, Article ID 6493712, 7 pages
https://doi.org/10.1155/2021/6493712

Research Article

A Modified Transverse Process-Pedicle Approach Applied to Unilateral Extrapedicular Percutaneous Vertebroplasty

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Received 31 August 2021; Revised 1 October 2021; Accepted 12 October 2021; Published 22 October 2021

Academic Editor: Sidong Yang

Objective. To introduce a modified transverse process-pedicle puncture technique applied to unilateral extrapedicular percutaneous vertebroplasty (PVP) for the treatment of osteoporotic lumbar vertebral compression fractures. *Methods*. A retrospective study was performed on 91 patients with osteoporotic vertebral compression fractures (OVCFs) who underwent unilateral extrapedicular PVP from June 2016 to September 2018. Lumbar and back pain was assessed through the visual analogue scale (VAS). Function recovery was assessed through the Oswestry disability index (ODI). Radiologic outcomes were assessed mainly on the basis of bone cement distribution and anterior vertebral height. *Results*. A total of 101 fractured vertebrae were successfully treated using the extrapedicular technique without any recognized clinical complications. The postoperative VAS and ODI values were significantly lower than the corresponding preoperative values ($P < 0.01$). Radiologic outcomes in all fractured vertebrae showed that the diffusion of bone cement could exceed the midline of the vertebral body. There was no significant difference between preoperative and postoperative anterior vertebral heights ($P < 0.05$). *Conclusion*. The modified transverse process-pedicle approach applied to unilateral extrapedicular percutaneous vertebroplasty is a simple, safe, and effective surgical method.

1. Introduction

Osteoporotic vertebral compression fractures (OVCFs) are one of the most common complications of osteoporosis in the elderly and often lead to severe back pain, kyphosis, impaired mobility, and reduced quality of life [1–3]. Currently, percutaneous vertebroplasty (PVP) is a widely used procedure for the clinical treatment of OVCFs and can obviously relieve pain, reduce bed rest time, and prevent deformity due to collapse of the vertebral body [4–6]. It is generally known that PVP through a bilateral transpedicular approach is the classic procedure performed to treat OVCFs [7, 8]. In recent years, unipedicular PVP has been advocated, reducing the operation and radiation exposure time periods and lowering the risk of cement leakage and complications caused by vertebral pedicle puncture [2, 9, 10]. However, due to the large sagittal diameter of the spinal canal, the long pedicle length, and the small angle of the pedicle in the coronal position, it is difficult to achieve proper bilateral diffusion through unilateral pedicle puncture in the treatment of lumbar vertebral compression fractures. In addition, it is difficult to detect cement diffusion in bilateral puncture, which increases the risk of this surgery. In this article, we will demonstrate a simple and easy unilateral puncture method for extrapedicular PVP and show that it has the advantages of safety, efficiency, and less pain.

2. Materials and Methods

Before surgery, informed consent was obtained from all patients after fully explaining the treatment process. This study was approved by the medical ethics committee of the Third Affiliated Hospital of Chongqing Medical University.

2.1. Study Patients

Inclusion criteria were as follows: (1) vertebral compression fractures from L1 to L5; (2) less than 50% loss of vertebral height; (3) bone mineral density (BMD) of −2.5 or lower; (4) on magnetic resonance imaging (MRI), the fractured vertebral body showed a hypointense signal on T1-weighted images and hyperintense signal on T2-weighted images; and (5) able to tolerate local infiltration anesthesia and to lie prone or laterally for 30 minutes without serious underlying diseases.

Exclusion criteria were as follows: (1) History of malignancy, infection, or tumor; (2) spinal cord compression or stenosis of the vertebral canal >30% of the local canal diameter; (3) neurologic deficits; (4) uncorrectable bleeding disorders; and (5) severe comorbidity in the heart, lung, or kidney or other serious underlying diseases resulting in intolerance to surgery.

There were 91 patients (age range from 61 to 89 years, mean of 75.75 ± 7.03 years) who underwent vertebral compression fracture treatment. A total of 101 vertebral compression fractures were treated by the modified transverse process-pedicle approach in the authors' institution between June 2016 and September 2018. The locations of the collapsed lumbar vertebrae were as follows: L1, 2 in 5 cases; L1, 3 in 3 cases; L2, 3 in 2 cases; L1 in 31 cases; L2 in 27 cases; L3 in 15 cases; L4 in 5 cases; and L5 in 3 cases. Among the 91 patients enrolled in this study, 22 had sprains, 11 had car accident-related injuries, 37 had fall-related injuries, and the other 21 cases had no definite trauma history. Table 1 summarizes the detailed characteristics of the patients.

All patients underwent preoperative imaging assessment using a combination of conventional radiography, MRI, and computed tomography (CT). Surgical indications were high signal intensity in the fat-lipid suppression phase on MRI and definite clinical symptoms of sustained severe lumbar and back pain. Out-of-bed activity was allowed 6 hours after the operation. Antiosteoporotic drugs (bisphosphonates, calcitriol, and vitamin D) were prescribed for at least 6 months after the operation.

2.2. Surgical Management. The surgical procedure was performed under local infiltration anesthesia with the patient in the prone or lateral position. C-arm fluoroscopy was used for simultaneous viewing of anteroposterior and lateral projections of the spine to identify the point of the vertebral body. Lidocaine (2%) was injected into the skin, lumbar fascia, and deep soft tissues. A 5 mm skin incision was performed at point B (Figure 1). The left transverse process of the fractured vertebral body was located under C-arm fluoroscopy (Figure 2(a)). The needle punctured the transverse process along the BA trajectory, overstrode the superior margin of the transverse process, and proceeded forward, scratching the lateral cortex of the pedicle. During this puncture process, the craniocaudal angle of the needle was increased to reduce the risk of damage to the dural sac and the traveling nerve root and the extraversion angle was increased to avoid injuring the paraspinal venous plexus.

Table 1: Characteristics of the study patients.

Characteristics	Patients
Case	91
Age (years)	75.75 ± 7.03
Sex (male/female)	21/70
BMD T-score	3.53 ± 0.61
Follow-up duration (months)	8.55 ± 1.47

BMD, bone mineral density.

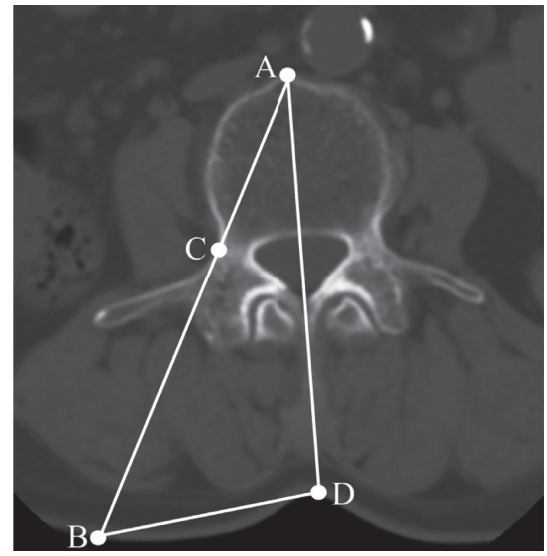

Figure 1: The skin entry point design for unilateral extrapedicular PVP. The skin entry point was determined from the axial image of preoperative CT at the target level. Point A is the junction point of the midline and the anterior edge of the vertebral body. Point D is the junction point of the midline and the skin. Point C is the entry point of the vertebral body. Point B is the junction point of the AC line and the skin, which is also the skin entry point of the unilateral extrapedicular PVP.

After reaching the hard and smooth lateral wall of the pedicle, the needle was slid forward and the needle tip was then stuck in the depressed bone groove at the superolateral junction between the pedicle and the vertebral transitional location. Anteroposterior and lateral views were essential for identifying the optimal position of the needle tip (Figures 2(b) and 2(c)). When the needle continued to penetrate the cortex, the occipital core was pulled out, the bone drill was inserted, and the drill was advanced until the end of the drill was placed in the anterior cortex of the vertebral body. Lateral views confirmed that the midline of the vertebral body was reached or exceeded. The bone drill was then replaced with a working cannula (Figures 2(d) and 2(e)). After successful puncture, bone cement was slowly injected into the vertebral body under C-arm monitoring (Figures 2(f)–2(h)).

2.3. Clinical and Radiographic Assessments. The VAS and ODI were recorded preoperatively at 1 day and 6 months postoperatively. Lumbar and back pain was assessed by the VAS. Function recovery was assessed by the ODI. The

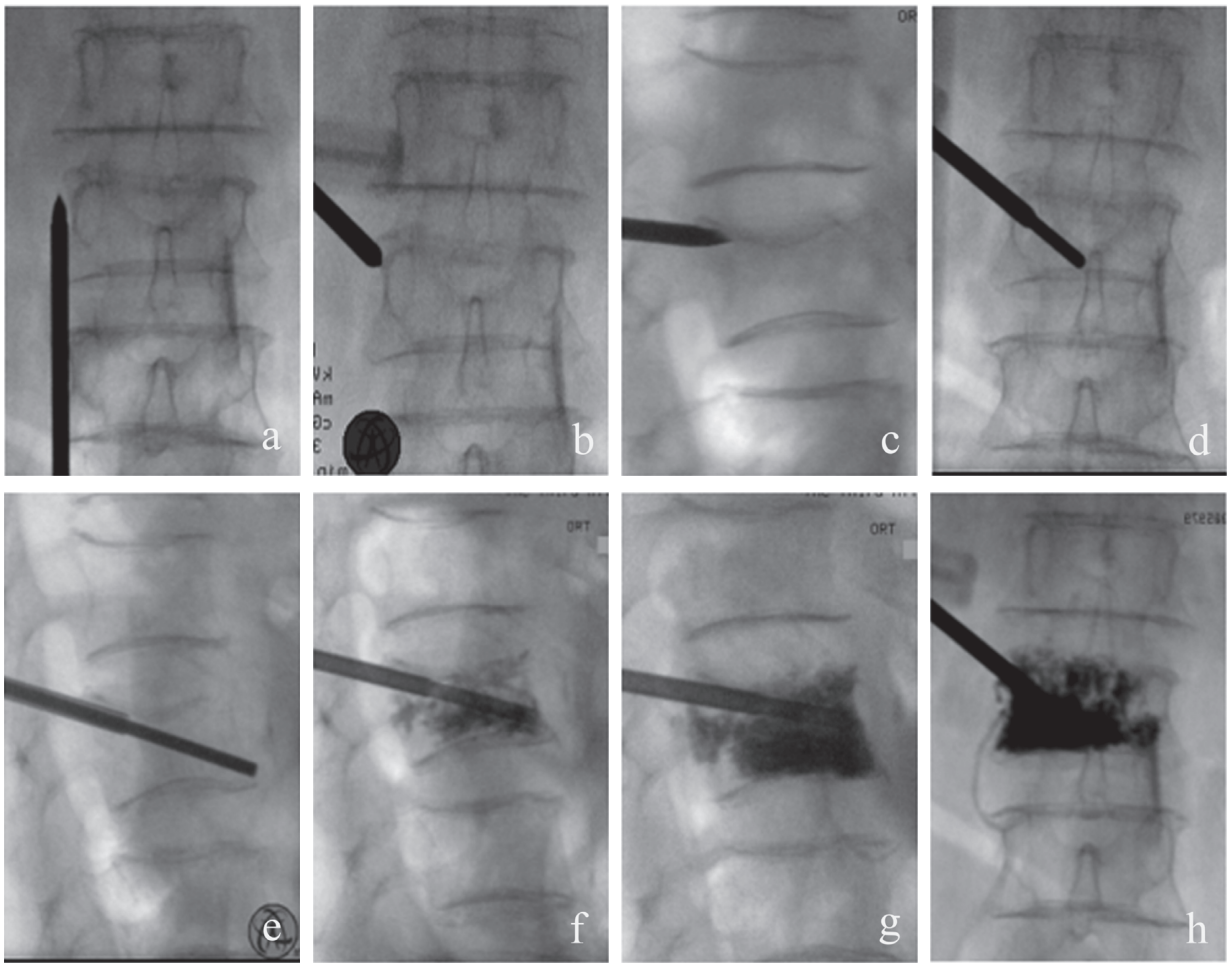

Figure 2: Anteroposterior and lateral views of the needle trajectory inserted into the vertebral body via a unilateral extrapedicular puncture method. (a) Anteroposterior radiograph showed the left transverse process of the fractured vertebral body. (b, c) The needle tip of the bone entry point was located at the bone groove at the junction between the pedicle and the vertebral transitional location. (d, e) Anteroposterior and lateral radiographs showed the optimal position of the working cannula. (f, g) The position of the cement cannula could be adjusted according to the dispersion of cement during the operation. (h) Anteroposterior radiograph showed the bone cement distribution.

quantity of injected bone cement, incidence of leakage of bone cement, and other complications were recorded during the surgery. The anterior vertebral height was measured and compared according to preoperative and postoperative imaging (1 day and 6 months).

2.4. Statistical Analysis. Statistical analyses were performed using SPSS version 23.0 statistical software. All the measurement data were presented as the mean ± standard deviation ($\overline{x} \pm s$). Preoperative and postoperative values between different subgroups were compared using the one-way ANOVA. Differences were considered significant at $P < 0.05$.

3. Results

All patients were followed up for 6–12 months, with an average 8.55 ± 1.47 months. The VAS pain and ODI scores at day one (1.63 ± 0.74, 19.70 ± 2.85) after operation were significantly lower than the preoperative scores (7.23 ± 0.79, 40.12 ± 3.92) ($P < 0.01$), but there were no significant differences with the scores at six months (1.52 ± 0.79, 18.84 ± 2.46) ($P < 0.05$) after operation. The anterior vertebral height at day one (24.77 ± 6.02) after surgery was slightly higher than that before surgery (23.86 ± 6.15), but there was no significant difference ($P < 0.05$). The anterior vertebral height at six months (24.14 ± 5.72) after surgery was slightly lower than that at day one after surgery, but there was no significant difference ($P < 0.05$) (Table 2).

All patients were successfully treated using the modified extrapedicular technique without any recognized clinical complications. The average operation time and the mean volume of the injected cement in a single level were 20.22 ± 4.51 min and 6.04 ± 0.98 mL, respectively. Radiologic outcomes in all fractured vertebrae showed that the diffusion of bone cement could exceed the midline of the vertebral body (Figure 3). Postoperative bone cement leakage was found in 8 patients in the current study. The bone cement leaked into the intervertebral space in 4 cases, the anterior edge of the vertebral body in 3 cases, and the vertebral canal in 1 case, without obvious clinical symptoms. Refracture of

Table 2: Changes in VAS and ODI scores and anterior vertebral height during follow-up periods.

Parameters	Preop	1 day postop	6 months postop	P_1	P_2
VAS ($n_1 = 91$)	7.23 ± 0.79	1.63 ± 0.74	1.52 ± 0.79	< 0.01	0.34
ODI ($n_1 = 91$)	40.12 ± 3.92	19.7 ± 2.85	18.84 ± 2.46	< 0.01	0.084
Anterior vertebral height ($n_2 = 101$)	23.86 ± 6.15	24.77 ± 6.02	24.14 ± 5.72	0.56	0.779

VAS, visual analogue scale; ODI, Oswestry disability index; P_1, preoperative vs. postoperative day 1; P_2, postoperative day 1 vs. postoperative month 6; n_1, total number of patients; n_2, total number of vertebrae.

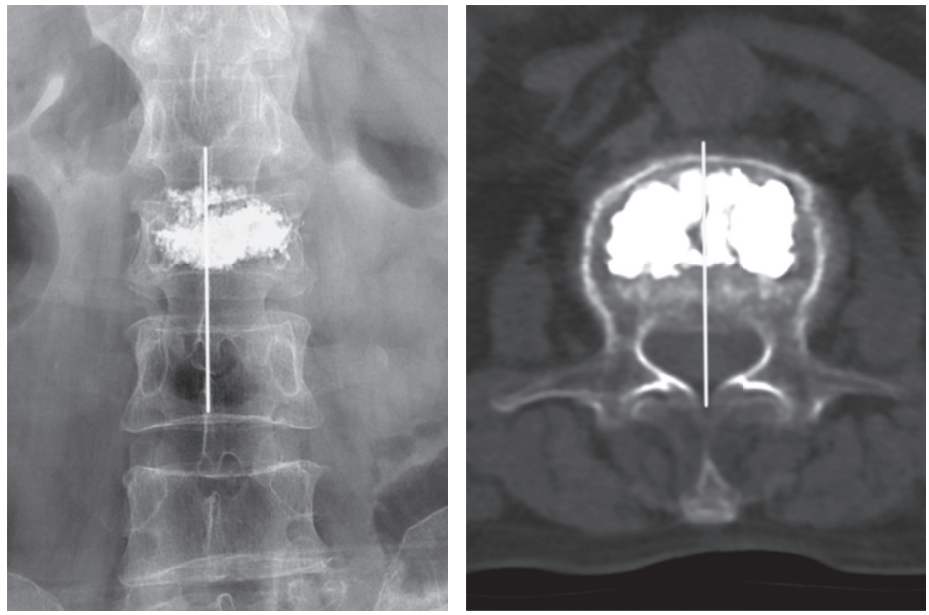

Figure 3: X-ray and CT showed that the distribution of bone cement crossed the midline with satisfactory diffusion.

the adjacent vertebral body occurred in 1 case at 2 weeks after the surgery (Figure 4).

4. Discussion

In relative terms, bilateral PVP showed increased operation time and injected cement volume, while unilateral PVP showed reduced operation time, surgery-related complications, and radiation exposure. In recent years, unilateral PVP has been increasingly used in surgery, resulting in reductions in exposure time to radiation, risk of cement leakage, and complications [2, 10, 11]. Soon et al. found that unilateral PVP using a modified surgical instrument with a directional needle was an excellent example of advancement and refinement in spinal surgery without increased clinical risk and the novel directional needle technique can potentially provide better radiological outcomes than a straight needle [12]. The unilateral extrapedicular needles, advanced through the costopedicular joint, had proper bilateral cement diffusion in the treatment of lumbar vertebral compression fractures [13]. Beall et al. reported an effective extrapedicular modified inferior endplate access to the vertebral body for lumbar vertebral compression fractures. The entry point of the needle was 0.5–1.0 cm above the inferior endplate anterior to the ipsilateral pedicle [14]. However, these techniques were generally complex and required repeated fluoroscopy, which also increased the patients' pain.

The modified transverse process-pedicle extrapedicular pathway in this study had the following advantages: (1) There was improved safety of the operation. This new technology can be applied to puncture the working cannula from the bottom of the "Kambin" triangle [15] to the contralateral fractured vertebral body. The wide and safe margin from the dural sac and nerve root of the triangle can reduce the risk of intraoperative nerve injury. In addition, the bone entry point of this approach was located in the safe puncture zone of extrapedicular vertebroplasty of lumbar vertebral bodies and was more superior to the midline of the pedicle, reducing the risk of segmental vertebral body artery injury [16]. (2) It alleviated patient pain. Because the puncture path of this technique is within the soft tissue, good local infiltration of anesthesia can be carried out, which can alleviate patient pain during the puncture process. (3) The operative procedure was simplified and controllable. This extrapedicular puncture technique had three definite bony markers (Figure 5), the upper edge of the transverse process, the outer wall of the pedicle, and the posterolateral cortex of the vertebral body, all of which had obvious landmarks, which made it possible to complete the single puncture with the use of C-arm guided fluoroscopy. Moreover, this extrapedicular puncture technique was free from the

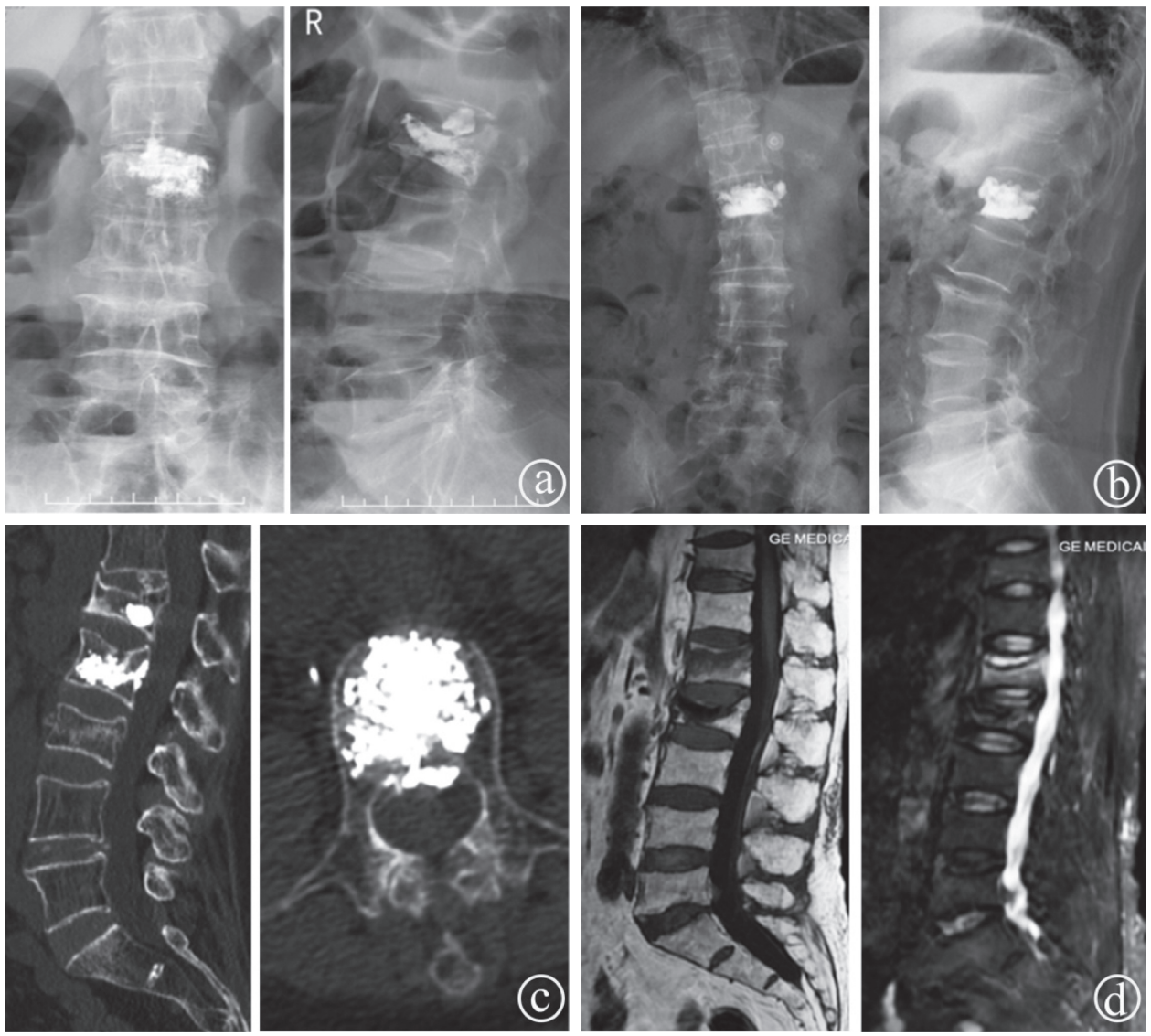

Figure 4: Images of bone cement leakage and adjacent level fracture in PVP cases. X-rays showing that the bone cement had leaked into the intervertebral disk (a). The anterior edge of the vertebral body (b). CT showing that the bone cement had leaked into the vertebral canal (c). MRI scan with compression fracture of the L1 vertebra after PVP of the L2 vertebra (d).

constraints of a pedicle. During the operation, the direction and depth of the cement cannula can be adjusted flexibly, which made it possible to ensure the ideal dispersion of the cement. (4) Different positions can be maintained according to the patient's condition. The puncture technique was easy to perform because of its clear bony markers. It can be used in prone, lateral, and semilateral positions according to the patient's condition and was especially suitable for patients with poor pulmonary function or those who are unable to lie prone due to pain.

This technique was mainly suitable for L1-3 vertebral fractures, and the degree of fracture compression was less than 50%. Because the puncture path was at the upper edge of the transverse process, the puncture point of the vertebral body was slightly higher than that of the pedicle puncture and it was difficult to penetrate the anterior part of the vertebral body, which limited the application of this technique in patients with vertebral compression degrees greater than 50%. The L4 vertebral body, and especially the L5 vertebral body, are essentially half-elliptic. The flattening of the vertebral body resulted in the difficulty of detecting the third bony marker, which limited the application of the puncture technique to a certain extent. For L4 and L5 vertebral fractures, the shape of the vertebral body should be judged by preoperative CT examination, and then the surgeon decides whether the puncture technique should be applied or not be applied. In patients with hypertrophy and a high position of the transverse process, the adjustment of the sagittal puncture angle was limited. It was difficult to puncture the cement cannula to the ideal position of the vertebral body. If the diffusion effect of unilateral puncture was poor, a contralateral pedicle puncture was necessary.

There were some limitations in this study. The number of patients included in this study was relatively small. The

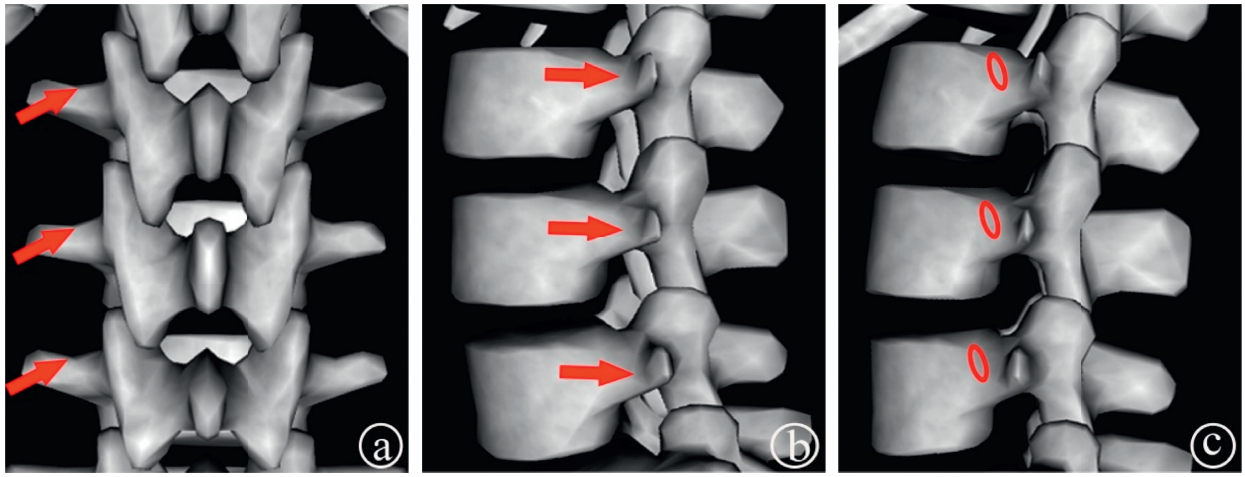

Figure 5: The three bony markers. (a) The superior margin of the transverse process (red arrow). (b) The outer wall of the pedicle (red arrow). (c) The posterolateral cortex of the vertebral body (red circle).

follow-up period was relatively short. In addition, no control group was established in this study. Further long-term follow-up studies in a large patient population are warranted to generalize our results.

5. Conclusion

A needle trajectory with a modified transverse process-pedicle approach can be easily and precisely planned using unambiguous anatomical landmarks under fluoroscopic guidance, enabling sufficient bone cement distribution and tremendous pain relief.

Data Availability

The data generated in this study are available from the corresponding authors upon request.

Conflicts of Interest

All authors declare that they have no conflicts of interest.

Authors' Contributions

PL, QZ, and YGL contributed to the conception and design of the study. YYZ, LHL, and HMW were responsible for the data collection, analysis, and article drafting. All authors gave the final approval.

References

[1] A. T. Malik, S. Retchin, F. M. Phillips et al., "Declining trend in osteoporosis management and screening following vertebral compression fractures-a national analysis of commercial insurance and medicare advantage beneficiaries," *The Spine Journal*, vol. 20, no. 4, pp. 538–546, 2020.

[2] S. Yang, C. Chen, H. Wang, Z. Wu, and L. Liu, "A systematic review of unilateral versus bilateral percutaneous vertebroplasty/percutaneous kyphoplasty for osteoporotic vertebral compression fractures," *Acta Orthopaedica et Traumatologica Turcica*, vol. 51, no. 4, pp. 290–297, 2017.

[3] Z. Wu, Y. Linqiang, and L. Mo, X. Jiang, J. Cui, Y. Feng et al., "Comparison of cement leakage rate and severity after percutaneous vertebroplasty for osteoporotic vertebral compression fractures using front-opening versus side-opening cannulas," *Orthopedics*, vol. 44, no. 3, pp. 134–140, 2021.

[4] C. Griffoni, J. N. M. Lukassen, L. Babbi et al., "Percutaneous vertebroplasty and balloon kyphoplasty in the treatment of osteoporotic vertebral fractures: a prospective randomized comparison," *European Spine Journal*, vol. 29, no. 7, pp. 1614–1620, 2020.

[5] A. Jurczyszyn, R. Czepko, M. Banach, B. Godlewski, P. Masłowski, and A. Skotnicki, "Percutaneous vertebroplasty for pathological vertebral compression fractures secondary to multiple myeloma-medium-term and long-term assessment of pain relief and quality of life," *Advances in Clinical and Experimental Medicine*, vol. 24, no. 4, pp. 651–656, 2015.

[6] P. P. Ng, L. P. Caragine Jr, and C. F. Dowd, "Percutaneous vertebroplasty: an emerging therapy for vertebral compression fractures," *Seminars in Neurology*, vol. 22, no. 2, pp. 149–156, 2002.

[7] M. J. Nieuwenhuijse, S. P. J. Muijs, A. R. van Erkel, and S. P. D. Dijkstra, "A clinical comparative study on low versus medium viscosity PolyMethylMetAcrylate bone cement in percutaneous vertebroplasty," *Spine*, vol. 35, no. 20, pp. E1037–E1044, 2010.

[8] B. S. Kim, B. Hum, J. C. Park, and I. S. Choi, "Retrospective review of procedural parameters and outcomes of percutaneous vertebroplasty in 673 patients," *Interventional Neuroradiology*, vol. 20, no. 5, pp. 564–575, 2014.

[9] L. Zhang, Z. Liu, J. Wang et al., "Unipedicular versus bipedicular percutaneous vertebroplasty for osteoporotic vertebral compression fractures: a prospective randomized study," *BMC Musculoskeletal Disorders*, vol. 16, p. 145, Article ID 145, 2015.

[10] Y. C. Chen, L. Zhang, E. N. Li et al., "Unilateral versus bilateral percutaneous vertebroplasty for osteoporotic vertebral compression fractures in elderly patients: a meta-analysis," *Medicine*, vol. 98, no. 8, Article ID e14317, 2019.

[11] W. Wang, K. Duan, M. Ma et al., "Can an unipedicular approach replace bipedicular percutaneous vertebroplasty for osteoporotic vertebral compression fracture?" *Journal of Back and Musculoskeletal Rehabilitation*, vol. 32, no. 2, pp. 261–267, 2019.

[12] W. C. Soon, R. K. Mathew, and J. Timothy, "Comparison of vertebroplasty using directional versus straight needle," *Acta Radiologica Open*, vol. 4, no. 3, Article ID 2047981615569268, 2015.

[13] A. Cianfoni, F. Massari, S. Ewing, M. Persenaire, Z. Rumboldt, and G. Bonaldi, "Combining percutaneous pedicular and extrapedicular access for tumor ablation in a thoracic vertebral body," *Interventional Neuroradiology*, vol. 20, no. 5, pp. 603–608, 2014.

[14] D. P. Beall, B. Parsons, and S. Burner, "Technical strategies and anatomic considerations for an extrapedicular modified inferior endplate Access to thoracic and lumbar vertebral bodies," *Pain Physician*, vol. 19, no. 8, pp. 593–601, 2016.

[15] A. F. Ozer, T. Suzer, H. Can et al., "Anatomic assessment of variations in kambin's triangle: a surgical and cadaver study," *World neurosurgery*, vol. 100, pp. 498–503, 2017.

[16] D. H. Heo and Y. J. Cho, "Segmental artery injury following percutaneous vertebroplasty using extrapedicular approach," *Journal of Korean Neurosurgical Society*, vol. 49, no. 2, pp. 131–133, 2011.

Hindawi
Pain Research and Management
Volume 2021, Article ID 2262837, 8 pages
https://doi.org/10.1155/2021/2262837

Research Article

Postoperative Management Strategy of Surgical Site Infection following Lumbar Dynesys Dynamic Internal Fixation

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Received 1 September 2021; Accepted 22 September 2021; Published 7 October 2021

Academic Editor: Sidong Yang

Aim. To research the incidence of surgical site infection (SSI) following lumbar Dynesys dynamic internal fixation and its management strategy. *Methods*. We retrospectively analyzed all cases of lumbar Dynesys dynamic internal fixation performed from January 2010 to December 2019, and the data from patients with SSI were collected. The observational indicators included the incidence of SSI, general information of the patients, surgical details, inflammatory indicators, pathogenic bacteria, and treatment. SSI was defined as both early infection and delayed infection, and the cases were divided into Groups A and B, respectively. The relevant indicators and treatment were compared between the two groups. *Results*. A total of 1125 cases of lumbar Dynesys dynamic internal fixation were followed up. Twenty-five cases of SSI occurred, and the incidence of SSI was 2.22% (25/1125). There were 14 cases of early infection (1.24%) and 11 cases of delayed infection (0.98%). Fourteen cases of early infection occurred 12.3 ± 8.3 days postoperatively (3–30), and 11 cases of delayed infection occurred 33.3 ± 18.9 months postoperatively (3–62). The inflammatory indicators of Group A were significantly higher than those of Group B (all $P < 0.05$), except for procalcitonin. The main infection site in Group A was located on the skin and subcutaneous tissue and around the internal instrument, while the main infection site in Group B was around the internal instrument. The main treatment for Group A was debridement and implant replacement, and the main treatment for Group B was implant removal. *Summary*. The incidence of SSI following lumbar Dynesys dynamic internal fixation was 2.22%, the incidence of early SSI was 1.24%, and the incidence of delayed SSI was 0.98%. If the main infection site of early infection is in the incision, debridement should be the main treatment method; if the infection site is around the internal fixation, implant replacement is recommended on the basis of debridement. Once delayed infection is diagnosed, implant removal is suggested.

1. Introduction

Surgical site infection (SSI) is a serious complication after lumbar spine surgery that increases the length of hospital stay, medical expenses, and rate of unplanned reoperations, bringing great challenges to both doctors and patients [1, 2]. At present, lumbar spine surgery that requires internal fixation is becoming increasingly common [3, 4]. Picada et al. [5] reported that the incidence of SSI in deep tissue after lumbar fusion and internal fixation was 3.2%. Reames et al. [6] reported that the incidence of SSI after pediatric scoliosis correction surgery was 2.6% (505/19360). Zhou et al. [7] conducted a meta-analysis including 603 cases of SSI in 22475 spine surgeries, with an incidence of 3.1%; the incidences in the cervical, thoracic, and lumbar spines were 3.4%, 3.7%, and 2.7%, respectively.

Lumbar transpedicular dynamic fixation could preserve the mobility of the fixed segment, maintain the height of the intervertebral space, and reduce adjacent segment degeneration [8, 9]. The Dynesys system is a representative transpedicular dynamic instrument that has been used clinically for more than 20 years [10, 11]. Correspondingly, lumbar Dynesys dynamic internal fixation also had a certain SSI incidence. For example, Welch et al. [12] and Grob et al.

[13] reported that the infection rate after Dynesys dynamic stabilization was 0.9% (1/101) and 3.2% (1/31). However, their sample size was limited, and the infection rates were not representative.

At present, the application of lumbar Dynesys dynamic internal fixation is not widespread. The most published literature mainly reports its clinical efficacy and imaging changes [11, 14, 15]. To our knowledge, there are no studies that have specifically reported on postoperative infection following lumbar Dynesys dynamic internal fixation. Therefore, the author retrospectively researched the incidence of SSI following more than 1000 cases of lumbar Dynesys dynamic fixation and its postoperative management strategy.

2. Materials and Methods

A retrospective study of all cases after lumbar Dynesys dynamic internal fixation performed by the author's team from January 2010 to December 2019 was performed, and the data from patients with SSI were collected. This research project was reviewed and approved by the Scientific Research Ethics Committee of Southwest Hospital, Army (Third) Military Medical University.

2.1. Inclusion and Exclusion Criteria. Inclusion criteria were as follows: (1) cases diagnosed as lumbar degenerative disease and following lumbar Dynesys dynamic internal fixation; (2) followed up for more than 12 months; and (3) the main observational content must include management after SSI was diagnosed.

Exclusion criteria were as follows: (1) revision surgery and (2) if the clinical data were incomplete.

2.2. Diagnosis of SSI. The SSI after the surgery or during the follow-up could occur at the incision (skin and subcutaneous tissue) or below the deep fascia, spinal canal, intervertebral space, paravertebral space, and around the internal instrument [16, 17]. Diagnostic criteria: (1) clinical manifestations included fever, low back pain and/or lower limb radiating pain, swelling, exudation, sinus around the incision, etc.; (2) inflammatory indicators were increased, such as white blood cells (WBC), neutrophils (N), thrombocytes, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and procalcitonin; (3) MRI showed that the low signal on the T1-weighted image and the high signal or mixed signal on T2-weighted image in subfascial tissue around the surgical site; (4) color ultrasound indicated that there was an abscess in the surgical site; and (5) bacterial culture was positive. (1) was the main criterion, (2), (3), (4), and (5) were the secondary criteria, and the SSI was diagnosed by meeting (1) and any one of (2)–(5).

2.3. Treatment Methods

2.3.1. Antibiotic Treatment. Vancomycin and (or) imipenem and cilastatin sodium were early selected empirically, and subsequently sensitive antibiotics were selected based on pathogenic bacteria and drug susceptibility test results. The total course of treatment was 8–12 weeks, and intravenous medication was performed for 4~8 weeks and then oral antibiotics for 4 weeks.

2.3.2. Surgical Intervention. (1) The incision was healed without local infection, but MRI showed some localized fluid around the internal fixation with no high or slightly higher inflammatory indicators. Puncture aspiration could be used to retain specimens, and repeated puncture and irrigation was suggested. (2) If the infection was only confined to the skin and subcutaneous tissues without involving the internal fixation below the deep fascia, a thorough debridement and suture was recommended. (3) If the infection was around the spacer below the deep fascia, and the pedicle screw did not show bone absorption "halo" sign in X-ray, it was advisable to take out the spacer and connector, completely debride, and then install new spacers and connectors. (4) If the infection mainly occurred below the deep fascia, the internal instrument was soaked with pus, the pedicle screw showed bone absorption "halo" sign in X-ray, the pedicle screw was loosening during surgery, the infection involved the screw trajectory in the vertebral body, and/or paravertebral abscess/the psoas major muscle abscess was formed, removal of the internal instrument should be performed.

2.3.3. Systemic Supportive Treatment. Albumin was supplemented for correcting hypoalbuminemia and anemia and maintaining albumin above 35 g/L and hemoglobin above 90 g/L.

2.4. Observational Indicators and Grouping. Incidence of SSI: the patients' age, sex, smoking and drinking behavior, previous surgical history, primary disease, and concomitant disease; intraoperative conditions: number of fenestrations, number of discectomy, number of fixed segments, operation time, blood loss, blood transfusion, and dural rupture; and postoperative infection time, symptoms, inflammatory indicators, pathogenic bacteria, and treatment. Infection that occurred within 3 months after lumbar Dynesys dynamic internal fixation was defined as an early infection, and infection that occurred 3 months after lumbar Dynesys dynamic internal fixation was defined as a delayed infection [18, 19]. The infected cases were divided into two groups, namely, the early infection group and delayed infection group, referred to as Groups A and B, respectively. The relevant indicators and main treatments of the two groups were compared.

2.5. Statistical Analysis. SPSS (version 19.0 IBM, NY, USA) software package was used for statistical analysis. Count data were recorded as yes or no, and measurement data were recorded as mean ± SD. For comparison between Groups A and B, the enumeration data were analyzed using the chi-square test or Fisher's exact test. If the measurement data were normally distributed, the independent-sample t-test was used; if the measurement data were not normally distributed, data conversion or Mann–Whitney test was used. $P < 0.05$ was taken to indicate that the difference was significant.

3. Results

A total of 1125 patients were followed up after lumbar Dynesys dynamic internal fixation, including 663 cases of lumbar disc herniation, 201 cases of lumbar spinal stenosis, 115 cases of lumbar spondylolisthesis, 71 cases of lumbar degenerative scoliosis, and 75 cases of lumbar discogenic pain. Twenty-five cases of SSI occurred, and the incidence of SSI was 2.22% (25/1125). There were 14 cases of early infection, with an infection rate of 1.24% (14/1125) and 11 cases of delayed infection, with an infection rate of 0.98% (11/1125).

3.1. General Information of the Patients and Surgical Details. The twenty-five patients included 21 males and 4 females, aged 49.4 ± 18.2 years (21–78). The primary diseases were lumbar disc herniation, lumbar spinal stenosis, lumbar degenerative spondylolisthesis, and lumbar degenerative scoliosis. There were 10 patients with a drinking history, 9 patients with a smoking history, 8 patients with hypertension, 4 patients with diabetes, and 4 patients with a history of lumbar surgery. The follow-up time was 58.4 ± 32.9 months (12–131). The number of fenestrations was 1.7 ± 1.0 (1–4), the number of discectomy was 1.2 ± 0.5 (0–2), and the number of fixed segments was 2.1 ± 0.811 (1–3). The operation time was 179 ± 74 minutes (80–330), the blood loss was 332 ± 253 ml (100–1200), and the blood transfusion was 154 ± 283 ml (0–1000). There was 1 case of dural rupture.

3.2. Postoperative Infection Time, Symptoms, and Inflammatory Indicators of SSI. Fourteen cases of early infection occurred 12.3 ± 8.3 days postoperatively (3–30); and 11 cases of delayed infection occurred 33.3 ± 18.9 months postoperatively (3–62). The main symptoms were low back pain (or lower limb radiating pain), incision exudation, redness and swelling, and fluid accumulation. Some inflammatory indicators increased, such as white blood cells, the percentage of neutrophils, platelets, C-reactive protein, erythrocyte sedimentation rate, and procalcitonin.

3.3. Secondary Surgery for SSI and Pathogenic Bacteria. A total of 20 cases underwent secondary surgery. The surgical methods mainly included debridement, implant replacement, and implant removal. The other 3 patients underwent puncture (irrigation), and 2 patients received only antibiotic treatment. Eleven cases of pathogenic bacteria were identified, accounting for 44%, 13 cases had negative cultures, and no specimens could be cultured in 1 case. Pathogenic bacteria included 4 cases of Staphylococcus epidermidis, 2 cases of Staphylococcus aureus, and 1 case each of Salmonella, Pseudomonas aeruginosa, Enterobacter, Acinetobacter baumannii, and Streptococcus lactis. The follow-up time after the second surgery for SSI was 42.2 ± 25.1 months (5–105), and there was no reinfection during the follow-up period.

3.4. Comparison of Surgical Details, Clinical Symptoms, Inflammatory Indicators, Pathogen Detection Rate, Main Infection Site, and Main Treatment Measures between Groups A and B (Table 1). There were no significant differences in the number of fenestrations, the number of discectomys, the number of fixed segments, operation time, blood loss, or blood transfusions between Groups A and B ($P > 0.05$). The fixed segment, operation time, blood loss, and blood transfusion in Group A were slightly higher than those in Group B. The inflammatory indicators of Group A were significantly higher than those of Group B (all $P < 0.05$), except for procalcitonin. The detection rates of pathogenic bacteria in Groups A and B were 62.5% and 27.3%, respectively ($P > 0.05$). The main infection sites in Group A were located at the skin and subcutaneous tissue and around the internal instrument, while the main infection sites in Group B were located around the internal instrument. Group A mainly used treatment measures such as debridement, implant replacement, and mere antibiotics. Group B mainly used treatment measures such as implant removal and puncture (irrigation).

The typical case is shown in Figure 1. A 40-year-old female patient with low back pain and left lower limb pain for 4 days was admitted to the hospital on July 6, 2020. Three years prior, she had undergone L4-5 discectomy and Dynesys dynamic internal fixation due to L4-5 disc herniation. She had a history of diabetes for 3 years. Laboratory results showed WBC 18.9×10^9/L, neutrophil 91.2%, CRP 170.0 mg/L↑, procalcitonin 0.35 ng/ml, and ESR 120 mm/h. Lumbar X and MRI results showed loose internal fixation, empyema around the internal fixation, and psoas major abscess (Figure 1). The diagnosis was delayed SSI after lumbar internal fixation. Treatment measures were implant removal, debridement, drainage, antibiotic therapy, support, and other treatments.

4. Discussion

In this research, 24 patients who underwent lumbar Dynesys internal fixation had SSI, with an infection rate of 2.22%. Goldstein et al. [20] reported 10 patients undergoing Dynesys dynamic surgery, of whom 3 cases had deep wound infections, with an infection rate as high as 30%. Pham et al. [21] reviewed the complications after Dynesys fixation. A total of 21 studies included 1166 patients, the average follow-up time was 33.7 months (12.0–81.6), and the incidence of SSI was 4.3%. Wiseman et al. [22] believed that titanium and titanium alloy compounds were less likely to be infected at the surgical site than other implant materials, including polymethylmethacrylate (PMMA), stainless steel, and hydroxyapatite. Titanium is one of the best implant materials compatible with human tissues, especially for fixing bones. The surface of titanium and titanium alloys was easily colonized by osteoblasts and soft tissues, thereby preventing the adhesion and colonization of bacteria and other pathogenic microorganisms on the surface of the internal instrument [23]. The pedicle screws of the Dynesys system are not connected by titanium rods but by a combination of a connector and spacer. The connector is woven from

Table 1: Comparison of the observational indicators between Groups A and B.

		Group A	Group B	P
Age (years)		56.9 ± 18.4	39.8 ± 13.0	0.016
Surgical situation	Number of fenestration	1.7 ± 1.1	1.7 ± 1.0	0.903*
	Number of discectomy	1.1 ± 0.4	1.2 ± 0.6	0.769*
	Number of fixed segment	2.2 ± 0.9	1.9 ± 0.7	0.323*
	Operation time (min)	195.8 ± 81.984	158.1 ± 70.7	0.208*
	Blood loss (ml)	385.7 ± 293.2	263.6 ± 180.4	0.134*
	Blood transfusion (ml)	182.1 ± 334.9	119.1 ± 210.8	0.809*
Clinical symptom	Incision exudation	8	0	0.007#
	Low back pain (leg pain)	4	7	
	Incision hydrops	3	0	
	Red and swollen incision	3	1	
	Sinus tract	2	2	
	Fever	2	1	
	Abscess	0	3	
Inflammation indicator	WBC ($\times 10^9$/L)	11.4 ± 3.0	8.2 ± 2.5	0.008
	N (%)	79.6 ± 12.3	68.9 ± 9.9	0.029
	Thrombocyte ($\times 10^9$/L)	296.7 ± 88.4	222.8 ± 54.1	0.023
	SR (mm/1 h)	54.2 ± 26.8	34.2 ± 27.1	0.048*
	CRP (mg/L)	64.9 ± 88.0	13.7 ± 15.8	0.012*
	Procalcitonin (ng/ml)	2.5 ± 5.3	0.5 ± 1.0	0.639*
Pathogenic bacteria	Positive rate	8/14 (57.1%)	3/11 (27.2%)	0.467#
Main infection site	Skin and subcutaneous tissue	9	0	0.001#
	Around internal instrument	3	10	
	Spinal canal	1	1	
	Intervertebral space	1	0	
Main treatment	Mere antibiotics	2	0	0.001#
	Puncture (irrigation)	1	2	
	Debridement	8	1	
	Implant replacement	2	0	
	Implant removal	1	8	

*Mann-Whitney test; #Fisher's exact test.

polyethylene terephthalate materials, and the spacer is made up of polycarbonate polyurethane. There is no soft tissue growth in the gap between the connector and the spacer, and the gap between the spacer and the pedicle screw during spinal flexion and extension activities might be where bacteria colonize. At the same time, the braided suture of the connector has greater bacterial adhesion, which might increase the likelihood of infection [24]. Goldstein et al. [20] postulated that intraoperative bacteria entered the surgical site, and the spacer acted as a medium for bacteria. However, the sample size was only 10 cases, and the results were hard to be convinced.

This study showed that the age, fixed segment, operation time, blood loss, and blood transfusion in Group A were higher than those in Group B, indicating that elderly patients and those with greater surgical trauma were prone to early SSI perioperatively. Early infection mainly manifested as incision exudation, low back pain (leg pain), and hydrops in the surgical site, while delayed infection mainly manifested as low back pain, sinus tract, abcess, etc. The inflammatory indicators were increased in most cases of early infection, while they were mostly normal in cases of delayed infection. The main infection site of early infection was located at the skin, subcutaneous tissue, and around the internal fixation, while the main infection site of delayed infection was located around the internal instrument. When delayed infection was suspected, MRI was performed. The hydrops around the internal instrument had obvious changes on the MRI, such as the high signal around the screw on the T2 image. The second invasive operation for early infection was mainly debridement, with complete removal of necrotic and inactivated tissue, and drainage and sealing of the incision. Early infection mainly occurred in the incision, and deep cavity infection was not common. If the infection around the internal instrument was serious, then replacement of the connector and spacer should be considered. The pedicle screw cannot be easily loosened in cases of early infection, so the screw might not need to be replaced. The author advocates the use of chlorhexidine (or iodophor), hydrogen peroxide, and physiological saline to repeatedly wash the infection site. For delayed infection, the main infection site was around the internal instrument, so for most patients, the internal instrument need to be removed.

Regardless of early infection or delayed infection, there are fewer concerns regarding lumbar dynamic stabilization surgery than lumbar fusion. Posterior (transforaminal) lumbar interbody fusion damages the most posterior spine structure, such as the lamina and facet joints. In early infection, implant removal would cause intervertebral instability, false joint formation, and increased neurological

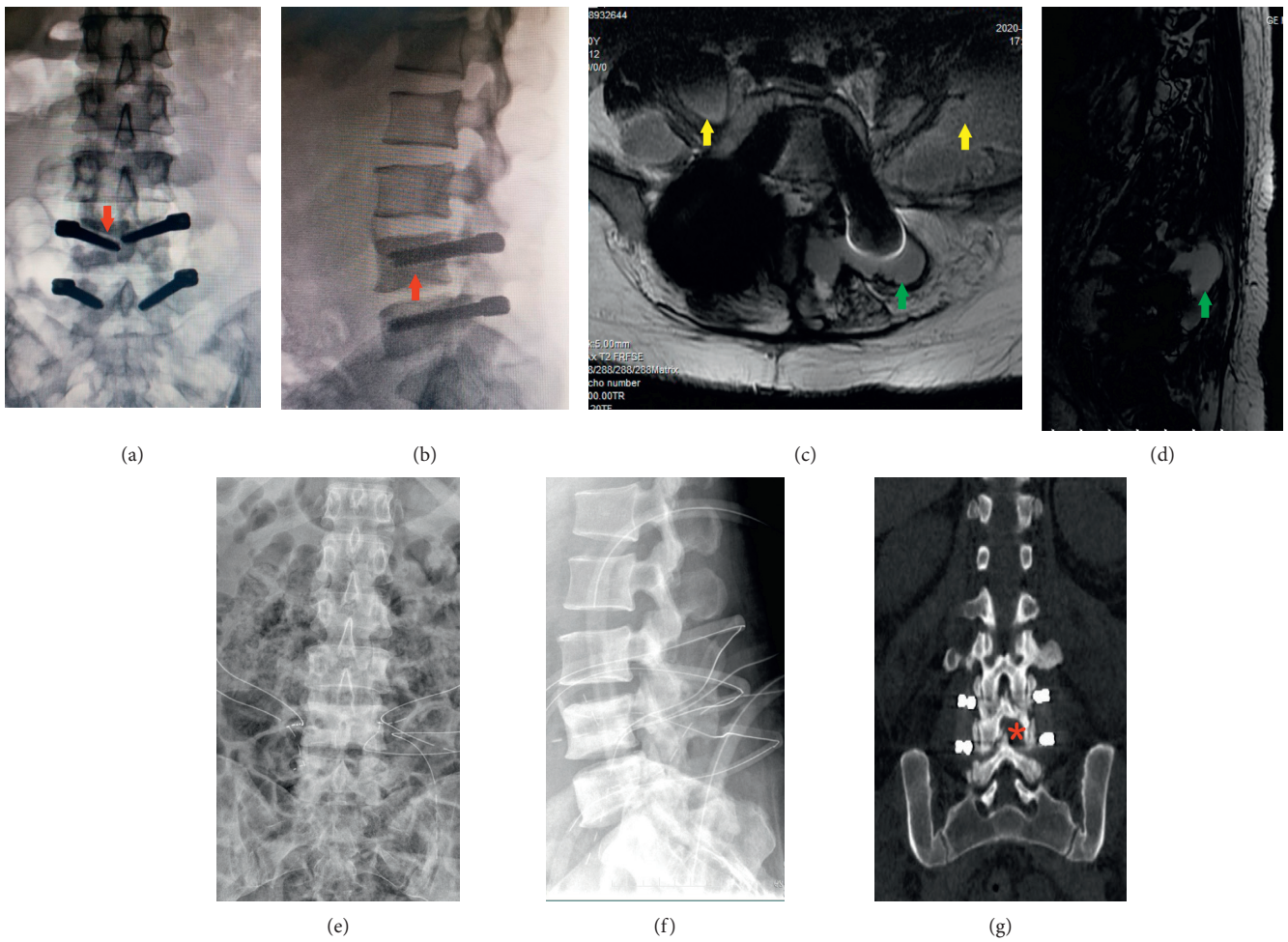

Figure 1: (a, b) Three years after L4-5 Dynesys dynamic internal fixation, anteroposterior and lateral X-view: the red arrow indicates bone resorption and loosening of the pedicle screw (halo sign). (c, d) Lumbar MRI: the green arrows indicate empyema around pedicle screws and spacers, and the yellow arrows indicate bilateral psoas muscle abscesses. (e, f) Placing drainage tubes after removal of the implant. (g) Opening a window between the lamina, retaining the lateral 1/2 of the inferior articular process in L4.

dysfunction. Lumbar dynamic stabilization does not require an intervertebral cage, avoiding the difficulty of removing intervertebral implants. The author has always advocated opening a window between the lamina, retaining the lateral 1/2 of the inferior articular process (Figure 1(g)) and achieving complete decompression of the nerve root canal by subtly expanding the lateral recess. Even if bilateral decompression is performed at the same level, the spinous process and the upper part of the bilateral lamina could be retained. Therefore, in patients undergoing lumbar dynamic stabilization, most of the posterior structure can be preserved, maintaining the stability of the spine. Once SSI occurs in lumbar dynamic internal fixation, implant removal has almost no effect on the stability of the spine. Of course, there is no "gold standard" for implant removal or retention in SSI after lumbar dynamic internal fixation, and it depends mainly on the unique situation of the patient, such as infection site, infection severity, patient's general condition, nutritional status, pathogenic bacteria, drug susceptibility test, treatment affordability, compliance, and other factors [25, 26].

In terms of how to prevent and treat SSI after lumbar dynamic internal fixation, the author has some suggestions. Full attention should be paid to the risk factors for infection. Janssen et al. [27] pointed out that age, body mass index, American Society of Anesthesiologists (ASA) score, revision surgery, and the use of nonsteroidal anti-inflammatory drugs are risk factors for SSI after thoracolumbar internal fixation in adults. Other studies have indicated that a modified Glasgow prognostic score ≧1, BMI ≦20.39 kg/m^2 [28], postoperative hyperglycemia, poor postoperative blood glucose control [29], perioperative hypoalbuminemia, and chronic steroid use are risk factors for SSI in spinal internal fixation [30]. The use of prophylactic antibiotics during the perioperative period and the correction of anemia and hypoalbuminemia are very important [31, 32]. A strict aseptic technique should be the basis, and direct contact with the internal instrument should be avoided as much as possible (Figure 2). For example, the Dynesys screw should be installed on the screwdriver without direct touching. In the screw implantation process, contact with gloves, cloth sheets, hooks, and muscle tissue should be avoided to the

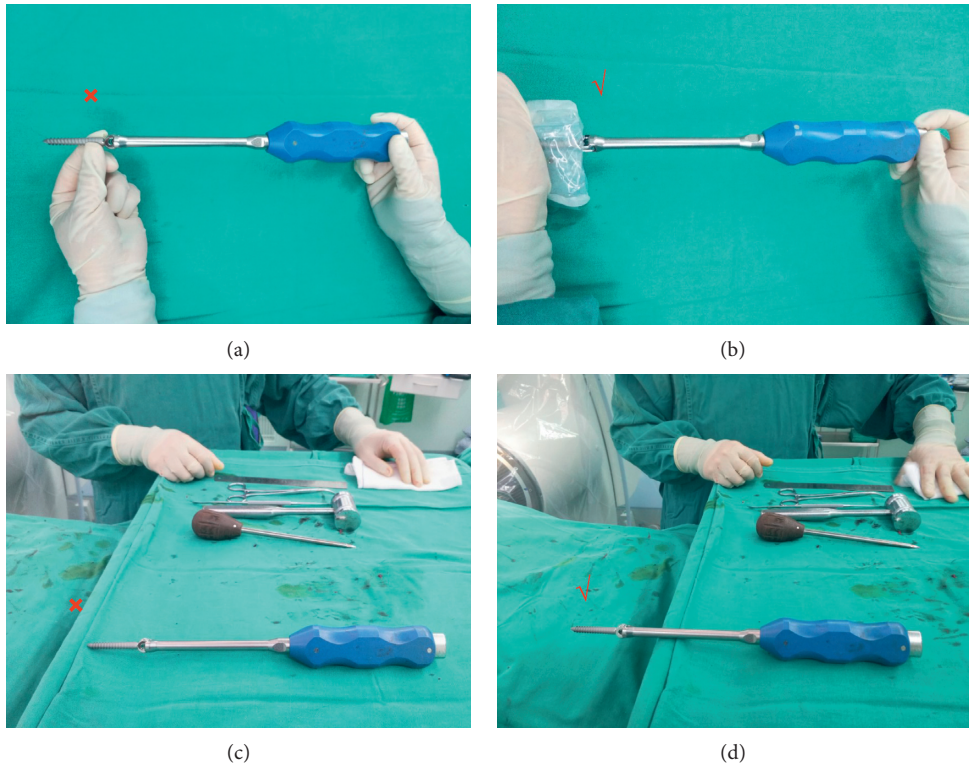

Figure 2: (a) Wrong: Dynesys screw was installed with direct touching; (b) correct: Dynesys screw was installed without direct touching. (c) Wrong: Dynesys screw was placed touching the cloth; (d) correct: Dynesys screw was placed without touching the cloth.

greatest extent possible. To ensure a sufficient extraversion angle of the screw and reduce the influence on the zygapophyseal joint, the author generally chose the Wiltse approach to complete the installation of the Dynesys system [33]. The muscle tissue should not be entrapped between the spacer and the screw because necrosis of the entrapped muscle is a good culture medium for bacteria. After the operation, the healing of the incision and inflammatory indicators needed to be carefully observed. Once SSI is suspected, specimens should be collected as soon as possible through incision exudate, drainage fluid, puncture fluid, etc. for pathogenic examination while using norvancomycin for empirical anti-infective therapy. After the drug sensitivity test is returned, the antibiotics may need to be adjusted, with an anti-infectious treatment of 8 to 12 weeks. Tsubouchi et al. [25] believed that timely use of effective antibiotics could help preserve implants. Lener et al. [34] reported that sensitive antibiotics should be administered intravenously for 2–4 weeks or until CRP drops significantly, followed by oral antibiotics for 6–12 weeks. Petilon et al. [35] advocated intravenous antibiotics for ≥6 weeks, followed by oral antibiotics for several weeks. Kowalski et al. [36] noted that even if the pathogenic test result is negative, long-term antibiotics are more effective in controlling and eradicating infection than short-term antibiotics (80%:33%). Of course, antibiotics could never replace surgical treatments such as debridement, implant replacement, or removal.

5. Conclusion

The incidence of SSI following lumbar Dynesys dynamic internal fixation was 2.22%, the incidence of early infection was 1.24%, and the incidence of delayed infection was 0.98%. If the main infection site of early infection is in the incision, debridement should be the main treatment method; if the infection site is around the internal fixation, implant replacement is recommended on the basis of debridement. Once delayed infection is diagnosed, implant removal is suggested.

Data Availability

The underlying data supporting the results of our study can be obtained by contacting the corresponding author via zhouqiang@hospital.cqmu.edu.cn.

Conflicts of Interest

The authors declare that there are no conflicts of interests regarding the publication of this study.

References

[1] A. Lazary, I. Klemencsics, Z. Szoverfi, and L. Kiss, "Global treatment outcome after surgical site infection in elective

degenerative lumbar spinal operations," *Surgical Infections*, vol. 22, no. 2, pp. 193–199, 2020.

[2] A. Jain, V. Puvanesarajah, E. N. Menga, and P. D. Sponseller, "Unplanned hospital readmissions and reoperations after pediatric spinal fusion surgery," *Spine*, vol. 40, no. 11, pp. 856–862, 2015.

[3] B. Welke, M. Schwarze, C. Hurschler, D. Nebel, N. Bergmann, and D. Daentzer, "In vitro investigation of two connector types for continuous rod construct to extend lumbar spinal instrumentation," *European Spine Journal*, vol. 27, no. 8, pp. 1895–1904, 2018.

[4] R. D. Murtagh, R. M. Quencer, A. E. Castellvi, and J. J. Yue, "New techniques in lumbar spinal instrumentation: what the radiologist needs to know," *Radiology*, vol. 260, no. 2, pp. 317–330, 2011.

[5] R. Picada, R. B. Winter, J. E. Lonstein et al., "Postoperative deep wound infection in adults after posterior lumbosacral spine fusion with instrumentation: incidence and management," *Journal of Spinal Disorders*, vol. 13, no. 1, pp. 42–45, 2000.

[6] D. L. Reames, J. S. Smith, K.-M. G. Fu et al., "Complications in the surgical treatment of 19,360 cases of pediatric scoliosis," *Spine*, vol. 36, no. 18, pp. 1484–1491, 2011.

[7] J. Zhou, R. Wang, X. Huo, W. Xiong, L. Kang, and Y. Xue, "Incidence of surgical site infection after spine surgery," *Spine*, vol. 45, no. 3, pp. 208–216, 2020.

[8] L.-Y. Fay, C.-C. Chang, H.-K. Chang et al., "A hybrid dynamic stabilization and fusion system in multilevel lumbar spondylosis," *Neurospine*, vol. 15, no. 3, pp. 231–241, 2018.

[9] A. Hu, C. Sun, Y. Liang, H. Wang, X. Li, and J. Dong, "Multisegmental lumbar spinal stenosis treated with Dynesys stabilization versus lumbar fusion in elderly patients: a retrospective study with a minimum of 5 years' follow-up," *Archives of Orthopaedic and Trauma Surgery*, vol. 139, no. 10, pp. 1361–1368, 2019.

[10] G. Akyoldas, O. M. Cevik, T. Suzer, M. Sasani, T. Oktenoglu, and A. F. Ozer, "Dynamic stabilization of the lumbar spine using the Dynesys® system," *Neurosurgery*, vol. 30, no. 2, pp. 190–193, 2020.

[11] Y. Zhang, Z.-C. Zhang, F. Li et al., "Long-term outcome of Dynesys dynamic stabilization for lumbar spinal stenosis," *Chinese Medical Journal*, vol. 131, no. 21, pp. 2537–2543, 2018.

[12] W. C. Welch, B. C. Cheng, T. E. Awad et al., "Clinical outcomes of the Dynesys dynamic neutralization system: 1-year preliminary results," *Neurosurgical Focus*, vol. 22, no. 1, p. E8, 2007.

[13] D. Grob, A. Benini, A. Junge, and A. F. Mannion, "Clinical experience with the Dynesys semirigid fixation system for the lumbar spine," *Spine*, vol. 30, no. 3, pp. 324–331, 2005.

[14] A. F. Ozer, T. Oktenoglu, E. Egemen et al., "Lumbar single-level dynamic stabilization with semi-rigid and full dynamic systems: a retrospective clinical and radiological analysis of 71 patients," *Clinical Orthopaedic Surgery*, vol. 9, no. 3, pp. 310–316, 2017.

[15] M. Ferraro, F. Luceri, D. Peroni, B. Misaggi, and G. M. Peretti, "Posterior dynamic neutralization and hybrid stabilization in degenerative spine diseases: long-term clinical and radiological outcomes," *Journal of Biological Regulators and Homeostatic Agents*, vol. 34, no. 4, pp. 91–Society, 2020.

[16] S. Garg, J. LaGreca, M. Hotchkiss, and M. Erickson, "Management of late (>1 y) deep infection after spinal fusion," *Journal of Pediatric Orthopaedics*, vol. 35, no. 3, pp. 266–270, 2015.

[17] P. J. Cahill, D. E. Warnick, M. J. Lee et al., "Infection after spinal fusion for pediatric spinal deformity," *Spine*, vol. 35, no. 12, pp. 1211–1217, 2010.

[18] J. Y. Du, C. Poe-Kochert, G. H. Thompson, J. P. Son-Hing, C. K. Hardesty, and R. J. Mistovich, "Risk factors for early infection in pediatric spinal deformity surgery: a multivariate analysis," *Spine Deformity*, vol. 7, no. 3, pp. 410–416, 2019.

[19] P. Lewkonia, C. DiPaola, and J. Street, "Incidence and risk of delayed surgical site infection following instrumented lumbar spine fusion," *Journal of Clinical Neuroscience*, vol. 23, pp. 76–80, 2016.

[20] I. M. Goldstein, N. Agarwal, A. Mammis, J. C. Barrese, and L. D. Christiano, "Dynamic stabilization: a nidus for infection?" *International Journal of Neuroscience*, vol. 125, no. 3, pp. 191–200, 2015.

[21] M. H. Pham, V. A. Mehta, N. N. Patel et al., "Complications associated with the Dynesys dynamic stabilization system: a comprehensive review of the literature," *Neurosurgical Focus*, vol. 40, no. 1, p. E2, 2016.

[22] D. B. Wiseman, C. I. Shaffrey, and G. Lanzino, "Posterior lumbar interbody fusion," in *Spine Surgery: Techniques, Complication Avoidance, and Management*, E. C. Benzel, Ed., vol. 1, pp. 452–473, Elsevier, Philadelphia, PA, USA, 2005.

[23] N. Kabirian, B. A. Akbarnia, J. B. Pawelek et al., "Deep surgical site infection following 2344 growing-rod procedures for early-onset scoliosis," *Journal of Bone and Joint Surgery*, vol. 96, no. 15, p. e128, 2014.

[24] L. Mahesh, V. R. Kumar, A. Jain et al., "Bacterial adherence around sutures of different material at grafted site: a microbiological analysis," *Materials*, vol. 12, no. 18, p. 2848, 2019.

[25] N. Tsubouchi, S. Fujibayashi, B. Otsuki et al., "Risk factors for implant removal after spinal surgical site infection," *European Spine Journal*, vol. 27, no. 10, pp. 2481–2490, 2018.

[26] A. Agarwal, A. Kelkar, A. G. Agarwal et al., "Implant retention or removal for management of surgical site infection after spinal surgery," *Global Spine Journal*, vol. 10, no. 5, pp. 640–646, 2020.

[27] D. M. C. Janssen, S. M. J. van Kuijk, B. d'Aumerie, and P. Willems, "A prediction model of surgical site infection after instrumented thoracolumbar spine surgery in adults," *European Spine Journal*, vol. 28, no. 4, pp. 775–782, 2019.

[28] Y. Kobayashi, H. Inose, S. Ushio et al., "Body mass index and modified Glasgow prognostic score are useful predictors of surgical site infection after spinal instrumentation surgery," *Spine*, vol. 45, no. 3, pp. E148–E154, 2020.

[29] Z. Pennington, D. Lubelski, E. M. Westbroek, A. K. Ahmed, P. G. Passias, and D. M. Sciubba, "Persistent postoperative hyperglycemia as a risk factor for operative treatment of deep wound infection after spine surgery," *Neurosurgery*, vol. 87, no. 2, pp. 211–219, 2020.

[30] Z. He, K. Zhou, K. Tang, Z. Quan, S. Liu, and B. Su, "Perioperative hypoalbuminemia is a risk factor for wound complications following posterior lumbar interbody fusion," *Journal of Orthopaedic Surgery and Research*, vol. 15, no. 1, p. 538, 2020.

[31] T. Tan, H. Lee, M. S. Huang et al., "Prophylactic postoperative measures to minimize surgical site infections in spine surgery: systematic review and evidence summary," *The Spine Journal*, vol. 20, no. 3, pp. 435–447, 2020.

[32] H. Ushirozako, T. Hasegawa, Y. Yamato, G. Yoshida, and T. Yasuda, "Does preoperative prognostic nutrition index predict surgical site infection after spine surgery?" *European Spine Journal*, vol. 30, no. 6, pp. 1765–1773, 2020.

[33] C. Zhang, L. Wang, T. Hou et al., "The influence of L4-S1 Dynesys dynamic stabilization versus fusion on lumbar motion and its relationship with lumbar degeneration: a retrospective study," *Journal of Orthopaedic Surgery and Research*, vol. 12, no. 1, p. 99, 2017.

[34] S. Lener, S. Hartmann, G. M. V. Barbagallo, F. Certo, C. Thomé, and A. Tschugg, "Management of spinal infection: a review of the literature," *Acta Neurochirurgica*, vol. 160, no. 3, pp. 487–496, 2018.

[35] J. M. Petilon, S. D. Glassman, J. R. Dimar, and L. Y. Carreon, "Clinical outcomes after lumbar fusion complicated by deep wound infection," *Spine*, vol. 37, no. 16, pp. 1370–1374, 2012.

[36] T. J. Kowalski, E. F. Berbari, P. M. Huddleston, J. M. Steckelberg, J. N. Mandrekar, and D. R. Osmon, "The management and outcome of spinal implant infections: contemporary retrospective cohort study," *Clinical Infectious Diseases*, vol. 44, no. 7, pp. 913–920, 2007.