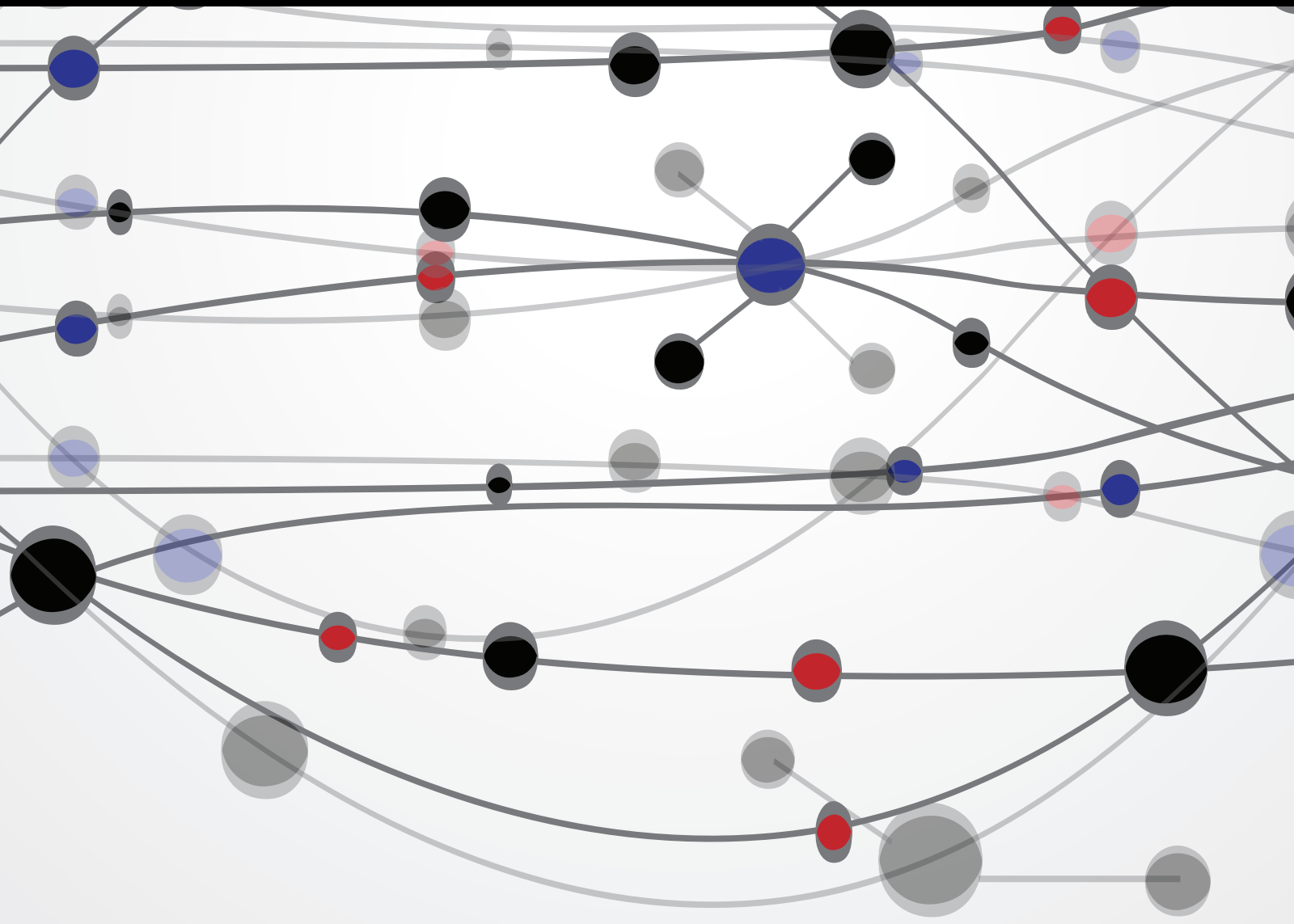
The Scientific World Journal

Perioperative Outcomes in Orthopedic Surgery

Guest Editors: Stavros G. Memtsoudis, Vassilios I. Vougioukas, Ottokar Stundner, and Lazaros A. Poultsides



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Editorial

Perioperative Outcomes in Orthopedic Surgery

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With millions of surgical procedures being performed worldwide annually, clinicians, researchers, patients, and administrators increasingly pursue understanding factors, which affect and determine perioperative outcomes. The last decades have been associated with extensive research and subsequent increased number of publications in the field of perioperative outcomes in orthopaedic surgery. The population is progressively involved in recreational and athletic activities increasing thus the prevalence of sport-related soft-tissue and bone injuries. Furthermore, the population is aging and the demand for joint replacement and spine surgery is increasing annually, raising inevitably the absolute numbers of surgery related complications such as infection, mechanical failure, and delayed union. Finally, the adoption of new technology and the introduction of minimally invasive surgical techniques still remain a controversial topic on whether evidence-based medicine has justified the risk of their use. Hence, it is important to critically evaluate the perioperative outcomes of modern orthopaedic surgery and further investigate whether a change in the perioperative management of the orthopaedic patient is warranted. Although the selected papers for this special issue are not an exhaustive representation of the area of perioperative outcomes in orthopaedic surgery, they represent an excellent panel for approaching and addressing this challenge. Without doubt they will provide significant knowledge to the readers, simulating further investigation and research and possible improvement of the current surgical technique and overall perioperative management of the orthopaedic patient.

The special issue contains six papers; of these, three papers are related to spine surgery and more specifically to fusion rates of various disc substitutes and outcomes and complications of minimally invasive surgery. One paper presents short-term outcomes of surgical reconstruction of chronic functional ankle instability. Another experimental study provides data that support the combined use of flexible intramedullary nailing and Ilizarov external fixation for bone repair enhancement. Finally, the last paper covers criteria for patient risk stratification with regard to the development of surgical site infection following total hip arthroplasty.

In the paper entitled "PEEK Cages versus PMMA Spacers in Anterior Cervical Discectomy: Comparison of Fusion, Subsidence, Sagittal Alignment, and Clinical Outcome with a Minimum 1-Year Follow-Up," authors compared radiographic and clinical outcomes after anterior cervical discectomy in patients with cervical degenerative disc disease using PEEK cages or PMMA spacers with a minimum 1-year follow-up. They found that the substitute groups showed differing fusion rates. However, clinical outcomes appeared to be generally not correlated with fusion status or subsidence. Authors concluded that they could not specify a superior disc substitute for anterior cervical discectomy.

In the paper "Minimally Invasive Technique for PMMA Augmentation of Fenestrated Screws" authors described the minimally invasive technique, as well as its safety and efficacy, for cement augmentation of cannulated and fenestrated screws using an injection cannula. The presented minimally invasive cement augmentation technique using an injection

cannula was proven to facilitate convenient and safe cement delivery through polyaxial cannulated and fenestrated screws during minimally invasive screw-rod spondylodesis.

In the paper "Accidental Durotomy in Minimally Invasive Transforaminal Lumbar Interbody Fusion: Frequency, Risk Factors, and Management," authors' purpose was to assess the frequency, risk factors, and management of accidental durotomy in minimally invasive transforaminal lumbar interbody fusion. Their results showed that the frequency of accidental durotomies in MIS TLIF is low, with overweight being a risk factor. They concluded that the minimally invasive approach seems to minimize durotomy-associated complications (CSF leakage, pseudomeningocele) because of the limited dead space in the soft tissue.

In the paper "Surgical Reconstruction with the Remnant Ligament Improves Joint Position Sense as well as Functional Ankle Instability: A 1-Year Follow-Up Study," they assessed functional improvement of chronic ankle instability after surgical reconstruction using the remnant ligament. This study showed that surgical reconstruction using the remnant ligament was effective not only for improving mechanical retensioning but also for ameliorating joint position sense and functional ankle instability.

In the paper "Bone Healing by Using Ilizarov External Fixation Combined with Flexible Intramedullary Nailing versus Ilizarov External Fixation Alone in the Repair of Tibial Shaft Fractures: Experimental Study," authors conducted an experimental study utilizing an open tibial shaft fracture canine model aiming to study the radiographic and histological outcomes of flexible intramedullary nailing (FIN) combined with Ilizarov external fixation (IEF) versus Ilizarov external fixation alone. Authors concluded that the combination of the Ilizarov apparatus and FIN accelerates bone repair and augments stabilization of tibial shaft fractures as compared with the use of the Ilizarov fixation alone.

Finally, in the paper "Patient, Surgery, and Hospital Related Risk Factors for Surgical Site Infections following Total Hip Arthroplasty" authors conducted an extensive review of the literature on reported patient, surgery, and hospital related risk factors for SSI after THA. This review can facilitate surgeons to identify patients at risk for infection and administrators to adopt preventive systems based strategies to reduce the overall risk and therefore the subsequent multifaceted burden of periprosthetic joint infections.

Acknowledgments

We would like to thank the authors for their excellent contribution and work on choosing the topics, preparing the manuscripts, and going through the revisions in a timely fashion. Furthermore, all reviewers should be congratulated and acknowledged for their essential work and time spent to improve the content of these papers.

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Clinical Study

Accidental Durotomy in Minimally Invasive Transforaminal Lumbar Interbody Fusion: Frequency, Risk Factors, and Management

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Purpose. To assess the frequency, risk factors, and management of accidental durotomy in minimally invasive transforaminal lumbar interbody fusion (MIS TLIF). *Methods*. This single-center study retrospectively investigates 372 patients who underwent MIS TLIF and were mobilized within 24 hours after surgery. The frequency of accidental durotomies, intraoperative closure technique, body mass index, and history of previous surgery was recorded. *Results*. We identified 32 accidental durotomies in 514 MIS TLIF levels (6.2%). Analysis showed a statistically significant relation of accidental durotomies to overweight patients (body mass index $\geq 25\,kg/m^2$; $P = 0.0493$). Patient age older than 65 years tended to be a positive predictor for accidental durotomies ($P = 0.0657$). Mobilizing patients on the first postoperative day, we observed no durotomy-associated complications. *Conclusions*. The frequency of accidental durotomies in MIS TLIF is low, with overweight being a risk factor for accidental durotomies. The minimally invasive approach seems to minimize durotomy-associated complications (CSF leakage, pseudomeningocele) because of the limited dead space in the soft tissue. Patients with accidental durotomy can usually be mobilized within 24 hours after MIS TLIF without increased risk. The minimally invasive TLIF technique might thus be beneficial in the prevention of postoperative immobilization-associated complications such as venous thromboembolism. This trial is registered with DRKS00006135.

1. Introduction

Surgical fusion techniques are used to treat degenerative, infectious, and traumatic pathologies of the lumbar spine [1–3]. The traditional open technique includes a long midline skin incision with dissection and retraction of the paravertebral musculature to expose the posterior structures of the spine. Minimally invasive techniques were shown to be equally effective as open procedures while leading to reduced blood loss, less postoperative morbidity, and faster recovery [4–6]. Accidental durotomies are an undesirable intraoperative complication with a reported frequency of 3.2 to 18.5% in spine surgery [7–12]. In minimally invasive transforaminal lumbar interbody fusion (MIS TLIF), however, accidental durotomies have scarcely been investigated [7].

We hypothesized that the frequency of accidental durotomies in MIS TLIF is comparable to other lumbar procedures.

2. Methods

2.1. Ethics Statement. The local ethics committee approved the study. The study is registered in the German Clinical Trials Register (DRKS00006135).

2.2. Data Collection. Through a retrospective review of our institutional database, we identified 372 consecutive patients (218 women and 154 men, age: 64.6 ± 13.6 years) who underwent MIS TLIF in 514 levels between January 2006 and March 2014. The vast majority of patients had degenerative

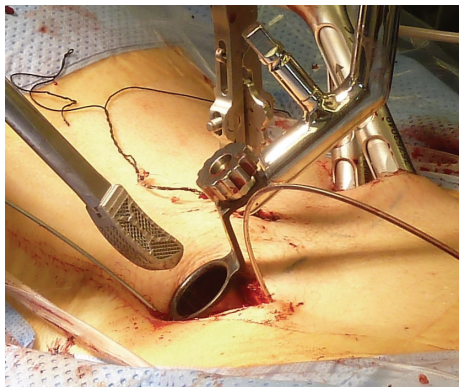

Figure 1: Minimally invasive cage implantation. An intervertebral cage made of titanium mesh is introduced minimally invasively through a nonexpendable tubular retractor (20 mm diameter) into the intervertebral disc space.

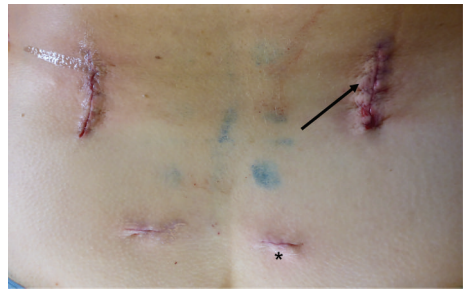

Figure 2: Wound closure. Subcutaneous sutures and skin adhesive were used for closing the wound. Placement of a drain is not necessary. The more lateral incisions (arrows) were used for minimally invasive implantation of screws, decompression of the spinal canal, and transforaminal insertion of the intervertebral cage (see also Figure 1). The stab incisions (asterisk) were used for minimally invasive rod insertion.

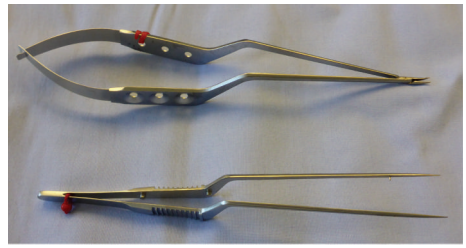

Figure 3: Microsurgical instruments. The figure shows a bayonet microneedle holder and bayonet microforceps that were used for suturing accidental durotomies.

disease (98.4%); few patients were operated on due to infection (1.6%). Based on operation reports and medical records, we collected details on the demographics, level of surgery, history of previous surgery at the same level, extent of decompression, intraoperative technique of closing durotomies, and durotomy-related complications. The frequency of accidental durotomies and their potential association with the body mass index (BMI), patient age, and history of previous surgery at the same level were investigated.

2.3. Surgical Technique. Each patient was placed in prone position on a radiolucent table under general anesthesia. Via bilateral short skin incisions (3 cm), a Jamshidi needle was introduced into the target vertebras through the pedicles using 3D C-arm navigation or C-arm fluoroscopic images, and Kirschner wires were inserted through the Jamshidi needle. A minimally invasive, transmuscular approach was created using a nonexpandable tubular retractor system (METRx, Medtronic, Minneapolis, USA). An operating microscope was used during the following transforaminal access including facetectomy, unilateral or bilateral decompression of the spinal canal and partial discectomy. After implantation of a TLIF cage (Figure 1), the 360-degree fusion was completed by insertion of cannulated screws via the Kirschner wires and minimally invasive rod insertion (e.g., CD Horizon Sextant II, CD Horizon Sextant Solera, and CD Horizon Longitude (Medtronic, Minneapolis, USA)). If bone density was considered to be low, additional cement augmentation of vertebral bodies was performed under fluoroscopic image guidance. Skin was closed with subcutaneous sutures and skin adhesive without placing a drain (Figure 2).

In case of durotomy, the dura was closed with nonresorbable suture (5/0 PremiCron, B. Braun, Melsungen, Germany) where possible and supported by a fibrinogen/thrombin-coated sponge (TachoSil, Takeda, Berlin, Germany) or gelfoam with fibrin glue to the surgeon's discretion. Commercially available, microsurgical instruments (bayonet microneedle holder and bayonet microforceps) were used for suturing the durotomy (Figure 3).

All patients, independent of occurrence of accidental durotomies, were mobilized within 24 hours of surgery unless the patient's clinical status prohibited mobilization.

2.4. Statistical Analysis. Results were expressed as mean with standard deviation. Statistical comparisons for categorical values between groups were accomplished using the two-tailed Fisher exact test. Prism 6 for Mac (GraphPad Software Inc., La Jolla, USA) and Excel 2011 for Mac (Microsoft Corporation, Redmond, USA) were used as statistical software and for data processing. P values < 0.05 were considered to be statistically significant.

3. Results

3.1. Frequency of Accidental Durotomies. Thirty-two accidental durotomies occurred in 514 MIS TLIF levels (6.2%) (Table 1). Table 2 shows the distribution of operated levels and accidental durotomies. MIS TLIF was performed most frequently at L4/5 (41.8%); furthermore, the highest percentage of durotomies was registered at L4/5 (9.8%).

3.2. Durotomy and Body Mass Index, Age, or Previous Surgery. We investigated a possible association between accidental durotomies and the BMI, patient age, and history of previous surgery at the same level.

Table 1: Characterization and dural closure technique in patients with accidental durotomies.

Patient number	Sex	Age (years)	BMI (kg/m^2)	Level of durotomy	Contralateral decompression?	Site of durotomy	Previous surgery?	Adhesions scarring?	Durotomy during	Closure	Mobilization
1	Male	76.4	29.8	L4/5	Yes	Ipsilateral	Yes	No	Cage implantation	Suture + TachoSil	1st postop. day
2	Female	73.0	27.0	L3/4	Yes	Ipsilateral	No	Yes	Cage implantation	TachoSil	3rd postop. day
				L4/5	Yes	Contralateral	No	Yes	Decompression	TachoSil	
3	Female	79.6	27.8	L3/4	Yes	Ipsilateral	No	Yes	Decompression	TachoSil	3rd postop. day
				L4/5	Yes	Contralateral	No	Yes	Decompression	TachoSil	
4	Male	68.6	38.2	L2/3	Yes	Ipsilateral	Yes	Yes	Decompression	TachoSil	1st postop. day
5	Male	71.6	33.2	L3/4	No	Ipsilateral	Yes	No	Cage implantation	TachoSil	1st postop. day
6	Female	65.2	32.3	L4/5	Yes	Contralateral	No	Yes	Decompression	TachoSil	1st postop. day
7	Female	71.4	34.0	L4/5	Yes	Ipsilateral	Yes	Yes	Decompression	TachoSil	3rd postop. day
8	Female	89.7	26.7	L4/5	Yes	Contralateral	No	Yes	Decompression	TachoSil	1st postop. day
9	Male	65.6	24.6	L4/5	Yes	Contralateral	No	No	Decompression	TachoSil	1st postop. day
10	Female	55.7	34.1	L3/4	Yes	Ipsilateral	No	No	Cage implantation	Suture + TachoSil	1st postop. day
11	Male	58.2	25.3	L5/S1	No	Ipsilateral	No	No	N/A	TachoSil	1st postop. day
12	Female	59.6	27.1	L4/5	Yes	N/A	No	No	Decompression	Suture + TachoSil	1st postop. day
13	Female	78.9	22.1	L3/4	Yes	Ipsilateral	Yes	No	Cage implantation	Gelfoam + fibrin glue	2nd postop. day
14	Male	66.2	28.4	L4/5	No	Ipsilateral	No	No	Decompression	TachoSil	1st postop. day
15	Male	64.4	34.3	L4/5	No	Ipsilateral	Yes	No	Decompression	TachoSil	1st postop. day
16	Female	55.0	33.8	L4/5	No	Ipsilateral	Yes	Yes	Decompression	TachoSil	1st postop. day
17	Female	74.2	44.3	L3/4	Yes	Ipsilateral	No	No	Decompression	Suture + TachoSil	6th postop. day due to transitory psychotic syndrome
18	Male	73.6	27.6	L4/5	No	Ipsilateral	Yes	Yes	Decompression	Suture + TachoSil	1st postop. day

Table 1: Continued.

Patient number	Sex	Age (years)	BMI (kg/m^2)	Level of durotomy	Contralateral decompression?	Site of durotomy	Previous surgery?	Adhesions scarring?	Durotomy during	Closure	Mobilization
19	Male	62.4	27.8	L4/5	Yes	Ipsilateral	No	Yes	Decompression	Suture + TachoSil	1st postop. day
20	Female	78.8	34.9	L2/3	No	Ipsilateral	Yes	No	Decompression	TachoSil	2nd postop. day
21	Female	71.7	27.3	L3/4	No	Ipsilateral	Yes	No	Decompression	Suture + TachoSil	1st postop. day
22	Female	75.3	31.0	L4/5	Yes	Ipsilateral	No	Yes	Decompression	Suture + TachoSil	1st postop. day
23	Male	66.0	24.8	L4/5	Yes	Ipsilateral	No	No	Decompression	TachoSil	1st postop. day
24	Male	62.5	30.7	L4/5	Yes	Ipsilateral	Yes	Yes	Cage implantation	TachoSil	1st postop. day
25	Female	75.2	27.9	L4/5	Yes	Contralateral	No	No	Decompression	TachoSil	5th postop. day
26	Female	70.1	40.4	L5/S1	Yes	Contralateral	No	No	Decompression	TachoSil	2nd postop. day
27	Female	65.5	24.2	L4/5	No	Ipsilateral	No	No	Decompression	TachoSil	1st postop. day
28	Male	78.5	24.4	L4/5	No	Ipsilateral	No	No	Decompression	Suture	N/A (died of multiple organ failure on postop. day 8)
29	Male	79.4	26.1	L4/5	Yes	Ipsilateral	No	Yes	Decompression	Suture	1st postop. day
30	Male	44.4	29.2	L4/5	No	Ipsilateral	Yes	Yes	Decompression	None (due to intact arachnoidea)	1st postop. day
Mean		69.2	30.0								1.6
Standard deviation		9.3	5.1								1.3
	16 × female			2 × L2/3	21 × yes	24 × ipsilateral	12 × yes	15 × yes	25 × decompression	20 × TachoSil	
	14 × male			7 × L3/4	11 × no	7 × contralateral	20 × no	17 × no	6 × cage implantation	8 × Suture + TachoSil	
				21 × L4/5		1 × N/A			1 × N/A	2 × suture	
				2 × L5/S1						1 × gelfoam + fibrin glue	
										1 × none	

BMI: body mass index.
N/A: not available.

Table 2: Distribution of operated levels and accidental durotomies.

Level of MIS TLIF	Number of MIS TLIF	Number of durotomies	Percentage of durotomies
L1/2	14	0	0.0%
L2/3	49	2	4.1%
L3/4	96	7	7.3%
L4/5	215	21	9.8%
L5/S1	140	2	1.4%
Total	514	32	6.2%

MIS TLIF: minimally invasive transforaminal lumbar interbody fusion.

Table 3: Number and relation of accidental durotomies and BMI.

Durotomy		BMI (kg/m^2)		Total
		<25	≥25	
No	**Levels operated**	**162**	**320**	**482**
	% without durotomy	33.6%	66.4%	100%
	% within BMI group	97.0%	92.2%	
Yes	**Levels operated**	**5**	**27**	**32**
	% with durotomy	15.6%	84.4%	100%
	% within BMI group	3.0%	7.8%	

The two-tailed Fisher exact test showed a statistically significant relation of accidental durotomies to overweight patients ($P = 0.0493$).
BMI: body mass index.

Table 4: Number and relation of accidental durotomies and patient age.

Durotomy		Age		Total
		<65 years	≥65 years	
No	**Levels operated**	**201**	**281**	**482**
	% without durotomy	41.7%	58.3%	100%
	% within age cohort	96.2%	92.1%	
Yes	**Levels operated**	**8**	**24**	**32**
	% with durotomy	25.0%	75.0%	100%
	% within age cohort	3.8%	7.9%	

The two-tailed Fisher exact test showed no statistically significant relation between accidental durotomies and age cohort ($P = 0.0657$).

Overweight patients (BMI ≥ 25 kg/m^2) had a higher incidence of durotomies (7.8% versus 3.0%, Table 3). The two-tailed Fisher exact test showed a statistically significant relation of accidental durotomies to overweight patients ($P = 0.0493$). Patients with an age of at least 65 years had a higher incidence of durotomies (7.9% versus 3.8%, Table 4). The two-tailed Fisher exact test showed no statistically significant relation between accidental durotomies and age cohort ($P = 0.0657$). Patients with history of previous surgery in the level of MIS TLIF had a higher incidence of durotomies (8.3% versus 5.3%, Table 5). The two-tailed Fisher exact test showed no statistically significant relation between accidental durotomies and history of previous surgery in the level of MIS TLIF ($P = 0.1535$).

Table 5: Number and relation of accidental durotomies and history of previous surgery.

Durotomy		Previous surgery		Total
		No	Yes	
No	**Levels operated**	**357**	**125**	**482**
	% without durotomy	74.1%	25.9%	100%
	% within group of previous surgery	94.7%	91.7%	
Yes	**Levels operated**	**20**	**12**	**32**
	% with durotomy	62.5%	37.5%	100%
	% within group of previous surgery	5.3%	8.3%	

The two-tailed Fisher exact test showed no statistically significant relation between accidental durotomies and history of previous surgery in the level of MIS TLIF ($P = 0.1535$).

3.3. Adhesions and Scarring. In 11 of the 32 levels with accidental durotomy (45.0%), neither history of previous surgery nor adhesions were recorded (Table 1). Twelve of the 32 levels (37.5%) with accidental durotomies had a history of previous decompression surgery. Six of these (50.0%) were stated in context with scar tissue that was adherent to the lacerated dura. Adhesions with subsequent accidental durotomy were found in 9 of 20 levels without history of previous surgery. Altogether, adhesions or scarring was found in 15 of 32 levels (46.9%), independent of a history of previous surgery.

3.4. Postoperative Complications. None of the patients with accidental durotomies developed a postoperative CSF fistula or needed revision surgery due to durotomy-associated complications. Apart from durotomy-associated complications, three patients experienced postoperative complications. Patient number 10 sustained an accidental durotomy during cage implantation with concomitant direct nerve injury. Postoperatively, the patient had new flexion and extension paresis of the right foot. Patient number 17 postoperatively sustained a transitory psychotic syndrome. After recovering from this syndrome, a hindered mobilization with an increased local pain level could be recognized. Imaging revealed a postoperative epidural hemorrhage, which was surgically evacuated without clinical sequelae. Patient number 28 sustained multiple organ failure and died on postoperative day 8.

4. Discussion

Accidental durotomies can lead to persistent CSF leakage with formation of a pseudomeningocele and CSF leak syndrome. The resultant symptoms include postural headache, nausea, back pain, intracranial hemorrhage, neurological deficits, and meningitis [8, 13]. Thus, if an accidental durotomy occurs, the surgeon has to ensure proper dural closure intraoperatively to prevent persistent CSF leakage. But even if accidental durotomy does occur in minimally invasive spine surgery, it is thought to be much less likely to cause sequelae because there is barely dead space available for formation

of a pseudomeningocele. The underlying cause is that the paraspinal musculature is not dissected during the approach and slides back to its original position after the tubular retractor has been removed [9, 10, 14].

4.1. Frequency of Accidental Durotomies. The present literature regarding the incidence and management of accidental durotomies in MIS TLIF is very limited and includes only smaller patient cohorts [7, 10, 15]. Senker et al. [7] retrospectively identified 10 accidental durotomies in 72 patients (13.9%) who underwent MIS TLIF or percutaneous lumbar stabilization. Half of the durotomies were closed with sutures. Sulaiman and Singh [15] reported 1 durotomy in 57 patients with MIS TLIF (1.8%) and 1 durotomy in 11 patients with open TLIF (9.1%). Than et al. [10] observed durotomies in 6.3% of 112 patients with minimally invasive lumbar spine procedures (decompressive and fusion procedures). Telfeian et al. [9] observed accidental durotomies in 16.7% of 12 patients with severe obesity (BMI > 40 kg/m^2) who underwent heterogeneous spine operations. Ruban and O'Toole [8] retrospectively examined minimally invasive operations (decompressive and fusion procedures) of the whole spine and found durotomies in 9.4% of 563 patients. Ross [16] stated an incidence for lumbar durotomies in 3.4% of 929 cases during minimally invasive decompression surgery. Khan et al. [17] reported an incidence for lumbar durotomies in 10.6% of 3,183 patients (decompressive and fusion procedures); the subgroup with history of previous surgery at the same level showed a higher incidence of 15.9%. Studies comparing open TLIF and open PLIF (posterior lumbar interbody fusion) procedures found higher numbers of durotomies in open PLIF procedures (17.1% (13/76 patients) versus 9.3% (4/43 patients) [18]; 7.7% (4/52 patients) versus 0.0% (0/50 patients) [19]).

Thus, the rate of accidental durotomies in our study with 6.2% in 514 levels with MIS TLIF is comparably low. Only two other studies with considerably less numbers of patients investigated durotomies in MIS TLIF procedures as well and reported durotomies in 1.8% [15] and 13.9% [7] of them, respectively.

4.2. Risk Factors. Accidental durotomies have been reported to occur more often in patients with older age, scars from previous surgery, ossificated ligamentum flavum, thinning of dura attributable to chronic compression, and surgeon inexperience [8, 10, 17, 20, 21]. In general, revision surgery is more demanding than primary surgery due to scarring and modifications of the anatomy. Thus, revision surgery may be associated with higher complication rates such as accidental durotomies or nerve root injury [8, 12, 17]. Likewise, levels with history of previous surgery showed an increased durotomy rate in our study (8.8% versus 5.3%, Table 5), though without reaching statistical significance. Our study demonstrated that accidental durotomies occur more often in overweight patients compared to normal weight patients. The longer approach to the spinal canal and, thus, the more difficult dissection with longer instruments might be an explanation for this finding. Consistent with Senker et al. [7], we did not find a statistical difference regarding durotomies between patients who were younger or older than 65 years ($P = 0.0657$), although the older age cohort tended to sustain more durotomies (7.9% versus 3.8%, Table 4).

4.3. Use of Drain. We generally use no drain in minimally invasive surgery. We agree with other authors [8, 10] that particularly the minimally invasive approach with its rather small corridor to the spine allows the soft tissue to slip back after removal of the tubular retractor and thus counters CSF accumulation in case of accidental durotomy. Thus, placing a drain is not necessary in our opinion. Moreover, we do not believe that placement of a subfascial drain prevents hematomas as stated by other authors [7]. Nevertheless, the use of drains after accidental durotomy in minimally invasive spine surgery remains controversial, since some authors describe their routine use [17, 22].

4.4. Mobilization after Durotomy. Early mobilization is recommended in elective spine surgery to reduce postoperative complications like venous thromboembolism [23]. We aimed to mobilize all patients on the first postoperative day, independent of occurrence of durotomy. Twenty-one of 30 patients with accidental durotomy could be mobilized on the first postoperative day (Table 1) without any complication. We therefore agree with Ruban and O'Toole [8] who also mobilized patients with durotomies within 24 hours of minimally invasive surgery without any complications. Than et al. [10] mobilized patients with durotomy within 48 hours after minimally invasive surgery without any complication, and Senker et al. [7] applied bed rest for 2.5 to 5 days in case of accidental durotomies after minimally invasive procedures. In contrast, bed rest after a durotomy during open spinal procedures has been recommended for up to 7 days [8, 17, 22], supporting that minimally invasive approaches are beneficial for early mobilization, even after durotomy. The underlying theory is that the minimally invasive approach with small skin incisions and the muscle-dilating technique causes only a very limited dead space in the soft tissue. This decreased space is believed to create less potential for CSF accumulation, permanent CSF leakage, and formation of a pseudomeningocele in comparison to the open approach [8, 10]. In this regard, we consider MIS TLIF superior to open TLIF or PLIF as patients with durotomy do not require extended bed rest after MIS TLIF and are recommended to be mobilized within 24 hours of surgery. Early mobilization is preventive regarding postoperative complications [23] and potentially reduces the length of hospital stay.

5. Conclusions

The frequency of accidental durotomies in MIS TLIF is low, and overweight is a risk factor for accidental durotomies. The minimally invasive approach seems to minimize durotomy-associated complications such as permanent CSF leakage or pseudomeningocele because of the limited dead space in the soft tissue. Furthermore, patients with accidental durotomy can usually be mobilized within 24 hours after

MIS TLIF without increased risk of complications. The minimally invasive TLIF technique might thus be beneficial in the prevention of postoperative immobilization-associated complications such as venous thromboembolism.

Limitations of the Study

The retrospective design is an obvious methodological weakness of this trial. Since patients were retrospectively included, no power analysis was performed. Furthermore the study lacks an open TLIF control group and does not compare differing durotomy repair strategies.

Abbreviations

BMI: Body mass index
CSF: Cerebrospinal fluid
MIS TLIF: Minimally invasive transforaminal lumbar interbody fusion
PLIF: Posterior lumbar interbody fusion.

Conflict of Interests

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

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Clinical Study

Minimally Invasive Technique for PMMA Augmentation of Fenestrated Screws

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Purpose. To describe the minimally invasive technique for cement augmentation of cannulated and fenestrated screws using an injection cannula as well as to report its safety and efficacy. *Methods*. A total of 157 cannulated and fenestrated pedicle screws had been cement-augmented during minimally invasive posterior screw-rod spondylodesis in 35 patients from January to December 2012. Retrospective evaluation of cement extravasation and screw loosening was carried out in postoperative plain radiographs and thin-sliced triplanar computed tomography scans. *Results*. Twenty-seven, largely prevertebral cement extravasations were detected in 157 screws (17.2%). None of the cement extravasations was causing a clinical sequela like a new neurological deficit. One screw loosening was noted (0.6%) after a mean follow-up of 12.8 months. We observed no cementation-associated complication like pulmonary embolism or hemodynamic insufficiency. *Conclusions*. The presented minimally invasive cement augmentation technique using an injection cannula facilitates convenient and safe cement delivery through polyaxial cannulated and fenestrated screws during minimally invasive screw-rod spondylodesis. Nevertheless, the optimal injection technique and design of fenestrated screws have yet to be identified. This trial is registered with German Clinical Trials DRKS00006726.

1. Introduction

Pedicle screw-rod instrumentation is an accepted technique to achieve rigid internal fixation in degenerative, deformative, tumor, and trauma disorders of the spine [1, 2]. With an aging patient population, spine surgeons encounter the challenge to obtain and maintain fixation in an osteoporotic spine [2, 3]. As the bone-screw interface is generally the region most susceptible to loosening and failure, modern techniques aim to improve the fixation of screws particularly in osteoporotic vertebras [3, 4]. Cement augmentation of screws with polymethylmethacrylate (PMMA) has been reported to increase resistance to pullout and toggle failure [3, 5–7]. However, the use of PMMA involves the risk of cement extravasation, which can lead to neural compression, neurological deficits, or pulmonary embolism [8]. Fenestrated screws have been developed to increase convenience and safety of cement delivery [9–11]. With the evolution of minimally invasive spinal fixation procedures comes the need for percutaneous cement delivery through polyaxial fenestrated screws and mounted screw extenders [12, 13]. The purpose of this study is to investigate the efficacy and safety of the minimally invasive technique for cement augmentation of cannulated, fenestrated screws using an injection cannula.

2. Methods

2.1. Patients. This study is a retrospective observational trial to assess the feasibility, effectiveness, and complication rate of injecting bone cement through cannulated and fenestrated screws in minimally invasive spine stabilization procedures. We identified 35 patients in our database of a single center who underwent minimally invasive posterior stabilization of the thoracic and lumbar spine with cement-augmented fenestrated screws due to degenerative/deformative disorders, spinal trauma, or pathological fracture between January and December 2012 (Table 1).

2.2. Surgical Treatment. The surgical technique of performing minimally invasive stabilization procedures with screw-rod instrumentation (CD Horizon Sextant II or CD

Table 1: Patient characteristics. The table shows demographics, underlying cause for performing minimally invasive cement-augmented screw-rod spondylodesis and spine region of the instrumentation.

Demographics	
Number of patients	35
Patient age (y)[#]	72.8 ± 8.8
Sex (female : male)	25 : 10
Body mass index (kg/m^2)[#]	27.3 ± 4.8
Diagnosis	
Degenerative/deformative disorder	22
Spinal trauma/osteoporotic compression/burst fracture	6
Spinal tumor/metastasis	7
Location of instrumentation	
Thoracic spine	2
Thoracolumbar junction	2
Lumbar spine	31

[#]Data are presented as mean with standard deviation.

Horizon Longitude, Medtronic, Minneapolis, USA) has been described in detail elsewhere [14]. For minimally invasive thoracic instrumentation we routinely use intraoperative spinal navigation for accurate screw placement (Cart II system, Stryker, Freiburg, Germany; software: SpineMap 3D navigation) [15, 16]. Usually, no drain was used in minimally invasive spine stabilization procedures. Patients were allowed to ambulate in the morning of the first postoperative day without orthosis, unless the patient's clinical status prohibited mobilization.

2.3. Cement Injection Technique. PMMA augmentation of the screws was performed at the discretion of the surgeon based on the knowledge of diagnosed osteoporosis or tactile findings during surgery. If the surgeon noticed abnormally reduced bone resistance while introducing the Jamshidi needle into the vertebral body, PMMA augmentation was performed [17, 18].

After screwing in the cannulated and fenestrated screws (CD Horizon Fenestrated Screw Spinal System, Medtronic; Figure 1), the bone cement injection cannulas (bone cement metallic injection cannula, Tsunami Medical, San Possidonio, Italy, distributed by Maxxspine, Bad Schwalbach, Germany, Figure 2) were first inserted empty into the polyaxial screw heads to check the proper fit and entry trajectory (Figure 3). After removal of injection cannulas, the PMMA cement (VertaPlex 1/2 Dose, Stryker, Duisburg, Germany) was prepared and filled into the injection cannulas, which can hold 1.5 mL of cement. The filled injection cannulas were reinserted into the screw heads sealed to avoid cement emersion into the screw heads, which could preclude rod insertion. Injection was performed with a toothpaste-like consistency of the cement. Per screw, approximately 2 mL of cement was injected in the lumbar spine and 1.5 mL of cement in the thoracic spine. For every 0.3–0.5 mL of cement injection, cement distribution was checked with fluoroscopic images in lateral projection. In case of evidence of epidural, intradiscal, or prevertebral/intravenous cement extravasation, the injection of cement was stopped.

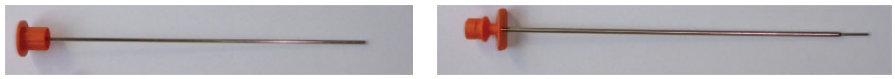
Figure 1: Polyaxial cannulated and fenestrated screw. The screw is fully cannulated with a total of six distal fenestrations (four fenestrations are in sight). Note the polyaxial screw head.

2.4. Radiographic and Complication Assessment. Cement extravasation was postoperatively evaluated in plain radiographs and additionally in available computed tomography (CT) scans using integrated software (IMPAX EE R20 VIII, Agfa HealthCare, Mortsel, Belgium). They were classified into prevertebral, paravertebral, epidural, and intradiscal cement extravasations. Moreover postoperative radiographic imaging was evaluated regarding screw loosening or breakage. Screw loosening was certified if radiographs or CT showed a clear zone around the screw and the radiolucency was 1 mm or wider at the bone-screw interface. Loss of lordosis from postoperative to final follow-up was calculated measuring the Cobb angle within the instrumented spine region in lateral plain radiographs. Complications and reoperations were gathered from patient records.

2.5. Statistical Analysis. Descriptive statistics were used to describe the basic characteristics of the data in the study. Results were expressed as means with standard deviations. Prism 6 for Mac (GraphPad Software Inc., La Jolla, USA) was used as statistical software.

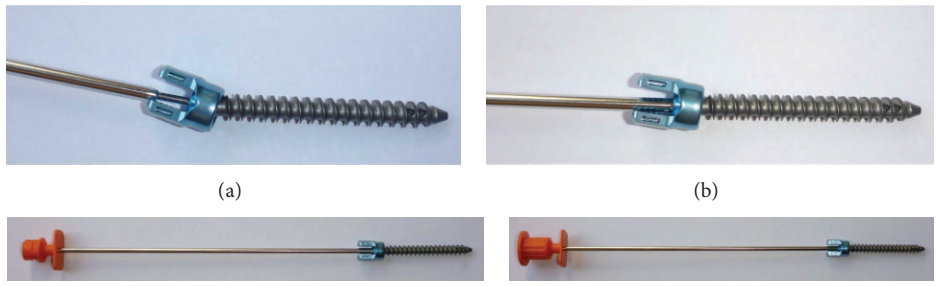
3. Results

3.1. Demographics. A total of 157 cannulated and fenestrated pedicle screws had been cement-augmented in 35 patients during minimally invasive posterior screw-rod spondylodesis. Surgery was mainly performed in the lumbar spine due to degenerative/deformative disorders (Table 1). Most operations were performed as minimally invasive transforaminal lumbar interbody fusion (MIS TLIF) (24/35 patients, 68.6%). Further instrumentation techniques included minimally invasive posterior screw-rod instrumentation only (2/35 patients, 5.7%), in combination with vertebral body replacement (6/35 patients, 17.1%) or in combination with balloon kyphoplasty (3/35 patients, 8.6%). Mean follow-up time was 12.8 months.



(a) (b)

Figure 2: Bone cement injection cannula. The injection cannula (b) can be filled with 1.5 mL of bone cement. With the pusher (a), the bone cement is poured in the cannulated screw and the surrounding vertebral body.



(a) (b)

(c) (d)

Figure 3: Exemplary assembly of injection cannula and polyaxial cannulated and fenestrated screw for percutaneous cement augmentation. The injection cannula is initially inserted unfilled into the polyaxial screw head (a) to check the proper fit and entry trajectory (b). After removing and filling the injection cannula with bone cement outside of the patient's body, the filled injection cannula is reinserted (c). Gradually inserting the pusher into the injection cannula (under fluoroscopic monitoring) bone cement is injected into the screw and surrounding vertebral body through the distal fenestrations (d) (bone cement not shown).

3.2. Radiographic Assessment, Cement Extravasations. Cement-augmented pedicle screws were largely placed in the lower lumbar spine. Table 2 demonstrates the distribution of minimally invasively cement-augmented screws and frequencies of cement extravasations assigned to the level of screw implantation. Overall, 27/157 (17.2%) cement extravasations were detected, at which multiple cement extravasations of one single level had been included. Most cement extravasations were located prevertebrally (20/27, 74.1%) and paravertebrally (4/27, 14.8%) (Table 3). These cement extravasations were often identified in pre- and paravertebral veins and were altogether small in amount (Figure 5). Two intradiscal (7.4%) and one minor epidural (3.7%) cement extravasations were discovered (Figure 5). None of the cement extravasations was causing a clinical sequela like a new neurological deficit.

Loss of lordosis during available follow-up time for plain radiographs (7.9 months) was $1.6^{\circ} \pm 3.7^{\circ}$.

3.3. Complications. We observed no mortality or cementation-associated complications like pulmonary embolism or hemodynamic insufficiency.

Screw loosening was found in one patient with minimally invasive posterior screw-rod spondylodesis L2–L4 in combination with lateral vertebral body replacement of L3 due to osteoporotic compression fracture of L3 13 months postoperatively at scheduled follow-up. Although bony fusion has not yet been achieved, revision surgery was not performed since the patient did not complain about a relevant pain level. Further follow-up examinations have been scheduled to assess fusion status and to avoid missing an early kyphotic deformity.

One patient experienced a new slight paresis of the left foot elevator (grade 4 according to the British Medical Council) after MIS TLIF. Since postoperative CT only discovered a minimal prevertebral cement extravasation, this complication was attributed to intraoperative manipulation of the L5 nerve root.

Further complications occurred, which we do not associate with cement augmentation of the screws: one superficial revision surgery 4 weeks after surgery due to wound dehiscence; one revision surgery 12 days after surgery due to epidural empyema; one revision surgery 12 days after surgery due to patient fall with screw breakage; one revision surgery 7 months after surgery due to screw breakage of a noncemented screw.

4. Discussion

Performing percutaneous cement-augmentation of cannulated and fenestrated screws is a further development in minimally invasive spine surgery [12, 13]. Since the inserted polyaxial screws are mounted with screw extenders (Figure 4), a connection device has to be used for injecting bone cement. We investigated the application and results using an injection cannula in 157 minimally invasive cement-augmented screws in 35 patients. In our experience, the injection cannula warrants a proper fit of its tip in the screw head and, hence, minimizes the risk of cement extravasation in the screw head. This is important, since hardened cement in the screw head might preclude minimally invasive insertion of the rod. Accordingly, we did not experience this phenomenon in our series. A further advantage of the injection cannula is the compatibility with different spine fixation systems (e.g., CD Horizon Sextant II, CD Horizon Longitude, or CD Horizon Sextant Legacy (Medtronic, Minneapolis, USA)).

Table 2: Distribution of cement extravasations. The table shows the numbers and frequencies of cement extravasations assigned to the level of minimally invasively cement-augmented pedicle screws. Note that the count of cement extravasations implies the assessment based on plain radiographs and computed tomography together.

Level of cemented screw	Count of screws studied	Count of cement extravasations	Percentage of cement extravasations	Symptomatic cement extravasations
Th1	0	n/a	n/a	n/a
Th2	2	0	0.0%	0
Th3	4	0	0.0%	0
Th4	2	0	0.0%	0
Th5	4	0	0.0%	0
Th6	2	0	0.0%	0
Th7	4	0	0.0%	0
Th8	0	n/a	n/a	n/a
Th9	2	0	0.0%	0
Th10	2	0	0.0%	0
Th11	2	1	50.0%	0
Th12	2	0	0.0%	0
L1	6	0	0.0%	0
L2	14	1	7.1%	0
L3	12	2	16.7%	0
L4	54	13	24.1%	0
L5	41	9	21.9%	0
S1	4	1	25.0%	0
Overall	157	27	17.2%	0

n/a: not applicable.

Table 3: Cement extravasations. The table shows numbers and locations of cement extravasations. Postoperative radiographs were available in all patients. Postoperative computed tomography (CT) was available in 24/35 patients (68.6%). Beside all cement extravasations detected on plain radiographs, CT additionally demonstrated slight prevertebral, paravertebral, and epidural cement extravasations.

Location of cement extravasation	Count on plain radiographs	Additional counts on CT
Prevertebral	18	2
Paravertebral	0	4
Epidural	0	1
Intradiscal	2	0

Since screw loosening only occurred in one of 157 minimally invasive cement-augmented screws (0.6%) in our series, we believe that cement-augmentation of fenestrated screws is an effective technique to support the fixation of a screw-rod spondylodesis in osteoporotic or osteopenic vertebras. Restrictively it has to be noted that the mean follow-up time of 12.8 months is rather short and fusion status was not assessed. Therefore, additional screw loosening might occur in the further course if bony fusion has not yet been achieved. Another study investigated open fusion procedures and showed no screw loosening (assessed in plain radiographs) at 12-month follow-up in 27 patients with 149 cement-augmented screws [19].

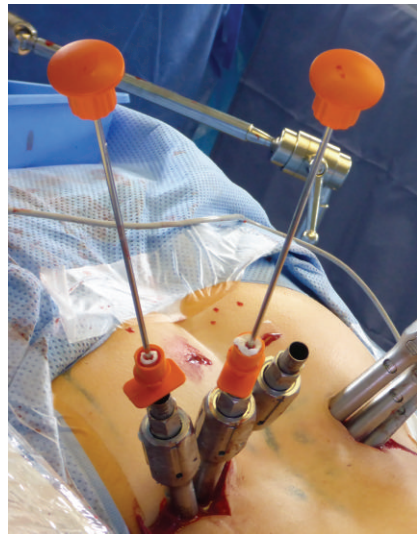


Figure 4: Intraoperative setting. The injection cannulas had been filled with bone cement and had been introduced through the screw extenders into the screw heads. The pushers were inserted to inject the bone cement through the cannulated screws and their fenestrations in the distal third of the thread into the vertebral body under fluoroscopic monitoring.

4.1. Other Clinical Studies Using Fenestrated Screws. Only four clinical studies have been published that examined cement augmentation using fully cannulated and fenestrated screws in spine stabilization procedures [10, 12, 13, 20]. Two of these studies used minimally invasive techniques [12, 13] with a total of 27 patients. First, Lubansu et al. [12] performed percutaneous cement augmentation of 78 fenestrated screws (titanium Expedium fenestrated screw, VIPER MIS Spine System, DePuy Spine) in 15 elderly osteoporotic patients. They used a cement delivery system (V-MAX, DePuy Spine) in combination with a specifically designed connector for percutaneous cement injection through the screw extenders. The authors evaluated cement extravasation on plain radiographs and observed 5 cement extravasations in 78 screws (6.4%) in 5 patients (33.3%), none of them classified as symptomatic. They stated two complications not associated with cement augmentation. The authors found no screw loosening after a mean follow-up of 36 months. Second, Pesenti et al. [13] performed percutaneous cement augmentation of 96 fenestrated screws (Longitude, Medtronic, or Mantis, Stryker) in 12 patients. No loosening or pullout of screws was observed in CT at the last follow-up. One cement-related pulmonary embolism occurred and was attributed to too liquid cement.

The other two studies examined cement-augmented fenestrated screws in open spine surgery. Amendola et al. [10] performed open cement augmentation of 81 monoaxial fenestrated screws (Legacy, Medtronic) in 21 patients. No

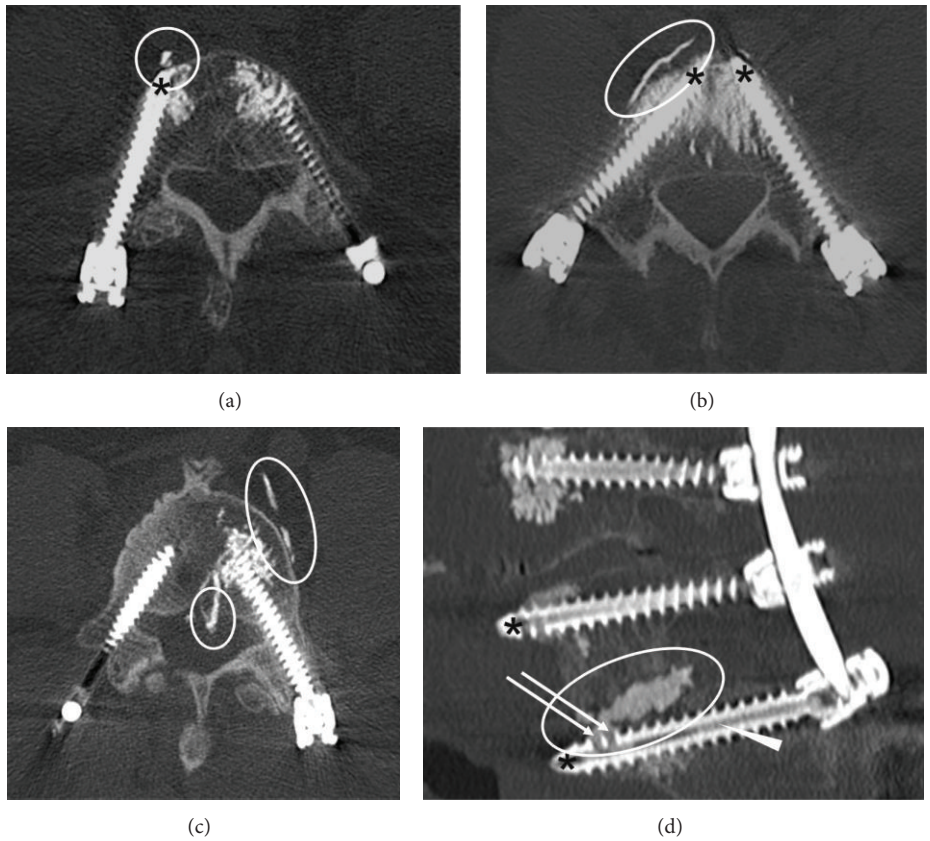


Figure 5: Cement extravasations. Postoperative computed tomography scans showing prevertebral ((a), (b)), paravertebral (c), epidural (c), and intradiscal (d) cement extravasations (encircled). Arrows (d) indicate fenestrations in the distal third of the thread; the arrowhead (d) indicates the hollow central shaft of the cannulated screw now filled with PMMA cement. Long screws with the tip of cannulated screws close to the anterior cortex of the vertebra (asterisks) might provoke prevertebral and paravertebral cement extravasations. Notice that the right screw (c) has not been cement-augmented due to local sclerosis of the vertebral body and therefore sufficient primary fixation strength.

loosening or pullout of screws was found in CT. The authors reported 5 cement extravasations in 81 screws (6.2%) in 5/21 patients (23.8%). One cement extravasation led to nerve root palsy; another one was noticed and removed during surgery without neurologic sequelae. The remaining three were small epidural cement extravasations stated as asymptomatic. Chang et al. [20] performed open cement augmentation in 255 monoaxial cannulated screws with one side hole (Wellong BMI Medical, Taiwan) in 45 patients. The authors evaluated 121 cement-augmented screws on CT and recorded 17 cement extravasations (14.0%) in 21 patients. One patient with epidural cement leakage had persistent left thigh pain after surgery; the remaining cement extravasations were reported to be "spotty or linear" without causing symptoms.

4.2. Further Techniques of Cement Augmentation. An earlier developed method is the retrograde injection technique. After preparing the screw tract by inserting and removing the screw, the bone cement is injected into the tract inside the vertebral body from anterior to posterior. Before the cement sets, the definite screw is inserted [21, 22]. Another method for screw augmentation is to perform an initial vertebroplasty or balloon kyphoplasty [19, 23]. A biomechanical study showed that balloon kyphoplasty augmentation is not superior to vertebroplasty augmentation in regard to pullout force [23]. Another technique is to coat solid screws with approximately 1 mL of PMMA cement before insertion [17]. The biomechanical effect of this technique is arguable.

The retrograde injection technique might carry an increased risk of epidural cement extravasation, since the bone cement might leak through an unrecognized violation of the pedicle wall while inserting the screw [20]. Accordingly, Chang et al. [20] reported a lower rate of cement extravasation using fenestrated screws compared to the retrograde injection method (14.0% versus 26.2% cemented screws). Using the retrograde injection method, Frankel et al. [24] stated asymptomatic cement extravasations in 9/158 screws (5.7%) in 9/23 patients (39.1%, evaluation on radiographs), and Hu et al. [11] observed asymptomatic cement extravasations in 26/145 screws (17.9%, evaluation on CT). Cement augmentation using fenestrated screws resulted in cement extravasation in up to 14% of screws in the current literature, though largely being asymptomatic [10, 12, 13, 20].

In our series, we observed cement extravasations in 27/157 fenestrated screws (17.2%) in 17/35 patients (48.6%). These numbers are in the upper range of reported frequencies of cement extravasations. This may be due to recording even the smallest cement extravasations on CT in our study

(Figure 5(a)). Another explanation of the relatively high number of prevertebral cement extravasations (20/27 cement extravasations, 74.1%) might be our insertion technique of screws. As can be seen in Figure 5, we tend to implant rather longer than shorter screws up to the anterior cortex of the vertebral body in order to increase the primary fixation strength. Performing cement augmentation at this position might more frequently lead to prevertebral cement extravasation through the tip of the screw.

More importantly, none of the cement extravasations in our study was causing a clinical sequela. Moreover, no pulmonary embolism, hemodynamic insufficiencies, or deaths had been observed. Therefore, all cement extravasations could be classified as asymptomatic.

However, when comparing different studies, one must take into account the imaging method used for evaluating cement extravasation. The frequency of cement extravasation is underestimated in plain radiographs compared to CT [8, 25].

4.3. Limitations of the Study. Obviously, the retrospective design is a methodological weakness. Furthermore, a comparison group might have helped to take the data in context with other cement augmentation techniques. The primary purpose of the study was to present the surgical technique; therefore the follow-up period is relatively short.

5. Conclusions

The reported minimally invasive technique with the aid of the presented injection cannula facilitates convenient and safe cement augmentation of polyaxial cannulated and fenestrated screws without increased complication rates regarding symptomatic cement extravasation or screw loosening. Nevertheless, the optimal injection technique and design of fenestrated screws have yet to be identified.

Abbreviations

ap:	Anterior-posterior
CT:	Computed tomography
MIS TLIF:	Minimally invasive transforaminal lumbar interbody fusion
PMMA:	Polymethylmethacrylate.

Ethical Approval

The local ethics committee approved the study.

Conflict of Interests

Ulrich Hubbe has consulting relationships with Medtronic and Maxxspine.

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Review Article

Patient, Surgery, and Hospital Related Risk Factors for Surgical Site Infections following Total Hip Arthroplasty

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Surgical site infections (SSI) following total hip arthroplasty (THA) have a significantly adverse impact on patient outcomes and pose a great challenge to the treating surgeon. Therefore, timely recognition of those patients at risk for this complication is very important, as it allows for adopting measures to reduce this risk. This review discusses literature reported risk factors for SSI after THA. These can be classified into patient-related factors (age, gender, obesity, comorbidities, history of infection, primary diagnosis, and socioeconomic profile), surgery-related factors (allogeneic blood transfusion, DVT prophylaxis and coagulopathy, duration of surgery, antibiotic prophylaxis, bearing surface and fixation, bilateral procedures, NNIS index score, and anesthesia type), and hospital-related factors (duration of hospitalization, institution and surgeon volume, and admission from a healthcare facility). All these factors are discussed with respect to potential measures that can be taken to reduce their effect and consequently the overall risk for infection.

1. Introduction

The success of total hip arthroplasty (THA) in relieving pain and improving function in patients with end-stage degenerative or inflammatory arthritis of the hip is undisputed. The number of procedures per year is estimated to further rise in the next years, as even younger patients with hip arthritis are expected to seek surgical treatment. Kurtz et al. [1] recently reported that, by the year 2020, the projected number of THAs per year will exceed 500,000. Periprosthetic joint infection (PJI) remains a devastating complication after THA, as its treatment may involve multiple surgical interventions and long-term administration of antibiotics and is associated with poor patient satisfaction and increased socioeconomic costs [2, 3]. PJI is also correlated with increased mortality, particularly in the group of elderly patients [4]. The rate of surgical site infection (SSI) has been reported to range from 0.2% during hospitalization to 1.1% up to 5 years after surgery [5]. Therefore, the projected increase in the number of THA will also reflect a respective increase in the absolute number of patients presenting with this complication.

Measures including perioperative antibiotics, exhaust suits, laminar air flow operating rooms, ultraviolet lighting, and antibiotic-impregnated cement have been introduced in an attempt to control infection rates after joint replacement surgery. However, before treating a patient with arthritis, it is very important that surgeons are able to identify potential risk factors for developing an infection. The purpose of this review is to summarize those risk factors predisposing to SSI following THA.

2. Search Strategy and Selection Criteria

An unrestricted computerized search of MEDLINE and OVID SP for studies published in the English language between 1990 and 2014 was conducted. The following terms were used in various combinations: "total hip arthroplasty," "risk factors," "infected joint arthroplasties," "surgical site infection," "periprosthetic joint infection," "prosthesis-related infection," "joint replacement infections," "musculoskeletal wound infections," and "osteomyelitis." Abstracts were reviewed and studies reporting on risk factors for superficial or deep PJI following THA were selected for full text review.

3. Patient-Related Factors

3.1. Age and Gender. The risk for infection after THA has been found to be higher in older patients [6–8]. In comparison to the younger population, these patients are usually characterized by impaired immune response to infectious agents, inferior nutritional status, and possibly more comorbidities. On the other hand, other investigators have determined younger age as a risk factor for infection after total joint arthroplasty [9]. In another study [10], the same association between younger age and infection risk was found for total knee arthroplasty but not for THA. The higher odds for future revision surgery related with younger patients has been proposed as an explanation of the increased infection risk in this population [9].

Male gender has been also reported as an independent risk factor for infection after THA [10–13]. Higher activity levels increase the risk for subsequent revision surgery, and also gender differences in skin microbial colonization [13] might account for this effect. In contrast to this, other studies showed an association for increased infection risk with female gender [6, 14].

3.2. Obesity. As obesity is considered a contemporary pandemic and its association with degenerative joint disease is known [15], obese patients present very frequently for THA. Nonetheless, morbidly obese patients undergoing THA have been found to have significantly higher rates of complications compared to nonobese patients, within 5 years postoperatively [16]. A more specific correlation between obesity and a higher risk for SSI after THA has been reported by several investigators [7, 9, 14, 17–26]. It has been shown that a BMI $\geq$ 35 is associated with a higher risk for positive intraoperative cultures during THA [26]. Furthermore, morbid obesity has been correlated with prolonged wound drainage [27], which is a known risk factor for deep SSI [8, 28]. Treating morbid obesity before THA can be therefore beneficial to patients not only from a general health perspective, but also in terms of reducing the risk of developing a postprocedural SSI. Diet and lifestyle modifications, pharmaceutical interventions, psychological support, and even bariatric surgery can be considered in these patients. This requires a multidisciplinary approach, involving the collaboration between the treating surgeon and a clinical dietician, an internist, a psychiatrist, and a bariatric surgeon. However, even with these measures, it is very unlikely that an obese patient scheduled to undergo THA will achieve such a preoperative weight loss that can have an effect on the risk for infection. It appears that a substantial preoperative weight-loss before surgery is needed for a significant effect to take place [29].

3.3. Comorbidities. The American Society of Anesthesiologists (ASA) score reflects the impact of existing comorbidities on the patient's general health status. An ASA score equal to or more than 3 has been determined by some investigators as an independent risk factor for SSI after THA [6, 14, 30]. Other studies have found an association between an increased risk for infection and the presence of more than 2 comorbidities [20, 24, 31], with each additional comorbidity significantly increasing this risk [31]. A Charlson comorbidity index of more than 5 has been also determined as an independent risk factor for PJI [12].

It is well established that, in patients undergoing surgery, diabetes mellitus (DM) is associated with increased risk for complications and increased length of hospital stay [32]. In the perioperative period, optimal glycemic control can be a challenge, as surgical stress in addition to modifications of the patient's usual diet needs to be taken into account. In general, hyperglycemia may cause disruption of the host's physiologic response to a bacterial load [33]. Diabetes has been identified as an independent risk factor for developing SSI after total joint arthroplasty, including THA [7, 9, 24, 31, 34, 35]. Even in patients without a diagnosis of DM, a fasting blood glucose of >140 mg/dL has been associated with a 3-fold increase in the risk of infection [24]. HbA1c is used to provide an estimate of the average blood glucose concentrations for a period expanding to 3 months before testing [32, 36]. However, its importance in predicting the risk for infection after total joint arthroplasty has not been confirmed [35]. Recognition of those patients with uncontrolled DM or even with perioperative fluctuations of the blood glucose levels is thus very important. In addition to interventions aiming to reduce bacterial load (e.g., use of antibiotic-impregnated cement), close monitoring of patients' perioperative blood glucose levels, and control of hyperglycemia (e.g., insulin sliding scale) can help minimize the risk of infection.

Connective tissue disease has been also correlated with increased risk for PJI after THA [11, 19, 37]. This group of conditions, including rheumatoid arthritis (RA), systemic lupus erythematosus, and psoriatic arthritis, is associated with modulation of the patient's immune system, resulting in predisposition to infection. Patients with longer duration of RA are at increased risk [38]. Moreover, these patients often receive chronic immunosuppressive treatment. Chronic glucocorticoid treatment has been identified as a risk factor for infection after THA [8, 18]. Novel biologic agents (TNFa blockers) used in the treatment of many of these conditions are known to adversely affect the patient's ability to fight infection and their use has been identified as a risk factor for PJI following total joint arthroplasty [38, 39]. It has been reported that patients with RA that have never received TNFa blockers have lower rates of bacteremia than those patients under biologic treatment [39]. Interruption of TNFa blockers before surgery has been advocated [38, 40]; however,

other studies have failed to prove that this measure actually decreases the infection risk [41].

The presence of malignancy has been confirmed to increase PJI risk [8, 10, 42]. It remains unclear, however, whether this correlation is due to the potential effects of malignancy on the immune response to infection per se or to the associated treatment such patients receive, which frequently consists of chronic administration of glucocorticoids and cytotoxic agents [42].

A number of other comorbidities have been also described as independent contributors to the infection risk after THA. These include preoperative anemia [19], liver disease [8, 10, 43], alcohol [7, 8] and intravenous drug abuse [8], previous myocardial infarction [24, 25], congestive heart failure [10, 24], postoperative atrial fibrillation [25], renal insufficiency [24, 25], fluid and electrolyte disorders [10], and pulmonary circulatory disease [10].

3.4. History of Infection and Staphylococcus aureus Colonization. It has been supported that infection involving the superficial layers of the surgical site is an independent risk factor for subsequent deep PJI [8, 18, 42]. Furthermore, increased drain output has been correlated with superficial infection and therefore with indirectly elevated risk for deep infection following THA [18, 27]. Prolonged wound drainage and other signs of superficial infection should alert the treating surgeon and prompt to further diagnostic testing and management [8]. It should be noted that, even though a direct association between the use of drains and the risk for SSI after THA has not been proven [13], it is recommended that drains should be removed in a timely fashion [44].

Patients with previous PJI of the same or different site have been recognized to be at increased risk for an ensuing infection [37, 45]. However, this effect is not attributed to the multiple number of artificial joints, but rather to contamination from surgery or to patients' poor general health status and immunocompromise [45].

Despite the fact that direct contamination of the wound during surgery seems to be the primary pathogenetic mechanism, especially with regard to *Staphylococcus aureus* and *Staphylococcus epidermidis*, bacteremia related with the presence of infection at sites other than joints may also lead to hematogenous seeding of a prosthetic joint and development of PJI in a considerable percentage of patients [46]. Patients with THA and infections of the skin [8], respiratory [8], or urinary tract [8, 25], as well as dental [47] and abdominal infections [8], were found to be at increased risk for PJI. The bacterial load seems to play a critical role in this effect [48]. Asymptomatic bacteriuria has been also determined as a risk factor for infection with gram negative bacteria following THA [49]. Therefore, an aggressive treatment protocol and close monitoring of patients undergoing THA and an infection at another site is warranted.

Colonization with *Staphylococcus aureus*, when combined with other variables including active tobacco use and BMI $\geq 30\,kg/m^2$, has been identified as a risk factor for infection after THA [23]. Similarly, other investigators have found that colonization or prior infection with *Staphylococcus aureus* as remotely as 10 years before presentation increases the risk for SSI after total joint arthroplasty [50]. Moreover, patients colonized with *methicillin-resistant Staphylococcus aureus* (MRSA) are known to be at increased risk for SSI after elective orthopaedic surgery [51, 52]. For these patients, the use of vancomycin for perioperative prophylaxis is advocated, as it is related with reduced infection rates [53].

3.5. Primary Diagnosis. Patients subjected to THA for posttraumatic osteoarthritis have been found to be at increased risk for infection [8]. In addition, higher rates of PJI have been reported in patients that underwent THA for traumatic hip injury (e.g., hip fracture) [6, 11, 34]. The local effects of a traumatic injury (hematoma formation, tissue necrosis, etc.), as well as its systemic consequences, may account for this correlation [6]. Dislocation, associated with local trauma and often requiring multiple reoperations, is another risk factor reported [8]. Analysis of the data retrieved from the Nordic Arthroplasty Register Association revealed that avascular necrosis of the femoral head was also correlated with increased risk for PJI [11]. Finally, several studies have indicated revision surgery [23, 34, 37] or prior joint arthroplasty [42] as an independent risk factor for developing infection following THA.

3.6. Socioeconomic Factors. Lower socioeconomic status, as indicated with entitlement to public assistance for Medicare, has been correlated with the risk of PJI [12]. Moreover, minority race has been also determined as an independent risk factor for SSI [10]. An increased risk for infection following THA has been also described for patients living in rural areas [7]. Poor living conditions, comorbidities, failure to adequately follow medical instructions, and delay in seeking help may predispose all these patients to increased infection risk.

4. Surgery-Related Factors

4.1. Allogeneic Blood Transfusion. Several studies have pointed out allogeneic blood transfusion as an independent risk factor for SSI after total joint arthroplasty, including THA [17, 25, 54, 55]. Transfusion of allogeneic blood is considered to induce immunomodulation to the recipient, due to the presence of white blood cells (WBC) above a critical level [56]. However, even transfusion of WBC-filtered allogeneic blood has been found to independently increase the risk of infection after THA [54]. Preoperative autologous blood donation, regional anesthesia [57], and prevention of excessive intraoperative blood loss can reduce the need for allogeneic blood transfusion [58] and therefore the risk of developing SSI.

4.2. DVT Prophylaxis and Coagulopathy. It has been reported that patients receiving low molecular weight heparin (LMWH) for DVT prophylaxis have significantly more prolonged wound drainage [27]. This has been attributed to the faster onset of action of LMWH in comparison to Coumadin. Nonetheless, aggressive anticoagulation both

with warfarin and with heparin has been identified as an independent risk factor for SSI [17, 59, 60]. Thus, DVT prophylactic medications should be closely monitored during the early postoperative period and any adverse events, including prolonged drainage and hematoma formation, should be recognized and addressed in a timely fashion. Coagulopathy has been also correlated with an increased SSI risk [10, 19]. Coagulopathy can be the result of a wide spectrum of disorders, including those inherited (e.g., hemophilia) and those acquired (e.g., liver disease). However, in most cases, appropriate pharmacologic interventions can maintain the coagulation mechanism on a level that may permit surgery while minimizing the risk for complications.

4.3. Prolonged Duration of Surgery. Several studies have identified prolonged operating time as an independent risk factor for PJI of the hip [6, 8, 12, 13, 23, 24, 30, 34, 37]. Procedures requiring more time usually relate to complex cases and may involve extensile exposures and considerable tissue damage [6]. Dealing with issues such as suboptimal surgeon training, inadequate preoperative planning, and substandard cooperation of operating room staff may lead to improvement of surgical times and therefore contribute to the decrease of the infection risk [23].

4.4. Antibiotic Prophylaxis and Skin Preparation. Antibiotic prophylaxis is a well-established measure to control postoperative infections. Failure to adhere to protocols of prophylactic antibiotic administration, both in terms of dosing and timing, has been associated with increased risk for PJI in patients undergoing THA [8, 30]. Additionally, for cemented implants, the use of plain cement (i.e., nonimpregnated with antibiotics) has been correlated with increased risk for revision due to infection [11]. Finally, although a recent international consensus meeting on periprosthetic joint infections did not acknowledge any differences between different agents [61] and in contrast to previous data [62], in one study skin preparation with chlorhexidine was found to be associated with increased rates of superficial wound infection when compared to povidone iodine [17].

4.5. Bearing Surface and Fixation Type. An increased infection risk has been linked with the use of metal-on-metal bearings in THA [63]. Metallosis-related local soft-tissue damage and increased rates of revision associated with this type of implants may be contributing factors. Moreover, in a study of arthroplasty register data, hybrid fixation was identified as a risk factor for revision of a THA due to infection [11]. However, the authors suggested that this effect might be due to confounding factors not recorded in the register.

4.6. Bilateral Procedures. Bilateral THA has been associated with an increased risk for infection in some studies [14, 25]. It is therefore recommended that bilateral procedures should be reserved for patients without major comorbidities [25]. Nonetheless, as other researchers have supported the safety of this treatment modality [64, 65], further investigation of the role of bilateral procedures is warranted.

4.7. National Nosocomial Infections Surveillance (NNIS) Index Score. The NNIS index score reflects the patient's general health (as related to the ASA score) but also takes into account the procedure's duration and the condition of the surgical wound. A NNIS index score equal to or more than 1 has been identified as an independent risk factor for PJI [42].

4.8. Anesthesia. In recent years, a number of publications have suggested that the choice of regional versus general anesthesia may have a profound influence on the general and possibly the local infection risk in orthopedic patients [57, 66, 67]. Possible mechanisms suggested by various authors are beneficial effects of neuraxial anesthesia on tissue perfusion, immune function, and blood loss. While the effect on short-term outcomes is increasingly well documented, long-term outcome data are rare at this time.

Other aspects of anesthesia may also play a role in preventing SSI after THA. For example, given the effectiveness of intraoperative high FiO_2 in preventing SSI in the general surgery population [68], the value of implementing such strategies in the field of elective orthopaedic surgery, including THA, needs to be further clarified. Additionally, controlled epidural hypotension has been shown to significantly reduce blood loss and improve tissue perfusion through vasodilatation. As hematoma formation and need for blood transfusion have been linked to increased risk of infection, hypotension may actually be beneficial. Care has to be taken however to not equate hypotension with hypo perfusion, which may be more likely during episodes of hypovolemia due to blood loss or general anesthetic effects.

5. Hospital-Related Factors

5.1. Duration of Hospitalization. Patients undergoing THA were found to have an increased risk for developing PJI if their hospitalization was prolonged [25, 42]. Similarly, non-same day surgery has been identified as an independent risk factor for PJI [23]. Hence, it is suggested that patient admission for an elective procedure such as THA should be avoided prior to the day of surgery, as longer hospitalization predisposes patients to greater exposure to nosocomial bacteria [25].

5.2. Hospital and Surgeon Volume of Procedures. Higher infection rates have been associated with low institution volume of THA procedures [69, 70]. It is likely that high-volume institutions have organized SSI control departments and strictly adhere to measures for prevention and early detection of infections. Additionally, low surgeon volume is another variable identified as a risk factor for SSI after THA [70, 71]. The number of cases surgeons perform seems to be conversely related to the duration of surgery and therefore may have an impact to the infection risk as well.

5.3. Admission from a Healthcare Facility. Patients admitted for THA from a healthcare facility have been found to have

Table 1: Studies of risk factors for surgical site infection in patients undergoing total hip arthroplasty (THA).

Study	Type	Number of THAs	Risk factors identified
Berbari et al. [42]	Retrospective	526	Superficial surgical site infection, NNIS index score ≥1, malignancy, prior arthroplasty.
Bongartz et al. [37]	Retrospective	328	Revision surgery, prolonged duration of surgery, previous joint infection, and rheumatoid arthritis.
Bozic et al. [19]	Retrospective	40,919	Obesity, rheumatologic disease, coagulopathy, and preoperative anemia.
Bozic et al. [63]	Retrospective	57,047 THAs with different bearing surfaces	Metal-on-metal bearing surfaces.
Carroll et al. [17]	Retrospective	453	Obesity, allogeneic blood transfusion, coagulation with warfarin, and surgical skin preparation with 0.5% chlorhexidine in 70% alcohol.
Choong et al. [20]	Retrospective	819	Obesity and presence of >2 comorbidities.
Cordero-Ampuero and de Dios [8]	Retrospective	47	Older age, systemic corticosteroid treatment, prolonged duration of surgery, trauma, malignancy, liver disease, alcohol abuse, IV drug abuse, inadequate antibiotic prophylaxis, persistent wound secretion, dislocation, skin infection, urinary tract infection, abdominal infection, and pneumonia.
Dale et al. [11]	Retrospective	432,168	Trauma, male gender, hybrid fixation, cement without antibiotics, inflammatory arthritis, and avascular necrosis.
Dowsey and Choong [21]	Retrospective	1,207	Obesity.
Font-Vizcarra et al. [26]	Prospective	402	BMI ≥ 35.
Friedman et al. [22]	Retrospective	12,355	Obesity.
Geubbels et al. [69]	Prospective	13,608 THAs and hemiarthroplasties	Low annual institution volume.
Gilson et al. [39]	Retrospective	22 patients receiving TNFa blockers subjected to hip, knee, shoulder, and ankle arthroplasty	Treatment with TNFa blockers.
Smith et al. [53]	Prospective	308 THAs and TKAs	Allogeneic WBC-filtered blood transfusion.
Iorio et al. [35]	Retrospective	1,659	Diabetes.
Jafari et al. [45]	Retrospective	55 THAs and TKAs	Previous joint infection.
Jiang et al. [43]	Retrospective	878 THAs	Liver cirrhosis.
Katz et al. [70]	Retrospective	58,521	Low institution volume and low surgeon volume.
Lai et al. [31]	Retrospective	22	Diabetes and presence of >2 comorbidities.
Lee et al. [72]	Retrospective	74	Admission from a healthcare facility.
Malinzak et al. [9]	Retrospective	2,775	Younger age, diabetes, and obesity.
Maoz et al. [23]	Retrospective	3,672 primary THAs, 406 revision THAs	Obesity, revision surgery, prolonged duration of surgery, and non-same day surgery.
McDougall et al. [59]	Retrospective	1,047	Anticoagulation with warfarin or IV heparin.
Momohara et al. [38]	Retrospective	81	Treatment with TNFa blockers and longer duration of rheumatoid arthritis.
Mraovic et al. [24]	Retrospective	101 THAs and TKAs versus 1,847 controls	Diabetes, obesity, prolonged duration of surgery, presence of >2 comorbidities, history of myocardial infarction, congestive heart failure, and renal insufficiency.
Muilwijk et al. [71]	Retrospective	15,906	Low surgeon volume.
Namba et al. [14]	Retrospective	30,491	Obesity, female gender, ASA score ≥3, and bilateral THAs.
Newman et al. [55]	Retrospective	1,622	Allogeneic blood transfusion.
Ong et al. [12]	Retrospective	39,929	Prolonged duration of surgery, Charlson index >5, male gender, and lower socioeconomic status.
Parvizi et al. [60]	Retrospective	35	INR > 1.5.

Table 1: Continued.

Study	Type	Number of THAs	Risk factors identified
Patel et al. [27]	Retrospective	1,221	Obesity, coagulation with LMWH, and increased drain tube loss.
Peel et al. [18]	Prospective	36	Obesity, superficial surgical site infection, increased drain tube loss, and systemic corticosteroid treatment.
Poultsides et al. [10]	Retrospective	412,356	Malignancy, coagulopathy, liver disease, male gender, congestive heart failure, fluid and electrolyte disorders, pulmonary circulatory disease, and minority race.
Pulido et al. [25]	Retrospective	5,060	Obesity, allogeneic blood transfusion, urinary tract infection, history of myocardial infarction, renal insufficiency, bilateral THAs, postoperative atrial fibrillation, and prolonged hospitalization.
Ridgeway et al. [6]	Prospective	16,291 primary THAs, 2,550 revision THAs	Older age, prolonged duration of surgery, trauma, and ASA score ≥3.
Saleh et al. [28]	Prospective	33 THAs and TKAs	Hematoma formation and persistent drainage.
Song et al. [34]	Retrospective	3,422	Diabetes, revision surgery, prolonged duration of surgery, and trauma.
Sousa et al. [49]	Prospective	1,248 THAs	Asymptomatic bacteriuria.
van Kasteren et al. [30]	Prospective	1,922	Prolonged duration of surgery, ASA score ≥3, and administration of prophylactic antibiotics after incision.
Willis-Owen et al. [13]	Prospective	1,750	Male gender and prolonged duration of surgery.
Wu et al. [7]	Retrospective	198	Older age, diabetes, obesity, alcohol abuse, and rural residence.

increased risk for developing SSI [72]. These patients have generally inferior health status than home-residing patients and are likely to be more prone to infections.

6. Conclusions

Identification of risk factors for SSI in patients undergoing THA allows for implementing measures to tackle those variables that can be modified and therefore to reduce the relevant infection risk. These measures may include adequate perioperative glycemic control, adjustment of the DVT prophylactic regimen to the needs of each individual patient and close monitoring of the coagulation status, increased awareness for early signs of superficial infection, both surgeon and patient education, stringent protocols of perioperative antimicrobial prophylaxis, and so forth. It should be noted that most studies reporting on the aforementioned risk factors are of retrospective nature, yielding lower quality evidence (Table 1). On the other hand, conducting prospective studies on this field can be very difficult, given the low prevalence of PJI after THA. Moreover, many series have determined certain independent risk factors, while others have failed to confirm the role of the same variables in increasing the infection risk (Table 1). One should be therefore very careful in interpreting the results of these studies. Further investigation with higher-quality trials is warranted, in order to formulate evidence-based guidelines for managing patients with risk factors for infection, scheduled to undergo THA.

Conflict of Interests

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

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Clinical Study

Surgical Reconstruction with the Remnant Ligament Improves Joint Position Sense as well as Functional Ankle Instability: A 1-Year Follow-Up Study

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Introduction. Chronic functional instability—characterized by repeated ankle inversion sprains and a subjective sensation of instability—is one of the most common residual disabilities after an inversion sprain. However, whether surgical reconstruction improves sensorimotor control has not been reported to date. The purpose of this study was to assess functional improvement of chronic ankle instability after surgical reconstruction using the remnant ligament. *Materials and Methods*. We performed 10 cases in the intervention group and 20 healthy individuals as the control group. Before and after surgical reconstruction, we evaluated joint position sense and functional ankle instability by means of a questionnaire. *Results and Discussion*. There was a statistically significant difference between the control and intervention groups before surgical reconstruction. Three months after surgery in the intervention group, the joint position sense was significantly different from those found preoperatively. Before surgery, the mean score of functional ankle instability in the intervention group was almost twice as low. Three months after surgery, however, the score significantly increased. The results showed that surgical reconstruction using the remnant ligament was effective not only for improving mechanical retensioning but also for ameliorating joint position sense and functional ankle instability.

1. Introduction

Lateral ankle sprain is an extremely common injury in sporting activities, with rupture of the lateral ankle ligaments accounting for more than 85% of all ankle sprains [1]. The anterior talofibular ligament (ATFL) and calcaneofibular ligament (CFL) are most often injured, especially the former [1, 2]. Repeated ankle inversion sprains result in chronic ankle instability. Chronic ankle instability may be defined in 2 ways: mechanical and functional. Mechanical ankle instability is the objective measurement of instability. It is the motion beyond the physiologic range of motion. The anterior drawer translation and talar tilt angle are used to objectively document the degree of mechanical ankle instability. On the other hand, functional ankle instability was described by Freeman as the subjective unstable feeling or complaint of a giving-way sensation of the ankle joint, with the etiology involving proprioceptive disorders as a result of previous ankle injuries [3]. Freeman suggested that the nerve fibers in capsular structures and ligaments of the ankle subserve the proprioceptive response, which helps stabilize the foot and ankle. Not only mechanical disruption of articular structures following ankle sprain, but also the deficit of proprioception may have a profound effect on neuromuscular control. Several mechanoreceptors have been observed in lateral ankle anatomical components, including the lateral ligaments, capsule, and retinaculum [4, 5]. The aim of this study was to assess functional improvement in chronic ankle instability after surgical reconstruction using the remnant ligament. We hypothesized that surgical reconstruction using the remnant ligament should improve decreased mechanoreceptor activity. Here, we describe functional improvement in chronic ankle instability after surgical reconstruction using the remnant ligament.

Table 1: Patient clinical data.

	Control ($n = 20$)	Intervention ($n = 10$)
Age: median (range)	24.5 (19–29)	27.6 (21–30)
Height (cm)	166.1 ± 7.3	165.5 ± 8.7
Weight (kg)	56.8 ± 6.6	55.6 ± 9.2
Male/female	10/10	5/5
Affected side (R/L)		5/5
Talar tilt angle (°)		9.7 ± 2.2
Anterior talar translation (mm)		6.0 ± 1.9

2. Materials and Methods

2.1. Patients. The patients with a history of repeated unilateral ankle sprain participated in this study (intervention group). The patients were 5 men and 5 women, with an average age of 25 (range, 16–30) years. All patients had chronic lateral instability both mechanical and functional with symptoms of a giving-way sensation. All patients were undergoing conservative treatment including rehabilitation prior to surgical intervention (range, 3 months–1 year). The patients whom conditions have not improved participated in the study. All patients were diagnosed clinically as having a lateral ankle ligament injury according to a preoperative assessment tool such as stress radiography (Table 1). Twenty healthy individuals (10 men and 10 women) who did not have a history of ankle sprain or any ankle pain were enrolled as the control group. Their average age was 25 (range, 15–30) years. The study design was approved by the institutional review board of the Human Experimental and Ethics Committee in our clinic, and written informed consents were obtained from all patients or their relatives.

2.2. Surgical Intervention. A modified Broström method was used for all patients with chronic ankle instability [6]. With the patient in a supine position, a short carved 5 cm incision was made over the ATFL. Subcutaneous dissection was carried down to the level of the capsule and joint of the anterolateral lesion of the ankle. In most cases, the remnant of the ATFL was confirmed by identification of the scar tissue adhered to the capsule and a thickened capsule. Then, the loosened CFL was seen from the tip of the fibula to its attachment on the calcaneus. The indication of this surgical procedure was based on the condition that the quality of the remnant of the ATFL and CFL, with 3–5 mm of thickness and 8–12 mm of width, was enough for the repair of the lateral ankle ligament, while the talar side of the ATFL and CFL attachment remained intact. The remnant of the ATFL, CFL, and capsule complex was completely detached from their attachment to the fibula, and decortication was performed to improve the possibility of union between bone and ligament. The remnant of the ATFL and CFL was sutured to their original attachment to the fibula through the pull put technique with the ankle in neutral position (Figure 1). After the tension of the repaired ligament and the ankle stability were checked, the wound was closed in layers.

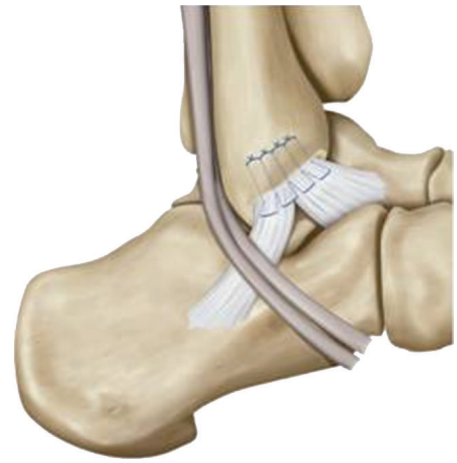


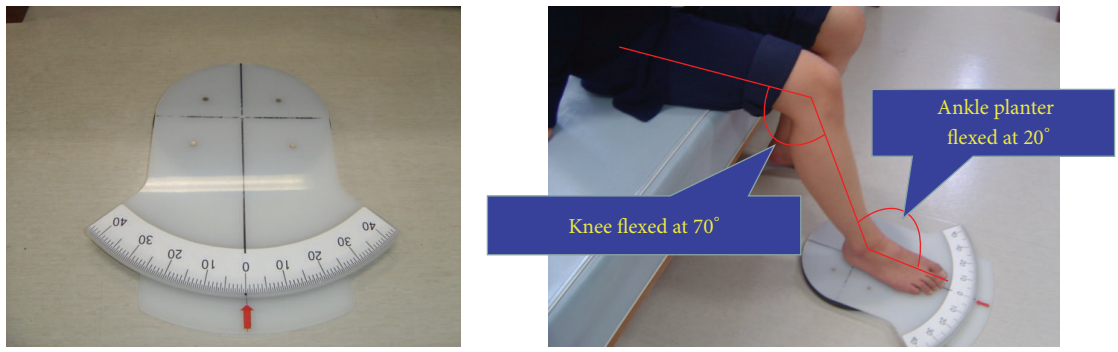
Figure 1: Our modified Broström method. Decortication was performed to improve the possibility of union between bone and ligament. And the remnant of the ATFL and CFL was sutured to their original attachment to the fibula through the "pull put technique" with the ankle in neutral position.

The first measurement was performed on the day before operation in all patients. After surgery, all patients wore a cast for 4 weeks. After cast removal, physiotherapy was performed, which involved range of motion training and muscle training (Table 2). All patients received rehabilitation every day till one month postoperatively, and at least 3 times per week till three months postoperatively. In previous study, it is suggested that the reproduction of damaged lateral ankle ligament progresses at least 7 weeks [7]. So we conducted a follow-up assessment 3 months after surgery, when the operated ankle had regained similar range of motion to the healthy ankle, plantar flexion, dorsiflexion, inversion, and eversion. We additionally conducted follow-up assessments at the 6 months and 1 year after surgical treatment. The primary outcome measures were joint position sense and functional ankle instability, as described below.

2.3. Measurement of Joint Position Sense. The goniometer footplate (Nakamura Brace Co., Shimane, Japan; Figure 2) described by Nakasa et al. was used to assess joint position sense [8]. The subjects took off their shoes and socks. Then, they sat down with the knee flexed at 70°, one at a time, on the goniometer footplate at a plantar flexion angle of 20°. The goniometer footplate can rotate internally, which means that the axis of the foot movement is aligned with the axis of the ankle inversion movement. The center of rotation of the goniometer footplate is just below the tuberosity of the calcaneus. When the subjects moved their ankle to the index angle of inversion, they were asked to memorize the angle. Then, the ankle was returned to the 0° position. After that the subjects were blindfolded to eliminate visual input, and they moved their ankle actively to match the previous index angle. The index angle was decided using a table of random numbers to 1 of 6 positions (5°, 10°, 15°, 20°, 25°, 30°), always starting from 0°. The absolute difference between the index angle and replication angle was recorded as the joint position

Table 2: Rehabilitation protocol after surgical intervention.

Surgery	p.o.2W	p.o.4W	p.o.2M	p.o.3M
	Partial weight bearing exercise →	Full weight bearing		
		Cast off		
		Range of motion exercise Muscle strength exercise (dorgi flexion, planter flexion) →	Range of motion exercise Muscle strength exercise (inversion, eversion)	
			Balance disk exercise	⟶
				Functional training (running, jump exercise, etc.) →



(a) (b)

Figure 2: Goniometer footplate (a) and angles for the measurement of joint position sense (b).

error. The absolute error of joint position sense was measured in triplicate. The mean of the 3 trials was used for analysis.

2.4. Evaluation of Functional Ankle Instability. We investigated subjective sensation of instability—the chief complaint in cases of functional ankle instability—by means of a questionnaire. We used a scoring list for the evaluation of functional ankle instability [2]. This scoring list is composed of 8 items: pain, swelling, sensation of instability, difficulty of motion, walking up and down stairs, running, activities of daily living (ADL), and need of some support. The total number of scoring point is 100, with levels divided into excellent (91–100 points); good (81–90 points); fair (61–80 points); and poor (<60 points). The subjects with less than 81 points were considered to have functional ankle instability.

2.5. Statistical Analysis. Statistical analysis was performed using SPSS version 6.xJ (SPSS Inc., Chicago, IL). We employed Dunnett's test for multiple comparison of the joint position sense error between the control and intervention groups. For comparison of the functional ankle instability score between the 2 groups, an unpaired t-test was used. A one-way analysis of variance (ANOVA) was performed, followed by paired sample t-test. A P value of less than 0.05 was considered to be statistically significant.

3. Results

3.1. Joint Position Sense. In the control group, the mean absolute error of joint position sense was 1.4 ± 0.5° at 5°, 1.2 ± 0.6° at 10°, 1.4 ± 0.6° at 15°, 1.4 ± 0.7° at 20°, 1.5 ± 1.0° at 25°, and 1.7 ± 0.7° at 30°. There were no significant differences in the degree of error of joint position sense between the dominant and nondominant ankle. There were also no differences between male and female patients. Therefore, we used the data of all 40 control ankles as a baseline for later comparisons. In the intervention group, the mean absolute error was 1.5 ± 0.6° at 5°, 1.7 ± 1.0° at 10°, 1.5 ± 0.8° at 15°, 1.9 ± 0.7° at 20°, 2.0 ± 1.0° at 25°, and 2.5 ± 1.2° at 30° before surgical reconstruction. There was a statistically significant difference between the control and intervention groups at all index angles over 15° before surgical reconstruction. Three months after surgical reconstruction in the intervention group, the mean absolute error of joint position sense was 1.1 ± 0.5° at 5°, 1.1 ± 0.5° at 10°, 1.2 ± 0.6° at 15°, 1.6 ± 0.9° at 20°, 1.4 ± 0.8° at 25°, and 1.1 ± 0.6° at 30°. These values were significantly different from those found preoperatively for all index angles over 15°. At six months after surgical reconstruction, the mean of absolute error was 1.3 ± 0.6° at 5°, 1.1 ± 0.2° at 10°, 1.2 ± 0.4° at 15°, 0.9 ± 0.5° at 20°, 1.0 ± 0.5° at 25°, and 1.2 ± 0.7° at 30°. One year after surgery, the mean of absolute error was 0.9 ± 0.3° at 5°, 1.4 ± 0.7° at 10°, 0.9 ± 0.5° at 15°, 1.1 ± 0.6° at 20°, 0.8 ± 0.7° at 25°, and 1.1 ± 0.4° at 30°. There was no significant difference in the absolute error between 3 months, 6 months, and 1 year after surgery (Figure 3).

3.2. Functional Ankle Instability. In the control group, the mean score of functional ankle instability was maximum,

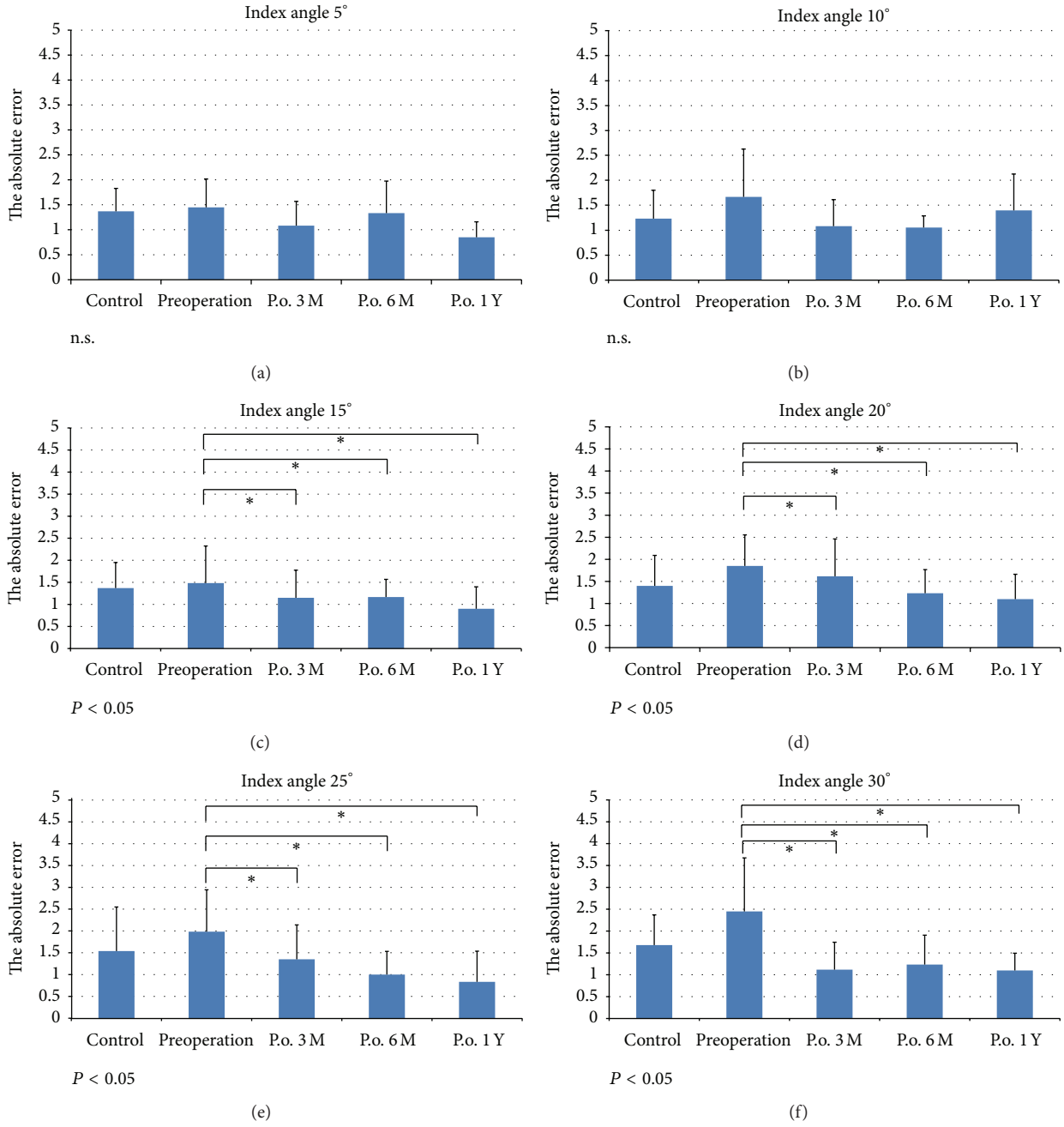


FIGURE 3: Joint position sense angles over the 1-year follow-up period. (a) and (b); there were no significant differences in the degree of error of joint position sense between control groups and unstable groups at index angle 5° and 10°. (c), (d), (e), (f); these values were significantly different from those found preoperatively for all index angles over 15° ($P < 0.05$). And there was no significant difference in the absolute error between 3 months, 6 months, and 1 year after surgery.

100 points. Before surgical reconstruction, the mean score of functional ankle instability in the intervention group was almost twice as low (56.0 ± 11.6 points). Three months after surgical reconstruction, however, the score significantly increased to 84.0 ± 9.1 points. The score increased further at six months and one year (96.6 ± 4.6 and 99.0 ± 2.1 points, resp.) after surgery. The difference between three and six months was also statistically significant (Figure 4).

4. Discussion

Adequate proprioceptive sensorimotor function of the ankle is a key factor in the treatment of ligament injury and chronic ankle instability [9]. Previous studies have reported significant differences in joint position sense between stable and unstable ankles [2, 8, 10, 11]. Indeed, in our study, the absolute error of joint position sense of the intervention

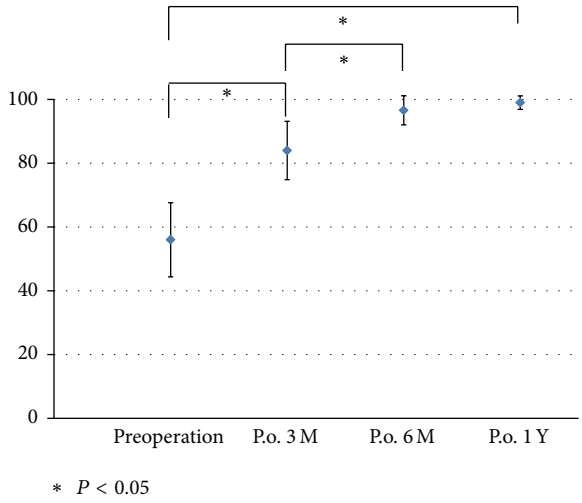


Figure 4: Functional ankle instability over the 1-year follow-up period. Three months after operative reconstruction, the score significantly increased ($P < 0.05$). The score increased further at 6 months and 1 year after operation.

(unstable) was significantly higher than in the control group. Importantly, we show that surgical reconstruction using the remnant ligament is efficient in improving ankle position sense and functional ankle instability in patients who had experienced an ankle sprain.

Halasi et al. reported that surgical treatment could improve the joint position sense of the unstable ankle [11]. This suggested that surgical reconstruction should be effective not only for mechanical ankle instability but also for functional ankle instability. In accordance with that study, Broström reported that 51 of 60 patients who underwent mid substance primary ligamentous repair reported minimal or no symptoms of instability at follow-up [6]. Now, using the remnant ligament, we also demonstrated excellent improvement of both joint position sense and functional ankle instability at three months after surgical reconstruction. Takebayashi et al. observed and mapped tension sensitive receptors in the lateral ankle ligaments [5]. Interestingly, the authors reported that the distribution of mechanoreceptor is not even in the lateral ankle ligament, and 93% of units were found either near the proximal or distal ends of the ligament, adjacent to the bone attachment. They also concluded that, from the viewpoint of the operative procedure, those who preserve the integrity of ligamentous detachments should be selected, as the density of the receptors is much greater in that area. Using the remnant ligaments in our operative treatment may be the reason for the excellent improvement of mechanoreceptor function and joint position sense, in addition to retensioning of the ligaments by surgical reconstruction. Surgical reconstruction using the remnant ligaments may be effective not only for retensioning of the lateral ankle ligaments but also for recovering the proprioceptive function. From the current study, it appeared that joint position sense was sufficiently improved at three months after surgery, as there were no differences between this and the later time points (six months and one year). In contrast, functional ankle instability continued to improve until six months after surgery. Hence, joint position sense was restored earlier than functional ankle instability.

These findings suggest that joint position sense could serve as an index to determine the appropriate time to start functional exercise for safe return to sports activity after ankle injury. Actually, functional ankle instability represents a loss of neuromuscular control, including proprioception, muscle weakness, muscle reaction time, and posture control [12]. If an appropriate rehabilitation program is offered to the patients, we may hasten improvement of functional ankle instability. Development of a rehabilitation program following ligament reconstruction is needed in the future.

The limitation of our study is that the number of patients was small, and surgical reconstruction using the remnant ligament was not compared with other ligament reconstruction techniques. A previous study has described that both primary and secondary repair yielded excellent or good results on perception of ankle stability [13]. Moreover, they concluded that each of those techniques yielded both good clinical and surgical outcomes. Further investigation with a larger number of patients and ligament reconstruction techniques would be required.

This study has 2 important results. First, before surgical reconstruction, the mean absolute error of joint position sense of the afflicted ankle was significantly larger than that of the healthy ankle. The scores of functional ankle instability of the intervention group were also significantly lower than those of the control group. This shows that proprioceptive malfunction has a role in the development of chronic ankle instability. Thus, deficit of joint position sense is a causative factor of functional ankle instability. Second, joint position sense with chronic ankle instability improved after surgical reconstruction using the remnant ligament. Using the mechanoreceptor-rich remnant ligament may have been the reason for the excellent improvement of joint position sense.

5. Conclusions

Based on these findings, we concluded that surgical reconstruction using the remnant ligament was effective not only for improving mechanical retensioning but also for ameliorating joint position sense and functional ankle instability. Joint position sense might be used in the future as a clinical assessment tool for determining the time to start functional exercise for safe return to sports after ankle injury.

Conflict of Interests

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

Authors' Contributions

Kamizato Iwao participated in the design of this study. Fukuhara Kohei carried out the study, together with Deie

Masataka, collected the important background information and drafted the paper. All authors read and approved the final paper.

Acknowledgments

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Research Article

Bone Healing by Using Ilizarov External Fixation Combined with Flexible Intramedullary Nailing versus Ilizarov External Fixation Alone in the Repair of Tibial Shaft Fractures: Experimental Study

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Purpose. Our research was aimed at studying the radiographic and histological outcomes of using flexible intramedullary nailing (FIN) combined with Ilizarov external fixation (IEF) versus Ilizarov external fixation alone on a canine model of an open tibial shaft fracture. *Materials and Methods*. Transverse diaphyseal tibial fractures were modelled in twenty dogs. Fractures in the dogs of group 1 ($n = 10$) were stabilized with the Ilizarov apparatus while it was combined with FIN in group 2 ($n = 10$). *Results*. On day 14, a bone tissue envelope started developing round the FIN wires. Histologically, we revealed only endosteal bone union in group 1 while in group 2 the radiographs revealed complete bone union on day 28. At the same time-point, the areas of cancellous and mature lamellar bone tissues were observed in the intermediary area in group 2. The periosteal layers were formed of the trabeculae net of lamellar structure and united the bone fragments. The frame was removed at 30 days after the fracture in group 2 and after 45 days in group 1 according to bone regeneration. *Conclusion*. The combination of the Ilizarov apparatus and FIN accelerates bone repair and augments stabilization of tibial shaft fractures as compared with the use of the Ilizarov fixation alone.

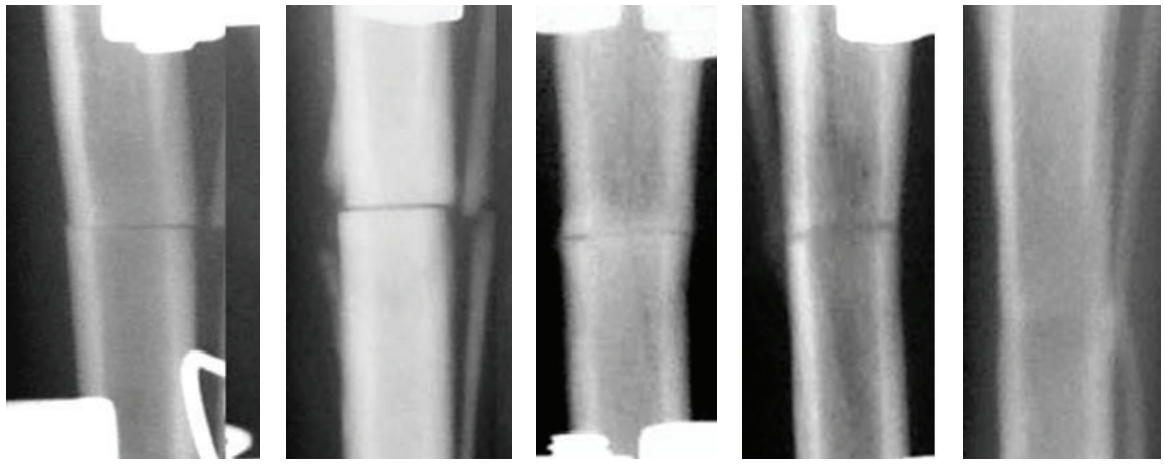
1. Introduction

The rise in the number of severe injuries due to high energy and traffic trauma has resulted in the search for more efficient and faster methods of fracture and nonunion repair. External and internal fixation methods have been widely used for their operative management and evolved a lot [1]. Recently, the techniques that combine external fixation and intramedullary nailing have proven to be more efficient in regard to outcome, patients' comfort, and a shorter inpatient stay both for cases of fractures and for orthopaedic diseases [2–5]. Most studies of their application demonstrate the radiographic and clinical findings that confirm the reasonability of their combination. However, there is little fundamental experimental research that could reveal the consolidation process by the application of the combined techniques for fracture healing.

Our research was aimed at revealing the differences in radiographic and histological outcomes of bone repair by using flexible intramedullary nailing (FIN) combined with the Ilizarov external fixation (IEF) versus the Ilizarov external fixation alone on a canine model of an open diaphyseal tibial fracture.

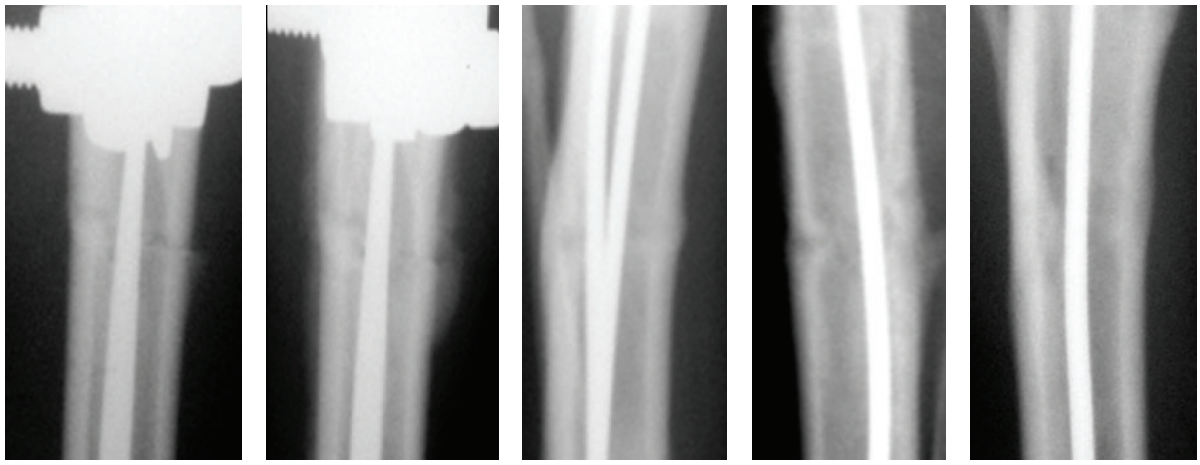
2. Materials and Methods

Open transverse diaphyseal tibial fractures (Gustilo type I) [6] were modelled in twenty adult mongrel dogs aged from



(a) (b) (c) (d) (e)

Figure 1: Group 1 radiographs: (a) day 7, (b) day 14, (c) day 30, (d) day 45, and (e) day 75.



(a) (b) (c) (d) (e)

Figure 2: Group 2 radiographs: (a) day 7, (b) day 14, (c) day 30, (d) day 45, and (e) day 75.

one to 5 years that had their tibial physes closed. Their mean body mass was 20 ± 2.9 kg.

The tibia was broken from a soft tissue incision on the medial side at the level of the middle diaphysis. The osteotomies of the tibia and fibula were performed with a chisel. Tibial transverse fractures were obtained in all cases.

Fractures in group 1 ($n = 10$) were stabilized with the Ilizarov apparatus (Figure 1) while in group 2 dogs ($n = 10$) the IEF was combined with FIN (Figure 2). Soft tissues were stitched.

We used two 1.8 mm hydroxyapatite-coated titanium wires for performing tibial FIN. The wire diameter measures from 20 to 25% of the bone marrow cavity diameter. Such a range of the wire diameter is used for bone lengthening with the combination of IEF and FIN [4]. They were inserted from the medial and lateral sides at the level of the tibial tuberosity and were introduced into the medullary cavity by pushing them down to the level of the distal metaphysis. The wires were cut at the entrance into the bone, and the wound was closed. Those wires remained in the canals of group 2 dogs during the entire experiment.

The Ilizarov apparatus assembly comprised four external rings. Two crossed Kirschner wires were inserted at each ring level and attached to the rings. The rings were connected with threaded rods. This variant of IEF assembly is considered to be stable enough both for experimental studies and for clinical use [4, 7–9]. Full weight bearing was allowed immediately for all dogs without any holder.

The postoperative radiographic images showed transverse fractures in the middle third of the tibial diaphyses (Figures 1(a) and 2(a)). The radiographic images and histological samples were studied on days 14, 28, 45, and 75 after the intervention. The Ilizarov fixator was dismounted after 30 days in group 2 and after 45 days in group 1 according to the quality of regeneration.

Radiographic views were taken with the aid of VEP X Technology Premium Vet device (Spain) on the day of the operation and day 7. Further on, they were taken by the

end of each time-point before the histological material was harvested. Two dogs of each group were euthanized after 14, 28, 45, and 75 postoperative days using lethal doses of sodium thiopental for preparing histological sections. Two dogs in each of the groups were not euthanized.

The bone tissue samples for histological examination were sections sawed longitudinally along the tibial axis. They were placed into the mixture of aldehyde fixators and picric acid and dehydrated by ethyl in ascending concentrations. One section part was decalcified in the mixture of formic and hydrochloric acid. The second section part was not decalcified but was immersed into araldite. Histotopographic sections were stained with hematoxylin eosin and according to Van Gieson stain. The surfaces of araldite blocks were polished, sputtered with the platinum and palladium alloy in the ionic vacuum sputtering system IB-6 (Eiko, Japan), and were studied with the aid of the electron probe microanalyzer INCA-200 Energy (Oxford Instruments, UK).

Interventions, animal care, and euthanasia conformed to the requirements of the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (Strasbourg, 18.03.1986), principles of laboratory animal care (NIH publication number 85-23, revised 1985), and the national laws. The study was approved by the ethics board of the institution.

3. Results

3.1. Radiographic Findings. The periosteal response and shadows of endosteal bone formation at the fracture site were seen after two weeks in group 1 (Figure 1(b)) and after one week in group 2 (Figure 2(a)). The fracture lines were still well seen.

After 14 days, the fragments' ends in group 2 seemed vague and the osteotomy line was not well distinguished. Shadows of endosteal response were expressed and the periosteal response at the level of the fracture was presented by shadows of uneven and unclear contours which were 2.8 ± 0.2 mm thick and 14.7 ± 1.3 mm long. In most cases, the periosteal layers bridged the osteotomy line (Figure 2(b)).

In group 1, homogenous shadows were seen in the fracture gaps by day 28 (Figure 1(c)). Those shadows of endosteal regeneration were 3.5 mm deep into both fragments while the compact periosteal layer was 1.2 mm high. Complete bone union with the periosteal layer that was completely reduced was observed in this group by day 45 (Figure 1(d)). On postoperative day 75, the axis was aligned. The fracture line was hardly seen and both endosteal and periosteal reactions at the osteotomy level were not noted (Figure 1(e)).

In group 2, the radiographs revealed bone union on day 28 (Figure 2(c)). The fragments' ends merged with the fracture line so that it was hardly seen. Compact periosteal layers united the proximal and distal fragments. Endosteal response was seen along the FIN wires. The Ilizarov fixator was taken off in the remaining dogs of this group on day 30. On day 45 the osteotomy line featured only single light areas. Endosteal response was observed along the FIN wires but the periosteal layers decreased (Figure 2(d)). On day 75, we observed the unified medullary cavity and continuous cortex along the bone circumference at the fracture level (Figure 2(e)). The osteotomy line and periosteal reaction were not visualized. However, the shadows in the bone marrow cavity showed more contrast radiographically. Bone fragments in both groups were stable during the entire experiment period. Intramedullary wires were not displaced. Infection was not observed.

3.2. Histological Findings

3.2.1. Group 1. The histological study on day 14 revealed loose fibrous connective tissue and weakly mineralized bone trabeculae of reticulofibrous structure in the intermediary area of the fracture site (Figure 3(a)). The trabeculae were oriented in the perpendicular direction relative to the long bone axis (Figure 4(a)). Periosteal regeneration was presented by cancellous bone tissue of the middle-sized cellulae and areas of nonmineralized connective tissue. The distal and proximal periosteal layers were not bridged. The endosteal regeneration was also of spongy structure but the cellulae were of the middle or large sizes with insertions of chondroid areas and fibrous cartilage.

On day 28, we revealed endosteal bone union (Figure 3(b)). There were massive reticulofibrous trabeculae of cancellous bone in the gap between the fragments and loose fibrous connective tissue in the space between the trabeculae (Figure 4(b)). Periosteal cancellous bone was undergoing reorganization into the compact structure and its proximal and distal portions started to unite.

Complete bone union was seen on day 45 (Figure 3(c)) when the periosteal, intermediary, and endosteal regeneration areas featured reticulofibrous cancellous bone with red bone marrow in the space between the trabeculae (Figure 4(c)).

On day 75, the tibia consolidated through lamellar bone tissue in the intermediary area between the fragments' ends (Figure 3(d)). The new cortex at the fracture level was formed of osteons that were not oriented regularly yet (Figure 4(d)). The medullary cavity was filled with hematopoietic and fatty bone marrow.

3.2.2. Group 2. The sections on day 14 showed a similar picture as in group 1 (Figure 3(e)). However, the portion of bone tissue in the intermediary area was bigger as compared to group 1 (Figure 4(e)). The difference between the groups was the envelope formed of bone tissue that started developing round the FIN wires and this process persisted till the end of the experiment (Figure 2(a)). That envelope was made of a trabecular net that represented reticulofibrous bone tissue and osteoids (Figure 5(a)). In the spaces between the trabeculae of the envelope there were areas of granulated tissue that had numerous vessels and perivasculocytes that featured different stages of differentiation. The collagen fibres that formed the fibrous frame of the osseoosteoid envelope were attached to the rough HP-coated wire surface (Figure 5(b)) and were connected between each other with tiny spreading fibres that built the fibrous frame (Figure 5(c)).

On day 28, cancellous and mature lamellar bone tissues were observed in the intermediary area (Figures 3(f) and 4(f)). Periosteal layers that were formed of the trabeculae

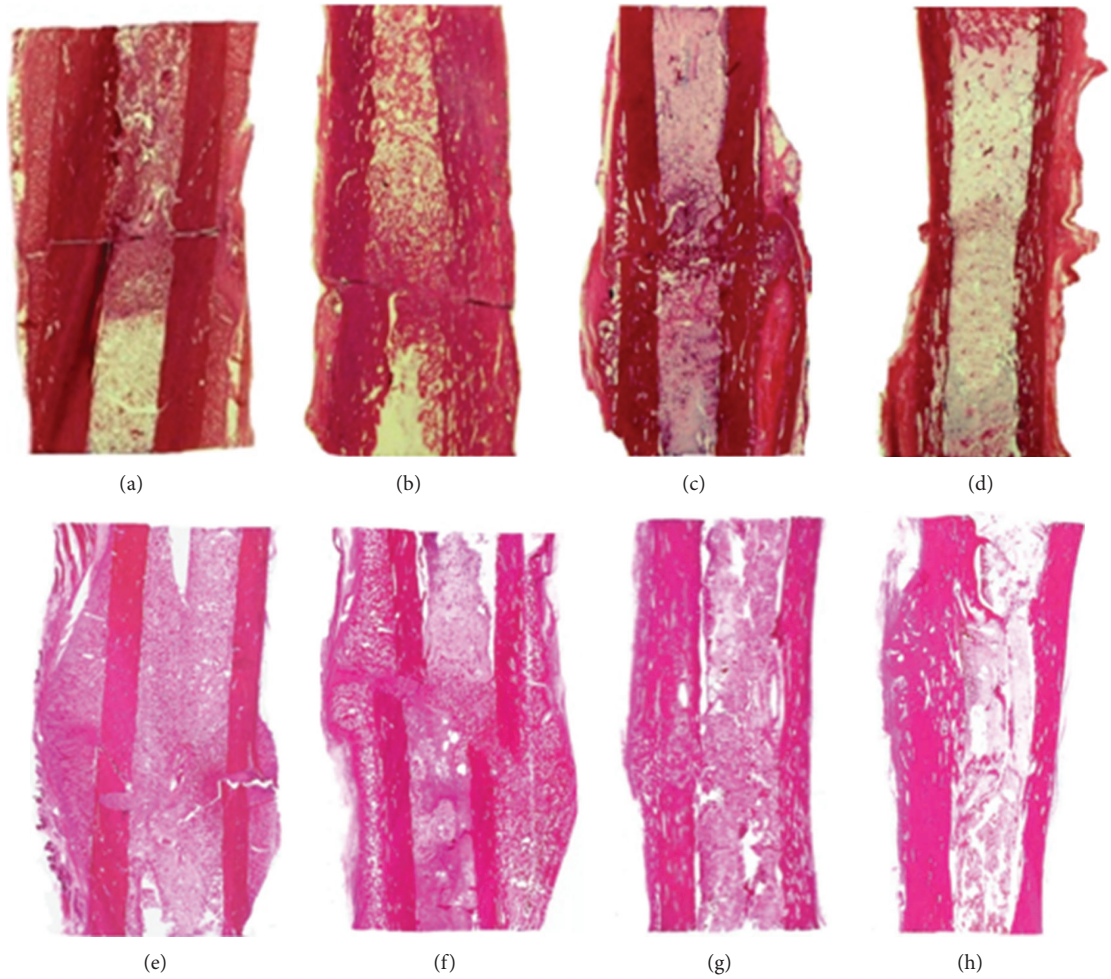


Figure 3: Tibial histotopograms. Group 1 (upper row) and group 2 (lower row): (a, e) day 14; (b, f) day 28; (c, g) day 45; and (d, h) day 75. Hematoxylin eosin staining, ×1.5.

net of lamellar structure united the bone fragments. The rough fibrous bone tissue in the envelope round the wires kept developing into a more mature and mineralized lamellar bone. Adhesion of osteogenic cells and amorphous bone matrix were also seen (Figure 5(d)).

Complete periosteal, intermediary, and endosteal bone union was observed on day 45 (Figure 3(g)). In the intermediary area, the bone fragments were united through the trabecular net of narrow cellulae and osteons that had various maturity stages (Figure 4(g)). The cortical layer was undergoing the phase of compactization. The bony envelope round the FIN wires was presented by the compact bone of lamellar structure in which osteons were under formation as well as by cancellous bone tissue that was filling in the medullary cavity of bone fragments and fixed it like a rod.

The histotopograms on day 75 showed the regenerated bone that had a more typical and organic structure of the regular bone tissue than in group 1. It was expressed by a more compact structure of the new bone on the fracture site (Figures 3(h) and 4(h)). Electron probe X-ray microanalysis on that day revealed a better calcium saturation at the fracture level than in group 1 (Figure 6).

4. Discussion

Open fractures of the tibial shaft often occur after a high energy direct trauma and their operative treatment is demanding [7, 10]. The studies that compare different methods of their fixation show high rate of nonunion when managed by the available methods of stabilization such as intramedullary nailing, plating, or external fixation when they are used independently [1, 2].

The Ilizarov techniques have shown to be useful in the management of difficult fractures and nonunions of the tibia but practicing surgeons call attention to their main drawbacks such as the long time the patients have to spend with the fixator on, much discomfort, and pin tract infections [3, 4]. Therefore, the techniques that combine the external device with intramedullary nailing have been advocated to avoid these problems. The combined techniques resulted in the reduction of the usual IEF duration and good union rates [3–5]. There were many clinical studies of using the external fixator over the nail or FIN for orthopaedic conditions and injuries [4, 5, 11, 12].

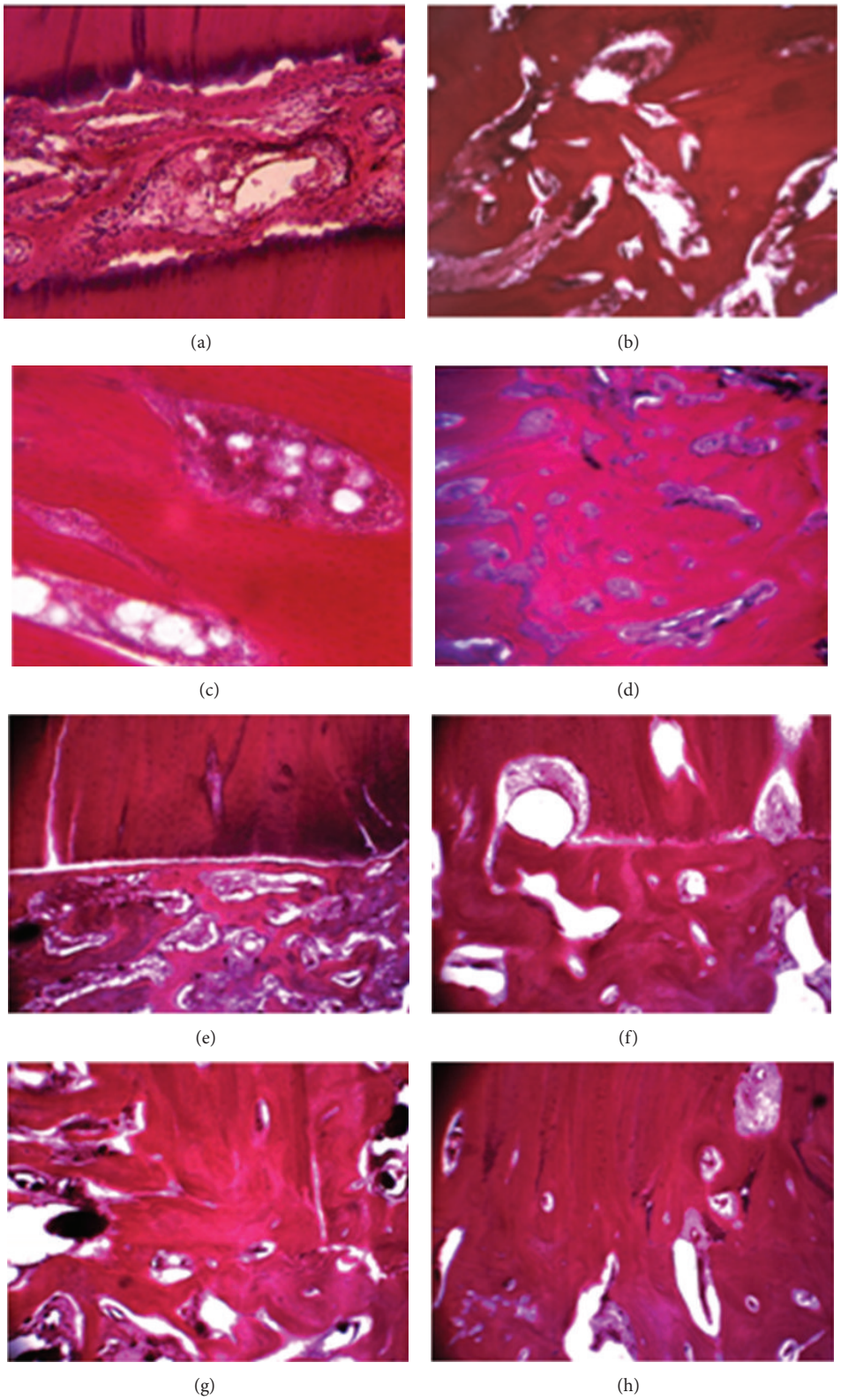


Figure 4: Microphotos of the intermediary regeneration areas. Group 1 (a–d) and group 2 (e–h): (a, e) day 14; (b, f) day 28; (c, g) day 45; and (d, h) day 75. Hematoxylin eosin staining. Magnification: (a, b, d–h) ×40 and (c) ×63.

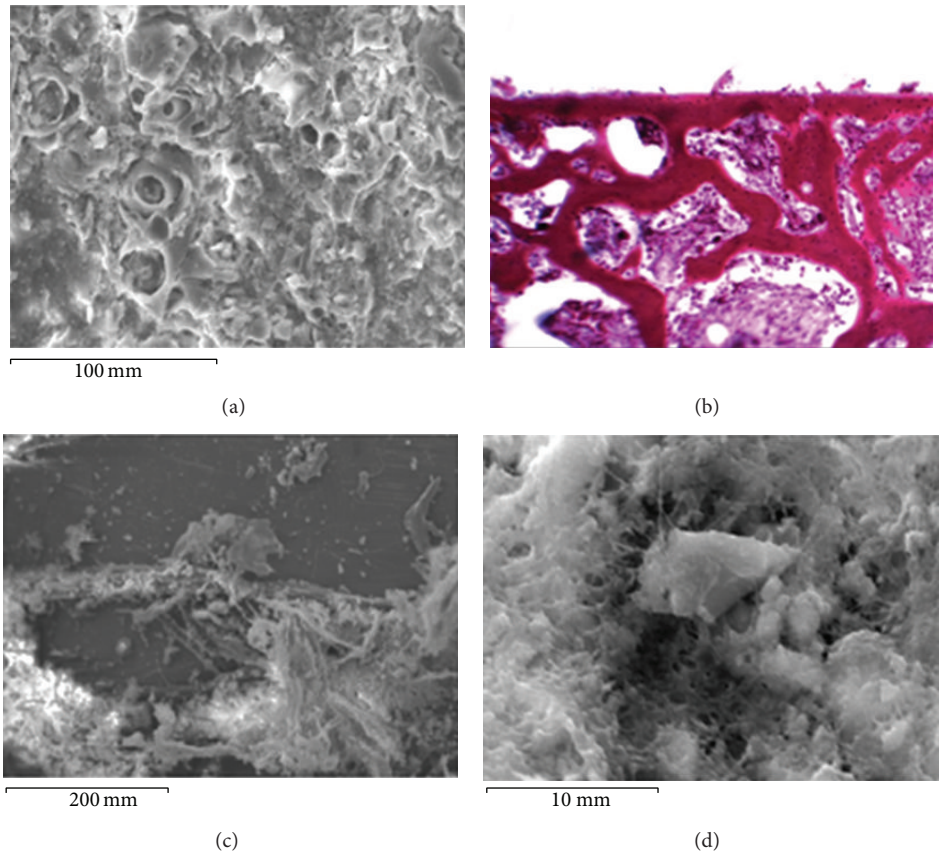


Figure 5: Structural features of the FIN wire surface and its adjacent area: (a) architectonics of the FIN wire, SEM ×1300; (b) osseoosteoid trabecular net envelope in the area adjacent to FIN wire, day 14, hematoxylin eosin staining, ×100; (c) fixation of collagen fibres of the osseoosteoid envelope to the rough FIN wire surface, day 14, SEM ×400; and (d) adhesion of osteogenic cells to the FIN wire surface and amorphous bone matrix in the pericellular space, SEM ×2500.

In fact, the IEF provides optimal reduction of complex tibial fractures while internal nailing augments their stabilization. Accurate reduction and stabilization will both be gained by such a combination. When primary consolidation happens, the external fixator can be removed and the nail can be left inside. However, there is much discussion of the condition of vascularisation during reaming and nailing due to possible damage of the medullary vessels and content. Undoubtedly, nailing affects the osteogenic potential of the bone marrow. Unreamed nailing is favoured nowadays as it produces less compression of the medullary contents though other studies show higher consolidation rates with reamed nailing [2, 13].

Bone regeneration has been widely studied using a canine model [9, 14, 15]. Our study has combined the Ilizarov fixator assembly for diaphyseal fractures with FIN that uses a couple of thin wires aimed at a lesser damage of the medullary content as compared to a single nail. The optimal diameter of such wires was calculated [16] and their combination with the Ilizarov fixator was already used and showed good outcomes in limb lengthening situations both experimentally and clinically [4, 9].

The available literature does not give a clear picture of the process of bone healing during the repair of shaft fractures and management of nonunions when combined external and intramedullary fixation is used to explain how the healing process develops.

Our study demonstrated that the healing process of a diaphyseal tibial fracture was faster and was completed by day 28 in group 2 whereas in group 1 it continued till day 45. The time difference of 15 days in the confirmed bone union in our groups is obviously in favour of the combined technique. The quality of regeneration was better in group 2 at all time-points studied. The endosteal bone formation along the wires was an additional reinforcing factor. Moreover, we suppose that the endosteal envelope was also an additional inducer of the periosteal osteogenesis and fragments' ends cambial cells osteogenesis.

We assume that the possible mechanism of the effect of using FIN is also associated with a prolonged formation of granulation tissue foci in the marrow cavity that stimulate the population of osteoproductive cells and angiogenesis that result in the activation of bone reparation.

Another advantage of the use of FIN technology is the fact that fracture consolidation in group 2 of our series was of primary type that featured neither cartilaginous nor connective tissues. No reaming is required in our technology. No damage to the intraosseous artery with the wires

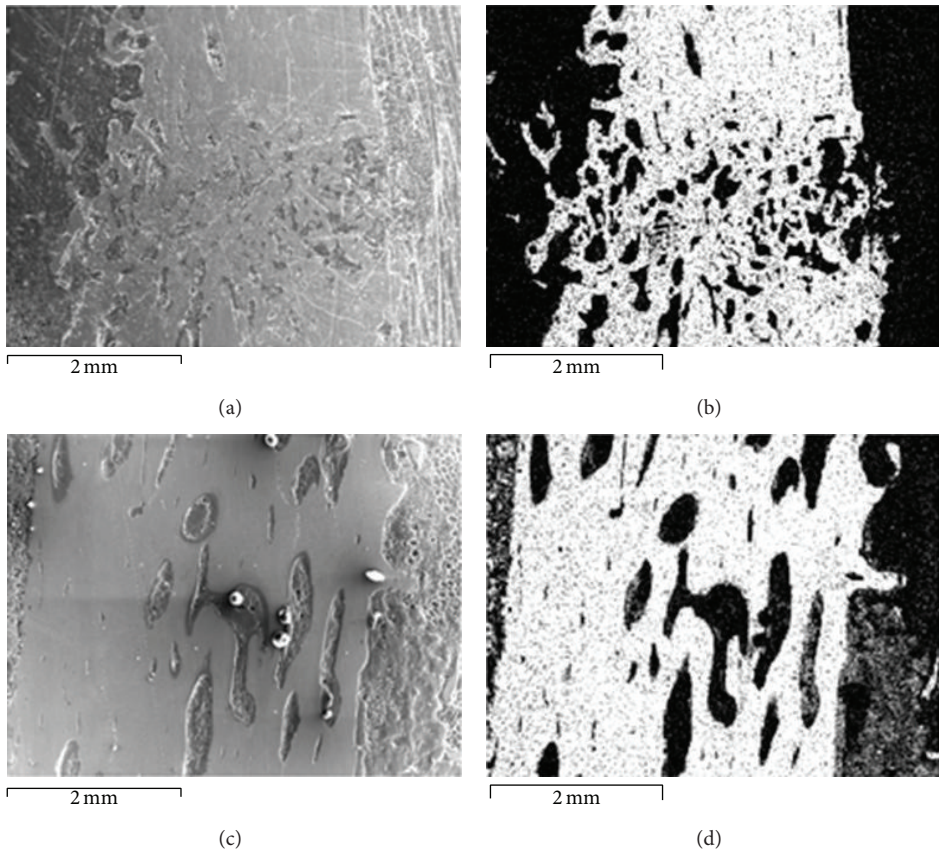


Figure 6: Bone regeneration in the intermediary area on day 75. Group 1 (upper row) and group 2 (lower row): (a, c) scans, ×20; (b, d) calcium distribution in the intermediary area by electron probe X-ray microanalysis.

was observed. Moreover, the procedure of introducing intramedullary wires and taking them out is not technically demanding and does not injure the tissues that could affect the knee joint. Therefore, no knee problems may be expected. Those problems were not encountered by using the FIN technology for limb lengthening [4, 9].

5. Conclusion

We conclude that our experimental study proves that the combination of the Ilizarov apparatus and FIN augments fixation stability of bone fragments, accelerates the repair of tibial shaft fractures, and can be used in clinical settings. This combined technique does not contradict the biological principles of the Ilizarov method.

Conflict of Interests

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

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Clinical Study

PEEK Cages versus PMMA Spacers in Anterior Cervical Discectomy: Comparison of Fusion, Subsidence, Sagittal Alignment, and Clinical Outcome with a Minimum 1-Year Follow-Up

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Purpose. To compare radiographic and clinical outcomes after anterior cervical discectomy in patients with cervical degenerative disc disease using PEEK cages or PMMA spacers with a minimum 1-year follow-up. *Methods*. Anterior cervical discectomy was performed in 107 patients in one or two levels using empty PEEK cages (51 levels), Sulcem PMMA spacers (49 levels) or Palacos PMMA spacers (41 levels) between January, 2005 and February, 2009. Bony fusion, subsidence, and sagittal alignment were retrospectively assessed in CT scans and radiographs at follow-up. Clinical outcome was measured using the VAS, NDI, and SF-36. *Results*. Bony fusion was assessed in 65% (PEEK cage), 57% (Sulcem), and 46% (Palacos) after a mean follow-up of 2.5 years. Mean subsidence was 2.3–2.6 mm without significant differences between the groups. The most pronounced loss of lordosis was found in PEEK cages (−4.1°). VAS was 3.1 (PEEK cage), 3.6 (Sulcem), and 2.7 (Palacos) without significant differences. Functional outcome in the PEEK cage and Palacos group was superior to the Sulcem group. *Conclusions*. The substitute groups showed differing fusion rates. Clinical outcome, however, appears to be generally not correlated with fusion status or subsidence. We could not specify a superior disc substitute for anterior cervical discectomy. This trial is registered with DRKS00003591.

1. Introduction

Cervical degenerative disc disease includes disc herniation and spinal canal stenosis and is a common cause of neck pain with radicular and myelopathic symptoms. Surgical treatment is indicated if conservative treatment failed or neurological deficits occurred. Depending on the location and extent of the pathology, an anterior or posterior approach has to be considered. If cervical degenerative disc disease is limited to one or two levels, an anterior cervical discectomy (ACD) is usually performed including decompression of neural structures and implantation of a disc substitute. Traditionally, no disc substitute or an iliac crest autograft was used. Iliac crest autograft was found to provide higher fusion rates than other substitutes and also led to relevant donor site morbidity [1]. As part of further development, bone cement was implanted into the intervertebral disc space in order to restore segmental height and to avoid donor site morbidity [2–8]. Currently, spine surgeons are increasingly using intervertebral cages, which initially consisted of carbon [9–11] or titanium [2, 5, 8, 12–18] and later consisted mostly of polyetheretherketone (PEEK) [14, 16, 18–27]. The implantation of an artificial disc is a further surgical option; a clear superiority over ACD and fusion, however, has not been specified [28].

A direct comparative study between PEEK cages and the bone cement polymethylmethacrylate (PMMA) as cervical disc substitute has not been reported in the literature so far. The aim of this study was to compare radiographic and clinical outcomes after ACD in patients with cervical

degenerative disc disease using PEEK cages or PMMA spacers with a minimum 1-year follow-up. Primary outcome measures were bony fusion and pain level at follow-up. Secondary outcome measures were degree of subsidence, loss of lordosis, functional outcome (questionnaires), and number of reoperations. We hypothesized that fusion status and pain levels do not differ between the treatment groups.

2. Methods

2.1. Ethics Statement. The local ethics committee approved the study. Written informed consent was obtained from the patients. The study conforms to the Declaration of Helsinki and was registered in the German Clinical Trials Register (DRKS00003591).

2.2. Patients. We retrospectively identified 225 patients in our database of a single center who underwent ACD without anterior plating for cervical degenerative disc disease with or without posterior osteophytes between January 2005 and February 2009. Of these, 69 patients were excluded due to implantation of disc prosthesis, previous cervical spine surgery, and ACD of level C7/T1 or more than two cervical levels. 107 of the remaining 156 patients could be contacted to participate in the study (Figure 1).

2.3. Surgical Treatment. A standard right-sided anterior approach was performed for ACD in supine position with complete excision of the intervertebral disc. Posterior osteophytes and herniated disc fragments were resected microsurgically. Moreover, the neural foramens were decompressed on both sides, and the posterior longitudinal ligament was dissected and removed. After careful curettage of subchondral cartilage while preserving intact endplates, either a PEEK cage without additional filling or a PMMA spacer (Sulcem, Zimmer Germany GmbH, Freiburg, Germany; Palacos, Heraeus Medical GmbH, Wehrheim, Germany) was implanted into the intervertebral disc space. The optimal cage size was determined under lateral fluoroscopic guidance for restoring disc height and cervical lordosis. In the PMMA groups, absorbable gelatin sponges were used to protect the nerve roots and dura against thermic injury. Additionally, two small asymmetric holes were drilled in the middle of both endplates to prevent slippage of the hardened PMMA spacer.

2.4. Postoperative Care. Postoperative external collar fixation was routinely applied for two weeks. On the first postoperative day, the patients were mobilized under physiotherapeutic guidance.

2.5. Radiographic Assessment. Plain radiographs in anterior-posterior and lateral projections were obtained before surgery, after surgery before discharge, and at follow-up (at least 12 months postoperatively) according to the protocol of our department. Additionally at follow-up, a thin-sliced CT scan of the treated and adjacent levels was performed routinely. Two surgeons blinded to the clinical status of the patient assessed the digital radiographs and CT scans using integrated software to measure distances and angles (IMPAX EE R20 VIII, Agfa HealthCare, Mortsel, Belgium). The mean values of the two surgeons' measurements were used for further analysis. In case of conflicting evaluation of the fusion status, the surgeons reassessed the CT scan and came to an agreement.

Fusion was determined in three-dimensional reconstructed CT scans and confirmed if continuous trabecular bone bridges through or around the implant were clearly present (Figure 2).

Subsidence and *sagittal alignments* were measured in lateral radiographs. For evaluating subsidence, we measured the total segmental height, which includes the central heights of the two vertebras and the disc space of the treated level (Figure 3). The difference between the total segmental height at follow-up and after surgery before discharge was considered as subsidence provided that the vertebral bodies showed no reduced height, for example, due to vertebral fractures. Subsidence was indicated as positive values. Furthermore we assessed the interbody height ratio [21, 29], which is the total segmental height divided by the anterior-posterior diameter of the upper vertebral body and hereby eliminates magnification variation in radiographs (Figure 3).

For evaluating the *segmental sagittal alignment (SSA)*, we applied the Cobb angle. For evaluating the *cervical sagittal alignment (CSA)*, the angle of the tangent to the C2 and C7 posterior vertebral body margins was measured [30] (Figure 3). Changes in SSA and CSA were calculated as difference of the values between follow-up and after surgery before discharge. Change toward kyphosis was indicated as negative values.

2.6. Clinical Assessment. The patients' subjective condition at follow-up was obtained with the Visual Analog Scale (VAS) for pain with a range of 0–10 (0: no pain; 10: worst possible pain), Neck Disability Index (NDI) with a range of 0–100 (0: no functional disability; 100: complete functional disability), and Short Form 36 Health Survey (SF-36) with a range of 0–100 (0: worst scale value; 100: best scale value); physical and mental component summaries have been normalized to a mean of 50 and standard deviation of 10 to assess levels of pain, body function, and quality of life.

To evaluate patients' satisfaction with the postoperative result, the Patient Satisfaction Index was applied at follow-up [31]. The Patient Satisfaction Index is a modified subitem of the North American Spine Society outcome questionnaire. It is scored as follows: (1) "Surgery met my expectations"; (2) "I did not improve as much as I had hoped but I would undergo the same operation for the same results"; (3) "Surgery helped but I would not undergo the same operation for the same results"; and (4) "I am the same or worse as compared to before surgery."

2.7. Statistical Analysis. Results were expressed as mean with standard deviations. Analysis of independent continuous quantitative variables between groups was performed using the two-tailed Student's t-test. Statistical comparisons for categorical values between groups were accomplished using the two-tailed Fisher exact test and the χ^2 test. Pearson's

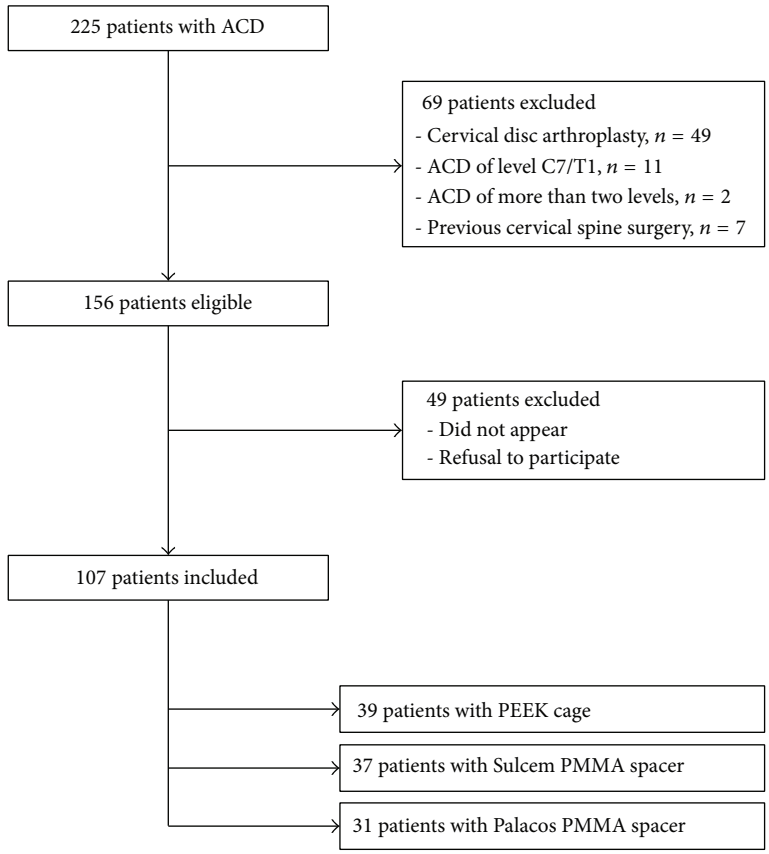


Figure 1: Patient flow diagram. Out of 225 patients with ACD between January 2005 and February 2009, 107 patients were included in one PEEK cage group and two PMMA groups. ACD: anterior cervical discectomy, PEEK: polyetheretherketone, and PMMA: polymethylmethacrylate.

correlation was used for regression analysis to evaluate the relationship between subsidence and change in SSA and between change in SSA and CSA. Prism 6 for Mac (GraphPad Software Inc., La Jolla, USA) and Excel 2011 for Mac (Microsoft Corporation, Redmond, USA) were used as statistical software and for data processing. P values <0.05 were considered to be statistically significant.

3. Results

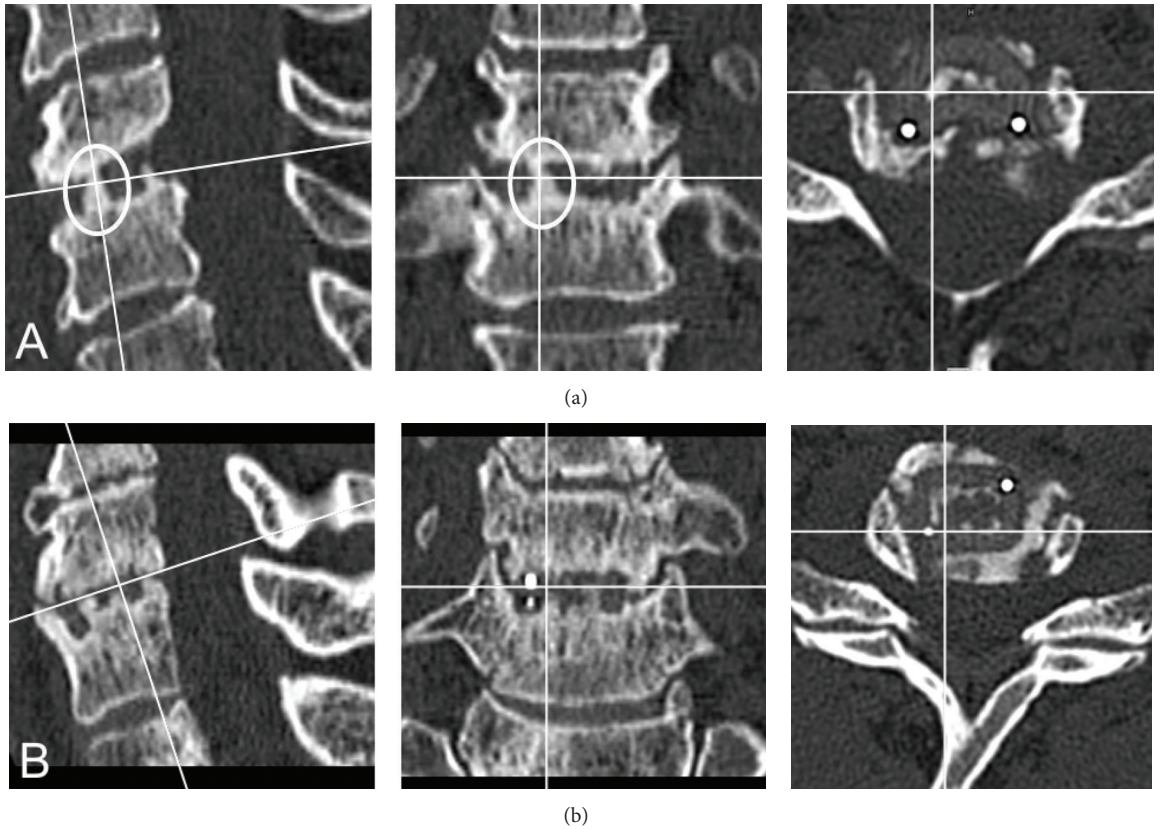
3.1. Patients. The study analyzed 107 patients (50 female, 57 male) who underwent ACD and implantation of a PEEK cage or PMMA spacer (Table 1). The mean age was 55 years (range: 29–82 years). Radicular symptoms were present in 87 patients (81.3%) and myelopathic symptoms were present in 25 patients (23.4%). 73 patients were operated on in one level and 34 patients in two levels leading to a total of 141 operated levels. Soft disc herniation was observed in 44 operated levels (31.2%), spinal canal stenosis in 67 levels (47.5%), and a combination of both in 30 levels (21.3%).

A cervical PEEK cage was implanted in 39 patients (51 levels), a Sulcem PMMA spacer in 37 patients (49 levels), and a Palacos PMMA spacer in 31 patients (41 levels). Different types of PEEK cages were used depending on surgeons' preference (14× C-MAXX, 12× Blackstone, 10× Arca Medica, 10× Acromed Depuy, 2× Solis Stryker, 2× Medicrea Impix-C, and 1× Shell-Cage). A majority of the patients were treated at C5/6. The follow-up times of the groups were significantly different (PEEK cage group: 16 ± 3 months; Sulcem PMMA group: 46 ± 8 months; Palacos PMMA group: 27 ± 7 months) with a mean of 29 ± 14 months (range: 12–57 months).

3.2. Radiographic Evaluation

3.2.1. Fusion. Bony fusion was confirmed in CT scans (Figure 2) in 64.6% of treated levels in the PEEK cage group, 57.1% of treated levels in the Sulcem PMMA group, and 46.3% of treated levels in the Palacos PMMA group. There was no statistically significant difference of the fusion status between the treatment groups (Table 2).

3.2.2. Subsidence. Lateral radiographs showed a mean subsidence from directly postoperative to follow-up of 2.3 mm in the PEEK cage group, 2.6 mm in the Sulcem PMMA group, and 2.3 mm in the Palacos PMMA group without being statistically significant between the groups (Table 2). Comparing the clinical outcome between the subgroups with a subsidence ≥3 mm versus <3 mm within each group, there were no significant differences except for the PEEK cage group; herein, the pain scores (VAS: 1.7 ± 1.2 versus 3.9 ± 1.8;



(a)

(b)

Figure 2: Fusion and nonfusion. Postoperative three-dimensional reconstructed CT scans after ACD with implantation of PEEK cages. (a) A continuous trabecular bone bridge through the cage (encircled) confirmed bony fusion; (b) no bony fusion was assessed due to the lack of continuous trabecular bone bridges.

Table 1: Selected demographic and clinical data.

	PEEK cage	PMMA Sulcem	PMMA Palacos	Overall	P (cage versus Sulcem)	P (cage versus Palacos)	P (Sulcem versus Palacos)
Number of patients	39	37	31	107			
Mean age (yr)[#]	53	57	57	55	0.096	0.130	0.759
Male : female ratio[^]	20 : 19	23 : 14	14 : 17	57 : 50	0.364	0.638	0.222
One level : two level ratio[^]	27 : 12	25 : 12	21 : 10	73 : 34	1.000	1.000	1.000
Radiculopathy[^]	31/39	33/37	23/31	87/107	0.348	0.775	0.124
Myelopathy[^]	10/39	5/37	10/31	25/107	0.252	0.601	0.082
C3/4[†]	2	5	5	12			
C4/5	8	3	5	16	0.265	0.505	0.612
C5/6	22	25	16	63			
C6/7	19	16	15	50			

The table shows demographics and clinical data with distribution of surgery levels.
[#]Student's t-test (two-tailed).
[^]Fisher exact test (two-tailed).
[†]χ^2 test.

Table 2: Bony fusion, subsidence, and sagittal alignment.

	PEEK cage	PMMA Sulcem	PMMA Palacos	Overall	P (cage versus Sulcem)	P (cage versus Palacos)	P (Sulcem versus Palacos)
Fused levels^	31/48 (64.6%)	28/49 (57.1%)	19/41 (46.3%)	78/138 (56.5%)	0.534	0.092	0.397
Fused patients^	23/37 (62.2%)	19/37 (51.3%)	13/31 (41.9%)	55/105 (52.4%)	0.482	0.143	0.474
Subsidence (mm)#	2.3 ± 2.8	2.6 ± 3.1	2.3 ± 2.9	2.4 ± 3.0	0.647	0.948	0.721
Change in SSA#	−4.1° ± 4.3°	−2.4° ± 6.2°	−1.0° ± 4.6°	−2.7°	0.129	0.003*	0.260
Change in CSA#	−3.1° ± 10.1°	−5.2° ± 10.7°	−1.3° ± 10.0°	−3.6°	0.420	0.500	0.168

The table shows ratios of fused levels and fused patients as well as means with standard deviations of subsidence and change in segmental and cervical alignment.
SSA: segmental sagittal alignment.
CSA: cervical sagittal alignment.
#Student's t-test (two-tailed).
^Fisher exact test (two-tailed).
*$P < 0.05$.

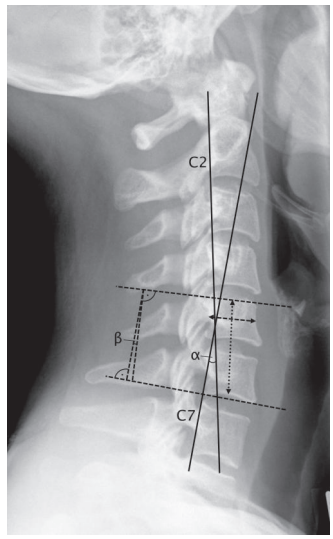


Figure 3: Measurement techniques for subsidence and sagittal alignments. The interbody height ratio of C5/6 is the total segmental height (vertical dotted line with arrowheads) divided by the anterior-posterior diameter of C5 (horizontal dashed line with arrowheads). α is the angle indicating the cervical sagittal alignment (CSA); β is the angle indicating the segmental sagittal alignment (SSA).

bodily pain (SF-36): 57 ± 21 versus 37 ± 13) and physical function (SF-36; 78±20 versus 58±25) showed better outcome in the subgroup with a subsidence ≥3 mm.

The interbody height ratio [21] at follow-up compared to directly postoperative was 0.91±0.08 (PEEK cage), 0.87±0.08 (Sulcem), and 0.90 ± 0.08 (Palacos).

3.2.3. Change in SSA and CSA. Change in SSA toward kyphosis of the treated level from directly postoperative to follow-up was the highest in the PEEK cage group (−4.1°), followed by the Palacos PMMA group (−2.4°) and the Sulcem PMMA group (−1.0°), yielding a statistically significant higher loss of segmental lordosis in the PEEK cage group compared to the Palacos PMMA group ($P = 0.003$) (Table 2).

Change in CSA toward kyphosis between C2 and C7 was −3.1° in the PEEK cage group, −5.2° in the Sulcem PMMA group, and −1.3° in the Palacos PMMA group without showing statistically significant differences.

3.3. Clinical Outcome. At follow-up, the mean VAS pain score was 3.1 in the PEEK cage group, 3.6 in the Sulcem PMMA group, and 2.7 in the Palacos PMMA group without significant differences between the groups (Table 3).

The mean NDI score was 26.5 ± 15.8 (range: 0–66) in the PEEK cage group, 34.7 ± 18.9 (range: 2–84) in the Sulcem PMMA group, and 24.9 ± 17.3 (range: 0–62) in the Palacos PMMA group with a statistically significant better NDI in the Palacos PMMA group compared to the Sulcem PMMA group ($P = 0.034$). Furthermore, the PEEK cage group showed a nearly statistically significant better NDI compared to the Sulcem PMMA group ($P = 0.051$) (Table 3).

Statistical analysis of the SF-36 revealed statistically significant worse physical function and physical component summary of the Sulcem PMMA group (49.7 and 33.4) compared to the PEEK cage (67.5 and 39.1) and Palacos PMMA group (63.2 and 39.4) ($P < 0.05$). The remaining scales of the SF-36 showed no statistically significant differences (Table 3).

The Patient Satisfaction Index as evaluation of patients' satisfaction with the postoperative result led to the following answers: "1" (46% PEEK cage, 32% Sulcem, and 48% Palacos); "2" (35% PEEK cage, 35% Sulcem, and 23% Palacos); "3" (5% PEEK cage, 9% Sulcem, and 23% Palacos); and "4" (14% PEEK cage, 24% Sulcem, and 6% Palacos). χ^2 test revealed no statistical difference of the Patient Satisfaction Index between the treatment groups ($P = 0.118$).

3.4. Comparisons

3.4.1. Fused Levels and Change in SSA. Within the PEEK cage group, fused levels showed statistically significant higher changes in SSA toward kyphosis compared to nonfused levels (−5.2° versus −2.1°; $P = 0.030$) (Table 4). The Sulcem and

Table 3: Clinical outcome.

	PEEK cage	PMMA Sulcem	PMMA Palacos	Overall	P (cage versus Sulcem)	P (cage versus Palacos)	P (Sulcem versus Palacos)
VAS[#]	3.1 ± 2.0	3.6 ± 2.5	2.7 ± 2.7	3.1 ± 2.4	0.342	0.565	0.193
NDI[#]	26.5 ± 15.8	34.7 ± 18.9	24.9 ± 17.3	28.7 ± 17.7	0.051	0.699	0.034[*]
SF-36							
Physical function[#]	67.5 ± 24.3	49.7 ± 28.8	63.2 ± 23.8	60.3 ± 26.6	0.007[*]	0.459	0.044[*]
Bodily pain[#]	46.4 ± 20.1	42.4 ± 24.0	49.9 ± 30.3	46.2 ± 24.7	0.444	0.588	0.277
General health[#]	53.9 ± 21.4	46.0 ± 20.5	51.5 ± 22.6	50.6 ± 21.5	0.116	0.662	0.309
Vitality[#]	47.2 ± 19.6	42.7 ± 20.8	44.3 ± 20.7	44.8 ± 20.2	0.360	0.557	0.769
Mental health[#]	57.4 ± 21.5	61.8 ± 22.4	65.5 ± 19.8	61.3 ± 21.4	0.403	0.110	0.475
Physical component summary[#]	39.1 ± 9.9	33.4 ± 11.8	39.4 ± 10.9	37.3 ± 11.1	0.036[*]	0.917	0.044[*]
Mental component summary[#]	43.3 ± 12.8	44.8 ± 14.5	46.2 ± 11.1	44.6 ± 12.8	0.661	0.335	0.670

The table shows means with standard deviations from self-reported questionnaires.
VAS: Visual Analog Scale.
NDI: Neck Disability Index.
SF-36: Short Form 36 Health Survey.
[#]Student's t-test (two-tailed).
[*]$P < 0.05$.

Palacos PMMA groups revealed no statistically significant differences.

3.4.2. Fused Patients and Outcome. Patients were classified as "fused" if all treated levels showed fusion and as "nonfused" if at least one level displayed no fusion. In this respect, 62.2% of the patients in the PEEK cage group were classified as fused, 51.3% in the Sulcem PMMA group, and 41.9% in the Palacos PMMA group (Table 2).

Analysis between fused and nonfused patients in respect to clinical outcome revealed that, in the Sulcem PMMA group, fused patients showed a statistically significant better physical component summary of the SF-36 than nonfused patients ($P = 0.024$) (Table 4). Interestingly, the fused subgroups in the PEEK cage and the Palacos PMMA groups did not even present a numerical improvement of the physical component summary or physical function compared to their nonfused subgroups. The remaining subitems of the SF-36 showed no statistically significant differences between fused and nonfused subgroups in respect to clinical outcome (data not shown). Fused patients in all substitute groups showed lower (better) VAS and NDI scores than the nonfused subgroups though without being statistically significant (Table 4).

3.4.3. Subsidence and Fusion: Subsidence and Change in SSA. There was no statistical difference with regard to fusion status between levels with subsidence of at least 3 mm compared to less than 3 mm (Table 5). Overall, fused levels displayed a higher mean subsidence (3.0 mm) than nonfused levels (2.1 mm) without reaching statistical significance ($P = 0.055$) (Table 4).

The mean change in SSA did not differ significantly between the subsidence categories with the threshold of 3 mm (Table 5).

3.5. Correlation Analyses

3.5.1. Subsidence and Change in SSA. To compare the effect of subsidence on the change in SSA, regression analyses were conducted. Subsidence was not a significant predictor of a change in SSA in any group (PEEK cage: $R^2 = 0.003$ and $P = 0.741$; Sulcem: $R^2 = 0.014$ and, $P = 0.449$; Palacos: $R^2 = 0.012$ and $P = 0.535$).

3.5.2. SSA and CSA. Correlation analysis between change in SSA and CSA was performed on patients solely operated on in one level to ensure homogeneous patient groups. Change in SSA was a significant predictor of a change in CSA in the Sulcem ($R^2 = 0.376$ and $P = 0.002$; Figure 4) and Palacos PMMA groups ($R^2 = 0.264$ and $P = 0.042$) but not in the PEEK cage group ($R^2 = 0.064$ and $P = 0.223$).

3.6. Reoperations. In the PEEK cage group, one patient experienced recurrent radicular pain and was reoperated 3 months after ACD due to anterior cage dislocation at level C5/6 and a new soft prolapse at level C6/7.

In the Sulcem PMMA group, two patients underwent revision surgery. One patient was relieved of newly developed radicular pain by unilateral posterior foraminotomy at level C7/T1 two years after ACD at level C6/7, which was now fused. Another patient developed new radicular pain with paresthesia one year after ACD at levels C4/5 (nonfused)

Table 4: Comparison of sagittal alignment, subsidence, pain level, and functional outcome according to fusion status.

	PEEK cage	PMMA Sulcem	PMMA Palacos	Overall
Change in SSA				
Fused *levels*	−5.2° ± 4.4°	−2.2° ± 7.4°	−1.4° ± 3.4°	−3.3° ± 5.7°
Nonfused *levels*	−2.1° ± 3.9°	−3.0° ± 3.8°	−0.5° ± 6.0°	−1.8° ± 4.6°
#*P*	0.030*	0.662	0.605	0.133
Subsidence (mm)				
Fused *levels*	2.7 ± 2.7	3.2 ± 3.2	3.1 ± 2.1	3.0 ± 2.8
Nonfused *levels*	1.7 ± 1.7	2.2 ± 1.8	2.3 ± 2.6	2.1 ± 2.1
#*P*	0.152	0.204	0.336	0.055
VAS				
Fused *patients*	2.9	3.4	2.0	2.8
Nonfused *patients*	3.1	3.8	3.3	3.4
#*P*	0.667	0.626	0.168	0.216
NDI				
Fused *patients*	24.1	32.7	19.9	26.0
Nonfused *patients*	28.0	37.0	28.6	31.2
#*P*	0.439	0.512	0.140	0.136
SF-36 Physical function				
Fused *patients*	66.4	56.4	63.0	62.2
Nonfused *patients*	72.1	42.2	63.3	58.9
#*P*	0.443	0.160	0.974	0.538
SF-36 Physical component summary				
Fused *patients*	39.6	37.7	37.8	38.5
Nonfused *patients*	39.7	28.5	40.7	36.3
#*P*	0.971	0.024*	0.489	0.349

The table shows means (with standard deviations) of change in segmental sagittal alignment, subsidence, pain level, and functional outcome according to the fusion status.
SSA: segmental sagittal alignment.
VAS: Visual Analog Scale.
NDI: Neck Disability Index.
SF-36: Short Form 36 Health Survey.
#Student's *t*-test (two-tailed).
*$P < 0.05$.

and C5/6 (fused) due to neuroforaminal stenosis; unilateral posterior foraminotomy at level C5/6 led to pain elimination.

In the Palacos PMMA group, one patient had to be surgically revised 18 months after ACD at level C3/4 (nonfused) due to retrospondylosis of C4 with spinal canal stenosis and kyphotic malalignment. Cervical alignment was restored by decompressive corpectomy of C4 and fusion with tricortical iliac crest autograft and anterior plating.

4. Discussion

4.1. Fusion. At the first sight, the present study displays comparatively high nonfusion rates after ACD in all treatment groups. The impact of using thin-sliced CT scans instead of lateral radiographs for assessment of bony fusion will be discussed below. However, higher fusion rates were not reflected in better clinical outcome except for Sulcem PMMA spacers with a significantly worse outcome in nonfused patients.

ACD with implantation of substitutes is a widely accepted surgical technique in cervical degenerative disc disease [1]. Intervertebral cages and PMMA spacers demonstrated good clinical outcome with differing fusion rates [1–3, 5, 12, 15–18]. Titanium cages filled with additional different materials revealed fusion rates of 47–97% [5, 16, 17, 32, 33]. Empty titanium cages showed fusion rates of 87% [2, 13]. Two comparative studies found higher fusion rates in filled PEEK cages than in filled titanium cages [14, 16]. In contrast, Cabraja et al. recently stated bone formation in 80% using empty titanium cages and 62% using empty PEEK cages [18]. But it has to be considered that a reliable assessment of trabecular bone formation and radiographic fusion signs is prevented in radiopaque titanium cages [23]. Besides the radiolucency of PEEK [15, 17, 22], a further advantage over titanium is supposed to be the elastic modulus of PEEK which is similar

Table 5: Comparison of fusion and sagittal alignment according to subsidence.

	PEEK cage (n = 45)			PMMA Sulcem (n = 42)			PMMA Palacos (n = 33)			Overall (n = 120)		
	n (levels)	Fused levels	Change in SSA[†]	n (levels)	Fused levels	Change in SSA[†]	n (levels)	Fused levels	Change in SSA[†]	n (levels)	Fused levels	Change in SSA[†]
Subsidence ≥ 3 mm	16	12/15	−5.5° (r, −15.1–3.5)	15	11/15	−2.0° (r, −15.6–16.4)	12	7/12	0.3° (r, −5.7–15.9)	43	30/42	−2.6° (r, −15.6–16.4)
Subsidence < 3 mm	29	17/28	−3.4° (r, −16.1–2.9)	27	15/27	−2.6° (r, −10.6–11.2)	21	8/21	−1.7° (r, −6.3–7.9)	77	40/76	−2.6° (r, −16.1–11.2)
P		0.308[^]	0.124[#]		0.330[^]	0.800[#]		0.300[^]	0.297[#]		0.053[^]	1.00[#]

The table shows ratios of fused levels and change in segmental sagittal alignment according to the degree of subsidence with a threshold of 3 mm.
[#]Student's t-test (two-tailed).
[^]Fisher exact test (two-tailed).
[†]Negative toward kyphosis; r: range.

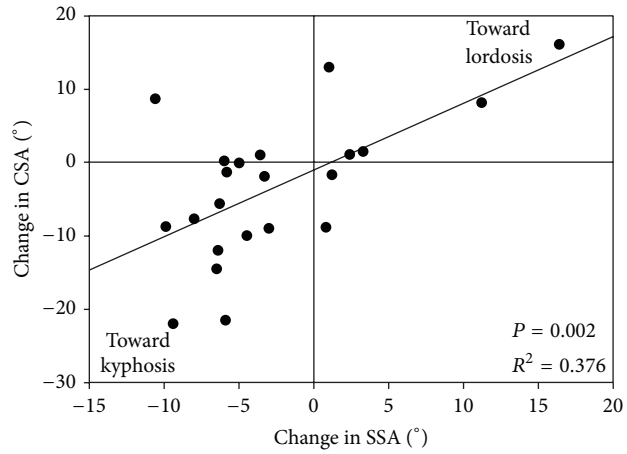


Figure 4: Correlation between SSA and CSA after ACD with implantation of Sulcem PMMA spacers. The diagram shows the positive correlation between SSA and CSA in the Sulcem PMMA group indicating that a change in SSA was a significant predictor of a change in CSA. The mean change in SSA was −2.4° and in CSA was −5.2°. ACD: anterior cervical discectomy, CSA: cervical sagittal alignment, PMMA: polymethylmethacrylate, and SSA: segmental sagittal alignment.

to that of cortical bone and is assumed to prevent cage subsidence [18, 20, 23, 29]. Since cervical vertebral endplates are thin layers of subchondral bone [34] and not cortical bone, the impact of this characteristic remains unclear.

PEEK cages filled with additional different materials showed fusion rates of 89–100% [14, 16, 20, 22–26, 35, 36]. Only few studies examined empty PEEK cages and reported bony fusion rates of 62% [18], 72% [19], and 76% (30% with "obvious fusion" and 46% with "probable fusion," only 6-month follow-up) [21], which are comparable with the present study.

PMMA spacers showed fusion rates of 0–66% [2–6, 37, 38], in an old publication by Böker et al. [7] of even 89%, though using radiographs for evaluation of bony fusion. Therefore, the fusion rates of the PMMA groups in the present study are in line with the published data.

The technique for assessment of bony fusion varies between the studies. Most authors use lateral radiographs [2, 3, 13, 14, 16–23, 25, 26, 33, 36], though CT imaging is clearly superior [22, 27] and was used in only few trials [5, 35]. We used thin-sliced CT scans with multiplanar reconstruction for the highest accuracy in assessing bony fusion. This might imply overestimation of bony fusion in previous studies due to inaccuracy in the measurement technique [27]. Therefore, comparisons of studies with different techniques have to be drawn very carefully. Nevertheless, our findings with higher fusion rates in PEEK cages (65%) than in Sulcem (57%) and Palacos (46%) PMMA spacers are in line with other reports showing higher fusion in titanium cages than in PMMA spacers (87% versus 66%, 2-year follow-up [2]; 97% versus 0%, 1-year follow-up [5]). In consequence of fusion rates of 65% and less, we prefer to use the term *ACD with implantation of a substitute* instead of *ACD and fusion (ACDF)*.

The higher rate of nonfusion in PMMA spacers could be attributed to a hindered ossification that can only develop around the PMMA spacer and not through the PMMA itself in contrast to a hollow cage [3, 6]. Moreover, missing attachment of PMMA to the bone with formation of a fibrous cement-bone interface was stated as a reason for nonfusion [6].

The clinical outcome, however, was generally not influenced by fusion status (Table 4), which was also observed by other authors [3, 18, 19, 21]. Only the Sulcem PMMA group showed a significantly better physical outcome in fused than in nonfused patients (Table 4). Although the Sulcem PMMA group revealed worse functional outcome than the PEEK cage and Palacos PMMA group, no clear beneficial substitute could be specified. Other studies found no difference in the clinical outcome between different substrates like titanium cages and PMMA [1, 2, 5, 6, 8, 37] or titanium and PEEK cages [18].

4.2. Subsidence. The loss of about 10% of the interbody height ratio in our patients over the course of time is consistent with results of other studies (up to 7.2% [21] and 9.2% [39] in PEEK cages). In addition, the overall mean subsidence (Table 4) is comparable to the results of Pechlivanis et al. [19] who reported a mean PEEK cage subsidence of 2.9 mm in fused and of 1.5 mm in nonfused patients. They found that the fusion group revealed a significant higher subsidence in PEEK cages [19]. Our data tended to correspond to their findings only after pooling all groups, though without reaching statistical significance (Tables 4 and 5). Why higher subsidence might promote fusion is unclear, but a broader contact of the substitute to cancellous bone and therefore promoting bone growth inducing factors were postulated as one reason [19].

In a biomechanical in vitro study, bone cement was found to exhibit a significantly lower subsidence than titanium or carbon fiber cages [40]. Besides, the elastic module of PEEK was hypothesized to be too flexible and could therefore lead to endplate failure with subsidence [19]. Our data with similar subsidence in the PEEK cage and PMMA groups conflict this hypothesis.

The incidence of subsidence (threshold in our study of 3 mm) was 36% in each group (Table 5). Other studies reported differing incidences of subsidence of 56% [41] (titanium cages, threshold of 3 mm); 44% [12] and 20% [18] (titanium cages, threshold of 2 mm); 15% [27] and 13% [19] (PEEK cages, threshold of 3 mm); and 29% [21], 26% [27], and 14% [18] (PEEK cages, threshold of 2 mm).

One patient in the Sulcem PMMA group needed further surgery with decompression of the neuroforamen on one side, which can be attributed to severe subsidence after ACD. No further associations between higher subsidence and worse clinical outcome were found. In the PEEK cage group, patients with a subsidence of at least 3 mm even showed a better outcome, which is an unexpected result and inconsistent with the general understanding. As usual, in

an academic center, several surgeons with different surgical skills and techniques operated on this patient cohort. This fact could have contributed to these unexpected findings. Other authors did not find significantly differing clinical outcome measures between subsidence and nonsubsidence groups [42].

4.3. Sagittal Alignment. The highest loss of lordosis (negative change in SSA) was found in the PEEK cage group and was significantly higher than in the Palacos PMMA group (Table 2). PEEK cages also had a significantly higher loss of lordosis in fused levels than in nonfused levels (Table 4) supposing that a higher loss of lordosis might promote bony fusion while bringing the anterior aspects of the endplates and their fracture fragments closer together. Moreover, in the PEEK cage group, the subgroup with a subsidence of at least 3 mm showed a higher, though not significant, loss of lordosis than the subgroup with a subsidence less than 3 mm (−5.5° versus −3.4°; Table 5). In the PMMA groups, however, these observations were not reflected.

Like in the Sulcem and Palacos PMMA groups of the present study, also prior studies showed a significant positive correlation of a change in SSA and CSA after ACD with filled PEEK cages [22].

4.4. Limitations of the Study. The retrospective design is an obvious methodological weakness of the study. Since patients were retrospectively included, no power analysis was performed. We intended to reduce a possible selection bias with precise patient selection criteria. The heterogeneity of patients with radicular and myelopathic symptoms can lead to bias in clinical outcome. In line with the retrospective design, differing follow-up times of the treatment groups come, which themselves can contribute to bias complication rates or radiographic measurements.

5. Conclusions

There are different fusion rates after ACD with implantation of PEEK cages and PMMA spacers. The results of the current study might indicate, in agreement with other reports, that fusion status and subsidence do not correlate with clinical outcome. No clear advantageous disc substitute could be specified; however, the PEEK cage and Palacos PMMA groups appeared to present better function in comparison to the Sulcem PMMA group.

Abbreviations

ACD: Anterior cervical discectomy
CSA: Cervical sagittal alignment
NDI: Neck Disability Index
PEEK: Polyetheretherketone
PMMA: Polymethylmethacrylate
SF-36: Short Form 36 Health Survey
SSA: Segmental sagittal alignment
VAS: Visual Analog Scale.

Conflict of Interests

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

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