

Retraction

Retracted: Red Cell Distribution Width: A Clinical Indicator to Assess Severity and Guide Anti-Inflammatory Therapy in Patients with Knee Osteoarthritis

Scientific Programming

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This article has been retracted by Hindawi following an investigation undertaken by the publisher [1]. This investigation has uncovered evidence of one or more of the following indicators of systematic manipulation of the publication process:

- (1) Discrepancies in scope
- (2) Discrepancies in the description of the research reported
- (3) Discrepancies between the availability of data and the research described
- (4) Inappropriate citations
- (5) Incoherent, meaningless and/or irrelevant content included in the article
- (6) Peer-review manipulation

The presence of these indicators undermines our confidence in the integrity of the article's content and we cannot, therefore, vouch for its reliability. Please note that this notice is intended solely to alert readers that the content of this article is unreliable. We have not investigated whether authors were aware of or involved in the systematic manipulation of the publication process.

Wiley and Hindawi regrets that the usual quality checks did not identify these issues before publication and have since put additional measures in place to safeguard research integrity.

We wish to credit our own Research Integrity and Research Publishing teams and anonymous and named external researchers and research integrity experts for contributing to this investigation.

The corresponding author, as the representative of all authors, has been given the opportunity to register their

agreement or disagreement to this retraction. We have kept a record of any response received.

References

- [1] H. Zhang, L. Shi, Z. Tang, G. Rong, and B. Gui, "Red Cell Distribution Width: A Clinical Indicator to Assess Severity and Guide Anti-Inflammatory Therapy in Patients with Knee Osteoarthritis," *Scientific Programming*, vol. 2022, Article ID 8368968, 6 pages, 2022.

Research Article

Red Cell Distribution Width: A Clinical Indicator to Assess Severity and Guide Anti-Inflammatory Therapy in Patients with Knee Osteoarthritis

Hongjing Zhang , Liwei Shi , Zhi Tang , Genxiang Rong , and Binjie Gui 

Department of Orthopedics, The First Affiliated Hospital of Anhui Medical University, Hefei 230022, China

Correspondence should be addressed to Binjie Gui; guibinjie@ahmu.edu.cn

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To explore the influence factors of the red cell distribution width (RDW) level in knee osteoarthritis (KOA) patients, the difference in RDW before and after total knee arthroplasty (TKA), and further explain the clinical value of the RDW level in KOA patients. Information of 195 patients with KOA and 43 patients with meniscus injuries undergoing surgical treatment in the Surgery Department of Joint and Microsurgery Repair and the Surgery Department of Sports Trauma and Joint Arthroscopy of the First Affiliated Hospital of Anhui Medical University from June 1, 2020, to December 1, 2020, were collected. All included patients' gender, age, height, medical history, blood lipid, erythrocyte sedimentation rate (ESR), CRP, RDW, anteroposterior and lateral X-ray images of the knee joint, and magnetic resonance imaging (MRI) of the knee joint were recorded. The difference in RDW of KOA patients with different severities before and after unilateral TKA surgery was compared, and the difference between KOA patients and patients with only meniscus injury was also compared for further analysis of the influence factors of the RDW level in moderate-severe KOA patients. Among moderate-severe KOA patients with different imaging severities, the RDW level was significantly different ($P=0.022$). There was no statistical difference between the groups with and without the TKA history. The RDW level was higher in KOA patients than in patients with only meniscus injuries, and the difference was statistically significant ($P < 0.05$). To some extent, the RDW level could be taken as a predictor for the severity of moderate-severe KOA patients, and its elevation was primarily related to chondritis and synovitis caused by KOA, so it was suggested that the patients receive adjuvant anti-inflammation therapy after TKA surgery.

1. Introduction

KOA is a common chronic joint disease that tends to occur in middle-aged and elderly people, especially females [1]. Its clinical manifestations might be pain and stiffness of the knee joint in the early stages [2] and deformity and dysfunction in the advanced stages. According to statistics, osteoarthritis is one of the top ten disabling diseases all over the globe [3, 4]. The pathogenesis of KOA is complex, and the specific pathogenesis is also under continuing study and exploration. Its main pathological characteristics are chronic synovitis of the knee joint, cartilaginous degeneration, and subchondral osteosclerosis [5]. The meniscus is composed of two half-moon-shaped fibrous cartilage structures. It is

wedged between the medial malleolus of the thighbone and the tibial plateau and is conducive to the stability of knee joint and stress absorption of the joint cartilage at the time of motion [6]. It was reported by some statistics that among symptomatic patients with confirmed KOA, the incidence rate of meniscus injury was 63%, while among asymptomatic patients, the incidence rate of meniscus injury was 60% [7]. The therapies included intraarticular cortisol injections, nonsteroidal anti-inflammatory drugs administered orally, exercise therapy, ultrasound therapy, and so on [8]. As for severe KOA patients, the therapy usually involves knee arthroplasty, and either unicompartmental knee arthroplasty (UKA) or TKA could achieve a satisfactory effect. Bilateral KOA patients often need to undergo surgery of the

counter-lateral after unilateral surgery to achieve a certain quality of life (QOL). RDW is one of the blood routine indicators used to indicate the varying degree of red blood cell size in blood. The higher the value, the higher the heterogeneity of cell size. Recent research found that RDW levels were significantly higher in OA patients, which was related to osteoarthritis, and that the RDW level and the risk of knee joint osteophyte had a positive correlation [9]. However, it is still debatable whether using RDW to predict the occurrence and severity of KOA is accurate. In this study, our purpose was to explore the influence factors of the RDW level in moderate-severe KOA patients, whether the elevation of their level is caused by primary osteoarthritis or secondary meniscus injury and or if there is a difference in the RDW level between bilateral KOA patients after undergoing unilateral knee arthroplasty and those without surgery. Besides, we aimed to explain further the clinical value of the RDW level in KOA patients.

2. Data and Methods

2.1. General Data. A total of 195 KOA patients, of which 43 patients with meniscus injury undergoing surgical treatment in the Surgery Department of Joint and Microsurgery Repair and the Surgery Department of Sports Trauma and Joint Arthroscopy of the First Affiliated Hospital of Anhui Medical University from June 1, 2020, to December 1, 2020, were selected as the study subjects. Among the KOA patients, there were 54 males and 141 females, aged 68 (65, 73) years old, 35 with a history of knee arthroplasty, and 160 without a history of knee arthroplasty. Among the patients with meniscus injury, 19 were males and 24 were females, aged 44 (32, 53) years old. The following were the inclusion criteria: KOA patients were included in accordance with the Joint Surgery Group of the Chinese Orthopedic Association's 2018 guidelines for diagnosis and treatment of osteoarthritis (Edition 2018); imaging of the knee joint (anteroposterior and lateral X-ray) revealed osteophyte formation, narrowing joint space, or joint deformity; and imaging (MRI plain scanning) evidence revealed meniscus injury but not osteoarthritis. The following were the exclusion criteria: the KOA group was required to exclude those with a history of acute trauma, tumors, infection history, and other types of arthritis, such as rheumatoid arthritis (RA), ankylosing spondylitis (AS), gouty arthritis, and so on, combined with severe liver and kidney diseases, hematologic diseases, and immune diseases; and the meniscus injury group was required to exclude those with a history of osteoarthritis and those with MRI examination taboos (metal and electronic implants) (Table 1).

This study conformed to the requirements of the Ethics Committee of the First Affiliated Hospital of Anhui Medical University, and all included patients have received informed consent and affixed signatures.

2.2. Study Method

2.2.1. Collection of General Data. Gender, age, height, weight, and medical history (history of knee arthroplasty,

hypertension, diabetes, and heart disease) of all included patients were recorded. All heights and weights were measured with the same weighing scale and height measuring instrument by wearing unlined clothes and taking off their shoes and hats, and the body mass index (BMI) ($\text{weight}/\text{height}^2$) was calculated.

2.2.2. Laboratory Examination. Fasting morning blood of all included subjects was collected and placed in a short purple tube and a short yellow tube to be tested by the Laboratory Department of The First Affiliated Hospital of Anhui Medical University, and the results included RDW, ESR, C-reactive protein (CRP), total cholesterol (TC), triglyceride (TG), HDL-C, and LDL-C. Hyperlipidemia (HLP) was defined as $\text{TC} \geq 6.2 \text{ mmol/L}$ or $\text{TG} \geq 2.3 \text{ mmol/L}$ or $\text{HDL-C} < 1 \text{ mmol/L}$ or $\text{LDL-C} \geq 4.1 \text{ mmol/L}$.

2.2.3. Imagological Examination. Anteroposterior and lateral X-ray images of the bilateral knee joints of all osteoarthritis patients were filmed, and the KOA severity was graded by two experienced joint surgeons using the Kellgren-Lawrence (K-L) grading and scoring system [10, 11] in accordance with the osteophyte condition and joint space, and the more severe side of the bilateral patients was selected for scoring. The two image-reading surgeons were blind to the age, symptoms, and test results of the study subjects (Table 2).

2.3. Statistical Analysis. The SPSS 26.0 software was used for processing and analysis. The normal distribution data were expressed by mean \pm SD, the data of abnormal distribution were expressed by median and interquartile range, and the qualitative data were expressed by frequency in the normal distribution test. The variance test was used to compare measurement data of multiple groups in normal distribution. The rank-sum test was used to compare measurement data of multiple groups in abnormal distribution. The chi-square test was used to compare qualitative data from multiple groups. Single-factor and multiple-factor regression analyses of the grading data were performed using the ordinal regression analysis method. As the pretest level $\alpha = 0.05$, $P < 0.05$ indicated that the difference was statistically significant.

3. Results

3.1. Comparison of KOA Patients with and without TKA. The ESR, CRP, and RDW of KOA patients were included in the study by dividing them into two groups with/without the TKA history, ESR, CRP, and RDW. Results showed that the difference in ESR, CRP, and RDW levels in the groups with and without the TKA history was not statistically significant ($P > 0.05$), as given in Table 3.

3.2. Comparison of Basic Characteristics of KOA Patients with Different K-L Grades. By anteroposterior and lateral images of the patients' knee joints and in accordance with K-L

TABLE 1: Criteria of guidelines for diagnosis and treatment of osteoarthritis (edition 2018) issued by Chinese Orthopedic Association.

No.	Conditions
1	Repeated arthralgia in recent 1 month
2	X-ray image (standing or weight-bearing position) shows narrow joint space, sclerosis and (or) cystic change of the subchondral bone, and osteophyte formation on the joint edge
3	Aged ≥ 50 years old
4	Morning stiffness time ≤ 30 min
5	Bone friction sound (sensation) at the time of friction

Meeting the conditions of 1 and any of 2, 3, 4, and 5 can be diagnosed as KOA.

TABLE 2: K-L grading and scoring system.

Grade 0	Normal knee joint
Grade 1	There is slight osteophyte with the articular cartilage
Grade 2	There is slight osteophyte with the articular cartilage and slightly narrowing joint space
Grade 3	There is moderate osteophyte with the articular cartilage, moderately narrowing joint space and sclerosis with subchondral bone
Grade 4	There is severe osteophyte with the articular cartilage, severely narrowing joint space, significant sclerosis with the subchondral bone, and joint deformity

TABLE 3: Comparison of KOA patients with and without the TKA history.

	With TKA history ($n = 35$)	Without TKA history ($n = 160$)	Z	P
ESR (mm/h)	11.00 (6.00, 23.00)	14.00 (8.25, 23.00)	-1.493	0.135
CRP (mg/L)	2.00 (0.80, 2.90)	1.45 (0.73, 3.00)	-1.042	0.297
RDW (%)	13.00 (12.60, 13.60)	13.10 (12.60, 13.60)	-0.338	0.736

grades, KOA patients were divided into three groups, where those with a K-L grade of 2 were defined as group I, those with a K-L grade of 3 were defined as group II, and those with a K-L grade of 4 were defined as group III. Analyses revealed that the difference in age, gender, weight, BMI, ESR, and CRP among patients of varying severity had no statistical significance ($P > 0.05$), as given in Table 4.

3.3. Comparison of RDW Levels in KOA Patients with Different K-L Grades. By comparing RDW levels in KOA patients with different K-L grades, it was discovered that RDW levels were of statistical significance in the three patient groups with different severities ($P = 0.022$), as given in Table 5. Further comparative analysis of the groups showed that the difference between group I and group II was of no statistical significance ($P > 0.05$). The difference between group I and group III was of no statistical significance ($P > 0.05$). The difference between group II and group III was of statistical significance ($P = 0.022$), and the RDW level of group III was higher than that of group II, as given in Table 6.

3.4. Influence Factors of RDW Level. All the 195 included patients were divided into four groups by referring to the quartile of the RDW level, where those with $RDW \leq 12.6$ were group I, those with $12.6 < RDW \leq 13.1$ were group II, those with $13.1 < RDW \leq 13.6$ were group III, and those with $RDW > 13.6$ were group IV. The effects of age, weight, BMI, ESR, CRP, history of hypertension, history of diabetes, and HLP on the RDW level were studied. The analysis of the ordinal multiple logistic regression model revealed that the model fitting information was of no statistical significance

($P > 0.05$), as given in Table 7. No variables entered the model, indicating that the above variables did not affect the RDW level.

3.5. Comparison between the KOA Patient Group and Meniscus Injury Group. The comparison of age, ESR, CRP, and RDW level was made between 195 KOA patients and 43 patients with a meniscus injury. The results showed that the KOA patients and the patients with meniscus injury had a statistical significance in age, ESR, CRP, and RDW level ($P < 0.05$). KOA patients were older than the patients with a meniscus injury in age and were also higher than the patients with a meniscus injury in ESR, CRP, and RDW level, as given in Table 8.

4. Discussion

It was discovered in this study that among KOA patients with K-L grade ≥ 2 , RDW level differed among patients with different imaging severities, and the patients with the higher K-L grade also showed the higher RDW level. KOA pathogenesis has been linked to IL-6, TNF- α , and other inflammatory factors, which may influence the RDW level by affecting the bone marrow function and iron metabolism [12]. As a result, it is possible that RDW is a predictor of osteoarthritis severity in moderate-to-severe KOA patients.

As an inflammatory disease, osteoarthritis has been linked to IL-1, IL-6, IL-8, IL-18, TNF- α , other proinflammatory factors, IL-4, IL-10, and other anti-inflammatory factors, matrix metalloproteinases (MMP-3 and MMP-13), and a disintegrin and metalloproteinase with thrombospondin motifs (ADAMTS-4 and ADAMTS-5) [13–16].

TABLE 4: Comparison of basic characteristics of KOA patients with different K-L grades.

Item	K-L group			$F/\chi^2/Z$	P
	Group I (n = 14)	Group II (n = 60)	Group III (n = 121)		
Age (years old)	68.14 ± 8.69	66.67 ± 7.99	68.35 ± 6.76	1.078	0.342
Gender (male/female)	3/11	13/47	38/83	2.195	0.344
Weight (kg)	65.75 ± 8.42	64.92 ± 10.70	64.87 ± 11.12	0.042	0.959
BMI	26.19 ± 3.28	25.82 ± 3.97	25.32 ± 3.63	0.592	0.554
ESR (mm/h)	14.00 (10.75, 16.75)	13.00 (9.25, 19.50)	14.00 (7.00, 23.00)	0.128	0.938
CRP (mg/L)	1.30 (0.75, 2.13)	1.15 (0.70, 2.75)	1.80 (0.80, 3.90)	2.607	0.272

TABLE 5: Comparison of RDW levels in KOA patients with different K-L grades.

	Group I	Group II	Group III	Z	P
RDW (%)	12.90 (12.40, 13.35)	12.80 (12.50, 13.40)	13.20 (12.70, 13.70)	7.610	0.022

TABLE 6: Comparison of RDW levels in groups with different K-L grades.

Group	Z	P
Group I vs. group II	0.468	1.000
Group I vs. group III	-22.564	0.468
Group II vs. group III	-23.032	0.029

TABLE 7: Model fitting information.

Model	-2 log likelihood	Chi-square	df	Sig.
Final	530.352	9.162	8	0.329

TABLE 8: Comparison between the KOA patient group and meniscus injury group.

	KOA	Meniscus injury	Z	P
Age (years)	68 (64, 73)	44 (32, 53)	-9.925	≤0.001
ESR (mm/h)	14.00 (7.00, 23.00)	9.00 (5.00, 16.00)	-2.815	0.005
CRP (mg/L)	1.60 (0.80, 3.00)	0.80 (0.30, 1.50)	-3.646	≤0.001
RDW (%)	13.10 (12.60, 13.60)	12.70 (12.20, 12.90)	-4.291	≤0.001

By studying and comparing the normal participants, Lippi et al. discovered that the higher the RDW value, the older the corresponding population was. On the other hand, the RDW level was also in positive correlation with ESR and CRP to a certain degree. In their study, Hanada et al. discovered that when compared with normal subjects, the osteoarthritis patients had higher ESR and CRP, which were positively correlated with K-L grade [17–20]. Existing studies have discovered that RDW is closely related to metabolic disease, cardiovascular disease (CVD), and cancer, and it is also related to the fatality rate of the elderly suffering from such diseases [21]. Nevertheless, this study showed that there was no significant difference in age, ESR, and CRP among the moderate-severe KOA patients. Besides, among the population with such conditions, age, weight, and other common pathogenic factors of KOA, hypertension, HLP, and other underlying diseases did not affect the patients' RDW

level. This study also prompted that as for bilateral KOA patients after undergoing unilateral TKA surgery, there was no significant change in ESR, CRP, and RDW levels compared with those without surgical treatment. Therefore, it is possible that after KOA patients progressed to moderate-severe condition, the RDW level did not have a specific relation with ESR, CRP, and some underlying diseases, and the increase of RDW could be attributed to other factors. In addition, since the level of an inflammatory factor in the bodies of KOA patients did not decrease after unilateral TKA surgery, their symptoms in the affected extremity might be aggravated. Therefore, it is necessary to perform subsequent anti-inflammatory therapy for bilateral KOA patients after surgical treatment.

The knee joint is the joint that bears the greatest weight in the human body and has a complex anatomical structure. In the progressive process of KOA, there can be corresponding changes in patellar articular surfaces, tibia, femur articular surfaces, patellar tendon, and meniscus [22, 23]. As a common sports trauma disease, the risk of chronic meniscus injury could be increased by both obesity and exercise. Englund concluded a study that showed the incidence rate of meniscus injury increased with the growth of age, and meniscus injury was related to BMI in females, but not in males [7]. Obesity in females and other factors were also identified as pathogenic factors for KOA. Some animal tests showed that under culture in vitro, the repair process of meniscus injury in pigs would be inhibited by IL-1, TNF- α , and other inflammatory factors [24]. Among the patients with meniscus tears, their meniscus cells also had a high expression of MMP-3, MMP-13, and ADAMTS-5 [25, 26]. It indicates that only meniscus injury may also cause a series of inflammatory responses and an increase in the patients' RDW level. By comparing the KOA patients and the patients with only meniscus injury in this study, the results showed that ESR, CRP, and RDW levels in KOA patients were higher than those in the patients with meniscus injury, which also indicated that the increased RDW level in KOA patients was mainly caused by chondritis and synovitis due to osteoarthritis, while secondary meniscus inflammation was not the main cause.

Study participants of this study were mainly selected from KOA patients with a K-L grade of 2–4, and such patients always required surgery to alleviate the symptoms

and improve their life quality, and they also required close attention from surgeons. RDW was a conventional examination indicator for hospitalized patients as a blood routine indicator. The RDW level was used as an indicator for the severity of moderate-severe KOA patients in this study, which could help to make a more comprehensive evaluation of the patients' condition. Moreover, the RDW level was used to indicate the necessity of the patients' performing bilateral TKA and guide postsurgery anti-inflammatory therapy to a certain degree.

The shortcomings of this study are that the study participants were severe KOA patients, with few cases of a K-L grade of 2. Second, it was very difficult to find elderly cases with only meniscus injury but not KOA. The patients with only meniscus injury were middle-aged and lacked a certain consistency in age compared with the high incidence rate of KOA elderly patients. In conclusion, the RDW level has played a certain role in the diagnosis and therapy of KOA, and its application value to other inflammatory diseases requires further study.

Data Availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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