

Bone and Arthroscopy Science

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Bone and Arthroscopy Science

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Table of Contents

- 1 Abnormal Brain Connectivity Networks in Patients with Knee Osteoarthritis: A Resting-state Functional MRI Study**
Huajuan Yang, Lei Zhang, Bo Zhang, Xiaoqian Zhou, Huizhi Mi, Jie Li, Cuiping Mao
- 16 The Effect of Psychological Intervention and Exercise Rehabilitation on the Improvement of Patients' Confidence in Osteoporosis Rehabilitation**
Haoxuan Ning
- 22 Effect Analysis of Muscle Strength Training in Sports Rehabilitation for Patients with Knee Joint Injuries**
Xinyu Wang
- 28 Investigation of the Causes of Inflammatory Reaction after Arthroscopic Anterior Cruciate Ligament Reconstruction**
Lifeng Wang, Wencang Jiao, Ke Wang, Lei Zhao, Suli Xie, Xinqi Li
- 36 Research on Serum Biomarkers in Knee Joint Diseases of the Elderly**
*Jikui Guan, Li Zhao**
- 43 Extrapedicular vs Transpedicular Percutaneous Kyphoplasty for Osteoporotic Vertebral Compression Fractures: A Systematic Review and Meta-analysis**
Fan Wu, Zhigao Wu, Xiang Shen, Wenjie Chen, Chizi Hao
- 54 Synthesis of the Best Evidence for Perioperative Pain Administration in Patients Having Total Hip Prostheses**
Sunjuan Dong, Weiting Liu, Yanling Zhou, Xiucheng Guo, Li Wu, Chi Wang
- 66 Exploring the Advantages of DWI Integrated with DCE Technology in the Diagnosis of AS-SIJ**
Maosheng Zhang

- 72 Analysis of Morphological Characteristics of Modic Changes in the Lumbar Spine Based on MRI Imaging Omics and Their Association with Low Back Pain**
Tuanmao Guo, Yuan Xiao, Yanli Xing
- 82 Clinical Study on the Treatment of Delayed Union After Long Bone Fracture Surgery with Platelet-Rich Plasma and Intramedullary Nail Dynamization**
Yalun Li, Xiang Zheng, Gang He
- 90 Prevention of Ocular Complications in Spine Surgery Patients in the Prone Position**
Yang Liu, Yan Cao, Long Wang, Yuling Zhong
- 94 A Systematic Evaluation of the Safety of Platelet-rich Plasma (PRP) in the Treatment of Osteoarthritis**
Ying Zhang, Hua Song, Xiaoyan Li, Qiangjin Ruan, Xihua Zhang
- 106 Research on Sport-Specific Adaptive Training Programs Following Repair of Upper Limb (Rotator Cuff and Elbow Joint) Impact Injuries in Rugby**
Xiaowei Wang

Abnormal Brain Connectivity Networks in Patients with Knee Osteoarthritis: A Resting-state Functional MRI Study

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Abstract: *Background:* Resting-state functional connectivity (FC) has been nominated as an effective method for elucidating the neural mechanisms underlying chronic pain. To date, whole-brain FC alterations in chronic knee osteoarthritis (KOA) remain largely unknown. *Purpose:* To investigate the functional connectivity patterns across the entire brain in patients with knee osteoarthritis (KOA) using resting-state functional magnetic resonance imaging (rs-fMRI). *Methods:* The current rs-fMRI analysis included 56 well-characterized KOA patients and 20 healthy controls (HCs), with data obtained from OpenNeuro. To identify aberrant topological organization in the brains of KOA patients, the study employed a graph theoretical approach. Additionally, the independent component analysis was conducted to characterize both intra-network and inter-network brain connectivity in these individuals. *Results:* Both the KOA cohort and healthy control cohort exhibited small-world characteristics in brain functional networks. Additionally, compared to HCs, KOA patients showed altered global properties, specifically characterized by reduced global efficiency and increased assortativity. At the nodal level, the KOA patients exhibited decreased degree centrality and betweenness centrality in the right thalamus. Furthermore, independent component analysis indicated abnormal FC within the anterior default mode network (DMN) and salience network (SN) in this patient cohort. The inter-network interactions did not show intergroup differences after multiple-test correction. *Conclusion:* The widespread functional abnormalities observed from a whole-brain network perspective in subjects with KOA pain may provide more comprehensive insights and reinforce the grasp of the neural mechanisms underpinning KOA.

Keywords: Knee osteoarthritis; Functional connectivity; Resting-state functional MRI; Graph theory; Independent component analysis

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1. Introduction

Knee osteoarthritis (KOA) represents the most common form of joint disorder, marked by progressive deterioration and subsequent breakdown of articular cartilage^[1,2], often leading to secondary damage to adjacent structures

such as bones and ligaments. Pain represents the predominant clinical manifestation of knee osteoarthritis (KOA), leading to reduced mobility and a diminished quality of life for patients^[3]. Given its high prevalence, significant functional limitations, and substantial socioeconomic burden, knee osteoarthritis (KOA) has become a critical global public health concern^[4–7]. Unfortunately, treatment regimens for KOA remain far from satisfactory. Limited understanding of the pathophysiological mechanisms is at least partially responsible for the experience, maintenance, and development of KOA.

Resting-state functional magnetic resonance imaging (rs-fMRI) over the past few decades has unraveled the neurophysiological processes underlying chronic pain disorders and created biomarkers related to cognitive, nociceptive, and social dimensions of pain^[8–12]. A wealth of functional neuroimaging research has demonstrated that KOA exhibited significant structural remodeling and functional alterations in brain regions^[13–16]. Functional connectivity (FC) denotes the temporal correlation of a neurophysiological index measured across distinct brain regions^[17] and has been extensively employed in studies using rs-fMRI. However, most studies have used narrow seed-based resting-state FC approaches to analyze rs-fMRI data^[13,18,19], knowledge about the functional integrity of whole-brain networks in individuals with KOA remains limited.

Analyses of rs-fMRI data, such as graph theoretical analysis and independent component analysis (ICA), have become increasingly popular for mapping brain activity, facilitating the investigation of the whole-brain network reorganization. Graph theoretical analysis views the entire brain as a complex network consisting of highly interconnected regions (referred to as nodes) that exchange bidirectional information^[20–22]. This approach provides structured frameworks for measuring topological and organizational characteristics of complex networks^[17,23]. In recent years, a handful of studies have tried to explore this method for analyzing rs-fMRI data of both normal and damaged human brains^[24–29]. By contrast, ICA is a data-driven method to decipher spatially independent components of coherent signals, enabling hypothesis-free and observer-independent assessment of interactions within and between resting-state networks (RSNs)^[30]. Chronic pain may be associated with metabolic alterations within large-scale distributed networks (e.g., default mode network, salience network, and central executive network) that comprise the pain connectome. Research into intra- and inter-network connectivity has significantly advanced our knowledge of large-scale functional organization in both healthy and disordered brains^[31–33]. However, it is unclear how brain networks change in functional connectivity within and between RSNs in KOA.

Considering the aforementioned factors, our objectives were to: (1) apply graph theory methods to quantify topological differences in whole-brain networks, and (2) utilize ICA to identify distinct FC patterns within and between RSNs. The study hypothesized that: (1) the small-world attribute of the whole-brain networks in KOA would be preserved, but KOA would be characterized by abnormal topological features (both globally and locally) of functional networks compared with HCs, and (2) specific regional FC changes would be observed linked to KOA of RSNs.

2. Materials and methods

2.1. Participants

The rs-fMRI data employed in our research were acquired from OpenNeuro (<https://openneuro.org/>). Participants provided written informed consent sanctioned by the Northwestern University Institutional Review Board committee (STU00039556). The open sharing of rs-fMRI data includes 76 subjects, categorized into three distinct groups, and the data was initially collected to identify and validate the predictability of clinical placebo response based on rs-fMRI brain connectivity^[34]. However, the data involved in our study were pre-treatment data, so these

data can be analyzed for two groups instead of four, including 20 HCs (mean age = 57.90 ± 6.66 years old, 10 males and 10 females) and 56 KOA patients (mean age = 57.91 ± 6.96 years old, 26 males and 30 females). No significant differences comparing demographic variables were observed in age ($p = 0.995$) and gender ($p = 0.784$). Inclusion and exclusion criteria for all participants can be found below.

Inclusion criteria:

- (1) Participants must be between 45 and 80 years old.
- (2) Confirmed by ACR guidelines, with radiographic evidence (Kellgren-Lawrence grade II-IV).
- (3) A visual analog scale (VAS) score exceeding 5 out of 10 within 48 hours before screening and the first visit.
- (4) Symptoms must have persisted for at least one year.
- (5) Daily pain relief drugs required to control osteoarthritis symptoms.

Exclusion Criteria:

- (1) Use of MAO inhibitors or centrally acting drugs for pain or depression.
- (2) Presence of narrow-angle glaucoma.
- (3) Poorly managed hypertension.
- (4) Other chronic conditions: Inflammatory arthritis, fibromyalgia, or persistent pain disorders.
- (5) Females who are pregnant, attempting conception, or breastfeeding.
- (6) Diagnosis of major depressive disorder.
- (7) Excessive alcohol consumption or prior liver disease.
- (8) Restricted medications: MAO inhibitors, triptans, serotonin precursors (e.g., tryptophan).
- (9) Drug interactions: CYP1A2 inhibitors, Thioridazine, or antidepressant usage.
- (10) Type 1 or type 2 diabetes.
- (11) Any condition that, in the investigator's judgment, may hinder compliance, distort findings, or pose risks.
- (12) MRI contraindications: Metal fragments in facial or ocular regions, or prior metalwork employment; Electronic implants (e.g., pacemakers, defibrillators, cochlear devices, neurostimulators); Prior cerebrovascular surgery; Severe claustrophobia (inability to tolerate confined spaces); Body piercings or tattoos; Weight exceeding 250 pounds; Detectable brain anomalies.

2.2. MR data acquisition

All subjects underwent MRI scanning (3T Siemens Trio whole-body) to acquire T1-weighted magnetization-prepared rapid gradient echo (MPRAGE) structural images (repetition time: 2.5 milliseconds; echo time: 3.36 milliseconds; flip angle: 9° ; voxel size: $1.00 \times 1.00 \times 1.00$ mm; field of view: 256 mm; matrix: 256×256 ; and slices: 160). High-resolution whole-brain rs-fMRI images were acquired using a T2*-weighted echo planar imaging (EPI) sequence (repetition time: 2500 milliseconds; echo time: 30 milliseconds; flip angle: 90° ; slice thickness: 3 mm; matrix: 64×64 ; number of slices: 40; and 300 volumes).

2.3. Functional data preprocessing

The rs-fMRI data were preprocessed using SPM12 (<https://www.fil.ion.ucl.ac.uk/spm/>) working on MATLAB R2016a. The preprocessing procedure for ICA analysis included the following stages: the first 10 volumes of each functional data set were removed to reduce equilibrium effects. The BOLD runs were subsequently corrected for slice timing and head motion. The BOLD images were spatially normalized to the Montreal Neurological Institute (MNI) standard template and resampled to 3-mm cubic voxels. Subsequently, the resulting data were smoothed by a 6-mm full-width at half-maximum Gaussian kernel. In addition to the first four steps of preprocessing for ICA,

further preprocessing for graph theory was conducted as follows: Detrending and nuisance regression procedures were applied to eliminate linear trends and non-neural-related signals, and the corrected functional images were further low-pass filtered (0.01–0.08 Hz).

2.4. Graph theoretical analyses

The whole-brain functional network construction and network metrics calculation were performed using the MATLAB-based software GREYNET toolbox (<https://www.nitrc.org/projects/gretna>). In topological networks, nodes and edges (FC between nodes) constitute the foundational structure. In the brain, nodes represent distinct brain regions, while edges signify the statistical relationships between BOLD signals across these regions. To define the brain nodes, a widely accepted AAL90 atlas was used to divide the entire brain into 90 cortical regions, each region representing a node within the network^[35]. Pearson correlation coefficients of BOLD signals between all possible pairs of nodes were calculated to derive the brain's connectivity matrix. Individual Pearson correlation matrices were then converted using Fisher's r-to-z transformation. Finally, topological metrics of the constructed FC matrix were calculated for each subject. For this study, the study selected commonly used global network metrics, including small-world attribute (lambda, gamma and sigma), global efficiency, and assortativity, to measure the properties of global networks. For the relatively stable nodal network, local metrics included nodal efficiency, betweenness centrality, and degree centrality. The results were visualized using BrainNet Viewer^[36] (<https://www.nitrc.org/projects/bnv/>).

To minimize bias resulting from choosing a single threshold, the study used an area under the curve (AUC) approach for each network measure. This method provides a comprehensive summary metric for assessing brain network topology and is effective in identifying topological changes associated with brain dysfunction^[37,38]. Consistent with previous studies^[38–40], Graph topological metrics were therefore calculated for all individual brain networks at network sparsity thresholds ranging from 0.10 to 0.34 with sparsity steps of 0.01, ensuring accurate estimation of “small-world” parameters and minimizing the inclusion of spurious edges^[41–44].

2.5. Independent component analysis

Group independent component analysis (GICA) was performed using the GIFT Toolbox (<https://trendscenter.org/software/gift/>). The steps for conducting group ICA and detecting intrinsic connectivity networks (ICNs) are shown as follows: the data was reduced in dimensionality through a two-step principal component analysis^[45]. 50 spatially independent components was auto-estimated through the Minimum Description Length (MDL) criteria. Infomax algorithm was employed for group independent component analysis, and the process was iterated 100 times using ICASSO (<http://research.ics.aalto.fi/ica/icasso/>) to ensure component consistency. The time courses and spatial maps for each subject were reconstructed, followed by a Fisher Z transformation for further investigation.

2.6. Statistical analysis

Analysis of the clinical and demographic data from all participants was performed using SPSS statistics software. Group comparisons were conducted by independent 2-sample t-tests for age and chi-square tests for sex.

For graph theory analysis, 2-sample t test with multiple comparisons (FDR corrected) was conducted to compare the differences in topological properties between KOA patients and HCs, including the AUC of each global network metric and each local network metric. The significance level was set at $p < 0.05$ (control covariates: age, gender).

For independent component analysis, to compare group differences in the intra-network FC, a one-sample t

test ($p < 0.05$, FWE corrected) was conducted separately for KOA patients and HCs to generate sample-specific spatial pattern masks for each group. Each mask of the KOA patients and HCs was subsequently merged into a total mask for each component. Furthermore, measures of inter-network FC between KOA patients and HCs were compared using 2-sample t tests with age and sex as covariates ($p < 0.05$, FWE corrected). In addition, for inter-network FC analysis, the study derived the time-series of each RSN from the ICA procedure and calculated Pearson's correlations between pairwise combinations. To enhance normality, these values were then transformed to Z-scores. Group differences in inter-network connectivity were compared using a 2-sample t test ($p < 0.05$, FDR corrected), controlling for age and sex as nuisance covariates.

3. Results

3.1. Group comparisons of global and nodal topological properties

In the wide-defined sparsity range, the lambda values hovered at 1, both gamma and sigma exceeded 1. These findings suggest that both two groups exhibit a “small-world” organization in resting-state networks (**Figure 1A**). For the global metrics, a decreased AUC of the global efficiency ($p = 0.048$, $t = 2.01$) and an increased assortativity ($p = 0.019$, $t = -2.39$) were observed in KOA patients compared with the HCs (**Figure 1B**). For the local metrics, patients with KOA had a decreased degree centrality ($p < 0.001$, $t = 4.28$) and betweenness centrality ($p < 0.001$, $t = 4.58$) of the right thalamus (**Figure 2**).

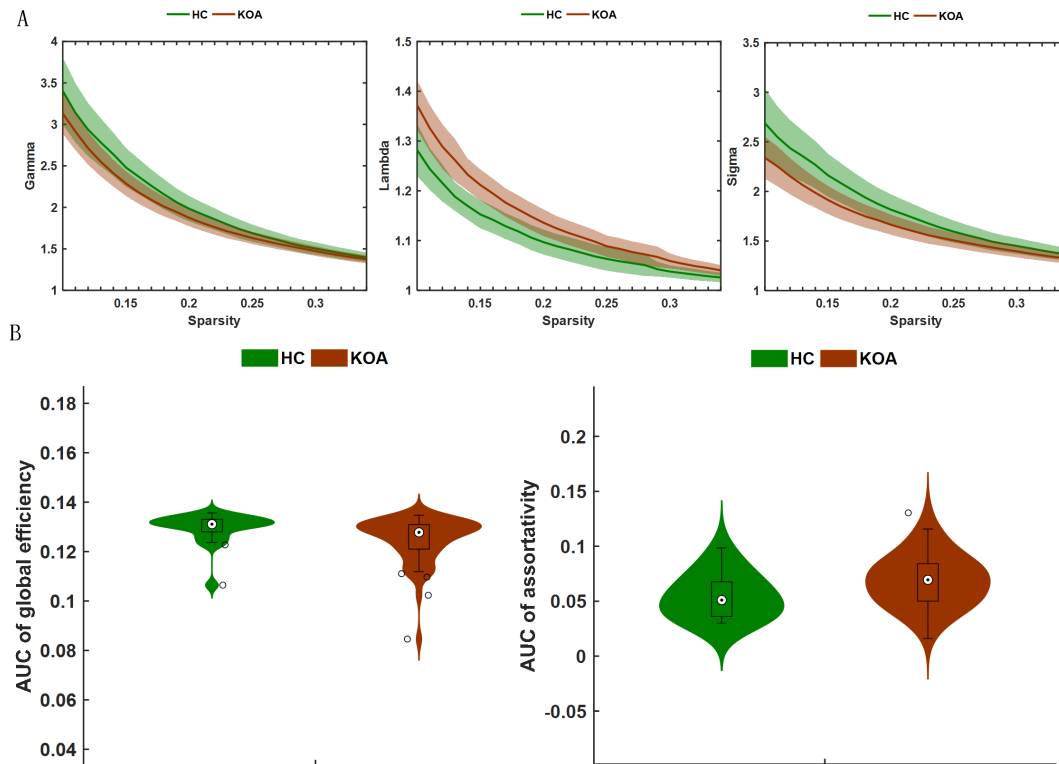


Figure 1. Group differences in global network metrics between KOA patients and HCs. (A) Small-world properties of sparsity threshold (10%-34%, with a step of 1%). The line and shading show the mean and 95% confidence interval of between-group differences. (B) Violin plots illustrating the area under the curve (AUC) parameters of the global efficiency and assortativity for KOA patients and HCs.

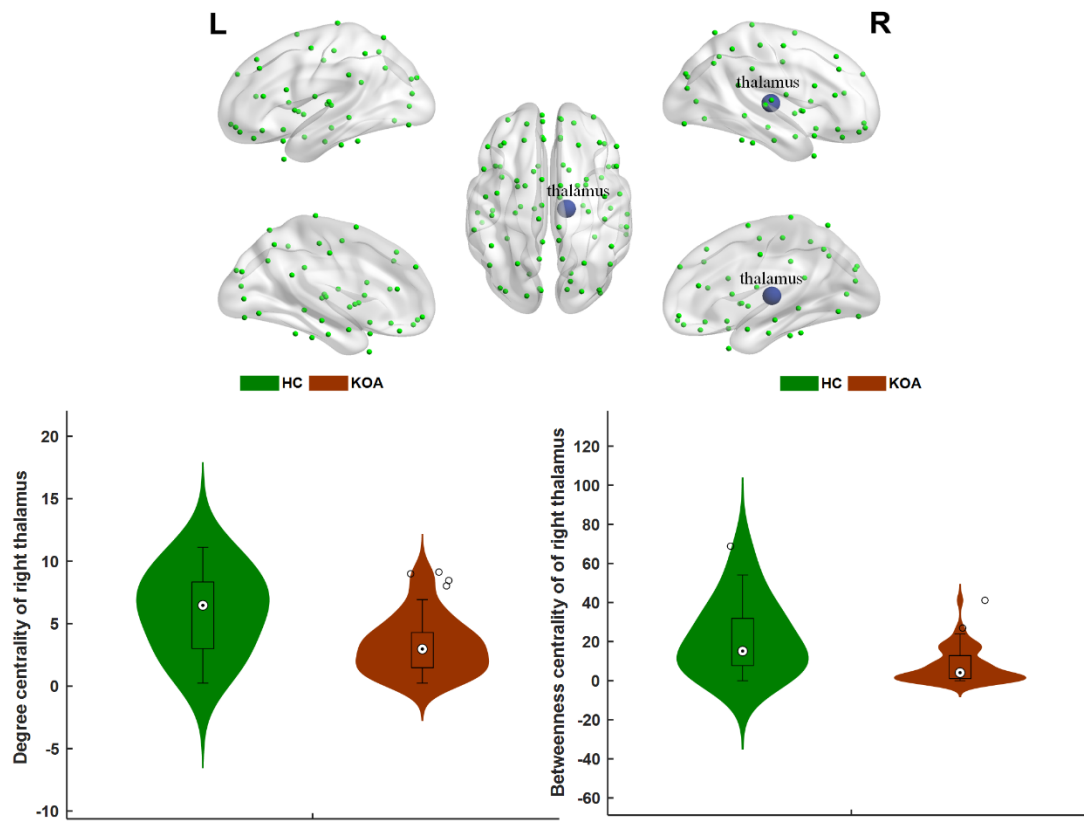


Figure 2. Group differences in degree centrality and betweenness centrality at the nodal level. Insignificant nodes are shown as green spheres, whereas blue (KOA < HC) spheres denote significant differences after FDR correction. Violin plots illustrating the area under the curve (AUC) parameters of degree centrality and betweenness centrality of the right thalamus for KOA patients and HCs.

3.2. Group comparisons of functional connectivity within and between RSNs

Nine functionally classical RSNs were extracted via visual inspection from all subjects (**Figure 3**). Compared with HCs, patients with KOA showed increased FC in left medial frontal gyrus of the anterior default mode network (aDMN), decreased FC in right insula of the salience network (SN), and reduced right superior temporal gyrus of the auditory network (AUN) compared with HCs (**Figure 4** and **Table 1**). No significant differences were observed in inter-network FC between KOA patients and HCs.

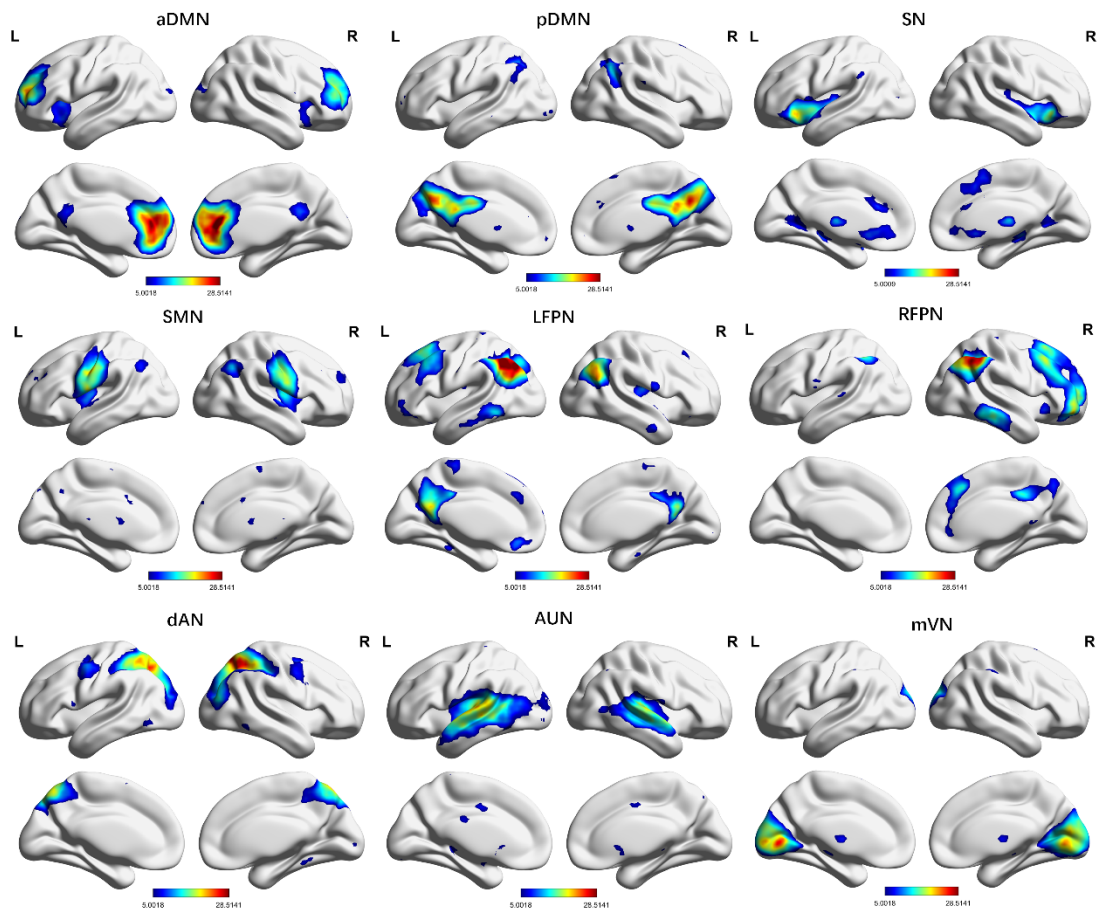


Figure 3. Spatial maps of one-sample t-test in nine RSNs of all subjects. The colorbar indicates the t value. aDMN: anterior default mode network; pDMN: posterior default mode network; SN: salience network, SMN: sensorimotor network; LFPN: left frontoparietal network; RFPN: right frontoparietal network; dAN: dorsal attention network; AUN: auditory network; mVN: medial visual network.

Table 1. Brain regions with significant differences in intra-network functional connectivity between KOA patients and healthy controls

RSN	Brain Regions	Cluster Size	MNI			Peak t Score
			X	Y	Z	
aDMN	L Medial frontal gyrus	43	-18	33	21	5.11
SN	R Insula	66	42	21	-9	-4.78
AUN	R Superior temprom gyrus	17	33	0	-18	-5.38

aDMN: anterior default mode network; SN: salience network; AUN: auditory network; MNI, Montreal Neurologic Institute; L, left; R, right.

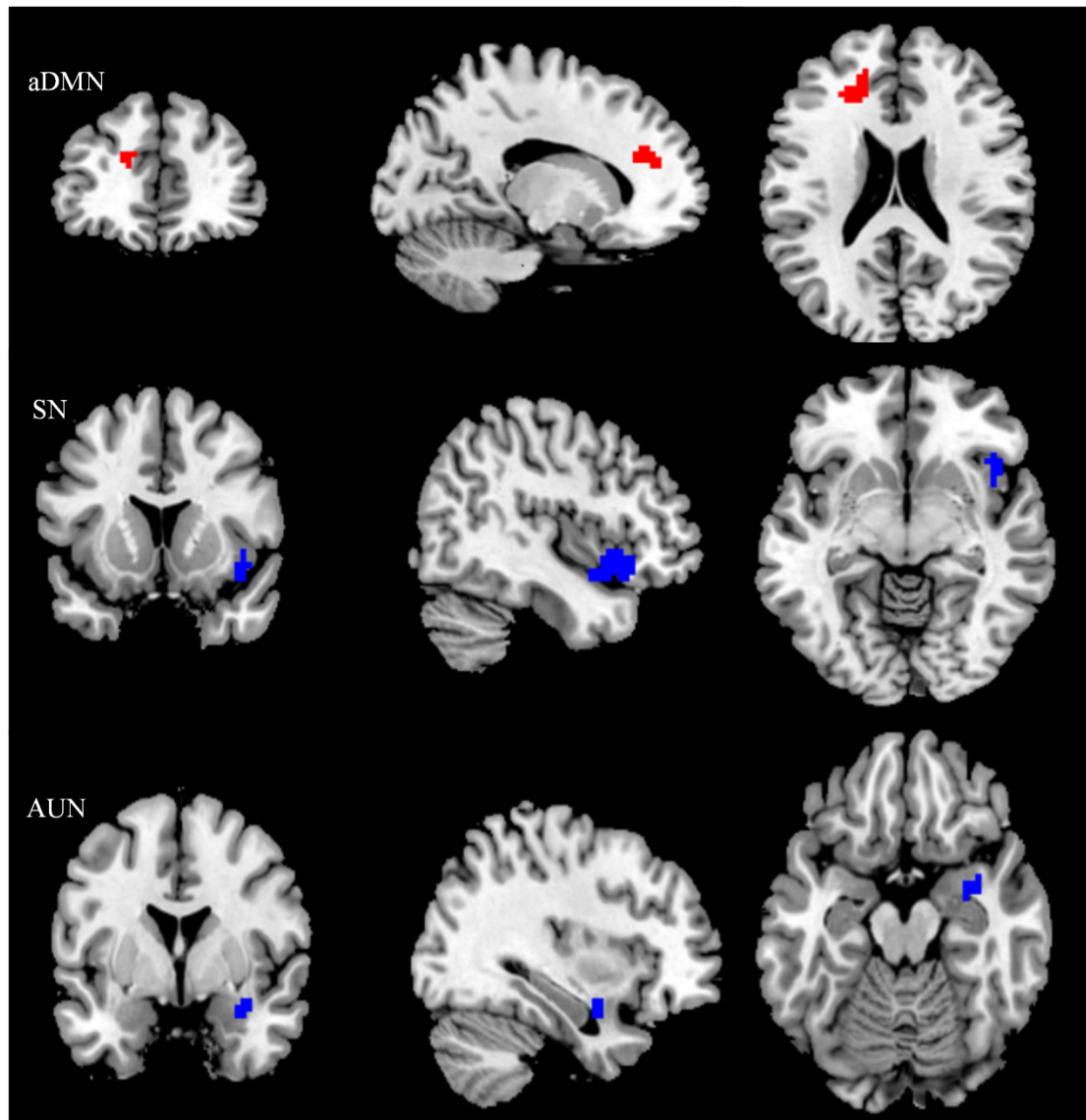


Figure 4. Comparison of intra-network functional connectivity between the KOA and HC groups. The red volume indicates a region whose functional connectivity was increased in KOA compared with HCs. Each blue volume indicates a region whose functional connectivity was decreased in the KOA .

4. Discussion

The study questioned whether differences existed in whole-brain network topology and how information transfer within intra- and inter-networks under chronic knee pain. Therefore, the study undertook unsupervised graph-theory-based analyses and ICA to identify a widespread network-level pathophysiological profile in KOA. Our key findings were as follows:

- (1) Both groups displayed a small-world structure. Patients with KOA exhibited a decreased AUC of global efficiency and an increased AUC of assortativity at the global level. Additionally, decreased degree centrality and betweenness centrality in the right thalamus were observed in patients with KOA at the local level.
- (2) Connectivity within the aDMN, SN, and AUN altered between the two groups.

4.1. Global and regional topological alterations of functional networks in KOA compared with HCs

At the global level, small-worldness, a fundamental trait of complex network structures^[41,46], signifies an optimal equilibrium between global integration and local segregation. Both groups exhibited the characteristic small-world property, which aligns with findings reported in previous research studies^[47,48]. Compared to controls, global efficiency was significantly decreased in the KOA group. Global efficiency is a robust indicator of information transmission within a network^[43] and is commonly used to estimate the integration of brain networks. In this study, the observed decrease in global efficiency among KOA patients compared to controls may indicate impaired integration of information between key brain hubs. Such disrupted connectivity across distributed neural regions could contribute to altered cognitive and perceptual processing^[49]. Abnormal topological organization has been reported in a previous study involving KOA cohorts^[48]. However, global efficiency showed no significant difference between KOA patients and HCs, which is inconsistent with our findings. By contrast, KOA patients showed a higher value for assortativity. Assortativity, which measures network segregation, indicates neural networks' susceptibility to detrimental matters or neuropathological conditions^[50,51]. A higher assortative value indicates that vertices are more likely to connect with other vertices of similar degree, leading to a more resilient network that can better inhibit the spread of information. Notably, the assortativity metric has been scarcely reported previously and may provide a more thorough assessment of the topological brain network architecture in KOA patients. Taken together, the decreased AUC of global efficiency and the increased AUC of assortativity indicate disruptions in brain networks related to functional integration and segregation in KOA patients. This suggests an imbalance between global integration and local segregation, highlighting disrupted energy expenditure in spontaneous brain activity and implying impaired parallel information transfer within the brain functional networks of these patients.

At the local level, the study found decreased nodal centrality in the right thalamus. Degree centrality measures the sum of links' weights connected to a node, depicting the significance of individual brain regions in influencing adjacent regions. Meanwhile, betweenness centrality evaluates how frequently a node participates in the shortest paths between all possible node pairs, reflecting its importance in facilitating communication within the network. Both metrics have been extensively used to assess brain network dysfunction across various clinical conditions^[38,52,53]. Interestingly, the changes in nodal network topology observed in our study were primarily evident in centrality properties, particularly in the degree centrality and betweenness centrality of the right thalamus. The thalamus serves as a vital element of the pain matrix and its role in modulating nociception in neuropathic pain conditions has been extensively studied^[54,57]. A seed-based analysis revealed abnormal resting-state and task-related functional connectivity and effective connectivity between the thalamus and cortex, with multiple regions involved, in the KOA cohort compared with HCs^[58]. Our results extends these previous studies by revealing abnormal degree centrality and betweenness centrality of the right thalamus, further highlighting the thalamus's significant and intricate role in KOA.

4.2. Intra-network connectivity alterations in KOA compared with HCs

Our study provides evidence that KOA patients showed impaired intra-network FC of the aDMN, SN and AUN compared to HCs. The default mode network (DMN) is related to higher-order functions and internal states monitoring for the detection of prominent events. Many neuroimaging studies have shown that the DMN could regulate the perception of pain through autonomic and antinociceptive descending modulation networks^[59,60].

Previous studies have consistently reported aberrant FC within the DMN in chronic pain conditions ^[8,61–65]. In our study, the medial frontal gyrus, a key component of the aDMN, exhibited reduced FC in KOA patients, highlighting its potential role in the functional reorganization of brain networks in KOA. The medial frontal gyrus, a region involving multiple psychological domains, including cognitive control, pain, and emotion ^[66–68], has been previously identified in fMRI studies on pain ^[69] and depression ^[70]. An epidemiological study estimated that 52% of patients with chronic pain contend with mental health challenges ^[71], including depression, experiencing a decline in quality of life. Thus, it is believed that impaired FC in the medial frontal gyrus may contribute to the development of mood and emotional instabilities such as depression in KOA. In addition, the medial frontal gyrus is essential for attentional processing in relation to pain, contributing to the integration and interpretation of sensory inputs ^[72]. Therefore, the observed reductions in FC within the medial frontal gyrus could be linked to impairments in attentional control and sensory information processing in KOA patients.

The SN, responsible for monitoring sensory input changes and coordinating brain activity to prompt behavioral responses, is anticipated to be pivotal in chronic pain. Network alterations in the SN are most commonly reported in chronic pain conditions ^[73–77]. As the primary causal output within the SN, the insula is recognized as a crucial brain region involved in pain-attention interactions and serves as a key hub in pain regulation pathways ^[78,79]. Numerous neuroimaging studies have demonstrated abnormal FC driven by the insular cortex in patients across various chronic pain conditions ^[13,80–83]. Prior research has demonstrated that individuals with KOA exhibit decreased gray matter volume in the bilateral insular cortex, alongside elevated fractional amplitude of low-frequency fluctuations (fALFF) in the left insula ^[84]. In our study, KOA patients exhibited significantly reduced FC in the insular cortex compared with pain-free controls, further pointing to the importance of insular cortex in the functional reorganization of brain networks associated with chronic KOA pain.

AUN is believed to be involved in memory processes, and the changes in AUN may be associated with the memory impairment in chronic pain patients. However, the specific role of the AUN in neuroimaging research on pain remains to be fully elucidated and warrants further investigation.

Several limitations constrain the interpretation of the results for consideration. Firstly, our study is limited by its cross-sectional design and cannot uncover causal relationships in the etiology and persistence of KOA. Longitudinal studies, including investigations into remission and recurrence patterns across the lifespan, are needed. Secondly, the graph theoretical approach provides insights into only one aspect of the complex neural mechanisms underlying chronic pain disorders. Future research should explore additional facets of network topology. Lastly, the study is constrained by a relatively small control group, therefore introducing some uncontrolled bias. Future studies should validate these findings by running a similar sample of patients.

5. Conclusion

In summary, the study found abnormal topological architecture in functional brain networks and aberrant FC in specific cognitive networks in KOA patients. Measuring whole-brain FC patterns in KOA patients may elucidate pain sensitization mechanisms, thereby perpetuating symptoms and contributing to KOA development. Overall, our findings may elucidate the pathophysiology of KOA and ultimately inform mechanism-based therapies for various chronic pain conditions.

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Disclosure statement

The authors declare no conflict of interest.

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The Effect of Psychological Intervention and Exercise Rehabilitation on the Improvement of Patients' Confidence in Osteoporosis Rehabilitation

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Abstract: The integration of psychological intervention and sports rehabilitation in osteoporosis rehabilitation aims to enhance patients' confidence in recovery through the synergistic effects of psychological regulation and functional training. Psychological interventions aim to strengthen self-efficacy, alleviate negative emotions, and stimulate the desire for rehabilitation. Sports rehabilitation improves bone metabolism, strengthens physical function, and enhances the overall rehabilitation experience. Through a multidisciplinary collaboration mechanism and personalized intervention approaches, this approach systematically improves rehabilitation compliance and self-management skills, significantly reduces the risk of falls and re-fractures, creates a supportive rehabilitation environment, promotes the internalization of health beliefs, and provides strong support for long-term rehabilitation outcomes.

Keywords: Osteoporosis; Psychological intervention; Exercise rehabilitation; Rehabilitation confidence; Individualized rehabilitation

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1. Introduction

Osteoporosis, a common chronic degenerative disease, not only weakens bone strength but also has a lasting impact on patients' psychological well-being and daily functioning. Traditional single-treatment approaches are no longer sufficient to meet the complex rehabilitation needs, leading to the emergence of a combined intervention approach. Integrating psychological support with physical rehabilitation not only improves patients' emotional state and physical function but also reshapes their rehabilitation beliefs and motivates self-management. Based on this new rehabilitation philosophy, a multidimensional intervention pathway is developed to enhance overall treatment outcomes through synergistic mechanisms. This approach shifts the rehabilitation model from passive acceptance to active participation, offering practical guidance and significant clinical implications.

2. Theoretical basis of psychological intervention and sports rehabilitation in the treatment of osteoporosis

Osteoporosis results from an imbalance in bone remodeling, with age and decreased estrogen levels being common triggers. Patients often face poor treatment outcomes due to both physical and psychological barriers during rehabilitation. Psychological interventions help enhance patients' motivation for recovery by regulating cognition, emotions, and behavior. For example, cognitive-behavioral therapy can reshape negative thoughts, supportive psychotherapy can reduce feelings of loneliness, and improving self-efficacy is crucial. Exercise rehabilitation activates the bone remodeling process through mechanical stimulation; weight-bearing and resistance exercises can improve bone metabolism and function, providing tangible benefits. Combining these approaches helps osteoporosis patients boost their confidence and improve their rehabilitation outcomes from both psychological and physiological perspectives.

3. Analysis of the intervention path of the combined mode of psychological intervention and sports rehabilitation

3.1. Operation strategies and procedures for integrating psychological intervention and exercise intervention

The treatment process typically begins with a preliminary psychological assessment and physical examination, evaluating the patient's emotional state, self-efficacy, and bone condition to set personalized rehabilitation goals. Psychological interventions, including cognitive-behavioral training, emotional guidance, and belief restructuring, help patients develop positive expectations for their recovery. Additionally, a gradual exercise plan is arranged, such as resistance training, gait balance exercises, and low-intensity aerobic activities, ensuring that patients can train with adequate mental preparation ^[1,2]. These two approaches are closely integrated during the intervention, with methods like motivational conversations and recording rehabilitation logs being used to reinforce the psychological recognition of the exercise's benefits.

3.2. The synergistic effect of the multidisciplinary team cooperation mechanism in intervention

Team members have clear roles and responsibilities, with information shared openly. The psychological counselor is responsible for conducting emotional interventions and building beliefs, while the rehabilitation therapist designs exercise programs based on bone density and functional levels. The doctor ensures medical safety and the control of intervention boundaries. During the implementation process, regular intervention meetings are held to discuss patient progress, reactions, and psychological adaptation, allowing for timely adjustments to the intensity and frequency of interventions. Nursing staff play a crucial role in daily management, providing life guidance, recording feedback, and promoting rehabilitation. By integrating resources from multiple specialties, not only is the professionalism and precision of interventions enhanced, but a supportive and trusting rehabilitation environment is also created for patients, increasing their willingness to actively participate. This approach helps to steadily boost both psychological and physiological confidence in recovery.

3.3. The implementation of an individualized evaluation and adjustment mechanism in the intervention program

In the initial diagnosis phase, patients undergo anxiety and depression assessments, self-efficacy evaluations,

bone density tests, and motor function evaluations using professional scales to understand their physiological and psychological foundations. During the intervention, a periodic follow-up mechanism is implemented, such as bi-weekly psychological status check-ups and motor endurance tests, to identify potential issues such as fluctuations in motivation, increased pain, or emotional fluctuations during rehabilitation ^[3,4]. Based on the feedback, intervention strategies are promptly adjusted. For instance, if anxiety significantly increases, the frequency of cognitive interventions is increased; if exercise fatigue becomes noticeable, the training intensity is reduced, and alternative exercises are introduced. This dynamic adjustment ensures that the intervention remains aligned with the patient's actual condition, ensuring the safety and effectiveness of the rehabilitation process while enhancing the patient's active participation and building their confidence over time.

4. The multidimensional influence of joint intervention on the rehabilitation confidence of osteoporosis patients

4.1. The psychological mechanism of emotion regulation and self-efficacy improvement

Enhancing emotional regulation is a key prerequisite for building confidence in rehabilitation. Osteoporosis patients often experience anxiety and depression due to pain, limited mobility, and uncertainty about their future health, which can hinder their willingness to actively participate in rehabilitation. Psychological interventions, such as cognitive restructuring and mindfulness training, help patients identify and manage these negative emotions, encouraging them to shift from passive coping to active control, thereby improving their emotional resilience. On this foundation, an increase in self-efficacy boosts patients' confidence in their ability to recover. By setting and achieving phased goals, patients receive positive feedback throughout the rehabilitation process, which reinforces their confidence in their recovery efforts ^[5-7]. The interaction between emotions and self-efficacy reduces inner stress and enhances motivation, building a strong psychological foundation that supports continuous recovery and effectively stabilizes and extends the duration of confidence in rehabilitation.

4.2. The supporting role of physical function improvement in the construction of rehabilitation belief

Patients with osteoporosis who undergo regular exercise rehabilitation often show improvements in bone density, muscle strength, and balance. These improvements directly alleviate their fear of falls or fractures. During this process, patients can perceive and quantify changes in their bodies, such as reduced pain, more stable gait, and greater ease in daily activities. These objective improvements reinforce their trust in the effectiveness of the treatment. Functional improvements not only reflect the outcomes of rehabilitation interventions but also serve as empirical feedback, helping patients transition from a state of doubt about whether they can recover to a positive mindset of being actively rehabilitated. When patients recognize that their efforts lead to tangible improvements, their belief in rehabilitation shifts from an abstract expectation to a realistic goal, significantly boosting their self-motivated confidence and willingness to continue with the intervention plan.

4.3. The effect of environmental security and social support on the enhancement of confidence in rehabilitation

In a safe physical environment and with strong family care, patients are more likely to engage in rehabilitation training, reducing anxiety caused by falls or setbacks. The design of barrier-free spaces, the proper use of assistive devices, and the attentive care provided by nursing staff all subtly enhance a sense of security. Social

support, particularly the emotional support and positive feedback from family, friends, and healthcare providers, reinforces the patients' sense of meaning and value in their rehabilitation. Peer interactions in group rehabilitation activities create a supportive psychological environment, making patients feel they are not alone. When patients feel understood, supported, and accompanied, their psychological resilience significantly increases, and their confidence in rehabilitation becomes more stable and profound.

5. Clinical value of combined intervention mode in the practice of osteoporosis rehabilitation

5.1. The improvement path of rehabilitation compliance and self-management behavior

Psychological intervention reshapes patients' perceptions of rehabilitation, reinforcing their sense of its value and encouraging them to view the treatment process as an intrinsic motivation. Sports rehabilitation, on the other hand, provides patients with positive feedback through visible physical improvements over a short period, boosting their confidence in ongoing participation. On this foundation, the intervention team can use tools like rehabilitation logs and goal planning sheets to guide patients in setting daily rehabilitation plans and self-assessment tasks, gradually fostering healthy habits. By involving family members, conducting remote follow-ups, and implementing an incentive feedback system, the continuity and standardization of rehabilitation are enhanced. Through continuous practice and feedback, individuals develop self-regulation and management skills, enhancing their control over the pace and content of rehabilitation. This leads to a dual improvement in psychological and behavioral adherence to rehabilitation, laying a solid foundation for long-term disease management.

5.2. The mechanism of action in fall prevention and risk control of re-fracture

Sports rehabilitation enhances lower limb muscle strength and balance, improves joint flexibility and posture control, which forms the physiological foundation for preventing falls. Psychological interventions effectively alleviate the fear and anxiety caused by fall experiences, preventing further muscle weakness due to fear of movement. During training, therapists can tailor gait simulation exercises and center-of-gravity shifting drills to enhance patients' adaptability to complex environments. Cognitive interventions help reduce the negative association of "movement = danger," enhancing patients' self-protection awareness and risk assessment skills. Environmental assessments and safety guidance, as supplementary measures, assist patients in identifying potential hazards in their daily lives. These multidimensional interventions collectively form a comprehensive fall prevention network that covers cognition, behavior, and environment. This not only effectively reduces the risk of re-fractures but also continuously reinforces patients' confidence in rehabilitation and their ability to live independently with each successful protection.

5.3. The extended effect of health belief establishment on long-term rehabilitation

In the combined intervention, psychological interventions guide patients to shift from a passive belief that "the disease is irreversible" to an active belief that "it can be improved and self-regulated" through education and cognitive restructuring. Exercise rehabilitation, on the other hand, strengthens patients' belief in the effectiveness of their efforts by quantifying physical improvements, making them more confident in their efforts. This confidence is reflected in daily behaviors such as actively following medical advice, regular exercise, and maintaining a healthy diet, which helps extend the benefits of rehabilitation ^[8-10]. Health beliefs help patients maintain psychological stability when facing health fluctuations or periods of stagnation in rehabilitation, reducing

their tendency to doubt the effectiveness of rehabilitation. The stability of these beliefs enables patients to transition from staged rehabilitation to continuous health management, thereby maximizing the clinical value of the combined intervention over time.

6. Conclusion

The combined use of psychological intervention and sports rehabilitation is increasingly recognized for its comprehensive value in osteoporosis rehabilitation. By improving emotional well-being, self-efficacy, and physical function, it significantly boosts patients' confidence in recovery. The multidisciplinary collaborative mechanism and personalized intervention approach support improved rehabilitation adherence and reduce the risk of re-fracture. Establishing a healthy belief system helps patients develop long-term self-management skills, which extends the benefits of rehabilitation. This model provides theoretical support and practical pathways for building a systematic, continuous, and effective osteoporosis rehabilitation system, with significant clinical value and potential for widespread application.

Disclosure statement

The author declares no conflict of interest.

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Effect Analysis of Muscle Strength Training in Sports Rehabilitation for Patients with Knee Joint Injuries

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Abstract: In this study, the theoretical relationship between knee joint injury and muscle strength training is explored, and the biomechanical changes caused by injury, the role of muscle on joint stability, and the physiological basis of training are clarified. The implementation strategies of personalized training programs based on injury type and stage, scientific training intensity control, and coordinated use of diversified training types are explained. Multi-dimensional evaluation is conducted from the aspects of joint function recovery, muscle strength and morphological recovery, and improvement of knee joint biomechanical properties, providing theoretical and practical references for muscle strength training in knee joint injury rehabilitation.

Keywords: Knee joint injury; Muscle strength training; Rehabilitation strategy; Effect evaluation; Biomechanics

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1. Introduction

The knee joint is the hub of human movement, but it is prone to injury in daily activities and competitive sports. The biomechanical imbalance and decreased stability of the knee joint after injury seriously affect limb function and quality of life. Muscle strength training, as the core means of rehabilitation, can reshape muscle structure from a physiological level and promote functional recovery through scientific strategies. In-depth exploration of its theoretical basis, implementation methods, and effect evaluation is not only related to the quality of patient rehabilitation, but also provides a key path for optimizing knee joint injury rehabilitation programs.

2. Theoretical relationship between knee joint injury and muscle strength training

2.1. Biomechanical changes caused by knee joint injury

As a complex and critical joint in the human body, the knee joint frequently bears pressure and stress in daily activities and sports. Once damaged, its biomechanical environment will change significantly. After anterior

cruciate ligament injury, the anterior-posterior laxity of the knee joint increases. When the tibia is completely ruptured, the forward displacement of the tibia can increase by 5 to 10 mm compared with the normal state, resulting in uneven distribution of pressure on the joint surface. The load originally borne by ligaments, muscles, and articular cartilage is transferred, the movement trajectory is offset, and the local wear of articular cartilage is aggravated, increasing the risk of traumatic arthritis. Meniscus injury also changes the biomechanical properties of the knee joint, and its function of buffering shock and dispersing load is lost. Injury to the medial meniscus will increase the pressure in the medial compartment, accelerate the wear of articular cartilage, change the mechanical conduction path, and increase the risk of injury to other structures. At the same time, knee joint injury will also cause pressure imbalance in the joint cavity, destroy the normal circulation of synovial fluid, further affect joint lubrication and nutrient metabolism, and aggravate the process of joint degeneration.

2.2. The key role of muscles in maintaining knee joint stability

The quadriceps, hamstrings, and gluteal muscles around the knee joint are important power structures for maintaining joint stability. The quadriceps, as an extensor, drives the calf to extend when contracted, ensures the normal position of the patella through the patellar tendon, and ensures the flexion and extension of the knee joint. Studies have shown that every 1 Newton increase in quadriceps muscle strength can reduce the pressure on the knee joint during daily activities. The hamstrings, as flexors, work together with the quadriceps to buffer the ground reaction force through eccentric contraction when running and jumping, reducing the risk of meniscus injury. The gluteal muscles are involved in maintaining the force line of the lower limbs. When walking, the gluteal muscles contract to stabilize the pelvis, reduce the additional torque of the knee joint in the support phase and swing phase, and lower the chance of joint injury^[1]. In addition, in actions such as going up and down stairs and squatting, these muscle groups need to work together to maintain the dynamic balance of the knee joint at different angles through fine force regulation to avoid secondary injuries due to uneven force.

2.3. Physiological basis of muscle strength training

From a physiological perspective, muscle strength training is of great significance to the rehabilitation of knee joint injuries. Training promotes muscle hypertrophy and increases muscle cross-sectional area. After repeated stimulation of muscle fibers, protein synthesis increases, myofibrils increase in number and size, and muscle contraction force is enhanced. Strength training can also improve the distribution of muscle fiber types. The human body's slow muscle fibers have strong endurance, and fast muscle fibers have high explosive power. Targeted training can transform some slow muscle fibers into fast muscle fibers to meet the needs of movement function recovery in knee joint rehabilitation. In addition, training improves neuromuscular coordination and enhances the precision of muscle control by the nervous system. During knee joint movement, muscles can respond quickly to mechanical changes, maintain dynamic stability of the joint, and reduce the risk of re-injury. Long-term and regular muscle strength training can also activate muscle satellite cells, promote muscle tissue repair and regeneration, optimize muscle metabolic capacity, and provide more lasting and stable mechanical support for the knee joint.

3. Implementation strategies of muscle strength training in knee injury rehabilitation

3.1. Development of personalized training programs based on injury types and stages

There are various types of knee injuries, such as ligament injuries (anterior cruciate ligament, posterior cruciate

ligament, medial and lateral collateral ligaments, etc.), meniscus injuries, cartilage injuries, etc. Different types of injuries have varying effects on knee stability and function, and rehabilitation training programs need to be accurately adapted. Taking ligament injuries as an example, in the early stage after anterior cruciate ligament reconstruction (0–2 weeks), in order to protect the graft, isometric contraction exercises of the quadriceps and hamstrings should be performed under brace fixation, such as static contraction of the quadriceps, multiple times a day, each time for 5–10 seconds, to prevent muscle atrophy; At 2–6 weeks, patients can gradually carry out active knee flexion and extension training, such as sitting knee flexion exercises, each flexion and extension range of motion is determined according to the progress of rehabilitation, and gradually increase the range of motion of the joint. During the rehabilitation of meniscus injury, if it is a mild injury, ankle pump exercise can be used to promote blood circulation in the lower limbs in the early stage. Lie flat on the bed and flex and extend the ankle joint slowly and evenly. Each flexion and extension should be maintained for 3–5 seconds, 10–20 times as a group, 3–4 groups per day; as recovery, straight leg raising training can be performed, supine position straighten the knee joint, slowly raise the lower limb to 30–60 degrees, hold for 5–10 seconds and then slowly put it down, 10–15 times as a group, 3–4 groups per day, to strengthen the quadriceps strength and reduce the pressure on the meniscus ^[2]. At the same time, according to the dynamic adjustment plan of the injury recovery stage, transition from the early joint range of motion and muscle basic strength recovery to the mid-term strength strengthening and stability training, and then to the later functional recovery and sports ability training.

3.2. Scientific and reasonable control of training intensity

Training intensity is a key element of muscle strength training in knee injury rehabilitation. In the initial stage, low-intensity training should be used to avoid increasing the burden on the injured part. For example, when performing isometric muscle contraction training in the early stage of injury, the contraction force should be controlled at 20–30% of the maximum muscle strength. The duration of each contraction should not be too long, 3–5 seconds is adequate, and each set should be repeated 10–15 times, 3–4 sets per day, to allow the damaged knee joint to adapt. As the rehabilitation process progresses, the training intensity is gradually increased. In the middle term, resistance training can be introduced, such as using elastic bands to perform simple knee flexion and extension resistance exercises. The resistance provided by the elastic band should start at a lower level, such as choosing an elastic band with a smaller elastic coefficient. Initially, perform about 10 times per set. As muscle strength increases, gradually increase to 15–20 times per set. At the same time, appropriately increase the resistance level of the elastic band, but make sure that there is no obvious pain or discomfort in the knee joint during training. When entering the late stage of rehabilitation, more challenging training can be carried out, such as moderately weighted leg strength training with the assistance of equipment. The weight is determined according to the individual's recovery situation. Generally, it starts from 10–20% of one's own body weight and gradually increases. The number of training times per set is maintained at 8–12 times. By scientifically adjusting the intensity, it can effectively promote muscle strength improvement and ensure the safe recovery of the knee joint.

3.3. Coordinated use of diverse training types

In order to comprehensively promote the rehabilitation of knee joint injuries, a variety of training types need to be used in combination. Isometric training plays an important role in the early stage. For example, isometric contraction of the quadriceps can enhance muscle strength and maintain basic physiological functions of muscles without obvious displacement of the joints. In the middle stage of rehabilitation, isotonic training can effectively improve muscle contraction and relaxation ability. For example, using dumbbells for leg curl exercises, choose

dumbbells of appropriate weight, such as 2–3 kg, and perform 10–15 times per set, 2–3 sets of training to enhance leg muscle strength and explosive power^[3]. Isokinetic training uses a special isokinetic muscle training device to provide precisely controlled resistance, which can effectively exercise muscles at different joint movement angles. For example, setting a specific angular velocity and performing knee flexion and extension exercises can significantly improve the coordination and strength balance of muscles around the knee joint. In addition, balance training cannot be ignored. For example, when standing on one leg, start with eyes open and gradually transition to eyes closed. Each standing time starts from 30 seconds. As the balance ability improves, the time is extended, which can effectively improve the proprioception and stability of the knee joint. Different types of training work together to help the recovery of knee joint function and muscle strength reconstruction in all directions.

4. Multi-dimensional evaluation of the effect of muscle strength training on knee injury rehabilitation

4.1. Evaluation based on joint function recovery

Joint function recovery is a key dimension for evaluating the effect of muscle strength training on knee injury rehabilitation. Knee injury is often accompanied by limited joint mobility, such as reduced range of motion, including flexion, extension, and rotation. During the rehabilitation process, it can be evaluated by measuring the active and passive range of motion of the knee joint. The normal knee extension position is 0 degrees, and the flexion can reach 135 to 150 degrees. If the patient's active knee flexion angle gradually increases from 90 degrees at the beginning of the injury to more than 120 degrees after muscle strength training, and the extension angle is close to 0 degrees, it shows that the training is effective in improving the range of motion of the joint. In addition, the performance of daily life functions is also crucial, such as whether the patient can independently complete walking, going up and down stairs, squatting, and other actions. Taking walking as an example, the patient's stride, step frequency, and knee stability during walking can be monitored. The stride of a normal adult is about 50 to 70 cm, and the step frequency is 80 to 120 steps per minute. If the patient's stride is close to the normal range after training, and there is no obvious pain, jamming, or weakness in the knee joint during walking, it means that the knee joint function has been effectively restored under muscle strength training and can better meet the needs of daily activities.

4.2. Evaluation of muscle strength and morphological recovery

As an important power structure to maintain the stability of the knee joint, the strength and morphological recovery of muscles are the core content of evaluating the rehabilitation effect. In terms of muscle strength, isometric, isotonic, and isokinetic muscle strength tests can be performed with the help of professional equipment. For example, a portable isometric muscle strength test device, such as a handgrip dynamometer, is used to test the isometric contraction strength of the quadriceps^[4]. The maximum isometric contraction strength of the quadriceps of normal adult males can reach 500 to 800 Newtons, and that of females is 300 to 500 Newtons. If the patient's muscle strength gradually approaches this range after training, it shows that the training has promoted muscle strength growth. Muscle morphology can be observed through imaging methods such as ultrasound and MRI. Muscle cross-sectional area is a key indicator of muscle morphology. MRI measurement data show that the cross-sectional area of the normal quadriceps in the middle of the thigh is about 50 to 70 square centimeters. Muscle atrophy often occurs after knee injury, and the cross-sectional area decreases. After a period of muscle strength training, if the cross-sectional area of the quadriceps gradually increases and approaches the normal range, it

indicates that the muscle gradually recovers to its normal form under the stimulation of training, providing stronger support for the knee joint.

4.3. Evaluation of improvement in the biomechanical properties of the knee joint

The biomechanical properties of the knee joint are of great significance for evaluating the rehabilitation effect. Biomechanical parameters such as the force line of the knee joint and the pressure distribution on the joint surface are abnormal after injury, and muscle strength training aims to correct these abnormalities. The three-dimensional motion analysis system can accurately measure the changes in the force line of the knee joint during movement. Under normal circumstances, the movement of the knee joint in the sagittal, coronal, and horizontal planes follows a specific trajectory. After injury, the trajectory may be offset, such as the abnormal increase in the knee valgus angle during the walking support phase. If, after muscle strength training, the knee valgus angle gradually decreases from more than 15 degrees after injury to the normal range of 5 to 10 degrees, it means that the training has effectively improved the force line of the knee joint. At the same time, with the help of pressure measurement insoles and other equipment, the pressure distribution of the joint surface can be monitored. The pressure distribution of the medial and lateral compartments of the normal knee joint is relatively balanced. After injury, the pressure of the medial compartment often increases significantly. When the pressure ratio of the medial and lateral compartments tends to be normal after training, it indicates that the pressure distribution of the joint surface is optimized, reducing the risk of articular cartilage wear, and further confirming the positive effect of muscle strength training on improving the biomechanical properties of the knee joint.

5. Conclusion

Knee injury rehabilitation is a complex system of engineering, and muscle strength training runs through it. From clarifying the biomechanical changes and muscle action mechanisms after injury to formulating personalized training strategies, and then verifying the effect through multi-dimensional evaluation, each link is closely related. Scientific application of muscle strength training can help improve knee joint function, enhance patients' quality of life, and provide solid theoretical and methodological support for knee joint injury rehabilitation practice.

Disclosure statement

The author declares no conflict of interest.

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Investigation of the Causes of Inflammatory Reaction after Arthroscopic Anterior Cruciate Ligament Reconstruction

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Abstract: *Objective:* To analyze the data of local inflammatory storm after anterior cruciate ligament reconstruction under knee arthroscopy, and to understand the causes and countermeasures. *Methods:* A retrospective analysis was performed on 135 patients who underwent anterior cruciate ligament reconstruction in the Third Surgical Group of the Department of Orthopedics, the 988th Hospital of the Joint Logistics Support Force from September 2020 to September 2023. The gender, age, injury time, operation time, blood loss, postoperative anticoagulant drug application time, drainage tube application, and other items were collected. The causes of postoperative local inflammatory storm in patients were obtained by binary logistic regression analysis. *Results:* There were no significant differences in gender, age, injury time, operation time, and blood loss ($P > 0.05$), but there were significant differences in the placement of drainage tubes and the initiation time of anticoagulant drugs ($P < 0.05$). Early application of anticoagulants for one day increased the risk of local inflammatory storm after arthroscopic anterior cruciate ligament reconstruction by 0.305 times, and the occurrence of inflammatory reaction without a drainage tube was 5.994 times higher than that with a drainage tube. *Conclusions:* Premature use of anticoagulant drugs and inadequate drainage may be the main causes of local inflammatory storm in these patients.

Keywords: Arthroscopic anterior cruciate ligament reconstruction; Local inflammatory storm; Anticoagulants; Drainage tube

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1. Introduction

Anterior cruciate ligament (ACL) injury is one of the most common knee ligament injuries. ACL rupture is often accompanied by bone contusion, other ligaments, and meniscus injuries, which can affect the stability of the knee joint, and long-term joint instability will lead to premature degeneration of the knee joint^[1]. Due to the very low chance of self-healing after ACL rupture and the poor effect of conservative treatment, the current treatment of ACL rupture is still mainly based on surgical treatment. Arthroscopic anterior cruciate ligament reconstruction is a minimally invasive surgical procedure under the arthroscope to replace the injured ligament to re-stabilize the knee

joint, which is the gold standard for the treatment of ACL rupture.

In 2020, according to statistics, China has more than 100000 cases of anterior cruciate ligament reconstruction under arthroscopy. With ACL reconstruction surgery gradually rising, its postoperative complications also attract more attention. Although the infection rate after ACL reconstruction is less than 1%, delayed treatment may lead to graft failure, articular cartilage destruction, secondary osteoarthritis, and other consequences^[2], which seriously affect the knee joint function. Although there was no purulent infection in this study, the symptoms found are very similar to infection, and the possibility of further development of infection cannot be excluded, so it has attracted full attention.

In this study, the clinical manifestations resembled those of a knee joint infection; however, no pathogenic organisms were detected in the synovial fluid obtained via joint puncture. Following arthroscopic anterior cruciate ligament reconstruction, patients developed knee effusion and swelling within three days. Subsequently, redness appeared in the calf area, accompanied by a low-grade fever, increased skin temperature, and a moderate elevation in white blood cell count. After joint puncture and administration of antibiotics, the patients' symptoms quickly resolved^[3]. A review of the relevant literature and medical texts revealed no prior reports of such a phenomenon. Therefore, this condition is temporarily referred to as a "local inflammatory storm." In order to understand the causes of this phenomenon and explore its coping methods, this study collected the data from the Third Surgical Group of the Department of Orthopedics, the 988th Hospital of the Joint Logistics Support Force, from September 2020 to September 2023.

2. Materials and methods

2.1. Study subjects

A total of 135 patients who underwent arthroscopic anterior cruciate ligament reconstruction from September 2020 to September 2023 in the Third Surgical Group of the Department of Orthopedics, the 988th Hospital of Joint Logistics Support Force were selected for retrospective analysis. Inclusion criteria: (1) patients met the diagnostic criteria of ACL rupture. (2) arthroscopic anterior cruciate ligament reconstruction; (3) complete medical records. Exclusion criteria: (1) patients with intra-articular fractures; (2) patients with joint infection and rheumatoid arthritis; (3) gouty arthritis; (4) patients with immune diseases and abnormal coagulation.

2.2. Clinical data

The general data of 135 patients included in this study were collected, including gender, age, injury time, operation time, blood loss, postoperative antibiotic application time, postoperative anticoagulant drug application time, drainage tube application, and other items. When the patients had clinical manifestations such as effusion and swelling of the knee joint, redness and swelling of the upper leg, low-grade fever, and elevated skin temperature after anterior cruciate ligament reconstruction under knee arthroscopy, blood routine, erythrocyte sedimentation rate, C-reactive protein, and other blood tests were performed immediately, and the joint cavity puncture fluid was collected for bacterial culture. According to the clinical manifestations, hematological examination, and joint fluid examination, it is necessary to quickly identify whether the knee joint infection is caused by pathogens^[4]. After excluding pathogenic infection, the clinical manifestations are attributed to a local inflammatory storm.

2.3. Treatment methods

Antibiotics were given within 24 hours after anterior cruciate ligament reconstruction under knee arthroscopy,

and low-molecular-weight heparin anticoagulation therapy was given 24 hours after surgery. In case of effusion, swelling, redness, low-grade fever, and elevated skin temperature in the upper leg, joint puncture was given in time. In order to relieve the patient's symptoms and avoid the occurrence of septic arthritis, antibiotic treatment was continued [5]. After treatment, the degree of knee joint effusion and swelling, the recovery of local symptoms such as calf skin temperature, and the recovery of hematological examination such as white blood cell count were used as evaluation indicators to evaluate the therapeutic effect, and then determine the subsequent treatment plan.

2.4. Statistical methods

SPSS 22.0 statistical software was used to process and analyze the data. The measurement data were expressed as mean \pm standard deviation (SD) and *t*-test was used. Count data were expressed as rate or constituent ratio, and χ^2 test was used. Using the Hosmer-Lemeshow test, the goodness of fit of the regression model was assessed; $P > 0.05$ means not statistically significant for binary logistic regression. $P < 0.05$ indicates a statistically significant difference.

3. Results

3.1. General information

A total of 135 patients who underwent arthroscopic anterior cruciate ligament reconstruction from September 2020 to September 2023 in the Third Surgical Group of Department of Orthopedics, 988th Hospital of Joint Logistics Support Force were selected, including 112 males and 23 females, aged from 15 to 61 years, with an average age of 29.39 ± 8.79 years. There were 35 cases of local inflammatory storm in the knee joint after operation, including 57 cases of old injury, 78 cases of fresh injury, 56 cases of drainage tube placement, and 79 cases of no drainage tube placement. See **Table 1** for details.

Table 1. Basic clinical data of 135 patients after anterior cruciate ligament reconstruction

Clinical data	<i>n</i> = 135	Percentage (%)
Gender		
Male	112	83%
Female	23	17%
Age (mean \pm SD)	29.39 ± 8.79	-
Nature of injury		
Fresh	57	42%
Old	78	58%
Operation time (mean \pm SD)	121.61 ± 41.09	-
Amount of bleeding (mean \pm SD)	28.19 ± 26.28	-
Antibiotic application time (mean \pm SD)	4.65 ± 3.30	-
Anticoagulant initiation time (mean \pm SD)	4.41 ± 3.44	-
Whether to place a drainage tube		
Yes	56	41%
No	79	59%

3.2. Binary logistic regression analysis

Logistic regression analysis of local inflammatory storm after anterior cruciate ligament reconstruction is presented in **Table 2**. A total of 135 patients who underwent arthroscopic anterior cruciate ligament reconstruction were selected as cases. The data on gender, age, injury type, operation time, blood loss, antibiotic application time, anticoagulation initiation time, and drainage tube placement were analyzed. Hosmer-Lemeshow test showed that $\chi^2 = 8.776$, $P = 0.362$. $P > 0.05$ indicated that the regression model fitted the data well, and the regression model was established. Through binary logistic regression model test results analysis, the initiation time of anticoagulation and whether to place a drainage tube were statistically significant ($P < 0.05$), and the odds of local inflammatory storm increased by 0.305 times when the initiation time of anticoagulation was used one day earlier. The risk of local inflammatory storm in patients without drainage tube placement was 5.994 times higher than that in patients with drainage tube placement.

Table 2. Results of binary logistic regression analysis.

Items	B	SE	Wals	df	Sig.	Exp (B)	95% CI of Exp (B)	
							Lower limit	Upper limit
Gender (1)	0.574	0.701	0.669	1	0.413	1.775	0.449	7.018
Age	0.015	0.030	0.249	1	0.618	1.015	0.957	1.077
Nature of injury (1)	0.086	0.480	0.032	1	0.857	1.090	0.425	2.794
Duration of surgery	0.003	0.006	0.189	1	0.663	1.003	0.990	1.015
Amount of blood loss	0.008	0.008	0.930	1	0.335	1.008	0.992	1.025
Duration of antibiotics	0.057	0.072	0.634	1	0.426	1.059	0.920	1.219
Initiation time of anticoagulation	-0.363	0.101	13.028	1	0.000	0.695	0.571	0.847
Placing a drain (1)	1.791	0.571	9.849	1	0.002	5.994	1.959	18.341

4. Discussion

4.1. Definition and clinical significance of local inflammatory storm

The Third Surgical Group of the Department of Orthopedics, the 988th Hospital of the Joint Logistics Support Force found that a part of the patients who underwent arthroscopic anterior cruciate ligament reconstruction had knee joint hemorrhage after surgery, followed by redness and swelling of the upper leg, elevated skin temperature, and low-grade fever. Blood routine examination showed a slight increase in white blood cells and C-reactive protein. After multiple cultures, no bacteria grew. After 7–10 days, the above symptoms gradually disappeared, and there was no long-term effect on the patients. The third surgical group began to pay attention to this phenomenon and began to search the literature and books, and found that this phenomenon had not been reported. Only Babalola *et al.* [6] reported a case of microbridge allergy with similar symptoms, but this situation excluded allergic reactions. After discussions, this phenomenon was named as local inflammatory storm after anterior ACL reconstruction, and relevant clinical data were collected for further analysis.

A total of 135 patients undergoing arthroscopic anterior cruciate ligament reconstruction were routinely treated with antibiotics and anticoagulant drugs after surgery, but the study found that 35 patients developed local inflammatory storm after surgery, with an inflammation rate of 26%. The patients presented with effusion and

swelling of the knee joint, redness and swelling of the upper leg, low-grade fever, and increased skin temperature. There were no obvious systemic symptoms, and the blood routine test showed mild leukocytosis. This local inflammatory storm is different from joint infection. From the perspective of etiology, the occurrence of this local inflammatory storm is not caused by the invasion of bacteria, viruses, and other microorganisms, which belongs to non-infectious local inflammatory storm^[7]. From the perspective of clinical symptoms, the local symptoms of this local inflammatory storm are obvious, and no systemic symptoms of infection occur. From the auxiliary examination, it can be found that the white blood cell count in the blood routine of these patients is increased, while other blood test indexes are in the normal range, and the bacterial culture of synovial fluid puncture is negative. From the perspective of the outcome of the disease, this local inflammatory storm is self-limited and can be clinically cured, but the appearance of local symptoms such as knee joint swelling and pain delays the recovery process. Although the outcome is good, it increases the course of the disease, hospitalization costs, and pain of the patient, which still needs to be paid attention to.

4.2. Cause analysis of local inflammatory storm

This study found that a total of 35 patients developed local inflammatory storm after surgery. To explore the causes of this phenomenon, in this study, binary logistic regression was used to analyze the correlation between gender, age, complications, operation time, blood loss, postoperative antibiotic application time, postoperative anticoagulant drug application time, and drainage tube application and postoperative local inflammatory storm, in order to determine the cause of postoperative local inflammatory storm. The results showed that the risk of local inflammatory storm after arthroscopic anterior cruciate ligament reconstruction was increased by 0.305 times when anticoagulant drugs were used one day earlier after surgery, and the risk of local inflammatory storm in patients without a drainage tube was 5.994 times that in patients with a drainage tube. However, there was no significant correlation between the patient's gender, age, operation time, intraoperative blood loss, and postoperative antibiotic application time and the postoperative local inflammatory storm. The results showed that the timing of anticoagulant use and the placement of a drainage tube were significantly correlated with the occurrence of local inflammatory storm, which further indicated that postoperative local hemorrhage may be the main cause of postoperative local inflammatory storm.

After anterior cruciate ligament reconstruction under knee arthroscopy, patients often have knee joint swelling, which is usually caused by knee joint effusion. The reasons may include rupture of local capillaries due to trauma caused by own ligaments and surgery, increased permeability of blood vessel wall, and interstitial edema caused by intravascular fluid penetration into the soft tissue space. During the operation, soft tissue traction and blunt dissection lead to postoperative soft tissue reactive swelling. When a large amount of normal saline is used to flush the joint cavity during the operation, swelling is caused by the absorption of normal saline by the nearby soft tissue.

When the accumulated blood reaches a certain pressure in the joint cavity, the accumulated blood will reach the other end of the bone tunnel along the tibia and femur^[8]. As the femoral end is rich in muscle tissue and has a strong ability to absorb blood accumulation, there is generally no local heat absorption and local inflammatory storm. The external mouth of the tibial bone tunnel is the anterior-medial side of the tibia, where there is no muscle tissue, so the blood accumulation cannot be absorbed in time and spreads along the tibia, resulting in local inflammatory storm with redness and swelling, low-grade fever, and high skin temperature in the upper leg^[9]. With a drainage tube placed at the end of the operation, the intra-articular blood can be drained out in time without

flowing out of the joint along the bone tunnel, and the occurrence of local inflammatory storm can be avoided. However, the placement of a drainage tube can also increase the risk of joint infection, and the drainage tube should be removed after 48 hours, so some patients may experience local inflammatory storm after the removal of the drainage tube^[10].

4.3. Prevention and treatment of local inflammatory storm

The use of anticoagulant drugs to prevent venous thrombosis of the lower extremities after surgery has become an expert consensus^[11]. As a small amount of blood accumulates in the joint after arthroscopic surgery, early use of anticoagulant drugs may increase the amount of blood in the joint cavity. However, if anticoagulant drugs are applied after the bleeding surface in the joint cavity has gradually healed, the chance of bleeding will be greatly reduced. Among the 35 patients with local inflammatory storm after surgery in this study, 30 patients (86%) were treated with anticoagulant drugs within 3 days after surgery, and 5 patients (14%) were treated with anticoagulant drugs after 3 days. Considering that most patients with anterior cruciate ligament injury are young adults, combined with the data, it is recommended to apply anticoagulant drugs to prevent thrombosis after 3 days of arthroscopic anterior cruciate ligament reconstruction^[12]. If the patient is older than 40 years old or has a higher thrombosis risk assessment score, it is recommended to place a drainage tube during the operation and apply anticoagulant drugs immediately after the operation to prevent the formation of lower extremity venous thrombosis.

According to the current research data, there are no cases of septic arthritis, and the results of the patient's symptoms and laboratory tests are very similar to bacterial infection, and the possibility of bacterial infection cannot be excluded, because the blood accumulation in the joint is a very good medium for bacteria, so the prophylactic antibiotics are changed to therapeutic antibiotics. After this phenomenon occurs, patients often panic and may feel that their postoperative symptoms are worsening. They may suspect a postoperative infection. Therefore, doctors should provide appropriate psychological support, clearly explain the causes and prognosis to the patient, help ease their anxiety, and encourage active cooperation with the treatment. Based on the study and understanding of inflammatory storms, a standardized treatment plan should be developed: (1) Joint cavity puncture aims to relieve intra-articular pressure, and the aspirated fluid should be sent for bacterial culture. (2) Prolonged use of antibiotics: For example, in anterior cruciate ligament reconstruction, antibiotics are generally administered for 24 hours. To prevent purulent infection, the duration of antibiotic use should be appropriately extended. (3) Local cold compresses should be applied, along with medications that promote venous drainage, such as aescinate.

5. Conclusion

The occurrence of local inflammatory storm after arthroscopic anterior cruciate ligament reconstruction may be related to the starting time of postoperative anticoagulant drug application and whether to place a drainage tube^[13]. The results of this study showed that the risk of local inflammatory storm increased by 0.305 times when anticoagulant drugs were used one day early after surgery. Therefore, attention should be paid to the initial application time of anticoagulant drugs in the routine treatment of anterior cruciate ligament reconstruction under knee arthroscopy. It is recommended to start anticoagulant drugs after 3 days^[14,15], and try to avoid the risk of local inflammatory storm. The risk of local inflammatory storm in patients without drainage tube placement is

5.994 times that of patients with drainage tube placement. For patients with high thrombosis scores and timely application of anticoagulant drugs after surgery, drainage tubes should be placed during the operation. In case of local inflammatory storm, the differential diagnosis between infection and medical history, clinical manifestations, physical examination, hematological examination, and bacterial culture of synovial fluid puncture should be made as soon as possible. Meanwhile, anti-inflammatory antibiotics, anti-swelling drugs, and local cold compress treatment should be given immediately to relieve symptoms.

Disclosure statement

The authors declare no conflict of interest.

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Research on Serum Biomarkers in Knee Joint Diseases of the Elderly

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Abstract: *Background:* Knee osteoarthritis (KOA) is characterized by chronic degeneration or wear of the articular cartilage, cartilage degeneration, fragmentation, and hardening, as well as bone spur formation and synovial inflammation. Over time, these changes occur slowly, and bone wear becomes more severe. This in turn causes pain, stiffness and swelling. It has an impact on normal work and life. To understand the mechanism and monitoring index of cartilage injury in the elderly population and prevent osteoarthritis. The purpose of this study was to compare the changes of serum cytokine biomarker levels in elderly patients with knee injury and osteoarthritis, and explore the correlation with the severity of lesions, which is conducive to early diagnosis and prevention of knee diseases. *Objective:* To investigate the differences in serum concentrations of matrix metalloproteinase-3 (MMP-3) and cartilage oligomeric matrix protein (COMP) in elderly patients with osteoarthritis, knee fracture or ligament injury. *Methods:* A total of 36 elderly KOA patients who underwent knee replacement in our hospital from July 2021 to May 2023 were selected as the observation group, and 36 elderly patients with knee fractures, patellar fractures, ligament or meniscus injuries who were treated during the same period were selected as the control group for the study. The age, gender, weight and other data of the patients were compared. The anteroposterior and lateral radiographs of the knee joints were examined for the first time, and the Kellgren and Lawrence (KL) score was used to compare the severity of KOA. The levels of serum MMP-3 and COMP in the two groups of patients were tested by enzyme-linked immunosorbent assay, and the changes and sensitivity of the two biomarkers in elderly knee diseases were compared and analyzed. *Results:* (1) Among the 72 knee joints included in the study, 36 cases were assigned to each group. No significant differences were observed in gender, age, or weight between the two groups ($P > 0.05$). (2) The concentrations of serum MMP-3 and COMP in the observation group were significantly higher than those in the control group. *Conclusion:* The elevated levels of COMP and MMP-3 in patients with knee osteoarthritis (KOA) suggest a potential correlation with disease progression, as their concentrations increased with worsening severity. These biomarkers may hold significant value for early detection, diagnosis, and prevention of KOA in elderly populations, warranting further investigation.

Keywords: Matrix metalloproteinases; Cartilage oligomeric matrix proteins; Biomarkers; Cartilage injury; Knee osteoarthritis

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1. Introduction

Knee osteoarthritis (KOA) is the most common arthritis of the knee in the elderly. It poses a huge burden on the affected elderly, healthcare providers and society. Current treatments focus on symptomatic relief, the use of non-steroidal painkillers and advanced arthroplasty. It is characterized by degeneration, erosion, wear and tear, injury, loss of articular cartilage, narrowing of the joint space, bone redundancy, subchondral sclerosis and synovial inflammation. In the pathogenesis of osteoarthritis of the knee, inflammation has been shown to underlie the pathogenesis. The inflammatory response promoted by inflammatory cytokines is a major factor and an important cause of chronic pain ^[1].

There are several high-risk factors for osteoarthritis of the knee, including age, trauma, and obesity. Current methods of clinical evaluation of disease severity often utilize imaging (radiographs and magnetic resonance imaging) and are assessed using the Kellgren and Lawrence scale, known as the KL grading system (grades 0-4). However, radiographs only show changes in bone and cartilage, which often occur late in the disease. In the clinical setting, when clinical signs of pain and reduced mobility have already appeared, the bone and cartilage lesions have become irreversible. Therefore, there is a need to find sensitive and predictive tests that could eventually replace current imaging methods and facilitate punctual, more targeted and personalized treatment ^[2]. Biomarkers (inflammatory cytokines) will likely be a better choice to reflect the severity of the lesion. Their concentrations can be measured in body fluids such as blood, urine or synovial fluid ^[3].

2. Data and methods

2.1. General information

36 elderly patients with KOA who underwent knee replacement admitted to our hospital during July 2021-May 2023 were selected as the observation group, and 36 elderly patients with knee fracture, patella fracture, ligament injury or meniscus injury who were hospitalized and received treatment at the same time were selected as the control group for the sexual study. Differences in age, gender, and weight between the two groups were compared. All of them took the frontal and lateral radiographs of the knee joint, and the severity of KOA was assessed by the Kellgren and Lawrence (K-L) grading system score. ELISA kits were used to detect the concentrations of serum MMP-3 and COMP in both groups. The correlation between the two biomarkers and the severity of knee disease was comparatively analyzed. The study was approved by the Ethics Committee of the First People's Hospital of Wuhu City under the informed consent of the patients.

2.2. Inclusion and exclusion criteria

Test group: (1) age ≥ 55 years old; (2) K-L grade 3-4; (3) X-ray frontal and lateral radiographs and MRI; (4) intermittent pain and activity limitation in the last month; (5) in line with the guidelines for the diagnosis and treatment of osteoarthritis ^[4].

Blank group: (1) age ≥ 55 years old; (2) K-L grade 0-1; (3) X-ray frontal and lateral radiographs and MRI; (4) patella fracture, femoral condyle fracture, tibial plateau fracture, meniscus injury or ligament injury.

Exclusion criteria: (1) medical diseases (respiratory, digestive, endocrine, cardiovascular and cerebrovascular and other systemic diseases); (2) rheumatism, autoimmune diseases or infectious diseases, etc.; (3) cognitive disorders, psychiatric disorders, and so on.

2.3. Research methods

2.3.1. Clinical data collection

On the day of admission, patients in both groups were measured for height, weight, blood pressure, etc., and asked about history, family history, clinical symptoms and other clinical data. On the next day, 5ml of fasting venous blood was collected, within 4h after collection, centrifuged at 2500 rpm for 10 minutes, and the serum was stored in the refrigerator at -20 °C. An ELISA kit was used to detect the concentration of MMP-3 and COMP in the serum; the COMP kit was provided by Shanghai Research Biotechnology Co., Ltd, and the MMP-3 kit was provided by the American Abcam Company.

2.3.2. Observation indexes

Compare the relationship between the MMP-3 and COMP levels of the two groups and the K-L classification and clinical symptoms of the patients.

2.3.3. Statistical methods

The data were analyzed using SPSS 25.0 statistical software. Continuous variables were presented as mean \pm standard deviation (SD), with between-group comparisons conducted using independent samples t-tests and analysis of variance (ANOVA). Categorical data were expressed as percentages, and group comparisons were performed using the chi-square (χ^2) test. A p -value of less than 0.05 was considered statistically significant.

3. Results

3.1. Comparison of cohort characteristics

In the 72 enrolled patients, there was no statistically significant difference in age, gender and weight ($P > 0.05$) (Table 1).

Table 1. Comparison of clinical data between the two groups

Groups (n = 36)	Age (years old)	BMI (kg/m ²)	Male/female	Left/right
Test group	67.3 \pm 8.3	28.73 \pm 3.69	11/25	17/19
Blank group	61.7 \pm 6.6	29.89 \pm 4.59	22/14	20/16
<i>P</i>	> 0.05	> 0.05	> 0.05	> 0.05

3.2. Comparison of MMP-3 and COMP

The serum MMP-3 and COMP levels of the observation group were higher than those of the control group, and the difference was statistically significant ($P < 0.05$) (Table 2).

Table 2. Comparison of MMP-3 and COMP levels between the two groups (ug/l, mean \pm SD)

Groups (n = 36)	MMP-3	COMP
Test group	4.38 \pm 0.78	5.62 \pm 1.65
Blank group	1.22 \pm 0.40	1.34 \pm 0.47
<i>t</i>	23.7034	25.7493
<i>P</i>	< 0.05	< 0.05

4. Discussion

KOA is characterized by chronic nonspecific inflammation with predominantly articular cartilage damage. The pathological mechanism is characterized by chondrocytopenia and extracellular matrix degradation. It includes degenerative changes in all tissue structures of the joint (bone, cartilage, synovium, ligaments and joint space)^[5]. Clinical manifestations are swelling, pain, stiffness, deformity, and consequently limited mobility and disability of the knee joint. The inflammatory process involves anabolic and catabolic metabolism with the involvement of multiple factors such as chemokines, cytokines, matrix metalloproteinases and their inhibitors. The current routine clinical adjuncts for knee disease are radiographs and other imaging tests, the positive manifestations of imaging examinations are often detected late in the development of the disease, indicating poor sensitivity in disease detection. Disruption of the metabolic balance of intra-articular cartilage is associated with the pathomechanism of osteoarthritis of the knee^[6]. Haraden *et al.*^[7] found in their study that six biomarkers in joint fluid, (including VEGF, MMP-3, TIMP-1, sICAM-1, sVCAM-1, and MCP-1), were associated with the severity of knee osteoarthritis. They also observed the association between these biomarkers and activated macrophages and neutrophils. Therefore, detecting the metabolic products of cartilage may be a method for early diagnosis, detection, and early warning of KOA.

Cartilage oligomeric matrix protein (COMP) is an extracellular matrix non-collagenous glycoprotein present in cartilage^[8]. It belongs to the thrombospondin family, also known as TSP-5, and is found mainly in human bone (articular cartilage, menisci, ligaments, tendons, and synovium)^[9–11]. COMP can interact with many other cartilage extracellular matrix (ECM) components, including type I, II, IX, IX, and XIV collagens, fibronectin, and proteoglycans^[12]. It promotes the secretion and assembly of collagen and maintains the stability of the extracellular matrix. It has obvious tissue specificity due to its high expression in cartilage. As one of the by-products of cartilage metabolism, it is now gaining increasing attention and research as a possible biomarker for early detection of osteoarthritis in the knee^[13].

Georgiev *et al.*^[14] observed that serum COMP levels were higher in patients with KOA than in controls, and that COMP was positively correlated with knee MRI scores, which suggests that COMP may reflect knee joint structural damage. In KOA, COMP expression is regulated by tumor necrosis factor (TNF- α). In this study, it was found that a portion of patients with knee joint trauma had elevated serum COMP. This research evidences indicate that COMP is involved in the molecular processes related to cartilage metabolism. Detecting COMP will pave the way for early prevention and treatment of synovitis and eventual cartilage degeneration in KOA patients^[15].

Matrix metalloproteinase 3 (MMP-3) is widely used as a serum biomarker. MMP-3 is the major enzyme involved in cartilage degradation. MMP-3 is thought to be a more specific indicator of a protein originally secreted by synovial fibroblasts. MMP-3 degrades a variety of extracellular substrates, including proteoglycans, fibronectin, laminin, and collagen type IV, and in addition initiates the MMP-3 can degrade various extracellular substrates, including proteoglycans, fibronectin, laminin, and collagen type IV, in addition to other matrix metalloproteinase family members. Therefore, MMP-3 is a degradation enzyme that plays a major role in cartilage destruction, and is the enzyme with the highest prevalence of KOA. However, serum MMP-3 is also significantly elevated in diseases involving synovitis. The biomechanical alterations of KOA stimulate the production of inflammatory mediators by chondrocytes, such as in interleukin-1 and tumor necrosis factor. These inflammatory mediators' response also triggers an increase in the synthesis of MMP-3, which, when activated, directly degrades proteoglycans in the extracellular matrix, while also activating other zymogens, leading to extracellular matrix degradation, and the products of the MMP-3 degradation are released into the joints, causing arthritis. The products of MMP-

3 degradation are simultaneously released into the joints, causing joint inflammation. Serum MMP-3 levels reflect the degree of inflammation and correlate with the level of disease activity. MMP-3 has a dominant role in joint disease damage. At the site of cartilage destruction, the level of MMP-3 in cartilage tissue increases. The expression of MMP-3 in the KOA group was significantly higher than that in the control group. Heard *et al.* [16] investigated the protein expression levels of MMP and TIMP in the synovial fluid of normal and early KOA joints. It showed that there was a significant difference in MMP-3 expression between normal and early KOA samples; the level of MMP-3 expression was significantly higher in advanced KOA. More importantly, MMP-3 can activate MMP-1, MMP-9, MMP-13 and other zymogens to produce a cascade amplification effect and accelerate cartilage destruction. The mRNA of MMP-3 is more strongly expressed in cartilage, showing different patterns in early and advanced disease, and more significantly in advanced disease.

Nonsteroidal anti-inflammatory drugs (NSAIDs) have demonstrated efficacy in alleviating symptoms and mitigating inflammation. Intra-articular injections of corticosteroids (CS), platelet-rich plasma (PRP), mesenchymal stem cells, and hyaluronic acid have been reported to relieve symptoms. However, the duration of action of these drugs and local side effects remain questionable.

The diagnostic criteria of clinical symptoms and imaging criteria are clinically relevant in the diagnosis of advanced stages. In clinical studies, diagnostic criteria for early osteoarthritis of the knee have good predictive power for individuals with knee pain, although more validation is needed [17]. Because when there is clear imaging evidence in clinical practice, the articular cartilage has already undergone irreversible degenerative damage, irreversible disease progression and joint degeneration have already occurred, thus delaying the optimal time for early treatment [18]. In addition, the onset of clinical symptoms of KOA (e.g., pain) is often delayed due to the patient's usually advanced age and pain tolerance, resulting in delayed diagnosis and treatment. Identifying reliable biochemical markers for early diagnosis of KOA and predicting disease progression is a top priority for KOA [19]. This is important for individuals at risk of OA (e.g., trauma) who may present with knee pain without observing obvious signs or radiographic evidence of KOA. This helps to identify patients with early KOA and monitor treatment at the individual level [20]. Studies have been conducted to analyze the correlation of various biomarkers and to identify the factors that are most easily and accurately used for early clinical diagnosis to provide a basis for early diagnosis of KOA.

The study analyzed serum levels of the biomarkers MMP-3 and COMP in elderly patients with patellar fractures, meniscus and ligament injuries, and knee osteoarthritis (KOA) to assess their variations in knee-related disorders and KOA. The findings revealed significantly higher MMP-3 and COMP levels in the observation group compared to the control group ($P < 0.05$), suggesting that these biomarkers are particularly elevated in KOA patients. Furthermore, patients with more severe disease exhibited even greater increases in MMP-3 and COMP levels, with these differences also being statistically significant ($P < 0.05$).

5. Conclusion

In conclusion, the serum biomarker COMP, MMP-3 levels were significantly elevated in elderly patients with KOA and gradually increased with the aggravation of the disease, which has a certain reference value for early warning, diagnosis, prevention and treatment of chronic cartilage damage in knee diseases.

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Disclosure statement

The authors declare no conflict of interest.

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Extrapedicular vs Transpedicular Percutaneous Kyphoplasty for Osteoporotic Vertebral Compression Fractures: A Systematic Review and Meta-analysis

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Abstract: *Background:* Osteoporotic Vertebral Compression Fractures (OVCFs) are one of the most common health problems in the elderly population. Percutaneous kyphoplasty is a minimally invasive technique that has gained widespread recognition. Transpedicular and extrapedicular are two approaches for kyphoplasty. But over the last decade, the safety and effectiveness of two approaches have remained unclear, and there is still a lack of evaluation of their therapeutic effects. *Objectives:* To assess the efficacy and safety of the two approaches as a treatment for patients with OVCF. *Methods:* The study searched CENTRAL, MEDLINE, EMBASE, Chinese Biological Medicine Database, VIP Journals Database, Wan-fang database, CNKI and Chinese Evidence-Based Medicine Database from their inception to December 2020 in both English and Chinese. The study searched Chinese-language journals and conference proceedings. Randomised-controlled trials that compared any form of the transpedicular approach to any form of the extrapedicular approach control intervention in the treatment of osteoporotic vertebral compression fracture patients were included. Two review authors (Wu and Huang) independently determined the studies to be included in the review based on inclusion and exclusion criteria and the extracted data were analysed by RevMan 5.3, and the level of evidence was assessed by the GRADE system. *Results:* Six randomised controlled trials with a total sample size of 395 patients were included; all of them were from Asian countries. Meta-analysis showed that the extrapedicular approach kyphoplasty is superior to the transpedicular approach kyphoplasty for less radiology exposure time, less cement volume, and a lower leakage rate. But there is no difference between the extrapedicular approach kyphoplasty and the transpedicular approach kyphoplasty with postoperative VAS scores and ODI scores. *Conclusion:* Based on the evidence of 6 RCTs, the effectiveness of extrapedicular kyphoplasty for the treatment of osteoporotic vertebral compression fracture patients is suggestive. Extrapedicular kyphoplasty has less radiology exposure time, cement volume and a lower leakage rate than transpedicular kyphoplasty, and there is no significant difference in VAS and ODI after surgery. With the methodological quality and the small number of the included studies taken into consideration, furthermore high quality and large-scale randomized controlled trials are needed.

Keywords: Extrapedicular percutaneous; Transpedicular percutaneous; Kyphoplasty; Osteoporotic vertebral compression fracture; Systematic review

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1. Introduction

Osteoporotic vertebral compression fractures (OVCFs) are common in the elderly population, with an estimated 1.4 million new fractures occurring every year worldwide^[1]. OVCFs cause a substantial economic burden, which will markedly increase over the coming decades^[2-4]. OVCFs have been traditionally treated with conservative management, such as bed rest, analgesics, braces, taking anti-osteoporotic agents, etc.^[5,6] However, in cases with persistent pain or being refractory to conservative management, percutaneous kyphoplasty (PKP) has been traditionally adopted^[7-9]. This minimally invasive technique has gained widespread recognition, effectively reducing pain both in the short and long term^[10,11]. Numerous clinical studies^[12,13] demonstrated that the treatment could rapidly relieve the pain of patients, restore vertebral height partially, and provide biomechanical stability by injecting bone cement into the fractured vertebrae. However, in light of previous literature, many studies^[14,15] have reported the disadvantages of surgery, such as the augmented vertebrae with significant vertebral height loss and aggravation of kyphotic deformity after surgery. There are still some reports of percutaneous injury to nerves or spinal cords in the surgery of percutaneous kyphoplasty^[16,17].

How to reduce intraoperative injury to nerves or spinal cords in the surgery of percutaneous kyphoplasty has become an important issue for clinicians to improve. Some research shows both the transpedicular approach and extrapedicular approach are relatively safe, but in the upper and middle thoracic spine, the risk of intraspinal mispositioning seems to be lower when using the extrapedicular approach^[18,19]. Due to the variable pedicle anatomy, two different approaches, the transpedicular and the extrapedicular approach, have been established. In particular, in the middle and upper thoracic spine, percutaneous procedures are challenging because of the difficult visualization of anatomical landmarks and a more unfavorable anatomy with smaller and differently orientated pedicles^[20]. But the actual effect and safety of extrapedicular kyphoplasty compared to transpedicular kyphoplasty is still unclear. As we know, this is the first Meta-analysis to discuss the effect of the extrapedicular approach kyphoplasty and transpedicular approach among treating OVCFs.

2. Methods

2.1. Search strategy and selection criteria

The study searched CENTRAL, MEDLINE, EMBASE, Chinese Biological Medicine Database, VIP Journals Database, Wan-fang database, CNKI, and Chinese Evidence-Based Medicine Database from their inception to December 2020. The search terms used were: the transpedicular approach and extrapedicular approach for treating OVCF in both English and Chinese. The study also searched files manually for relevant articles. The study searched Chinese-language journals and conference proceedings. The study included dissertations and abstracts, provided they contained sufficient detail for critical evaluation. The study submitted the details in the INPLASY register (registration number is INPLASY202330048).

The studies that met the following criteria were included: (1) the study evaluated the extrapedicular

kyphoplasty for treating OVCF and PKP; (2) the study must be conducted through case control design; and (3) the study provided sufficient raw data for the weighted mean difference (MD) with 95% confidence intervals (CI). Articles were excluded from our meta-analysis if they were duplicate publications or did not contain raw or usable data. Data from the included studies were extracted and summarized independently by two of the authors. Any disagreement was resolved by the adjudicating senior authors (D.L.).

2.2. Data analysis

For meta-analysis, the total effectiveness rates of dichotomous data were pooled using risk ratios (RRs). The aggregated results and 95% CIs for effect size were calculated using inverse-variance weighted random-effects meta-analysis. I^2 was used to assess heterogeneity across studies, with I^2 values of 0%, 25%, 50% and 75% representing no, low, moderate and high heterogeneity, respectively. Meta-regression was conducted to investigate the potential covariates that might have substantial impacts on between-study heterogeneity. Influence analysis was also conducted to determine whether an individual study affected the aggregate result or not. Subgroup analyses were performed according to the type of study design.

3. Results

The study identified 231 potentially relevant articles, and 225 articles were excluded for reasons given in **Figure 1**. Six studies, involving a total of 395 participants, met our inclusion criteria ^[21–26]. Key data are summarized in Table 1. All of them were from Asian countries, and 6 trials were from China and published in Chinese ^[21–26].

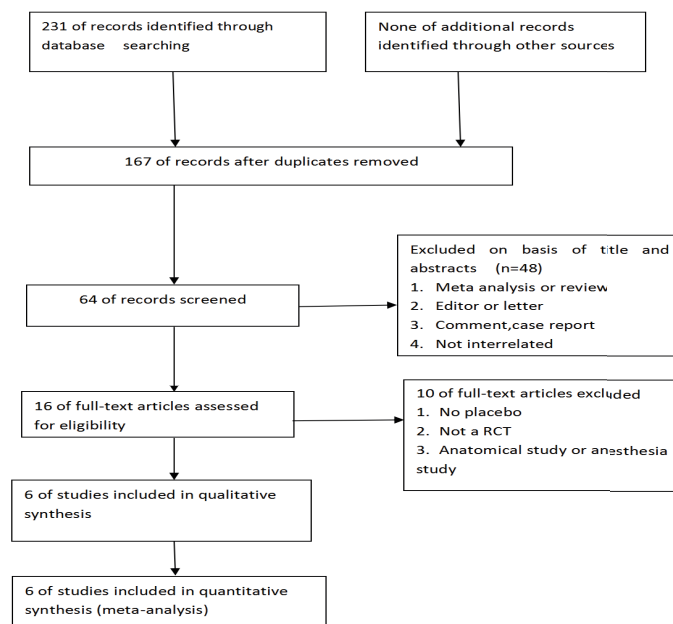


Figure 1. Flowchart of trials selection process.

Table 1. Summary of randomized controlled trials on the two approaches for treating OVCF

First author/year	Type of surgery	Intervention experimental	Intervention control	Outcomes
Chen, 2018 ^[21]	PKP	22	25	VAS, Surgery time, Cement volume, Leakage rate
Huang, 2019 ^[22]	PKP	60	60	VAS, ODI, Surgery time, Radiology exposure time, Leakage rate
Ma, 2019 ^[23]	PKP	30	28	VAS, ODI, Surgery time, Radiology exposure time, Cement volume, Leakage rate
Wang, 2012 ^[24]	PKP	28	26	VAS, Surgery time, Radiology exposure time, Cement volume
Yang, 2016 ^[25]	PKP	24	24	VAS, ODI, Cement volume, Leakage rate
Zhu, 2020 ^[26]	PKP	34	34	ODI, Surgery time, Radiology exposure time, Cement volume

PKP: percutaneous kyphoplasty, VAS: visual analogue scale, ODI: oswestry disability index

3.1. Study quality

Three articles of six trials were non-randomized control groups, and three trials were described as randomized, while one of the trials ^[22] had no detailed description of the method, and two of the trials ^[23,26] reported appropriate randomization, in which researchers used numerical table randomization method for randomization.

While all included trials reported favorable effects of extrapedicular kyphoplasty on treatment to osteoporotic vertebral compression fractures, none of the included trials reported the implementation of allocation concealment. All of the six studies did not mention either subjects or assessor blinding. And three reported follow up ^[22,23,26], none of the included trials reported dropout. Two of the included trials reported the ethical approval ^[21,23]. Three of the six trials showed a high risk of bias ^[21,24,25], while the other three trials showed a unclear risk of bias ^[22,23,26] (**Figure 2** and **Figure 3**). Based on GRADE system, all the evidences were level C and weak recommendation (2C). There was good agreement between the two reviewers.

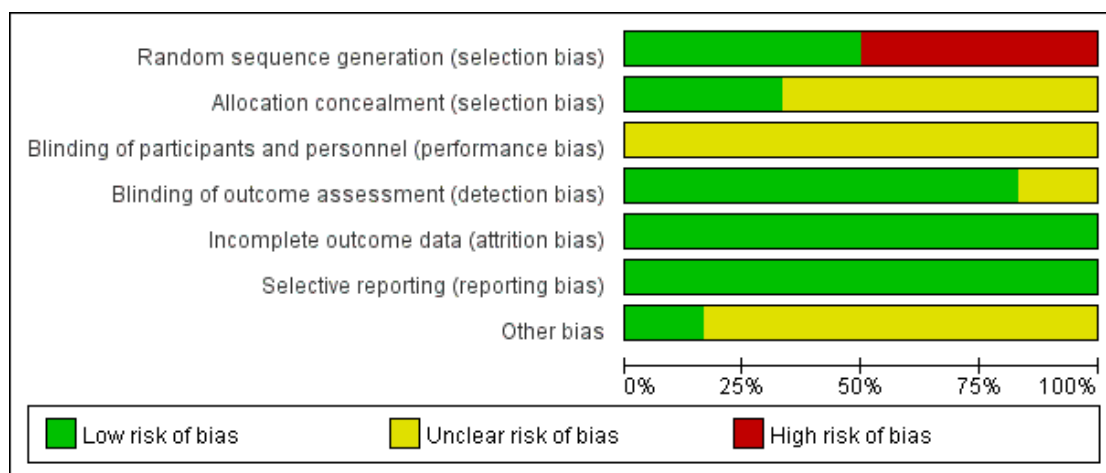


Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
2018	+	?	?	+	+	+	?
2019	+	?	?	+	+	+	?
2019	+	+	?	+	+	+	+
2012	+	?	?	+	+	+	?
2016	+	?	?	?	+	+	?
2020	+	+	?	+	+	+	?

Figure 3. Risk of bias summary: Review authors' judgments about each risk of bias item for each included study.

3.2. Outcomes

3.2.1. Fluoroscopy times

Adequate time of intraoperative fluoroscopy data were available in 4 studies ^[22–26]. Pooled data indicated a lower radiology exposure time of operation in the extrapedicular approach group, the difference was statistically significant (MD = -9.85, $P < 0.00001$, 95%CI -13.54 to -6.16, $I^2 = 96\%$, **Figure 4**).

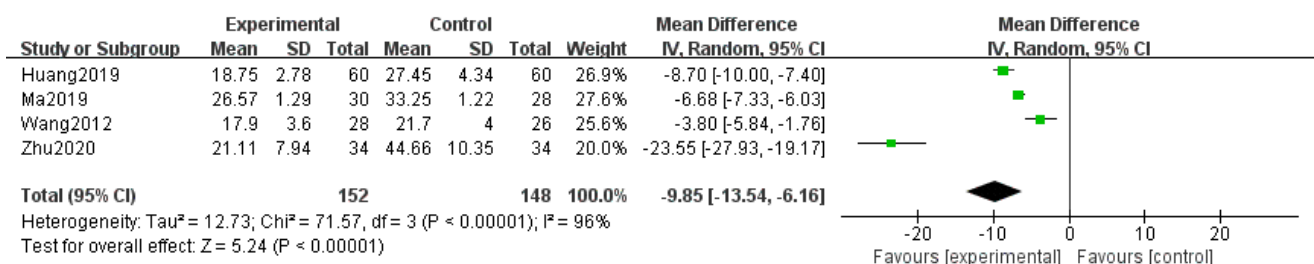


Figure 4. Meta-analyses of the radiology exposure time.

3.2.2. Bone cement injection volume

Five studies ^[21–26] provided adequate data about the mean and SD of the cement injection volume. Compared with the transpedicular approach group, the pooled estimate showed that the extrapedicular approach group used significantly less bone cement volume (MD = -0.96, $P = 0.003$, 95%CI -1.58 to -0.33, $I^2 = 95\%$, **Figure 5**).

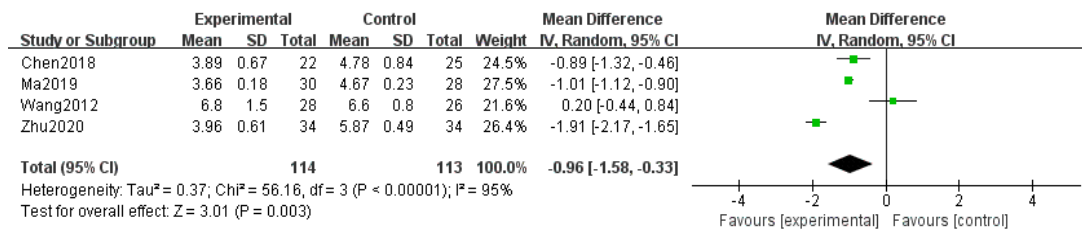


Figure 5. Meta-analyses of the bone cement injection volume.

3.2.3. Postoperative VAS and ODI

Five included articles ^[21–25] reported the VAS score at the time points of preoperative and postoperative. The meta-analysis found no significant differences in VAS after surgery between the extrapedicular approach group and the transpedicular approach group for OVCFs (MD = 0.04, $P = 0.43$, 95%CI -0.05 to 0.13, $I^2 = 66\%$, **Figure 6**). Four included studies ^[22,23,25,26] evaluated surgical outcomes by the ODI scores before and after the treatments. Result of pooled data indicated no statistical difference between the extrapedicular approach group and the transpedicular approach group with postoperative ODI (MD = -0.76, $P = 0.60$, 95%CI -3.60 to 2.08, $I^2 = 85\%$, **Figure 7**).

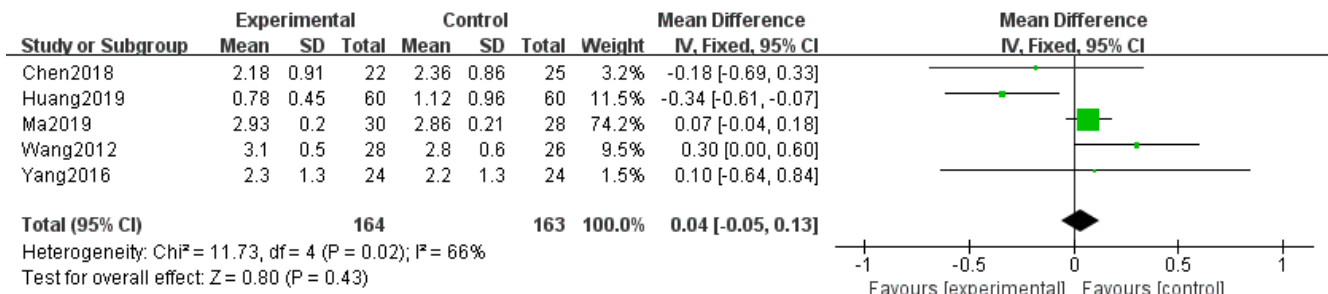


Figure 6. Meta-analyses of the VAS after surgery.

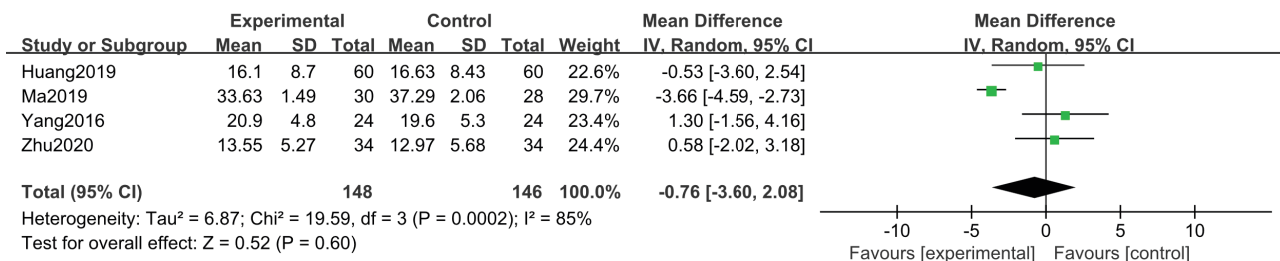


Figure 7. Meta-analyses of the ODI after surgery.

3.2.4. Complications

Four studies ^[21–23,25] provided relevant data on cement leakage, with 272 patients (135 in the extrapedicular approach group and 137 in the transpedicular approach group). The meta-analysis of the four studies showed that the transpedicular approach group had a significantly higher risk of cement leakage than the extrapedicular approach group (OR = 0.34, $P = 0.005$, 95%CI 0.16 to 0.73, $I^2 = 0\%$, **Figure 8**).

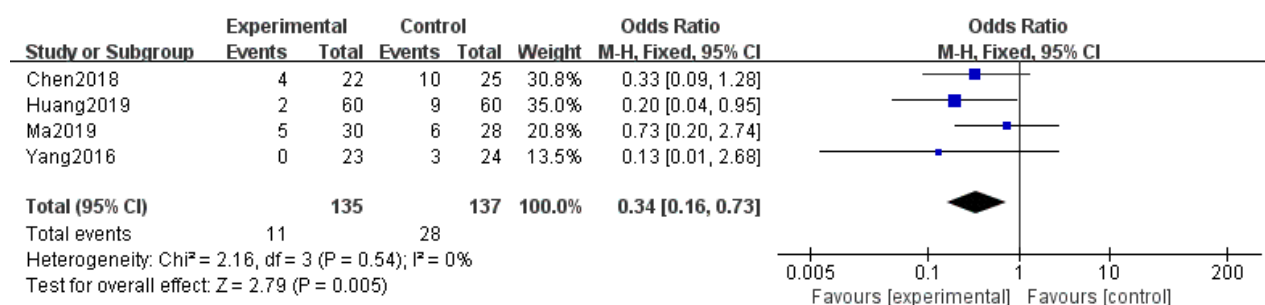


Figure 8. Meta-analyses of the cement leakage rate.

3.2.5. Adverse events

None of the 6 included trials mentioned adverse events at all.

4. Discussion

OVCFs are very common in elderly people, causing intractable pain, kyphosis and greatly impairing the quality of a patient's life. Percutaneous kyphoplasty is a minimally invasive operation used in the treatment of patients with OVCFs who have no improvement after 4 weeks of conservative therapy^[27–29]; it involves the insertion of the balloon plate into the vertebral body, followed by the injection of cement for the fixation of the vertebral body. Percutaneous kyphoplasty can provide rapid and constant pain relief, reduce the kyphosis deformity and improve the quality of life; thus, it has been regarded as one of the standard operations during the last decade.

Kim *et al.*^[30,31] described that a unilateral extrapedicular approach to kyphoplasty or vertebroplasty offers several benefits, including shorter operative time, which reduces perioperative risks that are considerable in seniors with multiple medical issues. Andrew *et al.*^[32] first reported step-by-step the percutaneous techniques used in the lumbar and thoracic extrapedicular approaches and the thoracic infrapedicular approach, with depiction in an accompanying video presentation. Liu *et al.*^[33,34] introduced the puncture methods in different extrapedicular approaches and recommended appropriate extrapedicular puncture methods for thoracolumbar PVP (PKP). However, the complications between two different approaches of percutaneous kyphoplasty were the main points that attracted the attention of those making the decisions. Cement leakage is a very serious and common complication. These controversial conclusions confused the clinical decision makers and did not standardize the therapy effectively.

Meta-analyses and systematic reviews were confirmed as the evidence with the highest quality in evidence-based medicine^[35]. This is the first systematic review of meta-analyses to compare the extrapedicular approach to the transpedicular approach in kyphoplasty for OVCFs. The study concluded that the extrapedicular approach kyphoplasty could reduce the radiology exposure time, cement volume, and cement leakage rate compared to that of the transpedicular approach kyphoplasty, while there were no differences in VAS scores, ODI scores. These findings are consistent in all included research, indicating that the extrapedicular kyphoplasty can significantly reduce the cement leakage rate and the radiology exposure time. The possible reason is that the extrapedicular approach is easier to puncture than the transpedicular approach, and there is no need to adjust the puncture too much during the operation^[36–38].

The study also found that the extrapedicular kyphoplasty group needed less bone cement than the

transpedicular kyphoplasty group. Yan *et al.* ^[39,40] described that, facing the small pedicle of the thoracic spine and the small included angle between the longitudinal axis of the pedicle and the sagittal plane, it is difficult for the pedicle approach to reach the target with a large lateral angle. These reasons may be causing the amount of bone cement injected in the extrapedicular kyphoplasty group to be usually less than the transpedicular kyphoplasty group. The pool analysis also suggests that there is no difference between the extrapedicular kyphoplasty group and the transpedicular kyphoplasty group with postoperative VAS and ODI scores. These results confirm that both extrapedicular kyphoplasty and transpedicular kyphoplasty can improve function and ease the pain of patients.

5. Limitations

There are several limitations in this meta-analysis. First, the search for studies those published in Chinese, so it may be difficult for English readers to assess. Second, several articles were excluded because they did not meet our inclusion criteria, so it is hard to conduct a global summary of all the evidence. Third, there was a high risk of bias attributable to the lack of blinding of participants and personnel due to both being involved directly in the treatment.

6. Conclusion

Although there is controversy, this systematic review comparing the extrapedicular approach kyphoplasty and the transpedicular approach kyphoplasty for treating OVCs demonstrates that the two minimally invasive procedures, extrapedicular approach kyphoplasty, are superior to the transpedicular approach kyphoplasty for less radiology exposure time, less cement volume, and a lower leakage rate. But in the future, large-volume, well-designed RCTs with extensive follow-up are awaited to confirm and update the findings of this analysis.

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Disclosure statement

The authors declare no conflict of interest.

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Synthesis of the Best Evidence for Perioperative Pain Administration in Patients Having Total Hip Prostheses

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Abstract: *Objective:* A methodical compendium of the best evidence on the management of pain in the Perioperative phase in patients undergoing total hip arthroplasty to offer evidence-based support for practice in the clinic. *Methods:* In the 6S pyramid model, we looked for guidelines, clinical decisions, expert consensus, evidence summaries, recommended practices, and systematic reviews of perioperative pain management in total hip arthroplasty patients in domestic and international guideline websites, websites of professional associations, and both English and Chinese data banks from December 16, 2014, to December 16, 2024, to obtain detailed statistics on perioperative patient pain monitoring and management in total hip joint arthroplasty patients, and to check the results of these results from the following sources. Literature quality assessment, evidence extraction, and summarization were done independently by 2 researchers. Literature quality assessment, evidence extraction, and summarization were done independently by 2 researchers. *Results:* A total of 20 papers were included, including 2 clinical decisions, 8 guidelines, 6 expert consensus, 3 Meta-analyses, and 1 randomized controlled trial. Forty pieces of evidence were summarized in six areas: preoperative preparation, principles of analgesic regimen development, choice of anesthesia, pharmacological analgesic modalities, nonpharmacological analgesic modalities, and post-discharge pain management. *Conclusion:* Perioperative pain management for THA patients is necessary, and healthcare professionals can refer to the summarized evidence to improve patients' perioperative pain, increase their postoperative exercise compliance, and accelerate the postoperative recovery process.

Keywords: Total hip replacement; Perioperative pain; Pain management; Summary of evidence

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1. Introduction

Total Hip Arthroplasty (THA) is an effective treatment for end-stage hip diseases ^[1,2]. With the intensification of population aging, the demand for THA has shown a continuous upward trend ^[3,4]. Although THA yields

favorable surgical outcomes, perioperative pain remains a major challenge for patients and a critical factor affecting prognosis^[5]. As the anesthetic effects gradually wear off postoperatively, patients often experience pain at the surgical incision site. Studies indicate that 27%-38% of patients suffer from persistent pain after surgery, which interferes with daily activities, leads to sleep disturbances, and reduces quality of life^[6,7]. Moreover, to alleviate the pressure on healthcare systems and medical institutions caused by the increasing volume of THA procedures, China is promoting same-day THA surgery. However, currently, only a few hospitals can safely perform such procedures under effective analgesia^[8]. Therefore, strengthening perioperative pain management for THA is crucial. Although some evidence on pain management exists, it spans a wide range of conditions and remains fragmented and unfocused for THA patients. Most published studies address only a single aspect of pain management (e.g., non-pharmacological therapies) and are outdated, failing to incorporate recent evidence from the past few years. Thus, this study systematically consolidates evidence on perioperative pain management for THA over the past decade based on existing research, aiming to provide a reference for healthcare professionals in developing perioperative pain management protocols for THA patients. This study has been registered with the Fudan University Center for Evidence-Based Nursing (Registration No.: ES20246663).

2. Data and methods

2.1. Formulating the evidence-based question

The evidence-based question was established based on PIPOST^[9]:

- (1) P (Population): Target population for evidence application – THA patients;
- (2) I (Intervention): Intervention methods – perioperative pain management measures;
- (3) P (Professional): Evidence users – healthcare professionals or patients;
- (4) O (Outcome): Outcome measures – degree of pain relief;
- (5) S (Setting): Settings for evidence application – hospitals, rehabilitation centers, etc.;
- (6) T (Type of Evidence): Types of evidence – clinical decisions, guidelines, expert consensus, evidence summaries, systematic reviews, etc.

2.2. Literature search strategy

Based on the “6S” pyramid model, a systematic search was conducted across the following databases and websites: UpToDate, BMJ, WHO, International Guideline Collaboration Network, Canadian Ontario Registered Nurses Association website, Scottish Intercollegiate Guidelines Network, New Zealand Guidelines Group, National Guideline Clearinghouse (USA), Medlive Guidelines Network, Australia JBI Evidence-Based Healthcare Database, UK National Institute for Health and Care Excellence (NICE) Guidelines Network, Cochrane Library, EMBASE, CNKI, Wanfang Database, VIP Database, Chinese Biomedical Literature Database (CBM), CINAHL, PubMed, Web of Science, American Academy of Orthopaedic Surgeons (AAOS), American Association of Hip and Knee Surgeons (AAHKS), International Association for the Study of Pain (IASP), and Chinese Orthopaedic Association (COA).

The Chinese search terms included: “total hip arthroplasty, hip arthroplasty, hip prosthesis implantation, hip fracture, femoral neck fracture,” “pain, pain management, pain intervention,” and “guidelines, expert consensus, clinical decision-making, evidence summary, systematic review, Meta-analysis.” The English search terms were: “total hip arthroplast / total hip replacement / hip fracture / femoral neck fracture,” “pain/ache / pain management

/ pain intervention,” and “guideline / consensus / best practice / systematic review / meta-analysis / evidence summary / randomized controlled trial.” Since guidelines are typically updated every five years ^[10], the search timeframe was set from December 16, 2014, to December 16, 2024.

2.3. Literature inclusion and exclusion criteria

Inclusion criteria:

- (1) Population: Patients undergoing total hip arthroplasty (THA);
- (2) Content: Studies related to pain management in THA;
- (3) Study types: Clinical decision-making, guidelines, expert consensus, evidence summaries, systematic reviews, etc.

Exclusion criteria:

- (1) Literature for which full text was unavailable;
- (2) Non-Chinese or non-English literature;
- (3) Literature rated as Grade C in quality assessment ^[11].

2.4. Literature quality assessment

- (1) Clinical decisions & evidence summaries: Evaluated using the CASE (Critical Appraisal Skills Programme for Evidence Summaries) tool ^[12].
- (2) Guidelines: Assessed using the AGREE II (Appraisal of Guidelines for Research & Evaluation II) instrument ^[13]. Based on standardized domain percentages, guidelines were classified as Grade A (strong recommendation), Grade B (weak recommendation), or Grade C (not recommended). Intraclass correlation coefficient (ICC) was used to assess inter-rater reliability between two researchers.
- (3) Expert consensus: Evaluated using the JBI (Joanna Briggs Institute) Critical Appraisal Checklist for Text and Opinion Papers (2016) ^[14].
- (4) Systematic reviews: Assessed using the JBI Critical Appraisal Checklist for Systematic Reviews (2016) ^[15].
- (5) Randomized controlled trials (RCTs): Evaluated using the Cochrane Risk of Bias Tool ^[16]. Two researchers independently conducted the quality assessments. Discrepancies were resolved through discussion or adjudication by a third researcher.

2.5. Evidence extraction and synthesis

Two researchers thoroughly reviewed the included literature, extracted relevant evidence, and synthesized the findings. The JBI Evidence Hierarchy (2014) ^[17] was used to initially classify evidence into Levels 1–5, followed by final grading using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) system to adjust for evidence quality. The JBI FAME (Feasibility, Appropriateness, Meaningfulness, and Effectiveness) framework was applied to determine Grade A (strong) or Grade B (weak) recommendations.

3. Results

3.1. Basic characteristics of included literature

A total of 5522 articles were retrieved, and 20 articles ^[18–37] were included after screening. The basic characteristics of the included literature are shown in **Table 1**.

Table 1. Basic characteristics of included literature ($n = 20$)

Included literature	Year	Source	Type	Topic focus
Edward R Mariano	2024	UpToDate	Clinical Decision	Acute pain management in adults
Enneking et al.	2024	UpToDate	Clinical Decision	Anesthesia for orthopedic trauma surgery
NICE	2020	NICE	Guideline	Joint replacement: hip, knee and shoulder
Hannon et al.	2022	AAOS	Guideline	Corticosteroids in Total Joint Arthroplasty
Anger et al.	2021	IASP	Guideline	PROSPECT guideline for total hip arthroplasty: a systematic review and procedure-specific postoperative pain management recommendations
Fillingham et al.	2020	AAOS	Guideline	Acetaminophen in Total Joint Arthroplasty
Hannon et al.	2020	AAOS	Guideline	Opioids in Total Joint Arthroplasty
Hannon et al.	2022	AAOS	Guideline	Ketamine in Total Joint Arthroplasty
Fillingham et al.	2020	AAOS	Guideline	Nonsteroidal Anti-Inflammatory Drugs in Total Joint Arthroplasty
Hannon et al.	2022	AAOS	Guideline	Periarticular Injection in Total Joint Arthroplasty
Shen Bin et al.	2016	Yimaitong	Expert Consensus	Accelerated Rehabilitation of Hip and Knee Arthroplasty in China - Expert Consensus on Perioperative Pain and Sleep Management
Zhou Zongke et al.	2016	Yimaitong	Expert Consensus	Accelerated Rehabilitation of Hip and Knee Arthroplasty in China - Expert Consensus on Perioperative Management Strategies
Chinese Geriatrics Association	2021	Yimaitong	Expert Consensus	Expert consensus on ERAS in hip/knee replacement perioperative care
Yao Xinmiao et al.	2017	Yimaitong	Expert Consensus	Chinese medicine orthopedics and traumatology clinical diagnosis and treatment guideline-expert consensus on perioperative rehabilitation of artificial hip replacement
Lei Guanghua et al.	2024	Yimaitong	Expert Consensus	Chinese expert consensus on clinical practice of daytime hip arthroplasty
Tian Hongtao et al.	2023	Yimaitong	Expert Consensus	Expert consensus on perioperative management of day surgery for hip and knee replacement in China
Hu et al.	2022	Web of Science	Meta-analysis	Efficacy of quadratus lumborum block for post-THA analgesia
Yang Min et al.	2022	VIP	Meta-analysis	Meta -analysis of postoperative outcomes of patients undergoing hip arthroplasty with transcutaneous electrical acupoint stimulation
Li et al.	2022	Web of Science	Meta-analysis	Non-pharmaceutical treatments to relieve pain or reduce opioid analgesic intake and improve quality of life after total hip replacement: a meta analysis
Steiness et al.	2024	Web of Science	RCT	Non-opioid analgesic combinations following total hip arthroplasty (RECIPE): a randomised, placebo-controlled, blinded, multicentre trial

3.2. Evaluation results of literature quality

3.2.1. Quality evaluation of included clinical decisions

This study ultimately included two clinical decision papers^[18,19]. Except for item 4, “Is the search transparent and comprehensive?” and item 5, “Is the grading of evidence clear?”, which were evaluated as “No”, all other evaluation items were rated as “Yes”. The literature quality is high and was approved for inclusion.

3.2.2. Quality evaluation of included guidelines

In this study, a total of 8 guidelines^[20–27] were finally included. The ICC of the two researchers was > 0.750 , indicating good agreement, and thus they were included. The quality evaluation results are shown in **Table 2**.

Table 2. Quality evaluation results of included guidelines

Guideline	Standardized percentage (%) of scores in each field						$\geq 60\%$ Domains (n)	$\leq 30\%$ Domains (n)	Grade	ICC
	Scope & Purpose (%)	Stakeholder Involvement (%)	Rigor (%)	Clarity (%)	Applicability (%)	Editorial Independence (%)				
NICE	75.00	83.33	63.54	97.22	75.00	50.00	4	0	A	0.968
Hannon et al.	55.56	36.11	38.54	91.67	22.92	100.00	2	1	B	0.946
Anger et al.	75.00	61.11	61.46	91.67	37.50	100.00	5	0	B	0.759
Fillingham et al.	66.67	58.33	64.58	86.11	43.75	87.50	4	0	B	0.845
Hannon et al.	69.44	72.22	61.46	97.22	66.67	100.00	6	0	A	0.850
Hannon et al.	69.44	72.22	35.42	91.67	27.08	87.50	4	1	B	0.973
Fillingham et al.	72.22	77.78	45.83	88.89	47.92	70.83	4	0	B	0.805
Hannon et al.	80.56	83.33	34.38	77.78	35.42	83.33	4	0	B	0.955

3.2.3. Quality evaluation of included expert consensus

A total of 6 expert consensus papers^[28–33] were included in this study. Except for one paper^[28] where items 4 and 5 were evaluated as “No” and item 6 as “Unclear”, three papers^[30,32,33] where item 6 was evaluated as “Unclear”, one paper^[29] where item 6 was evaluated as “No”, and one paper^[31] where items 2 and 6 were evaluated as “No”, all other evaluation items were rated as “Yes”. After the discussion, all papers were included.

3.2.4. Quality evaluation of included meta-analyses

This study included 3 meta-analyses^[34–36]. Two meta-analyses^[34,35] received “Yes” for all evaluation items. One meta-analysis^[36] received “No” for item 1, “Is the proposed evidence-based question clear and specific?” and item 9, “Has the possibility of publication bias been assessed?”, but “Yes” for all other items. The overall quality of the literature is high, and all were included.

3.2.5. Quality evaluation of included randomized controlled trials

This study included one randomized controlled trial^[37], and all evaluation results for each item were “low risk,” indicating high quality of the literature, which was therefore included.

3.3. Evidence summary and classification

Finally, 40 pieces of best evidence were summarized from six aspects: preoperative preparation, principles of

analgesic plan development, selection of anesthesia methods, pharmacologic analgesia, non-pharmacologic analgesia, and pain management after discharge. See **Table 3** for details.

Table 3. Summary of best evidence for perioperative pain management in THA patients

Evidence theme	Evidence content	Evidence level	Recommendation grade
Preoperative Preparation			
1. Patient Assessment	Assess the patient's age, physical and mental condition, medical history, fear/anxiety levels, substance use disorders, pain treatment history, and long-term medication use ^[18] . Older patients should have stabilized physiological status before surgery ^[19] .	1a	A
2. Pain Assessment	Evaluate joint pain severity and pain tolerance based on medical history and prior medication use ^[28] .	2a	A
3. Pain Assessment Tools	Routinely use the Numeric Rating Scale (NRS) and Visual Analog Scale (VAS). The Defense and Veterans Pain Rating Scale (DVPRS) may also be used. For children and nonverbal adults, use the Faces Pain Scale ^[18] .	1a	A
4. Health Education	Educate patients and families about analgesic plans ^[18] , surgical procedures, potential pain, and preventive measures ^[28] .	1a	A
5. Preoperative Counseling	Preoperative discussions can alleviate patient anxiety and establish a good physician-patient relationship ^[18] .	1a	A
Principles of Analgesia Planning			
6. Perioperative Analgesia	Optimal perioperative analgesia should balance pain control with functional goals while avoiding preventable complications ^[18] .	1c	A
7. Initial Analgesia Strategy	Begin with non-pharmacological therapies, non-opioid analgesics, and appropriate local/regional techniques to avoid excessive perioperative opioid use ^[18] .	1a	A
8. Multimodal Analgesia	Use preoperative multimodal analgesia with reduced opioids ^[18,19] and postoperative low-opioid multimodal strategies ^[19] .	1a	A
9. Patient Education Materials	Provide written materials (~6th-grade reading level) explaining perioperative multimodal analgesia ^[18] .	1c	B
10. Multimodal Components	Typically includes oral/injectable drugs + nerve blocks + peri-incisional injections, possibly combined with neuraxial anesthesia and patient-controlled analgesia (PCA). Avoid duplicate drug classes ^[28] .	2b	A
11. Preventive & Personalized	Use preventive and individualized analgesia ^[18] .	1a	A
12. Efficacy Monitoring	Regularly assess and adjust preventive analgesia ^[28] .	5b	A
13. Side Effect Monitoring	Monitor pain and treatment side effects, adjusting analgesia as needed ^[18] .	1b	A
Anesthesia Selection			
14. Pre-Anesthesia Evaluation	Establish a dedicated anesthesia clinic for THA outpatients. On surgery day, anesthesiologists should reassess based on prior evaluation ^[33] .	5b	A
15. Regional/General Anesthesia	For primary THA, use regional or general anesthesia with local infiltration analgesia (LIA). Avoid combining nerve blocks with regional/general anesthesia ^[20] .	1c	A
16. Neuraxial Anesthesia	Recommend neuraxial anesthesia for THA unless contraindicated ^[18,19] .	1c	A
17. Local Anesthetic Injection	For primary THA, inject local anesthetics (e.g., ropivacaine) around the joint, possibly with corticosteroids (e.g., betamethasone) and low-dose epinephrine (100–300 µg) ^[27,30] .	1b	A
18. Nerve Block Selection	For THA, lumbar plexus block is preferred ^[28,30] .	5b	B
19. Targeted Nerve Coverage	Post-THA nerve blocks should cover sensory nerves of the anterior hip capsule and acetabulum (e.g., femoral and obturator nerve branches) ^[19] .	1b	A

Table 3 (Continued)

Evidence theme	Evidence content	Evidence level	Recommendation grade
20. Positioning Caution	During nerve blocks or epidural analgesia, position patients carefully to avoid hip subluxation ^[19] .	1a	A
Pharmacological Analgesia			
21. Preoperative Medications	Use acetaminophen or selective COX-2 inhibitors ^[28-30] . For insomnia/anxiety, consider sedatives or anxiolytics ^[28,29] .	5b	A
22. Preemptive Analgesia	Outpatient THA patients should take oral COX-2 inhibitors 2 hours preoperatively ^[33] .	5b	B
23. Intraoperative Steroids	Intravenous dexamethasone reduces pain but may elevate blood glucose—use cautiously in diabetics ^[18,21] .	1a	B
24. Postoperative NSAIDs	Post-anesthesia, administer selective COX-2 inhibitors or NSAIDs IV/IM based on pain levels ^[22,28,30] .	2a	A
25. NSAID Caution	Avoid traditional NSAIDs in patients with peptic ulcers, long-term steroid/aspirin use; prefer COX-2 inhibitors ^[28] .	5b	B
26. PCA & Anxiolytics	Postoperatively, consider PCA ^[29-31] and anxiolytics ^[28] .	5b	A
27. Outpatient PCA Avoidance	Avoid IV/epidural PCA for outpatient THA ^[33] .	2b	A
28. Opioid Management	For severe pain, adjust analgesics or add weak opioids (preferably oral). Monitor closely to avoid dependence ^[18,28-30] .	5b	A
29. Ketamine Use	Low-dose IV ketamine may reduce pain but has side effects; use selectively ^[18,25] .	1c	B
30. Topical Agents	Options include NSAID gels/patches and opioid patches ^[28] .	5b	B
31. Pain Reassessment	Regularly assess resting/movement pain and adjust analgesics to tolerable levels ^[29] .	5b	B
32. Gabapentinoids	Avoid routine use of gabapentinoids for pain relief ^[18,22] .	1b	A
33. Postoperative Monitoring	Monitor pain relief, functional status, and side effects; adjust analgesia accordingly ^[18] .	1a	A
Non-Pharmacological Analgesia			
34. Preoperative Acupressure	Preoperative auricular acupressure or distal acupuncture may improve pain tolerance ^[30] .	5b	B
35. Intraoperative Acupuncture	Intraoperative distal acupuncture may be combined ^[30] .	5b	B
36. Postoperative Cryotherapy	Apply cold therapy, limb elevation, and lymphatic drainage postoperatively ^[30] .	5b	B
37. Acupuncture Points	Postoperative auricular points: Shenmen, Subcortex, Hip, Ashi. Body acupuncture points: BL23, GB29, GB30, GB34, BL40, ST34, ST36, BL57, BL60, Ashi ^[31] .	1c	B
38. Transcutaneous Stimulation	Transcutaneous electrical acupoint stimulation may reduce postoperative pain ^[35] .	2c	B
Post-Discharge Pain Management			
39. Oral Medications	Primary use of selective COX-2 inhibitors or NSAIDs ^[28] .	1a	A
40. Opioid Tapering	Opioid use post-discharge should involve shared decision-making among prescribers, patients, and caregivers, with clear tapering instructions ^[18] .	1a	A

4. Discussion

4.1. Good preoperative preparation is a necessary condition for successful surgery

Patient evaluation is the primary principle of perioperative pain management. Conducting a comprehensive evaluation of patients before surgery not only helps to understand their overall condition but also facilitates the smooth operation of the surgery. Pain evaluation, in particular, assists medical staff in understanding the degree and tolerance of patients' joint pain, thereby enabling the development of more effective analgesic plans. It is important to note that validated pain assessment tools should be used. Currently, the commonly used tools include the Numeric Rating Scale (NRS) and the Visual Analog Scale (VAS). Since THA patients often require evaluation of the severity of pain and its impact on functional status, the Defense and Veterans Pain Rating Scale (DVPRS) can be employed^[18]. Additionally, for children and adults who cannot communicate verbally, the Faces Pain Scale can be used, and it is recommended to consistently use the same assessment tool during the perioperative period^[18]. However, these assessment tools rely on self-reporting by patients and may be influenced by cultural backgrounds and individual differences, so their limitations should be considered in practical applications. Furthermore, THA patients often experience anxiety and nervousness. Preoperative conversations and educating patients and their families about the surgical process and postoperative recovery plan can alleviate these negative emotions and facilitate the establishment of a good doctor-patient relationship^[18,28].

4.2. Rational analgesic regimens and effective anesthesia methods are key to managing perioperative pain in THA

Optimal perioperative analgesic regimens should ensure effective pain relief, achieve functional goals, and avoid various complications. Among them, multimodal analgesia, as a comprehensive analgesic approach, not only reduces over-reliance on single-class drugs, especially opioids, but also shortens the onset time of drugs and prolongs the duration of analgesia^[18,28]. It has become the primary analgesic method for THA surgery, requiring multidisciplinary collaboration and strict management processes during implementation, with attention to avoiding repeated use of similar drugs. Preventive analgesia can prevent nociceptive sensitization caused by noxious stimuli at various stages of the perioperative period. Reasonable preventive analgesia can significantly reduce postoperative pain and decrease the amount of opioid medication used^[38]. However, due to individual differences in patients' responses to pain and analgesic drugs, it is necessary to evaluate the efficacy of preventive analgesic drugs on time and adjust medications accordingly.

Regarding the choice of anesthesia methods, it is recommended to establish a dedicated anesthesia assessment clinic for THA day surgery. On the day of surgery, the anesthesiologist should refer to the clinic evaluation results and re-evaluate the patient's condition. This dual assessment approach can identify potential risk factors and develop safer anesthesia plans for outpatient surgical patients. Secondly, when selecting anesthesia methods, it is necessary to consider both patient and surgical factors comprehensively. Regional anesthesia or general anesthesia combined with local infiltration analgesia (LIA) is often used^[20], which can significantly improve the analgesic effect. For patients without contraindications and special conditions, spinal anesthesia is recommended^[18,19]. Local anesthetics can also be injected around the joint to reduce postoperative pain^[27,30]. When performing nerve blocks or epidural analgesia postoperatively, operators should carefully position the patient to prevent hip subluxation^[19].

4.3. Drug and non-drug analgesia are key components of perioperative pain management

Perioperative drug analgesia for THA typically involves the use of selective COX-2 inhibitors or NSAIDs^[28-30]. Additionally, multiple intravenous injections of dexamethasone during surgery can reduce pain, but may

increase postoperative blood sugar levels, so diabetic patients should use it with caution. Currently, there is a lack of research on the specific effects of dexamethasone on joint replacement patients with diabetes, and further exploration is needed on the safety, dosage, and frequency of glucocorticoid administration for this patient population^[21]. For patients with a history of peptic ulcer or long-term use of glucocorticoids or aspirin, traditional NSAIDs should be used with caution, and selective COX-2 inhibitors are recommended^[28]. Postoperatively, patient-controlled analgesia can be selected as needed^[28–30]. However, it should be noted that self-controlled analgesia pumps are not recommended for patients undergoing daytime hip replacement surgery^[33], as these devices require longer monitoring and care, which is incompatible with the fast turnaround characteristics of daytime surgery. External medications can also be selected as needed^[28]. Postoperatively, patients' pain relief, functional status, and analgesic side effects should be monitored, and analgesia plans should be adjusted accordingly^[18].

Non-drug analgesic interventions during the perioperative period^[30–31,35] include acupuncture, auricular acupressure, transcutaneous electrical nerve stimulation, postoperative ice packs, and limb elevation. However, these measures have only been initially proven to reduce post-THA pain, and there is a lack of strong evidence to support their use, which limits their application to some extent. Future research is needed to develop more rigorous and standardized non-drug pain interventions for THA patients during the perioperative period.

4.4. Post-discharge pain management for THA: Oral medication as the mainstay, emphasizing regular follow-up and personalized guidance

Due to the short hospital stay for THA patients, most patients recover at home after discharge. Oral medication is more convenient and patient compliance is higher. Therefore, oral medication is the primary method for post-discharge analgesia, mainly selective COX-2 inhibitors or NSAIDs^[28]. The decision to use opioid medication is made jointly by the prescribing doctor, patient, and caregiver, adjusted according to the patient's condition, with clear guidance on reduction and discontinuation^[18]. Additionally, primary hospitals lack dedicated rehabilitation nurses, and patients often lack professional rehabilitation guidance after discharge. As recovery progresses, the level and nature of postoperative pain may change, requiring regular assessment and adjustment of analgesic regimens by medical staff. Therefore, regular follow-up and providing personalized analgesia and rehabilitation guidance are crucial. Furthermore, exploring more non-pharmacological interventions to develop more efficient, safe, and economical outpatient pain management strategies can improve THA patients' rehabilitation effectiveness and quality of life.

4.5. Innovations and limitations of this study

This study focuses on a specific topic, summarizing relevant content from various guidelines, covering perioperative pain management, incorporating the latest evidence, and adding content related to daytime THA patients. However, as daytime THA is still in its infancy stage in China^[39], there are few related studies and published papers, and the available evidence is limited. Future research should consider China's socio-medical conditions, studying the necessary conditions, clinical efficacy, and economic benefits of daytime THA to provide guidance for domestic practices.

5. Conclusion

This study summarizes the relevant evidence for perioperative pain management in THA patients, providing a

basis for medical staff to formulate relevant plans. When applying these findings, medical staff should consider domestic clinical situations, the actual medical environment, patient wishes and preferences, and fully evaluate the feasibility and suitability of each evidence item to carry out evidence-based transformation and application.

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Exploring the Advantages of DWI Integrated with DCE Technology in the Diagnosis of AS-SIJ

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Abstract: *Objective:* To observe the diagnostic advantages of MR diffusion-weighted imaging (DWI) integrated with dynamic contrast-enhanced (DCE) technology in ankylosing spondylitis (AS) with sacroiliac joint lesions (SIJ). *Methods:* 58 patients with AS-SIJ were selected and diagnosed with conventional MRI and DWI integrated with DCE, respectively, and the diagnostic differences were compared. *Results:* During the diagnosis of patients with AS-SIJ, the disease was graded. The detection rate of grade 1 was higher with DWI integrated with DCE, while there was no difference in the detection rates of the other grades between the two techniques. The detection rates of bone marrow edema, bone cystic changes, and L5-S1 articular process lesions were higher with DWI integrated with DCE. There was no difference in adverse reactions between the two diagnostic techniques. *Conclusion:* DWI integrated with DCE technology has a high early detection rate for AS-SIJ. It is recommended to use DWI integrated with DCE technology as the preferred diagnostic scheme to improve diagnostic accuracy.

Keywords: MR diffusion-weighted imaging; Ankylosing spondylitis; Sacroiliac joint lesions; Detection rate

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1. Introduction

Ankylosing spondylitis (AS) is a clinically common rheumatic immune disease and chronic inflammatory lesion that affects various parts, including the spine, peripheral joints, and sacroiliac joints. The main pathogenic factors include genetics, immunity, and infection. Early clinical symptoms of patients mainly include pain, morning stiffness, and fatigue in the lower back, hips, sacroiliac region, and groin, accompanied by peripheral arthritis. Some patients also experience extra-articular symptoms such as intestinal, lung, and eye abnormalities, while severe cases may involve spinal deformity or rigidity ^[1]. Clinical studies suggest that the sacroiliac joint (SIJ) is an early lesion of AS, and early diagnosis and effective therapeutic intervention of such lesions can lead to a high detection rate of AS. Imaging techniques, especially MRI, are commonly used to diagnose sacroiliac joint lesions in AS ^[2]. Pathological changes such as synovitis, inflammatory cell proliferation, and bone marrow fibrosis are common in AS-SIJ patients, affecting the diffusion rate of water molecules and elevating DWI signals.

DWI technology, which does not require the use of contrast agents, can observe fine tissue structures with high precision and has a high detection rate for early inflammation or small lesions. DCE, which requires the injection of a contrast agent, can monitor signal changes in the lesion area and generate a time-signal intensity curve (TIC). The volume transfer constant of the contrast agent (K_{trans}) can reflect the vascular permeability of the lesion area and assess the degree of inflammation, while indicators such as the extracellular volume fraction (V_e) can evaluate edema and predict the progression of fibrosis. Therefore, this study selected 58 AS-SIJ patients to evaluate the advantages of applying DWI integrated with DCE technology.

2. Materials and methods

2.1. General information

Fifty-eight patients with AS-SIJ were selected from January 2022 to June 2024, including 35 males and 23 females, aged between 29 and 38 years old, with an average age of (33.19 ± 3.75) years old. The disease duration ranged from 6 months to 4 years, with an average of (2.47 ± 0.45) years.

2.2. Methods

- (1) Instrumentation: A 3.0T MR scanner (750W) produced by GE was selected, using a body phased array coil.
- (2) Conventional MRI: Patients were examined in a supine position, and various parameters were adjusted based on the needs of patients with AS sacroiliac joint lesions. Images of STIR sequence, T2WI sequence, T1WI sequence, FS-T1WI sequence, FS-T1WI sequence, and 3D FLASH sequence were acquired. If patients were suspected of having active lesions, enhanced scanning-related operations were performed.
- (3) DWI Integrated with DCE Technique

During DWI scanning, the b-value was set at 800 s/mm^2 . Gadoteridol was injected intravenously through the elbow vein, and scanning was started. A high-pressure injector was used, with an injection flow rate set at 2 mL/s and a dose of 0.1 mmol/kg . Then, 20 mL of normal saline was injected. A total of 32 phases were acquired continuously without an interval, each with a duration of 10s , resulting in a total scanning time of 320s . For the axial plane, under the FSE-T1WI sequence, the TR value was set at 787 ms , the TE value at 15 ms , the field of view at 240240 mm^2 , the slice thickness at 4 mm , the matrix at 320256 , and acquisition was performed twice. Under the FRFSE-T2WI sequence, the TR value was set at 5225 ms , the TE value at 68 ms , the field of view at 240240 mm^2 , the slice thickness at 4 mm , the matrix at 320256 , and acquisition was performed twice. Under the DWI sequence, the TR value was set at 4000 ms , the TE value at 95 ms , the field of view at 360360 mm^2 , the slice thickness at 4 mm , the matrix at 128130 , and acquisition was performed six times. Under the DCE sequence, the TR value was set at 3.8 ms , the TE value at 1.2 ms , the field of view at 380304 mm^2 , the slice thickness at 4mm , the matrix at 256160 , and acquisition was performed once. For the coronal plane, under the FSE-T1WI sequence, the parameters were set at 639 ms , 15 ms , 240240 mm^2 , 3 mm , 320192 , with a slice gap of 1mm and acquisition performed twice. Under the FRFSE-T2WI sequence, the parameters were set at 1575 ms , 30 ms , 240240 mm^2 , 3 mm , 320256 , with a slice gap of 1 mm and acquisition performed twice. After acquiring the above images, they were transferred to a workstation where parameter maps were reconstructed using professional software, and multiple data points were measured. Post-processing of DCE images included

motion correction, adjustment of image swing differences, and removal of invalid phases. The diagnostic images were comprehensively observed to detect SIJ conditions. If a definite lesion was present, a region of interest (ROI) was placed in the center of the lesion. If no lesion was found, ROIs were placed in the central regions of both sides of the sacroiliac joint (sacral and iliac sides), ensuring that the area of each ROI was 25 mm². The apparent diffusion coefficient (ADC) value was measured from the ADC map, and ROI perfusion parameters, including K_{trans} , V_e , and the ratio of extracellular space volume to intravascular volume (K_{ep}) were obtained.

2.3. Statistical methods

Data were analyzed using SPSS 23.0 software. Measurement data mean \pm standard deviation (SD) were tested using the t-test, and enumeration data (%) were tested using the χ^2 test. A P -value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of detection rates of AS-SIJ at different levels by conventional MRI and DWI integrated with the DCE technique

As shown in **Table 1**, in the graded diagnosis of AS-SIJ, the detection rate of grade 1 by DWI integrated with the DCE technique was higher than that by conventional MRI ($P < 0.05$). There were no significant differences in the detection rates of other grades between the two methods ($P > 0.05$).

3.2. Comparison of detection rates of typical signs of AS-SIJ by conventional MRI and DWI integrated with DCE technique

As shown in **Table 2**, the detection rates of subchondral bone cystic changes, bone marrow edema, and L5-S1 articular process lesions by DWI integrated with DCE technique were higher than those by conventional MRI. The detection rates of joint erosion and joint surface hyperplasia and sclerosis were also higher than those by conventional MRI ($P < 0.05$).

3.3. Comparison of diagnostic results of DWI integrated with DCE technique for different disease activity levels

The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was used to evaluate disease activity. The stable phase was defined as a BASDAI score of no more than 4, with 22 cases; the active phase was defined as a BASDAI score of no less than 6, with 32 cases. For patients with scores exceeding 4 but below 6, if the erythrocyte sedimentation rate exceeded 20 mm/h or C-reactive protein exceeded 30 mg/L, they were considered to be in the active phase, with 3 cases. The remaining 1 case was in the stable phase.

The ADC values were $(1.16 \pm 0.53)10^{-3}$ mm²/s for patients in the active phase and $(0.81 \pm 0.27)10^{-3}$ mm²/s for patients in the stable phase ($t = 3.316$, $P = 0.002$). The K_{trans} values in the active phase were (0.77 ± 0.26) min⁻¹, and (0.20 ± 0.06) min⁻¹ in the stable phase ($t = 12.525$, $P = 0.000$). The V_e values in the active phase were (0.47 ± 0.10) , and (0.30 ± 0.05) in the stable phase ($t = 8.582$, $P = 0.000$). The K_{ep} values in the active phase were (1.08 ± 0.52) min⁻¹, and (0.54 ± 0.10) min⁻¹ in the stable phase ($t = 6.003$, $P = 0.000$).

3.4. Comparison of the incidence of adverse reactions

Both groups successfully completed the examination without any intolerable adverse reactions during the process.

4. Discussion

Relevant survey data statistics show that the incidence rate of AS in China is about 0.5%, with a higher incidence in males than in females. The majority of patients are young and middle-aged, and the causes of the disease include genetics, environment, immunity, and infection. The main clinical manifestations of patients are inflammatory low back pain, peripheral arthritis, and enthesitis. Some patients have multiple extra-articular symptoms, which can have a more severe impact on daily life [3]. Based on clinical practice analysis, the pathological feature of early-stage AS is SIJ. This type of lesion occurs earlier than tendonitis and ligament attachment points, and is prone to complications such as synovitis and osteomyelitis in the early stage of the disease. Further analysis reveals that SIJ originates from the bone marrow, and during the pathological process, pannus formation occurs, which can lead to lesions in the subchondral plate, ultimately resulting in damage to the cartilage. Therefore, early qualitative analysis of sacroiliac joint lesions and improving the early detection rate of AS are extremely important to shorten the treatment time. In addition, the occurrence of AS-SIJ can cause patients to experience dull pain in the hips and lower back, with increased pain after activity and at night, while some patients experience pain relief during rest. When patients sit for long periods or wake up in the morning, they are prone to develop stiffness in the sacroiliac joint, which is relieved by appropriate activity. In severe cases, the pain radiates to the back of the thigh but does not extend beyond the knee.

The diagnostic approach for AS-SIJ primarily relies on imaging techniques, with MRI being a commonly used examination method. The main advantage of MRI is its high density resolution, which provides better visualization of soft tissues [4]. DWI (Diffusion-Weighted Imaging) can evaluate the movement of water molecules within living tissues, allowing for highly sensitive observation of pathological changes. It is particularly effective in detecting early lesions and pathological processes, and can predict the extent of lesions. In the case of AS-SIJ, the accelerated movement of water molecules in inflamed areas is characterized by enhanced diffusion, resulting in a high signal on DWI. Additionally, increased water content in diseased tissues leads to an elevation in ADC (Apparent Diffusion Coefficient) values. DCE (Dynamic Contrast-Enhanced) imaging can assess tissue perfusion and has strong diagnostic validity for various systems in the body, especially the musculoskeletal system. During the active phase of AS-SIJ, there is an increase in microvascular permeability in the bone marrow tissue below the articular surface, resulting in significant bone marrow enhancement. By utilizing these principles, pathological changes can be effectively detected.

Table 1. Compares the detection rates of AS-SIJ using conventional MRI and the integrated DWI and DCE technique (n/%)

Group	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Conventional MRI (<i>n</i> = 58)	2 (3.4)	9 (15.5)	18 (31.0)	11 (19.0)	10 (17.2)
DWI integrated with DCE (<i>n</i> = 58)	0 (0.0)	19 (32.8)	22 (39.7)	13 (22.4)	12 (20.7)
χ^2 value	2.035	4.707	0.610	0.210	0.224
<i>P</i> -value	0.153	0.030	0.434	0.646	0.635

Table 2. Compares the detection rates of typical signs of AS-SIJ using conventional MRI and the integrated DWI and DCE technique (n/%)

Group	Subchondral bone cysts	Bone marrow edema	L5/S1 facet joint lesions	Joint erosion	Subchondral sclerosis
Conventional MRI (<i>n</i> = 58)	18 (31.0)	35 (60.3)	27 (46.6)	29 (50.0)	32 (55.2)
DWI integrated with DCE (<i>n</i> = 58)	32 (55.2)	46 (79.3)	41 (70.7)	40 (69.0)	44 (75.9)
χ^2 value	6.889	4.951	6.956	4.328	5.494
<i>P</i> -value	0.008	0.026	0.008	0.037	0.019

In this study, for the graded diagnosis of AS sacroiliac joint lesions, DWI combined with DCE technology had a higher detection rate for grade 1 lesions than conventional MRI, while there was no significant difference in the detection rates for other grades between the two methods. Relevant studies have shown that there are significant differences in pathological features among patients with AS sacroiliac joint lesions of different grades. Grade 1 and 2 AS sacroiliac joint lesions can be characterized by inflammatory cell infiltration, involving synovial adjacent tissues, increased synovial thickness, and the local generation of pannus, with some patients experiencing erosion of subchondral bone. Imaging diagnosis of such patients reveals a blurred or interrupted white line in the cortical area of the local articular surface, and a cystic structure with translucent features is observed below the articular surface of the affected limb. At this stage, the bone in the diseased area of the articular surface has been destroyed, resembling the skin of a bitter melon, and bone cortical defects can be observed in imaging. In patients with grade 3 AS sacroiliac joint lesions, the ligamentous tissue, synovial tissue, cartilage, and subchondral bone in the diseased area are all damaged, with severe synovial damage that can easily lead to secondary bone sclerosis. Close observation of the articular surface area reveals damage to the smooth structure, gradual narrowing of the articular space, and gradual sclerosis and hyperplasia of adjacent tissues. Grade 4 patients have relatively severe disease, with lesions involving the synovium and ligaments, severe joint ankylosis, and loss of joint space^[5]. Based on the above analysis, early AS-SIJ does not produce significant bone erosion, with soft tissue erosion as the main pathological feature, and pannus, increased synovial thickness, and inflammatory infiltration of bone adjacent tissues can be observed in the diseased area.

DWI combined with DCE technology has a higher detection rate for typical signs such as subarticular bone cystic degeneration and bone marrow edema than conventional MRI ($P < 0.05$). This is because DWI can detect the liquid components inside the cystic area, making it appear as a high signal. Inflammatory cells and fibrous tissues can affect the local diffusion effect, leading to changes in ADC values. DCE can detect active inflammation near the cystic area, causing leakage of the contrast agent, thus detecting bone cystic degeneration.

The activity of Ankylosing Spondylitis (AS) can be generally evaluated by disease progression, and a commonly used assessment method is the BASDAI score, which utilizes a graded scale to evaluate disease activity. However, this method has limitations in accurately and objectively capturing disease progression trends, and its role in evaluating treatment efficacy is limited. Therefore, it needs to be combined with advanced imaging techniques. Patients in the active phase of the disease have higher K_{trans} , V_e , and K_{ep} values than those in the stable phase ($P < 0.05$). Among these parameters, K_{trans} and K_{ep} can predict microvascular permeability. During the active phase of AS, continuous secretion of inflammatory factors in patients can lead to increased vascular permeability, resulting in a large amount of microvascular blood leaking into the tissue space, thus increasing the aforementioned numerical levels. V_e can evaluate tissue necrosis. During the active phase of AS, patients have obvious necrotic foci in their bone marrow tissue, which can elevate V_e levels. In DWI diagnosis, the ADC value may be interfered with by the parameter *b* value, and is related to tissue

structure and magnetic field uniformity. The diagnostic results of DCE are affected by the accuracy of data processing, scanning procedures, and the pharmacokinetics of the contrast agent, so a single diagnosis has certain defects. Therefore, this study adopts an integrated diagnostic approach that allows quantitative analysis of diagnostic images, eliminating subjective factors of patients, and objectively and comprehensively evaluating the blood perfusion and pathophysiological processes of AS-SIJ, thereby accurately determining the condition ^[6]. However, it should be noted that when AS-SIJ patients undergo DWI-integrated DCE technical diagnosis, it should be clarified whether the patient has any MRI contraindications, such as severe renal insufficiency or metal implants in the body, and patients should be instructed to maintain a steady breathing rate during the examination to prevent motion artifacts. Additionally, during DWI-integrated DCE technology, examination parameters should be adjusted based on the patient's actual physiological and pathological conditions to obtain clear imaging of different sequences. After confirming AS-SIJ, patients should be advised to avoid overexertion, correct poor posture, and actively receive rehabilitation treatment.

5. Conclusion

In summary, the integration of DWI and DCE technology has a better diagnostic effect on AS-SIJ, which can determine the disease grading, detect typical signs, and thus comprehensively grasp the disease status. In addition, the integration of DWI and DCE technology can effectively identify disease activity, screen out the differences in parameters between active and stable periods, obtain quantitative and accurate diagnostic information, and rationalize the follow-up treatment measures for the disease to improve the prognosis as much as possible.

Disclosure statement

The authors declare no conflict of interest.

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Analysis of Morphological Characteristics of Modic Changes in the Lumbar Spine Based on MRI Imaging Omics and Their Association with Low Back Pain

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Abstract: *Objective:* To analyse the MRI imaging characteristics, morphological features, and association with low back pain in different types of Modic changes (MC) of the lumbar spine. Features in different types of Modic changes (MC) in the lumbar spine and their association with low back pain. *Methods:* A retrospective analysis was conducted on the clinical data of 124 patients who underwent lumbar MRI examinations and were diagnosed with Modic changes between March 2024 and February 2025 at a certain hospital. Prospective collection of imaging and clinical data was conducted on 30 patients with different types of lumbar Modic changes and low back pain scores during the same period. Pyradiomics was used to extract MRI morphological and radiomics features in Modic changes, followed by Kruskal-Wallis test, Dunn's test, Mann-Whitney U test, correlation analysis, LASSO regression screening, and validation of differential features. A classification model was constructed using the support vector machine (SVM) algorithm, and heatmap analysis was performed to investigate the correlation between MRI morphological and radiomics features and low back pain scores. *Results:* Among 154 patients without low back pain, 34 were Modic Type I, 62 were Type II, and 58 patients with Modic Type III. A total of 7 morphological features and 19 radiomics features showed significant differences in mean values among the three Modic groups ($P < 0.05$). A Modic classification model based on the differential features was constructed using SVM, with an accuracy rate of 98%. In the correlation analysis, ODI scores were positively correlated with the long-to-short axis ratio and surface area-to-volume ratio of morphological features, and negatively correlated with sphericity and flatness ($P < 0.05$). Additionally, it was positively correlated with the radiomics feature FS_lbp_3D_m1_glszm_ZoneEntropy ($r = 0.380$, $p < 0.05$) and negatively correlated with T1_lbp_3D_m2_glszm_SmallAreaLowGrayLevelEmphasis ($r = -0.423$, $p < 0.05$) and FS_wavelet_LLH_firstorder_90thPercentile ($r = -0.376$, $p < 0.05$). *Conclusion:* Morphological and radiomics features differ among different subtypes of Modic changes (MC). An automatic classification model constructed based on these differential features demonstrates high accuracy, and key features are significantly associated with the low back pain functional disability index.

Keywords: Low back pain; Modic changes; Radiomics; Machine learning

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1. Introduction

Modic changes (MC) in the lumbar spine are characteristic signal abnormalities of the vertebral endplates and adjacent bone marrow on MRI, and are independent risk factors for severe and disabling low back pain. Although studies have shown that Type I MC is significantly associated with nonspecific chronic low back pain, the exact pathological mechanisms and specific associations with pain severity remain unclear. Current studies primarily focus on the presence, classification, and area of MCs, lacking precise quantitative analysis of lesion morphological characteristics, which limits a deeper understanding of the pathological progression of MCs and their pain-inducing mechanisms^[1]. In recent years, the emergence of radiomics has provided a powerful tool for in-depth analysis of medical images. It can high-throughput extract and quantify features such as texture, shape, and intensity distribution that are difficult to identify with the naked eye, thereby revealing potential pathological information. However, there are no studies investigating the morphological differences of lumbar MC using radiomics and exploring the association between these quantitative features and clinical symptoms of low back pain. Given this, the present study aimed to utilise radiomics methods based on conventional MRI sequences of the lumbar spine (T1WI, T2WI, FS), to precisely extract and quantitatively analyse morphological features of lesion regions in different types of MC (Type I vs. Type II). By analysing the relationship between cases where HIZ and Modic changes coexist on MRI and the occurrence of provoked consistent pain, and evaluating the specificity and sensitivity of combining these two features as a diagnostic marker, this study aims to establish a reliable and practical diagnostic method for DLBP^[2]. Additionally, by analysing the pathological changes in different regions of degenerative intervertebral discs represented by the HIZ zone and Modic signs, and combining these findings to study their relationship with DLBP, this study aims to deepen the understanding of the morphological characteristics of MC and its association with low back pain from an imaging quantitative perspective, thereby providing new imaging evidence for exploring the pathological mechanisms and potential therapeutic targets of MC-related low back pain.

2. Materials and methods

2.1. General data

A retrospective analysis was conducted on MRI data from 124 patients with lumbar Modic changes diagnosed between March 2024 and February 2025 at our hospital. Concurrently, 30 patients with lumbar Modic changes of different types and low back pain scores were prospectively enrolled, and their imaging and clinical data were collected. Imaging features were analysed to investigate their association with low back pain scores.

Inclusion criteria: (1) Confirmed Modic changes (Types I–III) by lumbar MRI; (2) Age 18–70 years old, no gender restrictions; (3) Complete T1WI, T2WI, and FS sequence imaging data.

Exclusion criteria: (1) Concurrent vertebral fractures, tumours, infections, or prior lumbar spine surgery; (2) Severe spinal stenosis (sagittal diameter ≤ 10 mm) or nerve root compression causing lower extremity radicular pain; (3) Incomplete key clinical data (e.g., classification records, pain scores) or damaged imaging data; (4) Patients with concomitant rheumatic immune diseases, metabolic bone diseases, congenital lumbar abnormalities, or scoliosis.

2.2. Methods

2.2.1. Modic change classification diagnosis

Assess the type of Modic changes in patients according to the diagnostic criteria for Modic changes in the lumbar

spine, excluding degenerative or infectious secondary changes: Type I: Low signal intensity on T1-weighted images (T1WI) of the endplates and adjacent bone, and high signal intensity on T2-weighted images (T2WI); Type II: High signal intensity on T1WI, and equal/slightly higher signal intensity on T2WI; Type III: Low signal intensity on both T1WI and T2WI.

2.2.2. Grading of lumbar disc degeneration and pain scoring

The degree of degeneration of Modic changes was assessed using the Pfirrmann criteria on T2WI sagittal images of lumbar MRI. Grade I-II was considered normal, and grades III-V corresponded to mild, moderate, and severe degeneration, respectively. The Oswestry Disability Index (ODI) and Visual Analogue Scale (VAS) were used to evaluate low back pain in 30 prospectively enrolled patients. The ODI assesses 10 dimensions of pain intensity, activities of daily living, lifting, walking, sitting, standing, sleep disturbance, sexual activity, social activity, and travel, with each item scored 0–5; VAS assessed pain intensity using a 10-cm scale (0 cm no pain, 10 cm severe pain), with continuous variables supporting parametric tests.

2.2.3. MRI normalisation and ROI segmentation

To eliminate the influence of different scanning devices, all MRI data were subjected to signal intensity normalization. Subsequently, using ITK-SNAP software, regions of interest (ROIs) were delineated on T1-weighted images (T1WI), T2-weighted images (T2WI), and fat-suppressed (FS) sequences for Modic lesions. Given that Modic changes often involve adjacent vertebrae, the ROI was defined within a single spinal functional unit containing the visible lesion and annotated on consecutive cross-sectional images across all relevant sequences. Cases with preliminary ROI delineation were reviewed by another senior physician with over ten years of clinical experience.

2.2.4. Imageomics feature extraction

Using the Python (v3.9.13) platform, the PyRadiomics toolkit is used to extract radiomics features from ITK-SNAP-annotated ROIs. A total of 107 quantitative parameters are calculated from each raw image, including first-order statistics, morphological features, and texture metrics based on the grey-co-occurrence matrix, grey-distance matrix, grey-size matrix, grey-dependence matrix, and adjacent grey-difference matrix. To enhance the information content of the features, filtering techniques were applied prior to feature extraction to strengthen the structural and textural pattern recognition of the ROI regions.

2.3. Statistical analysis

(1) Statistical distribution of morphological features in different types of Modic changes

All features extracted from the original and filtered images were standardised based on the distribution of imaging features (morphology, intensity, texture, etc.) with significant differences across various Modic changes. A Mann-Whitney U test ($p < 0.05$) was then used for preliminary screening. Subsequently, correlation analysis was performed on the screened features, and redundant features with high correlation ($r > 0.9$) were removed. We then applied the LASSO algorithm to calculate the coefficients of the remaining features, retaining those with non-zero coefficients as key differential features. Based on these features, we constructed machine learning classification models and further analysed their descriptive statistical differences (mean/variance) across different Modic types and their correlations with clinical baseline data.

(2) Statistical analysis of the distribution of imaging features among different Modic types

First, standardise the features extracted from the original and filtered images, and perform a Mann-Whitney U test ($p < 0.05$) to screen the features. Then, perform a correlation analysis on the screened features, remove redundant features with high correlation ($r > 0.9$), and apply the LASSO algorithm to calculate the coefficients of the remaining features, retaining the features with non-zero coefficients as the key difference feature set. Finally, a machine learning classification model is constructed based on this feature set to comprehensively evaluate the descriptive statistical differences (mean/variance) between different Modic types and their correlation with clinical baseline data.

3. Results

3.1. Baseline data

This study included 154 participants, including 124 without low back pain scores (88 males, 36 females), aged 18–70 years old, with an average age of 58.36 ± 5.10 years old. Among them, 34 were Modic Type I, 62 were Type II, and 28 were Type III; Among the 30 participants with low back pain scores prospectively collected, there were 7 males and 23 females, aged 19–71 years, with a mean age of 56.80 ± 6.62 years old. Among these, 7 were Modic Type I, 22 were Type II, and 1 was Type III. Due to the single case of Type III in the prospective cohort, its mean characteristics were not included in subsequent statistical analyses.

3.2. Morphological characteristics distribution of different modic types

Fifteen shape features were extracted from the ROI of T2WI images using PyRadiomics (**Table 1**). This table shows the mean (standard deviation) distribution of features in each Modic type, with means (SD) marked with “*” indicating that the feature followed a normal distribution in the corresponding type ($P < 0.05$). Kruskal-Wallis (KW) non-parametric tests were used to analyse intergroup differences, identifying seven morphological features with statistically significant differences ($P < 0.05$): elongation ($P = 0.000074$), flatness ($P = 0.014935$), major axis length (MajorAxisLength, $P = 0.030619$), major axis length to minor axis length ratio (MajorAxisLength/LeastAxisLength, $P = 0.014935$), axial maximum two-dimensional diameter (Maximum 2D Diameter Slice, $P = 0.022303$), sphericity (Sphericity, $P = 0.000012$), and surface area-to-volume ratio (Surface Volume Ratio, $P = 0.000010$).

Table 1. Distribution of Modic change morphological characteristics and KW test results for different subtypes

Feature	Mean (SD)			Difference Test (Kw test)
	Type I	Type II	Type III	
Elongation	0.816 (0.112)*	0.736 (0.124)	0.779 (0.111)	0.000074*
Flatness	0.629 (0.137)	0.575 (0.120)	0.609 (0.119)	0.014935*
Short axis ratio	25.259 (5.955)	24.620 (5.348)	24.956 (6.093)	0.774269
Major axis length	40.380(6.273)	43.425(8.399)	41.246 (7.495)	0.030619*
Long axis ratio	1.677 (0.416)*	1.835 (0.522)*	1.708 (0.348)	0.014935*
Maximum two-dimensional diameter (column direction)	44.065 (7.279)	46.258 (8.276)*	47.270 (8.102)	0.101193
Maximum two-dimensional diameter (row direction)	41.004 (8.084)	42.466(9.395)*	41.448 (9.250)	0.265319
Maximum two-dimensional diameter (axial)	40.312 (5.108)	39.012 (5.265)*	41.577 (5.597)*	0.022303*

Table 1 (Continued)

Feature	Mean (SD)			Difference Test (Kw test)
	Type I	Type II	Type III	
Maximum three-dimensional diameter	47.887 (7.108)	49.467 (7.981)	50.200 (8.074)	0.247682
Grid volume	12,226.669 (6,490.95)	10521.627 (5558.275)*	14,321.675 (9,160.341)	0.052316
Short axis length	32.596 (4.924)	31.306 (4.976)	31.774 (5.746)	0.333330
Spherical degree	0.438 (0.039)	0.405 (0.053)*	0.424 (0.045)	0.000012*
Surface area	5744.109 (2251.073)	5684.179 (2152.712)*	6473.510(2559.349)	0.348311
Surface area to volume ratio	0.520(0.116)*	0.592(0.124)	0.515 (0.116)	0.000010*
Voxel volume	12,416.356 (6,515.319)	10705.479 (5581.332)*	14,521.310 (9,205.617)	0.054961

To identify the specific intergroup differences among the seven morphometric features that showed overall significance in the Kruskal-Wallis test, Dunn's post hoc test was used for pairwise comparisons (**Table 2**). The analysis revealed that elongation rate, flatness, sphericity, surface area-to-volume ratio, and long-to-short axis ratio all exhibited statistically significant differences between Modic I and Modic II types. The surface area-to-volume ratio showed significant differences not only between Modic I and II types but also between Modic II and III types ($P < 0.05$). The long axis length and axial maximum two-dimensional diameter did not reach statistical significance ($P > 0.05$), but their P -values were close to the critical level. The Kruskal-Wallis test, as a non-parametric method, may be limited in effectiveness when sample sizes are small or the population distribution deviates from the assumption, and it is prone to outliers, leading to false positives. In contrast, Dunn's Test exhibits greater robustness, particularly for comparisons between small sample groups. The reason for this may be that the two features (long axis length and maximum two-dimensional diameter) exhibited marginal significance in the overall test (KW $P < 0.05$).

Table 2. Results of Dunn's Test for morphological features with significant differences

Features with significant differences		Dunn's Test results		
Elongation rate	P-value	1	2	3
	1	1.000000	0.000079	0.431213
	2	0.000079*	1.00000	0.180102
Elongation	3	0.431213	0.180102	1.000000
	P-value	1	2	3
	1	1.000000	0.018587	1.0000
Flatness	2	0.018587*	1.00000	0.46437
	3	1.000000	0.46437	1.00000
	P-value	1	2	3
Long axis length	1	1.000000	0.051191	1.000000
	2	0.051191	1.00000	0.375196
	3	1.000000	0.375196	1.000000

Table 2 (Continued)

Features with significant differences		Dunn's Test results		
Maximum two-dimensional diameter (axial)	P-value	1	2	3
	1	1.000000	0.178804	1.000000
	2	0.178804	1.000000	0.062015
	3	1.000000	0.062015	1.000000
	P-value	1	2	3
	1	1.000000	0.000022	0.601980
Sphericity	2	0.000022*	1.0000	0.057642
	3	0.601980	0.057642	1.00000
	P-value	1	2	3
Surface area to volume ratio	1	1.000000	0.000154	1.000000
	2	0.000154*		0.003347
	3	1.0000	0.003347*	1.000000
Long-to-short axis ratio	P-value	1	2	3
	1	1.000000	0.018587	1.0000
	2	0.018587*	1.0000	0.46437
	3	1.000000	0.46437	1.0000

3.2. Imagingomics differences in Modic changes of different types

Radiomics features were extracted from T1WI, T2WI, and FS sequences using PyRadiomics. Compared with a single sequence, the combination of T1WI+T2WI+FS significantly improved the accuracy of Modic classification. The feature extraction process includes raw images and seven types of transformation processing: wavelet, Gaussian-Laplace filtering (LoG), pixel square (Square), square root of intensity (SquareRoot), logarithmic transformation (Logarithm), exponential transformation (Exponential), local binary pattern (LocalBinaryPattern2D/3D), and gradient features (Gradient). Each sequence extracts 1,906 features. To screen for Modic classification-specific features, the following screening criteria are applied:

- (1) Mean-centred and variance-scaled the original data (mean = 0, variance = 1);
- (2) The standardised features were analysed using the Mann-Whitney U test to screen out 1,336 features with significant intergroup differences ($P < 0.05$). Their distribution relative to the threshold line ($P = 0.05$) is shown in the scatter plot in **Figure 1**. The points in **Figure 1** represent the features extracted from different image types, and the red horizontal line indicates the critical condition of $P = 0.05$.
- (3) Highly correlated features ($r > 0.9$) were removed, prioritising variables with the highest average absolute correlation, resulting in 823 features retained;
- (4) The LASSO algorithm (optimal $\alpha = 0.044984$) was used to calculate feature coefficients (**Figure 2**) and screen non-zero coefficient features.

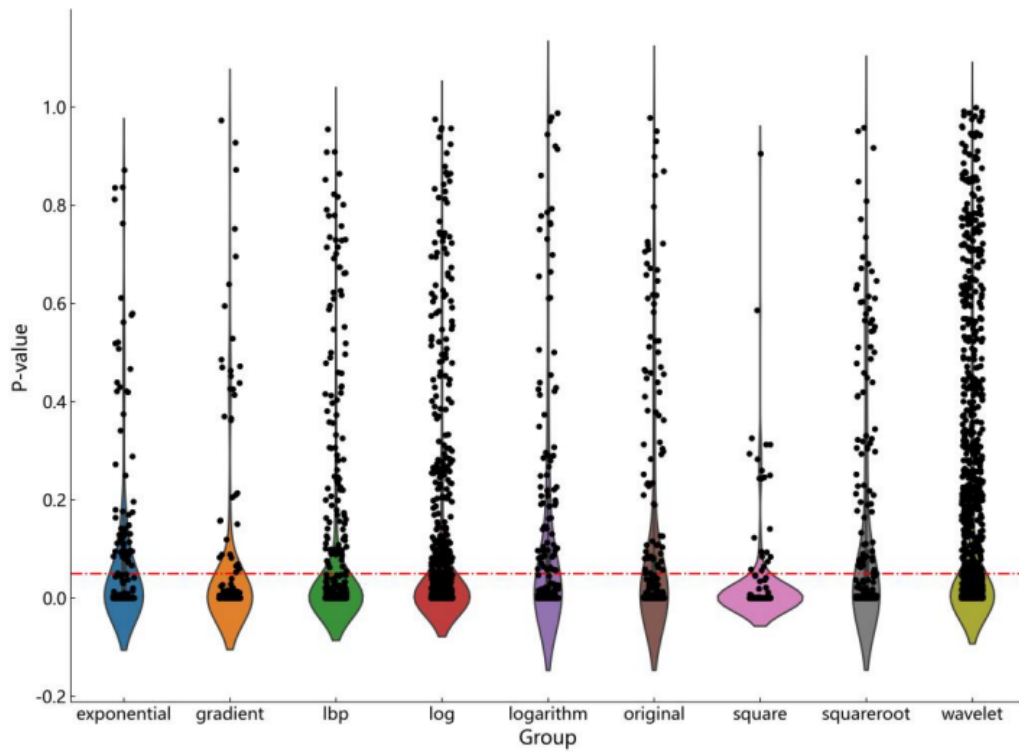


Figure 1. Mann-Whitney U test results.

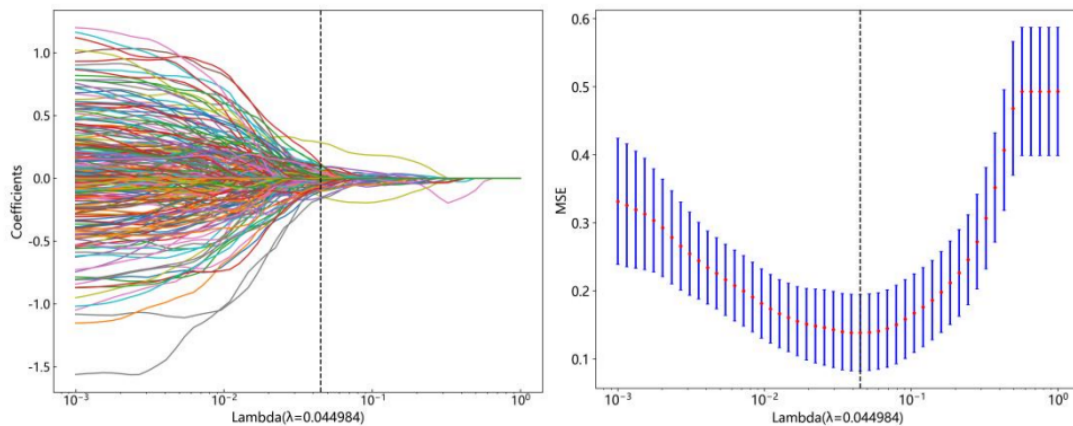


Figure 2. LASSO regression coefficient distribution plot.

Based on the 29 non-zero coefficient features selected by LASSO (threshold $> 1 \times 10^{-6}$), a Modic classification model was constructed using support vector machines (SVM). The model validation set achieved an accuracy rate of 98%, confirming that the selected features have significant discriminative efficacy for Modic classification. Further analysis using Kruskal-Wallis test and Dunn's test validated the differences between feature groups. The results showed that 15 features in the T1WI sequence exhibited significant intergroup differences ($P < 0.05$); 8 features in the T2WI sequence exhibited significant intergroup differences ($P < 0.05$); and 6 features in the FS sequence exhibited significant intergroup differences ($P < 0.05$). All 29 features reached a significant level in the Kruskal-Wallis test.

3.3. Correlation between radiomics features and low back pain

In this section, we used R language to analyse the correlation between the low back pain scores of the 30 patients prospectively collected and the aforementioned morphological and radiomic features. During the correlation analysis, since only 1 case in the prospectively collected cases belonged to Modic Type III, we only analysed data from Modic Type I and Modic Type II cases.

3.3.1. Correlation between morphological characteristics and low back pain

The study found that the Oswestry Disability Index (ODI) score was significantly correlated with specific lumbar morphological features. ODI was significantly positively correlated with the muscle fibre long-short axis ratio ($r = 0.391, p < 0.05$) and the surface area-to-volume ratio ($r = 0.506, p < 0.01$). Conversely, ODI scores were significantly negatively correlated with sphericity ($r = -0.499, p < 0.01$) and flatness ($r = -0.390, p < 0.05$). This indicates that elongated muscle fibre morphology, increased surface complexity, and deviation from spherical and flat states are associated with increased severity of low back pain.

3.3.2. Correlation between imaging group differences and low back pain

Research has found that the Oswestry Disability Index (ODI) score is significantly associated with specific radiological imaging features. ODI is positively correlated with the regional entropy of three-dimensional images from FS sequences (FS_lbp_3D_m1_glszm_ZoneEntropy, $r = 0.380, p < 0.05$); while it was negatively correlated with the low-greyscale small-area distribution in T1 sequences (T1_lbp_3D_m2_glszm_SmallAreaLowGrayLevelEmphasis, $r = -0.423, p < 0.05$) and the LLH wavelet 90th percentile (FS_wavelet_LLH_firstorder_90Percentile, $r = -0.376, p < 0.05$). Additionally, age is negatively correlated with the pixel grey level variability of the T2 sequence (T2_logarithm_firstorder_RobustMeanAbsoluteDeviation, $r = -0.390, p < 0.05$); while it was positively correlated with the uniformity of grey-level spatial distribution in the T1 sequence (T1_exponential_glszm_SizeZoneNonUniformityNormalized, $r = 0.492, p < 0.01$) and low grey-level large dependence (T1_lbp_3D_m1_gldm_LargeDependenceLowGrayLevelEmphasis, $r = 0.395, p < 0.05$).

4. Discussion

Modic changes are an independent risk factor for severe disabling low back pain^[3]. This study investigated the morphological and radiomic features of lumbar MCs and their association with low back pain through quantitative analysis. The baseline characteristics of the study population were consistent with the incidence patterns of MCs and previous studies^[4]. This study systematically revealed the imaging feature differences among MC subtypes for the first time: MC Type I exhibits higher elongation rate, flatness, and sphericity in morphology, suggesting a more spherical shape and flatter surface, which may be associated with its more active inflammatory state^[5]; whereas MC Type II exhibits a larger major axis length, major-to-minor axis ratio, and surface area-to-volume ratio, with a morphology tending toward elongated or irregular shapes. The larger surface area-to-volume ratio may be associated with tissue swelling and deformation caused by inflammation^[6], and this feature shows a significant positive correlation with the Oswestry Disability Index (ODI) ($r = 0.506, p < 0.01$); Additionally, ODI was positively correlated with the long-to-short axis ratio ($r = 0.391, p < 0.05$) and negatively correlated with sphericity ($r = -0.499, p < 0.01$) and flatness ($r = -0.390, p < 0.05$), indicating that elongated lesion morphology, surface complexity, and deviation from spherical and flat states are significantly associated with worsening low back pain severity.

Imageomics analysis further revealed that ODI was positively correlated with FS sequence regional entropy (FS_lbp_3D_m1_glszm_ZoneEntropy, $r = 0.380$, $p < 0.05$), while negatively correlated with the distribution of low-grayscale small regions in the T1 sequence (T1_lbp_3D_m2_glszm_SmallAreaLowGrayLevelEmphasis, $r = -0.423$, $p < 0.05$) and the FS sequence LLH wavelet 90th percentile (FS_wavelet-LLH_firstorder_90thPercentile, $r = -0.376$, $p < 0.05$). Reduced smoothness and increased regional entropy may be associated with oedema signals in the lesion, thereby influencing pain ^[7,8]. Additionally, age was significantly correlated with specific radiomic features: negatively correlated with pixel grey-scale variability in the T2 sequence (T2_logarithm_firstorder_RobustMeanAbsoluteDeviation, $r = -0.390$, $p < 0.05$); with the uniformity of grey-level spatial distribution in the T1 sequence (T1_exponential_glszm_SizeZoneNonUniformityNormalized, $r = 0.492$, $p < 0.01$) and the low grey-level large dependence (T1_lbp_3D_m1_gldm_LargeDependenceLowGrayLevelEmphasis, $r = 0.395$, $p < 0.05$), indicating that the texture and grey-level characteristics of lesion tissues change with age, supporting the role of age in the onset of MC ^[9]. A diagnostic model constructed using 29 significantly different radiomics features selected from T1 (15), T2 (8), and FS (6) sequences effectively distinguished MC subtypes, highlighting the diagnostic value of the T1WI sequence ^[10]. The innovation of this study lies in the first application of radiomics technology to quantitatively analyse MC characteristics and construct an automatic classification model, providing new insights into the pathogenesis of MC and the differentiation of MC-related low back pain.

5. Conclusion

The study demonstrates that morphological and radiomics features effectively differentiate between subtypes of Modic changes (MC). An automated classification model leveraging these discriminative features achieves high accuracy, with key features showing significant correlations with the low back pain functional disability index. These findings highlight the potential of radiomics-based approaches in improving MC subtype characterization and their clinical relevance in assessing functional disability. Further validation in larger cohorts could enhance the model's utility in personalized diagnosis and management.

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Clinical Study on the Treatment of Delayed Union After Long Bone Fracture Surgery with Platelet-Rich Plasma and Intramedullary Nail Dynamization

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Abstracts: *Background:* The purpose of this study was to investigate the clinical effect of platelet-rich plasma (PRP) combined with intramedullary nailing in the treatment of delayed union after long bone fracture surgery. *Methods:* To retrospectively analyze the clinical data of 60 patients with delayed healing of long bone fractures treated in the Department of Orthopaedics of the Fourth Affiliated Hospital of Guangzhou Medical University in 2023 from January 2021 to December 2021, patients were randomly divided into a combined treatment group (30 cases) and a control group (30 cases). PRP combined with intramedullary nail dynamic therapy was used for combined treatment, while only intramedullary nail dynamic therapy was used for the control group. *Results:* Bone healing was achieved in 28 patients in the combination group (93.3%), and the mean bone healing time was 4.2 ± 1.1 months. The former group was significantly better than the control group (76.7%, 6.5 ± 1.4 months) ($p < 0.05$). At the last follow-up, the recovery rate of limb function was 90.0% in the combined treatment group and 70.0% in the control group, and the former had an advantage in this aspect ($p < 0.05$). No disability or death occurred during follow-up in either group. *Conclusion:* PRP combined with intramedullary nailing has a significant clinical effect on delayed union after long bone fracture surgery, which can effectively promote fracture healing and improve patient prognosis.

Keywords: Platelet-rich plasma; Intramedullary nail dynamization; Long bone fracture; Delayed union; Clinical study

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1. Introduction

Bone healing is a complex biological process in the human body related to fracture repair, encompassing various stages such as hematoma organization, primary callus formation, and callus remodeling. It involves the participation of multiple cell types, including osteoblasts, osteoclasts, and vascular endothelial cells, as well as

numerous biomolecules like bone morphogenetic proteins and insulin-like growth factors ^[1]. However, when patients are affected by factors such as poor local blood circulation, infection, and malnutrition, the injured site is prone to delayed healing or non-union ^[2,3]. Long bone fractures are one of the common traumatic diseases in clinical practice, and issues of delayed healing or non-union after surgery severely impact patients' prognosis and quality of life. According to the "Guidelines for Perioperative Management of Accelerated Rehabilitation After Major Orthopedic Surgery in China," the incidence of delayed healing after long bone fracture surgery ranges from approximately 5% to 15%. This statistic not only signifies that a large number of patients endure long-term pain and suffering but also bear a heavy economic burden. For example, in the case of femoral shaft fractures, patients with delayed healing experience an extended hospital stay of 2–3 months and additional medical expenses of 30,000 to 50,000 yuan ^[4,5]. Therefore, addressing the issue of delayed healing in long bone fractures has become a focal point of research.

PRP is an autologous plasma preparation derived from human blood. Due to its unique origin, PRP often poses no risk of disease transmission or immune rejection, exhibiting high safety and tolerability in clinical applications. Furthermore, PRP is rich in various growth factors, including platelet-derived growth factor, transforming growth factor- β , and vascular endothelial growth factor. These growth factors work synergistically to accelerate the healing process of fractures ^[6]. In recent years, PRP has gained widespread application and research in the field of orthopedics, covering not only fracture non-union but also osteoarthritis, tendon injury repair, and other aspects ^[7].

Dynamic intramedullary nailing is one of the commonly used methods to treat delayed fracture healing ^[8,9]. Its principle is to remove the locking screw at one end of the intramedullary nail, breaking the original stable mechanical environment of the fracture end and increasing the micro-movement of the fracture end. Moderate micro-movement can simulate physiological stress stimulation, activate osteoblast activity at the fracture site, promote callus formation and remodeling, and thus promote fracture healing ^[10]. From a biomechanical perspective, after dynamic intramedullary nailing, the stress distribution at the fracture end is closer to the natural state, and the stress stimulation intensity increases by 15% - 20%. This change in the mechanical environment can effectively promote the mineralization and shaping of the callus ^[11]. However, there is currently no consensus in the academic community on the effect of using dynamic intramedullary nailing alone or combined with PRP to treat delayed healing of long bone fractures ^[12].

This study aims to deeply explore the clinical effect of PRP combined with dynamic intramedullary nailing in the treatment of delayed healing of long bone fractures. By comparing the efficacy of combined therapy with dynamic intramedullary nailing alone, the specific role of PRP in promoting fracture healing will be clarified. This study provides a scientific basis for clinically optimizing treatment plans, thereby improving the treatment effect of patients with delayed healing after long bone fracture surgery and filling some gaps in current research on combined therapy.

2. Research objects and methods

2.1. Research objects

From January 2021 to December 2023, a total of 71 patients with delayed healing of long bone fractures were treated at the Fourth Affiliated Hospital of Guangzhou Medical University. Sixty patients who met the inclusion and exclusion criteria were randomly selected, with 30 patients in the combined treatment group and 30 patients

in the control group. The combined treatment group received PRP combined with dynamic intramedullary nailing, while the control group only received dynamic intramedullary nailing. The grouping process strictly followed the principle of randomization to ensure that the two groups of patients were comparable in baseline data such as age, gender, fracture site, and fracture type.

This study is a Guangzhou Science and Technology Plan Project (No. 20220101064). The clinical data of patients was approved for use by the Ethics Committee of the Fourth Affiliated Hospital of Guangzhou Medical University (Approval No. 2021-D-037), and all patients were exempted from informed consent. This study does not involve any conflicts of interest.

2.2. Inclusion criteria

- (1) No signs of fracture healing after more than 6 months;
- (2) Reliable internal fixation at the fracture end, without breakage or loosening of the internal fixation;
- (3) Bone defect at the fracture end ≤ 5 mm;
- (4) Follow-up time exceeding 12 months with complete follow-up treatment.

2.3. Exclusion criteria

- (1) Infectious nonunion of bones;
- (2) Combined with severe metabolic diseases, such as diabetes, etc.;
- (3) Heavy smoking and drinking history that cannot be quit during treatment;
- (4) Pathological fractures.

2.4. Preparation of PRP

Autologous PRP was prepared using a two-step centrifugation method, as described below: 10 mL of blood was drawn from the patient's antecubital vein using a 10mL disposable syringe pre-filled with 1 mL of sodium citrate anticoagulant and an 18G needle, and this was repeated for a total of 2 tubes; under sterile conditions, the blood was centrifuged at a radius of 15 cm and a speed of 1500 r/min for 10 minutes, resulting in three layers of separation; the lower layer of red blood cells was slowly discharged; the remaining portion was centrifuged again at a radius of 15 cm and a speed of 2000 r/min for 10 minutes; subsequently, the lower layer of red blood cells was slowly discharged, and 2.0–2.5 mL of the middle layer from each tube was retained for injection, yielding PRP. Routine quality control was performed on the obtained PRP product, and the platelet concentration in the PRP prepared by the above method was 3–6 times that of whole blood.

2.5. Experimental methods

In the control group, the locking screws at one end of the intramedullary nail were removed under local or lumbar anesthesia to perform intramedullary nail dynamization. Strict aseptic techniques were followed during the surgical procedure to ensure the safety and effectiveness of the operation. The experimental group received an injection of PRP at the fracture site under local or lumbar anesthesia and C-arm monitoring, along with intramedullary nail dynamization. The specific steps were as follows: After completing the intramedullary nail dynamization, the fracture site was located through C-arm fluoroscopy, and the prepared PRP was slowly injected around the fracture end to ensure uniform distribution of PRP in the fracture area.

2.6. Evaluation of therapeutic effect

Detailed records were kept of patients' bone healing time, bone healing rate, and limb function recovery. X-ray films were used to evaluate fracture healing, and the Johner-Wruhs scoring system was employed to assess limb function recovery.

The recovery of limb function was evaluated using the Johner-Wruhs scoring system. This scoring system assesses the patient's limb function from multiple aspects such as pain, function, appearance, range of movement, etc., and is divided into four grades: excellent, good, medium, and poor.

2.7. Statistical analysis

SPSS 22.0 software was used for statistical analysis. The Shapiro-Wilk test was performed to determine whether the measurement data followed a normal distribution. Normally distributed measurement data were expressed as mean \pm standard deviation (SD), and comparisons between the two groups were made using the two-sample *t*-test. Comparisons of count data between the two groups were conducted using the χ^2 test, and the results were expressed as *n*(%). A *P*-value < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of general information between the two groups

The general information of 60 patients is shown in **Table 1**. The combined treatment group included 30 patients, with 18 males (60%) and 12 females (40%). The age range was 25 to 58 years old, with an average age of 42.5 ± 8.3 years old. In this group, there were 15 cases (50%) of femoral fractures and 15 cases (50%) of tibial fractures. 22 patients (73.3%) had closed fractures, and 8 patients (26.7%) had open fractures. In the control group, there were 19 males (63.3%) and 11 females (36.7%). The age range was 23 to 59 years old, with an average age of 41.8 ± 7.9 years old. 16 patients (53.3%) had femoral fractures, and 14 patients (46.7%) had tibial fractures. 21 patients (70%) had closed fractures, and the remaining patients had open fractures. There were no statistically significant differences in general information such as age, gender, fracture site, and fracture type between the two groups (*P* > 0.05), indicating comparability between the groups.

Table 1. Comparison of general information between the two groups

Item	Combination therapy group (<i>n</i> = 30)	Control group (<i>n</i> = 30)	<i>t</i> / χ^2 value	<i>P</i> -value
Age (years)	42.5 ± 8.3	41.8 ± 7.9	0.335	0.739
Gender (Male/Female)	18/12	19/11	0.070	0.791
Fracture Site (Femur/Tibia)	15/15	16/14	0.067	0.796
Fracture Type (Closed/Open)	22/8	21/9	0.082	0.775

3.2. Comparison of clinical data between the two groups

As shown in **Table 2**, the average fracture healing time in the combination therapy group was 4.2 ± 1.1 months, which was significantly shorter than the 6.5 ± 1.4 months in the control group, and the difference was statistically significant (*P* < 0.05).

Table 2. Comparison of fracture healing time between the two groups

Item	Combination therapy group (n = 30)	Control group (n = 30)	t-value	P-value
Mean fracture healing time (months)	4.2 ± 1.1	6.5 ± 1.4	6.97	< 0.001

3.3. Comparison of clinical healing rates between the two groups

At 12 months post-operation, the clinical healing rate in the combined treatment group was 93.3% (28/30), which was significantly higher than the 76.7% (23/30) in the control group. The difference was statistically significant ($P < 0.05$) (Table 3).

Table 3. Comparison of clinical healing rates between the two groups

Item	Combination therapy group (n=30)	Control group (n=30)	χ^2 Value	P Value
Number of clinical healings	28	23	4.320	0.037
Clinical healing rate	93.3%	76.7%		

3.4. Comparison of functional recovery between the two groups

In terms of functional recovery, the excellent and good rate of the Johner-Wruhs score in the combined treatment group was 90.0% (27/30), which was significantly higher than the 70.0% (21/30) in the control group. The difference was statistically significant ($\chi^2 = 4.800$, $P < 0.05$). The specific scoring results are shown in Table 4.

Table 4. Comparison of functional recovery between the two groups

Rating grade	Combination therapy group (n = 30)	Control group (n = 30)
Excellent	15	10
Good	12	11
Fair	2	7
Poor	1	2

3.5. Comparison of complications between the two groups

No severe complications occurred in both groups. In the combined treatment group, 2 patients experienced mild local pain and 1 patient had a short-term fever, all of which resolved spontaneously. In the control group, 1 patient developed a superficial infection that was successfully treated with antibiotics (Table 5). Overall, both treatment methods demonstrated good safety profiles.

Table 5. Comparison of postoperative complications between the two groups

Complication	Combination therapy group (n = 30)	Control group (n = 30)
Pain	2	0
Fever	1	0
Infection	0	1

4. Discussion

The core pathological feature of delayed fracture healing is the inhibition of osteogenesis caused by stress shielding at the fracture site^[13]. Dynamization of intramedullary nails changes the mechanical environment at the fracture site and increases micro-movement by removing the locking screw at one end of the nail. Longitudinal stress stimulation at the fracture site can promote callus formation and mineral deposition, which is beneficial for fracture healing. Moderate micro-movement can stimulate callus formation and remodeling, activate osteoblast activity at the fracture site, and promote the repair and regeneration of bone tissue. Furthermore, the various growth factors abundant in PRP play key roles in the treatment of delayed healing of long bone fractures: (1) Platelet-derived growth factor can chemoattract osteoblasts and mesenchymal stem cells, promote their proliferation and differentiation, and provide an adequate cell source for fracture healing; (2) Transforming growth factor- β can regulate the synthesis and deposition of extracellular matrix, promoting the formation and mineralization of bone matrix; (3) Vascular endothelial growth factor can stimulate angiogenesis, improve blood supply to the fracture site, and create a favorable nutritional environment for fracture healing^[14]. Throughout the treatment process, PRP provides a rich source of bioactive substances, while dynamization of intramedullary nails creates favorable mechanical stimulation. The combined application of these two treatment modalities further improves the therapeutic effect and accelerates the process of fracture healing. This study, through a prospective controlled design, verified the clinical efficacy of PRP injection combined with dynamization of interlocking intramedullary nails for the treatment of delayed healing of long bone diaphyseal fractures. The results fully demonstrate that PRP combined with dynamization of intramedullary nails has a significant clinical effect in the treatment of delayed healing after long bone fracture surgery. Compared with the dynamization of intramedullary nails alone, the combined treatment approach has clear advantages regarding bone healing time, bone healing rate, and limb function recovery ($P < 0.05$). These results suggest that early biomechanical intervention combined with PRP treatment can optimize the microenvironment for fracture healing and promote fracture healing.

The results of this study are consistent with most literature reports^[15,16]. However, the conclusion is not entirely consistent, and further research may be needed on the clinical efficacy of PRP. In some scholars' studies, the clinical efficacy of PRP is uncertain^[17]. This phenomenon may be closely related to factors such as PRP preparation methods, injection doses, and timing. Different preparation methods may lead to differences in the concentration and activity of growth factors in PRP, and insufficient injection doses or improper timing may not fully exert the role of PRP in promoting fracture healing. This study adopted standardized PRP preparation and injection methods, strictly controlling each link in the preparation process to ensure the quality and activity of PRP, while reasonably selecting the injection timing, which may be an important factors that help improve the treatment effect.

This study has certain limitations. Firstly, the sample size of this study is relatively small, with only 60 patients included. The small sample size may lead to certain sampling errors in the research results, affecting the universality and reliability of the results. Secondly, the follow-up time is relatively short, only 12 months, and the long-term effects and long-term complications of fracture healing have not been fully observed. Additionally, this study is a single-center study, and the research results may be influenced by factors such as patient sources, treatment levels, and research conditions of a single hospital.

Based on the limitations of this study, larger-scale, multi-center, long-term follow-up randomized controlled studies are needed to further verify the effectiveness and safety of PRP combined with intramedullary nail dynamization for the treatment of delayed union after long bone fracture surgery. During the research process,

research variables should be strictly controlled to ensure the scientificity and reliability of the research results. Furthermore, the optimal preparation method of PRP should be further explored to optimize indicators such as platelet concentration and growth factor activity; determine the optimal injection dose and timing of PRP to fully exert its role in promoting fracture healing. At the same time, actively explore the combined application of PRP with other biological agents or physical therapies, expand the selection of treatment methods, and provide better and more effective treatment options for patients with delayed union after long bone fracture surgery.

5. Conclusion

The combined therapy of PRP and dynamization of intramedullary nails for delayed union after long bone fracture surgery has significant clinical effects, effectively reducing fracture healing time and improving clinical healing rates and excellent functional recovery rates. This combined therapy is safe and feasible, providing a new option for the treatment of delayed union after long bone fracture surgery. However, further research is still needed to optimize the treatment regimen and explore its long-term efficacy and mechanism. In clinical practice, doctors can comprehensively consider and select appropriate treatment methods based on the specific conditions of patients to improve treatment effectiveness and patient prognosis.

Disclosure statement

The authors declare no conflict of interest.

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Prevention of Ocular Complications in Spine Surgery Patients in the Prone Position

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Abstract: *Objective:* To investigate the causes and preventive methods for blindness after spine surgery in the prone position. *Methods:* A retrospective analysis was conducted on the data of three patients who developed blindness after prone-position spinal surgery. *Results:* One patient died. Two patients were followed up 5 to 6 months after discharge, with no recovery of vision. Both patients remained blind in both eyes. *Conclusion:* Postoperative blindness in patients undergoing prone-position spine surgery is rare and difficult to treat once it occurs. Early recognition and prevention are essential to avoid this catastrophic complication.

Keywords: Ocular complications; Blindness; Spine; Prone-position surgery

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1. Introduction

Spinal surgeries are generally performed in the supine, prone, or lateral decubitus position, with the prone position being the most commonly used. Various complications may arise from the surgical position, particularly ocular complications, which often include pressure injuries to the periocular skin and postoperative visual loss (POVL).

POVL is an extremely rare but devastating postoperative complication. The first case of blindness after spinal surgery in the prone position was reported by Slocum *et al.* in 1948^[1]. The incidence of POVL in spinal fusion surgeries is about 3.09/10,000 according to the literature^[2]. Most studies on POVL are retrospective or case reports, with varying opinions on its causes and pathophysiology. Currently, there is no effective treatment, and once it occurs, the prognosis is extremely poor, often leading to permanent blindness.

Between December 2020 and January 2022, our department treated three cases of POVL. These included one case of posterior cervical spine surgery, one case of combined anterior and posterior cervical surgery, and one case of posterior lumbar spine surgery. This paper reviews the causes and preventive measures for POVL in these cases.

2. General information

2.1. Patient 1

A 71-year-old male was admitted on December 27, 2020, with “3 days of neck and shoulder pain and 1 day of limb weakness.” Upon admission, his vision was normal in both eyes. The patient underwent emergency surgery under general anesthesia for “posterior cervical laminectomy and bilateral screw fixation.” After surgery, he was placed in the supine position and noted to have severe swelling of the left eyelid, corneal epithelial defects, conjunctival congestion, and sluggish pupillary reflex. Following anesthesia recovery, the patient reported complete loss of vision in the left eye. A 3D CT of the optic nerve canal on January 2, 2021, revealed no significant bony abnormalities in the optic nerve canals bilaterally. However, left eye muscle hypertrophy was noted. The diagnosis of left central retinal artery occlusion was considered. Symptomatic treatments, including corticosteroid therapy, were given. Two weeks after surgery, the left eye had no light perception, slight exophthalmos, ptosis, and conjunctival congestion. The right eye appeared normal. The patient died on the 23rd day after admission due to systemic complications.

2.2. Patient 2

A 67-year-old male was referred from a local hospital on December 17, 2021, due to “sudden loss of vision and eye pain in the right eye for 2 days.” Prior to surgery, his vision was normal. He underwent “posterior lumbar decompression and internal fixation” at the local hospital. Postoperatively, he developed sudden loss of vision and eye pain in the right eye, along with limited ocular movements, without symptoms such as redness, photophobia, or tearing. Upon examination, the right eye had no light perception, limited ocular movement, conjunctival edema, mild corneal edema, and absent pupillary light reflex. The right retina showed gray-white edema, macular discoloration, and retinal hemorrhages. The left eye was normal. A diagnosis of right central retinal artery occlusion was made. The patient was treated with antibiotics (e.g., tobramycin eye drops, timolol eye drops) and supportive care. After 2 weeks, the patient was discharged with no recovery of vision in the right eye. Follow-up in June 2022 showed no light perception in the right eye and normal vision in the left.

2.3. Patient 3

A 59-year-old male was transferred to our hospital after experiencing sudden vision loss in the left eye for 1 week, following a fall. On December 24, 2021, he underwent “posterior cervical open reduction and fixation, combined with anterior decompression and interbody fusion” for cervical spine fractures at the local hospital. Prior to surgery, his vision was normal. Postoperatively, he developed sudden loss of vision in the left eye, with conjunctival edema, limited eye movement, and no pain, photophobia, or tearing. Examination revealed no light perception in the left eye, limited ocular movement, incomplete eyelid closure, conjunctival edema, clear cornea, and absent pupillary reflex. The fundus showed retinal pallor and edema. A 3D CT scan of the optic nerve canal suggested left extraocular muscle hypertrophy and a possible old fracture of the right orbital medial wall. A diagnosis of left central retinal artery occlusion was made. Despite treatment, the left eye did not recover vision. Follow-up in June 2022 showed no light perception in the left eye, with normal vision in the right.

3. Results

One patient died. Two patients were followed up for 5 to 6 months after discharge, with no recovery of vision. Both patients are permanently blind.

4. Discussion

Postoperative visual loss (POVL) is an extremely rare complication but often devastating. Once it occurs, treatment is usually ineffective, with almost no success rate^[3]. Although the mechanisms behind POVL have been recognized in recent years, it remains underappreciated by many surgeons due to its rarity.

POVL can be classified into three types based on the mechanism of blindness: ischemic optic neuropathy (ION), central retinal artery occlusion (CRAO), and cortical blindness^[4].

ION is caused by acute ischemia of the optic nerve, resulting in optic nerve fiber damage, often involving both eyes. Prolonged prone positioning during surgery is a significant risk factor for ION, likely related to increased intraocular pressure and head venous pressure, both of which reduce ocular perfusion pressure and can lead to ischemic optic nerve injury, resulting in vision loss^[5].

Hypotensive shock is another risk factor for ION. Significant intraoperative blood loss can cause hypovolemia and reduced mean arterial pressure, resulting in insufficient ocular perfusion and ischemia of the optic nerve^[6,7].

CRAO typically causes ischemic damage to the entire retina, leading to complete vision loss in the affected eye. The clinical presentation is characterized by sudden, painless loss of central and peripheral vision in one eye, accompanied by a relative afferent pupillary defect (RAPD). Fundus examination typically shows retinal pallor and edema, particularly in the macula, with a characteristic “cherry red spot” appearance. CRAO is most commonly caused by direct mechanical compression of the eye during surgery, which leads to a significant increase in intraocular pressure and occlusion of the central retinal artery^[8].

Cortical blindness is a rare complication of spinal surgery and is caused by damage to the visual centers in the occipital cortex.

The three patients in this study were all diagnosed with CRAO, likely due to prolonged intraoperative pressure on the eyes^[9]. Since all cases occurred after the 240-minute window, treatment was unsuccessful, and vision did not recover.

The prognosis of POVL is poor, with most cases leading to irreversible blindness. Therefore, prevention is crucial. The following preventive measures should be implemented^[4]:

- (1) Preoperative assessment: Evaluate patients for risk factors such as hypertension and diabetes. Ensure appropriate perioperative cardiovascular management. For high-risk patients, consider staging surgery and shortening operation times.
- (2) Positioning: Minimize the use of horseshoe headrests and avoid direct ocular pressure. Use Mayfield headrests to secure the head, and adjust positioning carefully to avoid relative movement of the head and pillow that may lead to ocular pressure^[10].
- (3) Intraoperative management: Continuously monitor blood pressure and hemoglobin levels, maintaining circulatory stability and avoiding severe hypotension.
- (4) Postoperative visual monitoring: Immediately check vision upon anesthesia recovery in high-risk patients, particularly those undergoing prolonged surgeries or at risk of significant blood loss^[11].

Postoperative ocular complications, especially POVL, are severe and difficult to reverse. Effective prevention, including optimal positioning, eye protection, careful patient selection, and monitoring, is essential to reduce the incidence of POVL and ensure patient safety.

5. Conclusion

Postoperative blindness following prone-position spine surgery, though rare, is a devastating complication with limited treatment options. Therefore, early recognition and proactive preventive measures are critical to minimizing the risk and ensuring patient safety.

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A Systematic Evaluation of the Safety of Platelet-rich Plasma (PRP) in the Treatment of Osteoarthritis

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Preface

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1. Scope

This document specifies the terms and definitions, basic principles, general requirements, safety evaluation indicators, safety evaluation methods, safety evaluation processes, and the content and format of evaluation reports for the systematic evaluation of the safety of platelet-rich plasma (PRP) treatment for osteoarthritis.

This document is applicable to the systematic clinical safety evaluation of PRP treatment for patients with osteoarthritis caused by degenerative diseases in orthopedic and joint surgery departments of general hospitals.

2. Normative references

The content in the following documents constitutes essential provisions of this document through normative references in the text. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

- (1) T/ZGCIT XXX Technical Specification for the Preparation of Platelet-Rich Plasma (PRP)
- (2) T/ZGCIT XXX Specification for Quality Control and Release Testing of Platelet-Rich Plasma (PRP)
- (3) T/ZGCIT XXX Clinical Application Guideline for the Treatment of Osteoarthritis with Platelet-Rich Plasma (PRP)
- (4) “Good Manufacturing Practice for Pharmaceutical Products”
- (5) “Expert Consensus on the Clinical Application of Platelet-Rich Plasma in Orthopedic Surgery” (2018 Edition)
- (6) “Expert Consensus on the Preparation Technique of Autologous Platelet-Rich Plasma (PRP)” (2021 Edition)

3. Terms and definitions

The following terms and definitions are applicable to this document.

- (1) Platelet-Rich Plasma (PRP): A platelet concentrate extracted from autologous blood by centrifugation.
- (2) Osteoarthritis (OA): Also known as osteoarthropathy, degenerative arthritis, hypertrophic arthritis, or senile arthritis, it is a chronic joint disease characterized by degenerative changes in articular cartilage and secondary bone hyperplasia, with an unclear etiology.
- (3) Safety Evaluation: The process of systematically monitoring, evaluating, and analyzing potential adverse reactions, adverse events, and their potential impacts on patient health during the clinical application of a specific treatment method, to determine the safety characteristics and risk level of the treatment.

4. Basic principles

4.1. Principle of comprehensiveness

The safety evaluation of PRP treatment for osteoarthritis should cover the entire process from patient selection, pre-treatment preparation, treatment implementation to post-treatment follow-up, comprehensively monitoring various potential adverse reactions and safety events to ensure no critical information is missed.

4.2. Principle of comprehensiveness

This should include the following aspects:

- (1) Comprehensive consideration of individual factors such as age, gender, underlying diseases, and genetic background;
- (2) PRP preparation parameters such as platelet concentration, activation method, and anticoagulant use;
- (3) Details of treatment operations such as injection site, injection dose, and injection frequency;
- (4) External environmental factors such as the sanitary conditions of the treatment institution and the professional skills of the operators.

4.3. Principle of dynamism

As the efficacy and safety of PRP treatment for osteoarthritis may change over time, a dynamic evaluation mechanism should be established to monitor and evaluate corresponding safety indicators at different time points (such as immediately after treatment, short-term follow-up, medium-term follow-up, and long-term follow-up), to timely detect potential delayed adverse reactions and long-term safety issues.

4.4. Principle of ethics

During the safety evaluation process, medical ethics principles should be strictly followed, fully respecting patients' rights to informed consent, privacy, and autonomous choice.

5. General requirements

5.1. Product quality

The product quality should comply with T/ZGCIT XXX “Specification for Quality Control and Release Testing of Platelet-Rich Plasma (PRP)”.

5.2. Treatment process

It should comply with the requirements of T/ZGCIT XXX “Clinical Application Guideline for the Treatment of Osteoarthritis with Platelet-Rich Plasma (PRP)”.

5.3. Institutional requirements

5.3.1. Legal qualification and practice license

The institution should have legal qualifications and a practice license that comply with local laws and regulations, to ensure its legal operation in the medical field.

5.3.2. Equipped with corresponding medical equipment and facilities

The institution should have relevant medical equipment and advanced laboratory facilities suitable for PRP treatment, which should comply with the relevant requirements of the “Good Manufacturing Practice for Pharmaceutical Products”.

5.3.3. Equipped with a professional medical team

It should include orthopedic surgeons, PRP experts, nursing staff, etc., who should have professional knowledge and clinical experience in related fields, to effectively carry out PRP treatment.

5.4. Personnel requirements

5.4.1. Medical background and professional qualification

Medical personnel should have a relevant medical background, usually requiring a medical degree or other medical professionals such as orthopedic surgeons.

5.4.2. Professional knowledge and skills

Medical personnel should have professional knowledge and skills in related fields, especially in the treatment of osteoarthritis and PRP therapy, as well as professional skills in aseptic techniques and joint injection techniques.

5.4.3. Familiar with the principles and techniques of PRP treatment

Medical personnel should be familiar with the principles, methods, and techniques of PRP treatment, including the extraction, culture, identification, and infusion processes of PRP.

5.4.4. Familiar with clinical practice guidelines

Medical personnel should be familiar with clinical practice guidelines and the latest research results related to PRP treatment for osteoarthritis, to ensure the scientific and reliable treatment.

5.4.5. Strict patient screening and evaluation ability

Medical personnel should have the ability to strictly screen and evaluate patients, to ensure that the treatment is suitable for patients who meet the corresponding criteria, while excluding cases with contraindications.

5.4.6. Communication skills and maintenance of doctor-patient relationship

Medical personnel should have good communication skills, be able to establish trust and cooperation with patients, and fully explain the treatment process, potential effects, and risks.

5.4.7. Compliance with medical ethical principles

Medical personnel should comply with medical ethical principles during PRP treatment to protect patients' rights and safety.

5.4.8. Continuous education and training

Medical personnel should participate in continuous education and training, keep track of the latest medical research achievements and clinical practices, and maintain professional standards in this field.

5.4.9. Emergency response capability

Medical personnel should have the ability to respond to unexpected situations and complications that may occur during the treatment process, and be able to quickly make correct emergency responses.

6. Safety evaluation indicators

6.1. Local adverse reaction indicators

6.1.1. Pain

Standardized pain assessment tools such as the Visual Analog Scale (VAS) or Numeric Rating Scale (NRS) should be used to record changes in the degree, nature, frequency, and duration of joint pain before, during, and after treatment, as well as during follow-up. Abnormal conditions such as increased pain or new pain should be identified, and their correlation with treatment should be analyzed.

6.1.2. Swelling

The degree of swelling should be evaluated by measuring joint circumference or observing local joint appearance (such as skin tension, color, and texture). The time of swelling occurrence, resolution, and whether it is accompanied by other symptoms such as pain and fever should be recorded to determine whether the swelling is a treatment-related adverse reaction.

6.1.3. Erythema

Observe whether there is erythema around the joint, including its range, color, and boundary clarity. Determine whether it is a manifestation of allergic reaction or inflammatory reaction, and record the duration and resolution process of the erythema.

6.1.4. Joint effusion

Methods such as ultrasound, MRI, or joint puncture should be used to detect the formation of effusion in the joint cavity. Evaluate the amount and nature of the effusion (such as clear, bloody, purulent, etc.) and its impact on joint function. Analyze the causal relationship between joint effusion and PRP treatment.

6.1.5. Local infection

Closely observe the presence of infection symptoms and signs such as redness, swelling, heat, pain, and suppuration at the treatment site. Regularly perform wound secretion culture and drug sensitivity tests. Once an infection is detected, effective anti-infection measures should be taken promptly, and the occurrence, development, and treatment results of the infection should be recorded in detail.

6.1.6. Local reactions related to joint surgical operations

When applied in the field of joint surgery, such as in combination with arthroscopic surgery, open surgery, and PRP treatment, additional attention should be paid to the healing of the surgical site. Record wound healing time, presence of dehiscence, bleeding, and drainage. Observe redness, swelling, induration formation, and scar hyperplasia around the surgical incision.

6.2. Systemic adverse reaction indicators

6.2.1. Fever

Monitor changes in patients' body temperature and record the degree of fever (low-grade, moderate, high), duration, fever pattern (such as continuous, remittent, intermittent), and accompanying symptoms (such as chills, headache, fatigue). Determine whether the fever is related to the immune response or infection after PRP treatment, and take appropriate measures to reduce the temperature.

6.2.2. Allergic reactions

Observe patients for allergic symptoms and signs such as skin itching, rash, urticaria, dyspnea, and blood pressure drop. Inquire about the patient's past history of allergies. For patients with suspected allergic reactions, allergen detection and corresponding anti-allergic treatment should be performed promptly, and the occurrence and severity of allergic reactions should be recorded in detail.

6.2.3. Gastrointestinal reactions

Inquire about gastrointestinal discomfort symptoms such as nausea, vomiting, abdominal pain, and diarrhea. Understand their frequency, severity, and relationship with diet and medication use. Evaluate whether gastrointestinal reactions affect patients' nutritional intake and quality of life, and take appropriate symptomatic treatment measures.

6.2.4. Abnormal blood system indicators

Regularly perform hematological tests such as blood routine and coagulation function before and after treatment. Monitor changes in indicators such as platelet count, white blood cell count, erythrocyte sedimentation rate, prothrombin time, and activated partial thromboplastin time. Timely detect possible adverse reactions in the blood system, such as abnormal platelet aggregation, increased bleeding tendency, or thrombosis. Adjust the treatment plan or take appropriate intervention measures based on the test results.

6.2.5. Abnormal liver and kidney function indicators

Test patients' liver function (such as alanine aminotransferase, aspartate aminotransferase, bilirubin, albumin, globulin, etc.) and kidney function (such as creatinine, urea nitrogen, uric acid, etc.) indicators. Observe the dynamic changes of these indicators before and after treatment to evaluate the potential impact of PRP treatment on liver and kidney function. For patients with liver and kidney function damage, further identify the cause and provide corresponding liver and kidney protection treatment.

6.3. Long-term safety indicators

6.3.1. Risk of tumorigenesis

Conduct long-term follow-up on patients with osteoarthritis undergoing PRP therapy, documenting the occurrence of neoplastic diseases during this period, including tumor type, location, diagnosis time, and other relevant epidemiological data. Analyze the potential association between PRP treatment and tumorigenesis, taking care to exclude the influence of other confounding factors.

6.3.2. Long-term changes in joint structure and function

Evaluate long-term structural changes such as joint cartilage wear, bone hyperplasia, joint space narrowing, and

functional changes like joint mobility, stability, and muscle strength through periodic imaging examinations (X-ray, CT, MRI) and joint function assessment scales (e.g., WOMAC score, Lequesne index). Determine whether PRP treatment has any adverse effects on the long-term structure and function of joints, providing a basis for further optimizing treatment plans.

6.4. Adverse event management

The handling of adverse events should comply with the requirements of T/ZGCIT XXX “Guidelines for the Clinical Application of Platelet-Rich Plasma (PRP) in the Treatment of Osteoarthritis.”

7. Safety evaluation methods

7.1. Clinical observation method

Trained healthcare professionals should conduct detailed physical examinations of patients before and after treatment and during follow-up, focusing on observing symptoms and signs of various local and systemic adverse reactions mentioned in the safety evaluation indicators. They should accurately and promptly record observations and classify the severity of adverse reactions (e.g., mild, moderate, severe) according to predetermined criteria for appropriate management and statistical analysis.

During each follow-up, inquire about the patient’s subjective experiences since the last visit, including abnormalities such as pain, swelling, fever, discomfort, and their impact on daily life and work. Encourage patients to report any potential treatment-related adverse reactions honestly, and combine these with objective examination results to comprehensively assess the patient’s safety status.

7.2. Laboratory examination method

Based on safety evaluation indicators, collect patient samples such as blood and synovial fluid at specific time points before and after treatment (e.g., 1 day, 1 week, 1 month, 3 months, 6 months, 1 year post-treatment). Send these to the laboratory for relevant tests, including blood routine, coagulation function, liver and kidney function, inflammatory markers (e.g., C-reactive protein, erythrocyte sedimentation rate), immunological markers (e.g., immunoglobulins, complement), and pathogen detection (e.g., bacterial culture, viral nucleic acid testing). Ensure the accuracy and reliability of laboratory results and promptly feedback any abnormalities to clinicians for further diagnosis and management.

For patients with joint effusion, besides routine physical and chemical analysis and cytology, special pathogen detection (e.g., tuberculin smear and culture, fungal culture) and biomarker testing (e.g., matrix metalloproteinases, cytokines) should be performed based on the patient’s condition. This clarifies the etiology and nature of the effusion, providing a basis for targeted treatment plans.

7.3. Imaging examination method

During pre-treatment and follow-up, select appropriate imaging methods like X-ray, CT, MRI, or joint ultrasonography based on the patient’s specific conditions to evaluate the treated joint. Focus on observing morphological and signal changes in structures such as articular cartilage, bone, synovium, meniscus, and surrounding soft tissues. Determine if there are any imaging abnormalities related to treatment, such as aggravated cartilage damage, bone destruction, synovial thickening, increased joint effusion, soft tissue swelling or calcification. Combine these findings with clinical symptoms and signs for comprehensive analysis,

assessing the impact of these imaging changes on joint function and quality of life.

Imaging examinations should be interpreted and diagnosed by experienced professional radiologists. Establish a standardized imaging report template, detailing any observed abnormalities and making an initial judgment on their correlation with PRP treatment. This provides accurate imaging information support to clinicians for timely treatment adjustments or interventions.

7.4. Patient-reported outcomes (PRO) survey method

Utilize validated PRO scales such as the Visual Analog Scale (VAS) for pain, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and the Short Form-36 (SF-36) health survey. Conduct questionnaire surveys at various follow-up time points before and after treatment to understand patients' subjective perceptions and evaluations regarding their health status, joint pain, functional limitations, and quality of life. Obtain information on treatment safety and efficacy from the patient's perspective.

During the PRO survey process, ensure questionnaire distribution, completion, and collection comply with standard requirements. Explain the questionnaire completion method and precautions to patients, guaranteeing they can express their feelings and experiences truthfully and accurately. Simultaneously, perform strict quality control and data analysis on collected questionnaires, integrating patient-reported outcomes with clinical observations, laboratory examinations, and imaging results for a comprehensive understanding of the safety of PRP treatment for osteoarthritis and its impact on patients' quality of life.

8. Safety evaluation process

8.1. Pre-treatment assessment

8.1.1. Patient selection

It should comply with the requirements of T/ZGCIT XXX "Guidelines for the Clinical Application of Platelet-Rich Plasma (PRP) in the Treatment of Osteoarthritis."

8.1.2. PRP preparation evaluation

It should conform to the provisions of T/ZGCIT XXX "Technical Specification for the Preparation of Platelet-Rich Plasma (PRP)."

8.1.3. Informed consent

Fully inform patients about the purpose, methods, expected effects, possible adverse reactions, and risks of PRP treatment for osteoarthritis. Ensure that patients sign the informed consent form based on a thorough understanding, protecting their right to information and choice. This also establishes a solid foundation of communication and trust for subsequent safety evaluations.

8.2. Treatment process monitoring

8.2.1. Treatment operation records

During the PRP injection process, detailed records should be kept of the specific operational steps, including sterilization methods for the injection site, injection routes (such as intra-articular injection, peri-articular soft tissue injection, etc.), injection dose, injection speed, and patient reactions during injection. This ensures the standardization and normalization of treatment operations and provides a basis for analyzing possible

relationships between adverse reactions and treatment procedures.

8.2.2. Immediate adverse reaction observation

After the injection, closely monitor the patient's immediate reactions at the treatment site, including symptoms such as increased pain, dizziness, palpitations, sweating, rash, and dyspnea. The observation should continue for at least 30 minutes. If any abnormalities occur, prompt emergency measures should be taken, and detailed records should be made of the adverse reaction's occurrence time, manifestations, severity, and management process.

8.3. Post-treatment follow-up evaluation

8.3.1. Follow-up plan development

Based on the characteristics of PRP treatment for osteoarthritis and the requirements of safety evaluation indicators, a detailed follow-up plan should be developed. This plan should clarify the follow-up time points (e.g., 1 day, 1 week, 2 weeks, 1 month, 3 months, 6 months, 1 year post-treatment), follow-up contents (including clinical symptom inquiry, physical examination, laboratory tests, imaging examinations, etc.), and follow-up methods (such as outpatient follow-up, telephone follow-up, online follow-up, etc.). This ensures comprehensive and systematic monitoring and evaluation of the patient's condition after treatment.

8.3.2. Data collection and organization

During each follow-up, collect various safety evaluation data from patients according to the predetermined follow-up content. This includes patient subjective feelings, clinical examination results, laboratory test reports, and imaging examination images. Ensure detailed recording and organization of the data, guaranteeing its completeness, accuracy, and timeliness. This provides a reliable foundation for subsequent data analysis and safety evaluation.

8.3.3. Safety evaluation and reporting

Based on the collected follow-up data, conduct a comprehensive evaluation of the patient's safety status at each follow-up time point according to the safety evaluation index system and methods specified in this standard. Determine the presence of adverse reactions, as well as their types, severity, frequency of occurrence, and prognosis. Regularly prepare safety evaluation reports, summarizing the results of PRP treatment for osteoarthritis and providing timely feedback to clinicians and relevant researchers. These reports serve as reference points for clinical decision-making and scientific research. For cases with severe adverse reactions, conduct detailed individual case analyses and reports, deeply exploring the mechanisms and possible risk factors of adverse reactions, and proposing corresponding prevention and management suggestions to improve the safety and effectiveness of PRP treatment.

9. Contents and format of the safety evaluation report

9.1.1. Basic information

Include the patient's name, gender, age, contact information, hospital admission number (or outpatient number), diagnosis (specific site and staging of osteoarthritis), and treatment time. This clarifies the patient's individual

characteristics and treatment background.

9.1.2. Treatment plan

Provide a detailed description of the PRP preparation method (such as the centrifugation technique used, type of anticoagulant, activation method, final platelet concentration, etc.), treatment operation process (including injection site, injection dose, injection frequency, whether combined with other treatment measures, etc.), and any special situations during the treatment (such as whether the treatment process was smooth or if any unexpected events occurred). This allows readers to clearly understand the specific treatment plan received by the patient.

9.1.3. Results of safety evaluation indicators

(1) Local adverse reactions

List the occurrence of adverse reactions such as pain, swelling, erythema, joint effusion, and local infection. Include information on the time of occurrence, duration, severity (described as mild, moderate, or severe), management measures (such as drug treatment, physical therapy, surgical intervention, etc.), and prognosis (such as complete resolution, partial resolution, no resolution or worsening). If relevant images or imaging data are available, annotate and explain their acquisition time and method. (2) Systemic adverse reactions

Report the occurrence of systemic adverse reactions such as fever, allergic reactions, gastrointestinal reactions, abnormalities in blood system indicators, and abnormalities in liver and kidney function indicators. Record the specific manifestations, time of occurrence, severity, diagnostic basis (e.g., laboratory test results, clinical manifestation characteristics, etc.), treatment process, and prognosis of each adverse reaction. For severe adverse reactions requiring hospitalization or special examinations, provide detailed medical records and examination report summaries.

(3) Long-term safety indicators

Summarize the monitoring results of tumor occurrence risk and long-term changes in joint structure and function. Include information on follow-up time, whether tumor cases were detected during the follow-up period (if so, describe the tumor diagnosis process, pathological type, treatment situation, etc.), and dynamic changes in joint imaging examinations and functional scoring scales. Analyze the potential relationship between these long-term safety indicators and PRP treatment, discussing and providing an outlook based on existing literature.

9.1.4. Conclusion and recommendations

Based on the safety evaluation results, make an overall evaluation of the safety of PRP treatment for the osteoarthritis patient in this case. Clarify whether severe adverse reactions occurred during the treatment process and the extent of their impact on the patient's health. Provide suggestions for subsequent treatment and follow-up for this patient. Additionally, discuss general safety issues of PRP treatment for osteoarthritis, summarizing lessons learned and providing reference points and improvement directions for future clinical practice and research work.

9.2. Report format

The format for the safety evaluation report of platelet-rich plasma in the treatment of osteoarthritis is as follows:

(1) Cover page

The cover should include the report title (e.g., “Safety Evaluation Report of Platelet-Rich Plasma in the Treatment of Osteoarthritis”), the patient’s name, the report date, the name of the reporting institution, and contact information. The format should be concise and clear, facilitating easy identification and archiving.

(2) Table of contents

List the main sections and corresponding page numbers of the report to allow readers to quickly locate the desired information.

(3) Main text

The main text should elaborate on each section in the order specified above. The language should be clear, accurate, and concise, avoiding overly complex or ambiguous vocabulary and sentence structures. For data and results, visual aids such as tables, bar charts, line graphs, and flowcharts should be used to enhance readability and persuasiveness. Additionally, appropriate references should be cited in the text to support the scientific validity and reliability of the conclusions.

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List all references cited in the report, formatted according to the national standard for citation (e.g., GB/T 7714-2015). Ensure the completeness and accuracy of reference information to facilitate further reading and traceability of relevant literature.

10. Application and feedback of evaluation results

Provide timely feedback of safety evaluation results to clinicians, serving as an important reference for developing individualized PRP treatment plans for osteoarthritis. For patients with higher safety profiles, clinicians can appropriately adjust treatment parameters (such as increasing injection dose, shortening injection intervals, etc.) based on the patient’s condition to improve treatment effectiveness. For patients who experience adverse reactions, clinicians should promptly adjust the treatment plan (such as suspending treatment, changing the treatment method, providing corresponding symptomatic treatment measures, etc.) based on the severity and type of adverse reaction to ensure patient safety and health.

Regularly summarize and analyze the safety evaluation results of PRP treatment for osteoarthritis in clinical practice.

Disclosure statement

The author declares no conflict of interest.

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Research on Sport-Specific Adaptive Training Programs Following Repair of Upper Limb (Rotator Cuff and Elbow Joint) Impact Injuries in Rugby

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Abstract: Rugby is a highly competitive sport with unique functional demands on the upper limbs, resulting in a high incidence of impact injuries to the rotator cuff and elbow joint. After the repair of such injuries, conventional rehabilitation training often fails to meet the specialized athletic requirements for athletes returning to competition, which can easily lead to secondary injuries or a decline in athletic performance. Based on the specialized mechanisms of upper limb impact injuries in rugby and the core needs after repair, this paper constructs a three-stage specialized adaptive training program: “clinical rehabilitation - specialized transition - competitive adaptation,” along with proposing individualized adjustment strategies and risk prevention measures. The aim is to provide a scientific basis for the Basketball and Rugby Sports Management Center to formulate rehabilitation plans for athletes after injury, enhance rehabilitation efficiency, and ensure the safe return of athletes to competition.

Keywords: Rugby; Rotator cuff injury; Elbow joint impact injury; Specialized adaptive training; Rehabilitation program

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1. Introduction

In rugby, the upper limbs are crucial for executing core technical movements such as passing, tackling, blocking, and ball-carrying breaks. The rotator cuff and elbow joints are subjected to repetitive traction, valgus stress, and instantaneous impact forces, leading to a high incidence of impingement injuries. According to statistics, upper limb injuries account for 35%–40% of all sports injuries among rugby players, with impingement-related injuries such as rotator cuff impingement syndrome, ulnar collateral ligament injuries of the elbow, and lateral epicondylitis of the humerus comprising over 60% of these cases^[1]. After surgical or conservative treatment and repair, if conventional rehabilitation methods such as range-of-motion recovery and basic strength training are solely employed, athletes may achieve “functional recovery.” However, upon returning to competition, they often experience limited power output and distorted movements due to inadequate load tolerance of the upper limbs for

specialized movements and uncoordinated movement patterns, resulting in a secondary injury risk that is 2-3 times higher than that of the general population ^[2]. The Basketball and Rugby Sports Management Center bears the core responsibility of ensuring athlete health and enhancing athletic performance, necessitating the establishment of a rehabilitation system that integrates both “clinical healing principles” and “specialized sports demands.” Therefore, it is essential to explore specialized adaptive training programs for upper limb (rotator cuff, elbow joint) impingement injuries in rugby following repair.

2. Specialized mechanisms and core rehabilitation needs of upper limb impingement injuries in rugby

2.1. Specialized injury mechanisms of rotator cuff impingement injuries

The rotator cuff muscle group (supraspinatus, infraspinatus, teres minor, and subscapularis) is the core structure for maintaining dynamic stability of the shoulder joint. In rugby, the following specialized movements are prone to inducing impingement injuries: First, overhand passing. During passing, the shoulder joint needs to complete a coherent sequence of “extension-abduction-internal rotation,” and the supraspinatus tendon repeatedly traverses the subacromial space. Studies have shown that the pressure in the subacromial space can reach 300–400 kPa during this process. If the athlete has a Type II/III acromion morphology (hooked acromion) or insufficient scapular stability, it can easily lead to repeated friction between the tendon and the acromion and coracoacromial ligament, triggering subacromial impingement syndrome. During high-intensity passing, the rotator cuff needs to withstand a pulling force of 3-4 times the body weight. If the repaired tendon has not adapted to this load, it is prone to re-tearing. Second, tackling and blocking ^[3].

During a frontal tackle, the upper limbs need to extend forward and resist the reactive force of the opposing player. The rotator cuff must rapidly undergo eccentric contraction to maintain shoulder joint stability. If the timing of force application is inappropriate or there is an imbalance in rotator cuff muscle strength (such as the infraspinatus being weaker than the subscapularis), it can easily lead to eccentric tendon injury ^[4]. During lateral blocking, the shoulder joint is subjected to lateral impact forces, which may trigger compound impingement between the rotator cuff muscle group and the joint capsule, exacerbating the extent of injury.

2.2. Specialized injury mechanisms of elbow joint impingement

The elbow joint serves as a crucial hub for force transmission in rugby, and its impingement injuries are mostly related to “valgus stress” and “repeated flexion and extension.” The specific mechanisms are as follows:

During passing, the elbow joint needs to rapidly extend from a 90° flexion position to nearly full extension. The origin of the common extensor tendon at the lateral epicondyle of the humerus is subjected to repeated traction, which, over time, can easily lead to lateral epicondylitis (“tennis elbow”). When breaking through with the ball, the elbow joint needs to resist the pulling force of the opposing player. The anterior bundle of the ulnar collateral ligament is subjected to continuous valgus stress, which can reach 200–250 N. When this stress exceeds the tolerance limit of the ligament, it can easily lead to strain or partial tearing.

When an athlete falls to the ground and supports their body with the palm of their hand, the elbow joint instantaneously bears an axial impact force (which can reach 5-6 times the body weight). This can lead to the impact between the articular surfaces of the olecranon process of the ulna and the trochlea of the humerus, potentially causing cartilage damage or osteophyte formation. This, in turn, may induce osteoarthritis of the elbow joint and increase the risk of subsequent impact injuries ^[5].

2.3. Core specialized needs after repair

After the repair of rotator cuff and elbow joint impingement injuries, the rehabilitation needs of athletes should go beyond “basic functional recovery” and focus on the specialized characteristics of rugby. Specifically, these needs include: restoring the “stabilizing strength” of the rotator cuff muscle group (to maintain dynamic stability of the shoulder joint and prevent joint instability and impingement during passing) and the “explosive strength” of the muscle groups surrounding the elbow joint (to meet the demands of rapid force generation during passing and resistance during tackling); rebuilding the coordinated force generation pattern of the upper limbs and trunk (such as the linkage between the shoulder, waist, and hip during passing) to avoid secondary injuries caused by compensation from a single body part ^[6]; gradually adapting to the “repetitive loads” (such as 10-15 consecutive passes) and “impact loads” (such as the instantaneous resistance during tackling) encountered in rugby; and conducting targeted training for specialized movements such as overhand passing, tackling, and blocking to ensure standardized and efficient movements and reduce the risk of injury recurrence.

3. Design of a specialized adaptive training program after repair of upper limb impingement injuries in rugby

3.1. Phase 1: Clinical rehabilitation period - tissue protection and basic functional activation

3.1.1. Training objectives

Maintain the repair environment of tissues surrounding the rotator cuff and elbow joint to prevent adhesion; activate the basic functions of the rotator cuff muscle group and the elbow joint flexor-extensor muscle group, and restore joint range of motion (shoulder flexion $\geq 120^\circ$, abduction $\geq 90^\circ$, elbow flexion-extension $\geq 135^\circ/0^\circ$); and alleviate postoperative/post-injury pain (VAS pain score ≤ 2 points).

3.1.2. Core training content

- (1) Range of motion training: The rehabilitation therapist assists in passive shoulder flexion and abduction (avoiding overhead movements), and uses resistance bands for passive elbow flexion and extension. Each movement is held for 15-20 seconds, with 3 sets per session and 1 session per day, laying the foundation for subsequent specialized movements.
- (2) Muscle activation training: Perform isometric contractions of the rotator cuff while standing against a wall (with the upper arm against the torso and external rotation against the wall), and isometric contractions of the elbow flexors/extensors while seated (with the forearm on a table and resisting hand pressure). Each contraction is held for 10 seconds, followed by a 5-second relaxation, with 15 repetitions per set and 2 sets per session, activating stabilization functions.
- (3) Core stability training: Perform prone planks with knees on the ground (30 seconds per set, 3 sets) and glute bridges (15 seconds per repetition, 12 repetitions per set) to strengthen the core and provide a stable foundation for specialized movements.

3.1.3. Intensity control and precautions

All movements should be performed under the premise of “pain-free.” If pain occurs (VAS score > 3), the exercise should be stopped immediately. Avoid active overhead movements (such as raising the arm above shoulder level) to prevent excessive strain on the rotator cuff tendons. A rehabilitation therapist should be present to provide

guidance, correct issues such as “shrugging” and “compensatory force generation,” and ensure proper movement form.

3.2. Phase two: Specialized transition period-muscle strength enhancement and establishment of basic specialized movements

3.2.1. Training objectives

Enhance concentric/eccentric strength of the rotator cuff muscles (especially the supraspinatus and subscapularis), and isotonic strength of the elbow flexors/extensors; establish a “simplified movement pattern” for rugby-specific actions (such as half-range passing and non-contact tackling simulations); restore the range of motion to normal levels (shoulder flexion $\geq 160^\circ$, abduction $\geq 120^\circ$, elbow flexion/extension $\geq 145^\circ/0^\circ$).

3.2.2. Core training content

- (1) Muscle strengthening training: For the rotator cuff muscle group, use elastic band shoulder abduction ($0\text{--}90^\circ$), internal/external rotation (upper arm against the torso), 3 sets per session, 2 sessions per day^[7]; for the elbow joint muscle group, perform dumbbell forearm flexion/extension (0.5–1 kg) and elastic band elbow flexion/extension, 12 repetitions per set, 3 sets per session, 2 sessions per day; for the scapular stabilizing muscle group, conduct prone “fly” exercises and elastic band pull-downs, 10 repetitions per set, 3 sets per session, 2 sessions per day.
- (2) Prototype training for specialized movements: Standing and holding a soft ball for half-range passing simulations (15 repetitions per set, 2 sets per session), facing a foam dummy for non-contact tackling simulations (10 repetitions per set, 2 sets per session), and holding a rugby ball for ball-carrying breakthrough simulations (8 repetitions per set, 2 sets per session).
- (3) Coordination training: Seated while holding a ball, perform shoulder extension and forward push passing in coordination with breathing, while tightening the abdomen, 12 repetitions per set, 3 sets per session, 1 session per day.

3.2.3. Intensity control and precautions

Gradually increase the load during muscle strength training, ensuring that muscle soreness does not persist for more than 24 hours after each training session (to avoid excessive fatigue that may hinder healing); use soft training equipment (such as soft balls and foam dummies) for specialized movement simulations to reduce impact loads on the upper limbs; conduct joint range of motion and muscle strength assessments once a week, and promptly adjust the training program if there is a stagnation in muscle strength growth or a decrease in joint range of motion.

3.3. Phase three: On-Field adaptation period—load tolerance and specialized confrontation adaptation

3.3.1. Training objectives

The primary objectives of this phase are to enhance the upper limb’s tolerance to rugby-specific loads (such as continuous passing and confrontational tackling); optimize the power efficiency of specialized movements to restore athletic performance (such as passing speed and tackling stability); and establish awareness of secondary injury prevention, mastering self-protection movements for unexpected situations on the field.

3.3.2. Core training content

During this phase, the core training content primarily encompasses three aspects: First, specialized load tolerance training. This involves coordinated passing drills with teammates over progressive distances of 5 to 15 meters (3 sets per session, 2 sessions per day), gradually increasing the passing frequency; engaging in light-intensity tackling drills against padded teammates (3 sets per session, 1 session per day), progressively increasing resistance; and conducting medicine ball overhead throws for distance and elastic band-assisted passing drills (10 repetitions per set, 3 sets per session, 1 session per day). Second, specialized movement optimization training. This includes correcting passing techniques through video playback, simulating falling scenarios to train self-protection movements, and performing specialized movements on different playing surfaces to enhance environmental adaptability. Third, organized comprehensive confrontation training in the form of 3v3 and 5v5 small-sided games (with restrictions on high-intensity collisions), conducting specialized training under fatigue conditions, and simulating late-game scenarios.

3.3.3. Intensity control and precautions

The intensity of confrontation training should be gradually increased, with the initial confrontation game intensity not exceeding 50% of the game intensity, and subsequent weekly increases of 10% to 15%. After each training session, apply ice packs to the upper limbs (15 minutes each for the rotator cuff and elbow joints) to alleviate muscle fatigue and inflammatory responses. A team doctor should be present on-site. If any upper limb pain, numbness, or abnormal force generation occurs during training, immediately suspend the training and conduct an assessment.

4. Evaluation and individualized adjustment of specialized adaptive training programs

4.1. Multidimensional evaluation system

To ensure the effectiveness and safety of the training program, an evaluation system combining “stage assessment + dynamic monitoring” has been established, with specific indicators outlined in **Table 1** below.

Table 1. Multidimensional evaluation system

Evaluation Dimension	Core Metrics	Frequency	Passing Standard
Pain Assessment	VAS Pain Score	Before each session	VAS ≤ 3 during training; returns to ≤ 1 within 24 hours after training
Function Assessment	UCLA Shoulder Score (rotator cuff) MEPS Elbow Score (elbow joint)	Every 2 weeks	UCLA Score ≥ 30 (Excellent) MEPS Score ≥ 90 (Excellent)
Strength Assessment	Isokinetic Strength Test (shoulder IR/ER, elbow flexion/extension at 60°/s & 180°/s)	Every 4 weeks	Affected side strength $\geq 85\%$ of the healthy side Strength symmetry error $\leq 10\%$
Sport-Specific Performance	Passing speed (radar gun) Passing accuracy (hits/10 attempts) Tackling stability (posture maintenance time under resistance)	Every 2 weeks	Passing speed $\geq 90\%$ of the healthy side Accuracy $\geq 80\%$ No difference in tackling stability compared to the healthy side
Imaging Evaluation	Ultrasound/MRI (rotator cuff tendon continuity, elbow ligament edema)	Pre- and post-training	Good rotator cuff tendon continuity, no re-tears No edema or worsened damage in the elbow ligaments

4.2. Individualized adjustment strategies

Based on the severity of the injury and the repair method, athletes undergoing surgery for complete rotator cuff tears should extend their clinical rehabilitation period to 8–10 weeks, while those undergoing conservative treatment can shorten it to 4–6 weeks. In terms of age, athletes under 25 years old can increase the intensity of explosive power training, while those over 30 years old should focus more on core training and extend their period of adaptation to the playing field. Regarding position, quarterbacks should intensify passing drills, while linebackers should prioritize elbow joint resistance and protective training.

5. Risk prevention and control and safeguard measures for training programs

5.1. Common risk points and response strategies

5.1.1. Risk of secondary impact

If there is a sudden worsening of shoulder cuff or elbow joint pain during training, training should be immediately suspended, and an ultrasound examination should be conducted to rule out tendon re-tearing. Response measures: Adequate warm-up before training (dynamic stretching + 5–10 minutes of light aerobic exercise), setting a “pain warning line” during training (stop if VAS score > 3), and performing static stretching for relaxation after training.

5.1.2. Risk of muscular compensation

If athletes exhibit actions such as “shrugging shoulders while passing” or “bending forward to compensate for elbow extension,” it can easily lead to secondary injuries in the neck and waist. Response measures: Rehabilitation specialists should be present to observe movements in real-time, use motion capture technology to analyze movement patterns, promptly correct compensatory actions, and apply kinesiology tape for fixation when necessary.

5.1.3. Risk of overtraining

If persistent upper limb soreness lasts more than 48 hours after training or if muscle strength declines, it indicates overtraining. Response measures: Establish a training log to record the load and physical response of each training session, schedule 1–2 rest days per week, avoid continuous high-intensity training, and supplement with protein and vitamins as necessary to promote recovery.

5.2. Safeguard measures

The center should establish a collaborative team consisting of “team doctors, rehabilitation therapists, and specialized coaches.” Team doctors are responsible for injury assessment and risk management, rehabilitation therapists design training programs and adjust intensity levels, and specialized coaches optimize movement details based on rugby-specific technical requirements, ensuring that training is both “safe” and “rugby-specific” [8,9]. Secondly, the center should be equipped with professional equipment such as soft training balls, resistance bands, isokinetic muscle strength training devices, foam dummies, and shoulder and elbow pads [10]. The training venue should be flat and free of debris, and grassy fields should undergo regular inspections for evenness to prevent accidental injuries caused by equipment or venue issues. Additionally, regular training sessions on upper limb injury prevention and rehabilitation knowledge should be conducted. Through case studies and movement demonstrations, athletes can understand their injury characteristics and training contraindications, enhancing their self-protection awareness and encouraging proactive cooperation with training programs.

5. Conclusion

The rehabilitation of upper limb (rotator cuff, elbow joint) impingement injuries in rugby should prioritize “safe return to the field and restoration of rugby-specific athletic abilities” as the core objective, rather than merely satisfying basic functional recovery. The “three-stage rugby-specific adaptive training program” developed in this paper can be further refined in the future by incorporating sports biomechanics technologies (such as three-dimensional motion capture and surface electromyography analysis) to optimize training details. This will provide more precise scientific support for the rehabilitation training of upper limb injuries in rugby, facilitating athletes’ efficient return to the field and enhancing their athletic performance.

Disclosure statement

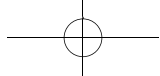
The authors declare no conflict of interest.

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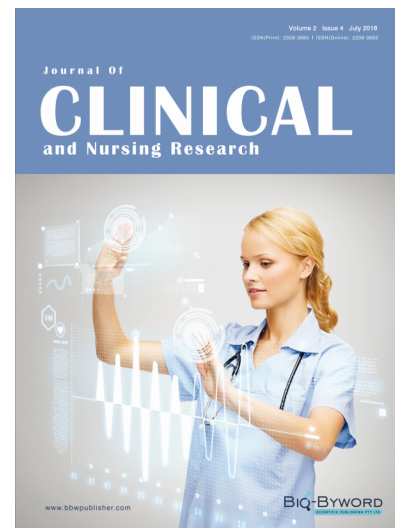
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