



Analysis of Risk Factors of Cartilage Wear in Lateral Compartment of Patients with Varus Knee Osteoarthritis

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ABSTRACT

The objective of this study was to investigate the risk factors of cartilage wear in the lateral compartment of patients with varus knee osteoarthritis (VKO). The sample consisted of 110 patients with VKO who underwent total knee arthroplasty at Fujian hospital. The patients were divided into the lateral compartment cartilage abrasion group (n=30) and the lateral compartment cartilage non abrasion group (n=80) according to the lateral compartment cartilage status. The clinical data and laboratory indexes of patients were collected, and the risk factors of cartilage wear in lateral compartment of patients with VKO were analyzed by single factor and multi factor logistic regression. Labor intensity, imaging grade, integrity of lateral meniscus and anterior cruciate ligament, and course of disease may be the risk factors for cartilage wear of lateral compartment in patients with VKO ($P<0.05$). The levels of IL-6, TNF- α and IL-1 β in the joint fluid of the cartilage wear group were significantly higher than those of the non-wear group ($P<0.05$). The results showed that the heavy labor intensity, the absence or insufficiency of the lateral meniscus, the absence or insufficiency of the anterior cruciate ligament, the long course of disease, and the high level of IL-6, TNF- α and IL-1 β was an independent risk factor for cartilage wear of lateral compartment in patients with VKO ($P<0.05$). It was concluded that heavy labor intensity, absence or incompleteness of lateral meniscus, absence or incompleteness of anterior cruciate ligament, long course of disease and high level of IL-6 and TNF- α in synovial fluid IL-1 β Level is an independent risk factor for cartilage wear of lateral compartment in patients with VKO.

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Authors' Contribution

YL and PZ conducted the experiments in this study. QW and DC contributed to the design and interpretation of the current study and wrote the article.

Key words

Varus type, Knee osteoarthritis, Lateral compartment, Cartilage abrasion, Risk factors

INTRODUCTION

Knee osteoarthritis is one of the common clinical chronic bone and joint diseases, which is often accompanied by varus deformity, which usually occurs in the middle-aged and elderly people. The patients mainly show clinical symptoms such as knee joint swelling, pain, limitation of movement, loss of function, local tenderness and so on. In severe cases, there are even knee joint deformities and even disabilities, seriously affecting the daily activities and quality of life of patients (Matsumoto *et al.*, 2022). At present, the clinical treatment of patients with knee osteoarthritis is still lack of radical treatment, mainly using symptomatic support treatment and ladder therapy,

although it can alleviate the clinical symptoms to some extent, but the effect on the prognosis of patients is limited (Liu *et al.*, 2022). With the continuous progress of clinical medical technology, total knee arthroplasty uses surgical methods to replace diseased joints, which provides an effective treatment for patients with knee osteoarthritis.

According to clinical studies, the wear and tear of cartilage in the lateral compartment of patients with knee osteoarthritis is a key factor affecting the implementation of knee arthroplasty (Tsubosaka *et al.*, 2018). Patients with knee osteoarthritis varus deformity with lateral compartment cartilage wear are not suitable for knee arthroplasty (Mortazavi and Vosoughi, 2022). Therefore, to explore the characteristics of lateral compartment cartilage wear in patients with varus knee osteoarthritis (VKO) and to study the risk factors of lateral compartment cartilage wear in patients with VKO. It has important clinical significance to slow down the pathological progress of osteoarthritis, improve the feasible treatment rate of knee arthroplasty and improve the quality of life of patients. The purpose of this study was to explore the risk factors of lateral compartment cartilage wear in patients with VKO in order to provide reference for the clinical diagnosis and treatment of knee osteoarthritis.

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MATERIALS AND METHODS

Sample

A total of 110 patients with inverted knee osteoarthritis who underwent total knee arthroplasty in our hospital from September 2019 to December 2021 were divided into two groups: Lateral compartment cartilage attrition group (n=30) and lateral compartment cartilage unworn group (n=80) according to the state of lateral compartment cartilage during operation.

Patients with VKO in both groups were eligible to join the study if they met the following inclusion criteria: Patients with inverted knee osteoarthritis were diagnosed by clinical symptoms, signs and imaging examination (Ihle *et al.*, 2022); patients were treated with total knee arthroplasty; and patients with complete clinical records. Patients with congenital malformations, traumatic arthritis and inflammatory arthropathy, severe cardiac and renal insufficiency, and previous knee surgery or osteotomy were excluded from both groups. Patients could withdraw from the study at any point without prejudice to their care.

Methods

During the operation, the wear and tear of cartilage was more than weidow 2 grade, and the lateral compartment cartilage was not full layer. After osteotomy, dehydration, embedding and section treatment, the paraffin sections were stained with HE, and the morphological changes of cartilage were observed under microscope to confirm the wear and tear (Zhang *et al.*, 2020).

Consult the case data and record the sex, age, body mass index and labor intensity of the two groups of patients (technicians, managers, intellectuals and other mental workers are defined as light physical labor intensity. Workers, fishermen, soldiers and farmers were defined as heavy physical labor intensity, lateral collateral ligament (stable and unstable during operation), imaging grade, location of lesion, lateral meniscus (missing or incomplete and intact during operation), anterior cruciate ligament (missing or incomplete and intact during operation), course of disease, varus angle, range of motion, HSS score. The synovial fluid was extracted before operation and the levels of interleukin-6 (IL-6), interleukin-8 (IL-8) and tumor necrosis factor- α (TNF- α) were detected according to the instructions of ELISA detection kit. Univariate analysis was used to analyze the related factors of lateral compartment cartilage wear in patients with VKO, and Logistic multivariate regression was used to analyze the independent risk factors of lateral compartment cartilage wear in patients with VKO.

Statistical analysis

All data were analysed with Statistical Package for Social Sciences version 20. χ^2 test was used to compare the counting data, mean \pm standard deviation ($\bar{x} \pm s$) was used to express the measurement data, t-test was used for comparison, and Logistic regression was used to analyze risk factors. The difference was statistically significant ($P < 0.05$).

RESULTS

There was no significant difference in sex, age, body mass index (BMI), stability of lateral collateral ligament, location of lesion, angle of varus, range of motion and HSS score between the two groups, but labor intensity, imaging grade, integrity of lateral meniscus and anterior cruciate ligament and course of disease may be the risk factors of lateral compartment cartilage wear in patients with VKO (Table I).

The levels of IL-6, TNF- α and IL-1 β in synovial fluid in cartilage wear group were significantly higher than those in non-cartilage wear group (Table II).

The results of multiple linear regression analysis showed that heavy labor intensity, absence or insufficiency of lateral meniscus, absence or insufficiency of anterior cruciate ligament, long course of disease and high levels of IL-6, TNF- α and IL-1 β in synovial fluid were independent risk factors for lateral interventricular cartilage wear in patients with VKO ($P < 0.05$) (Tables III and IV).

DISCUSSION

VKO is a chronic joint disease that often occurs in middle-aged and elderly people. In severe cases, joint deformities or even disabilities are easy to occur, which seriously affect the health and quality of life of patients (Wang *et al.*, 2022). With the aggravation of the aging problem in our society, the incidence of knee osteoarthritis is increasing year by year. According to the investigation of clinical epidemiology, the incidence of osteoarthritis in middle-aged and elderly people over 60 years old is as high as 50%. The disability rate of patients with osteoarthritis is as high as 53% (Zhang *et al.*, 2020). At present, there is still a lack of clinical methods for the radical cure of osteoarthritis, and the late stage is generally solved by surgical methods such as joint replacement. Knee arthroplasty is an effective method for the clinical treatment of knee osteoarthritis, but according to clinical studies, knee osteoarthritis patients with wear and tear of lateral compartment cartilage will fail in knee arthroplasty (Koh *et al.*, 2019). Knee arthroplasty is suitable for patients with inverted knee osteoarthritis with limited medial compartment lesions.

Table I. Comparison of general data and biomechanical indexes of knee joint.

Characteristics		Cartilage wear group (n=30)	Unworn cartilage group (n=80)	$\chi^2/t/Z$	P
Sex	Male	18	50	0.058	0.810
	Female	12	30		
Age		66.70±10.68	65.38±9.42	0.631	0.530
BMI (kg/m ²)		28.42±3.36	27.83±3.41	0.811	0.419
Labor intensity	Heavy	20	29	8.172	0.004
	Light	10	51		
Lateral collateral ligament (knee)	Instability	19	41	1.285	0.257
	Stability	11	39		
Imaging grading (knee)	1	0	3	2.140	0.033
	2	2	21		
	3	11	23		
	4	17	33		
Location of lesion (knee)	Right	13	41	0.547	0.459
	Left	17	39		
Lateral meniscus (knee)	Absence or imperfection	26	16	41.083	0.000
	Intact	4	64		
Anterior cruciate ligament (knee)	Absence or imperfection	21	14	27.720	0.000
	Intact	9	66		
Course of disease (year)		11.42±4.36	7.83±3.41	4.545	0.000
Varus angle(°)		9.50±1.44	8.91±1.65	1.726	0.087
Range of activity(°)		102.03±26.13	105.43±28.61	0.568	0.571
HSS score (score)		56.45±18.43	57.13±16.28	0.188	0.851

Table II. Comparison of biochemical indexes of articular fluid between the two groups.

Group	Cartilage wear group (n=30)	Unworn cartilage group (n=80)	P	t
IL-6 (μg·L ⁻¹)	150.37±16.09	97.86±11.28	0.000	19.236
TNF-α (ng·L ⁻¹)	121.41±13.14	50.71±8.22	0.000	33.742
IL-1β (pg·L ⁻¹)	16.36±2.13	9.34±1.76	0.000	17.567

Table III. Assignment.

Factor	Variable	Assignment
Cartilage tissue wear	Y	Not worn=0, worn =1
Labor intensity	X1	Light =0, heavy =1
Lateral meniscus	X2	Intact=0, absence or imperfection =1
Anterior cruciate ligament	X3	Intact=0, absence or imperfection =1
Course of disease	X4	Continuous variable
IL-6	X5	
TNF-α	X6	
IL-1β	X7	

Table IV. Analysis of multiple factors affecting cartilage wear in lateral compartment of patients with VKO.

Project	Regression coefficient (B)	P	OR	95% confidence interval of OR	
				Lower limit	Upper limit
Labor intensity	0.298	0.034	1.347	1.002	1.775
Lateral meniscus	0.168	0.015	1.071	0.896	1.652
Anterior cruciate ligament	2.798	0.009	16.415	2.025	33.071
Course of disease	0.031	0.004	1.031	0.801	1.180
IL-6	0.218	0.028	1.244	0.968	1.599
TNF-α	0.031	0.004	1.031	0.801	1.180
IL-1β	0.035	0.008	1.037	0.880	2.996

Wear and tear of lateral compartment cartilage is a contraindication for knee arthroplasty and the most common cause of surgical failure (Kim *et al.*, 2019). Therefore, to deeply study the pathogenesis and etiology of lateral compartment cartilage wear in patients with VKO, to explore the risk factors of lateral compartment cartilage

wear in patients with VKO, and to find possible preventive ways. It has important clinical significance to slow down the pathological progress of osteoarthritis, improve the feasible treatment rate of knee arthroplasty and improve the quality of life of patients.

The abnormal biomechanics of knee joint may be related to the mechanism of cartilage wear in lateral compartment of patients with inverted knee osteoarthritis (Bonano *et al.*, 2021). There are anatomical differences between the medial and medial compartments of the knee joint. When the human body is standing upright, about 60% of the body load is distributed in the medial compartment, and kinematics takes the medial compartment as the axis of movement, so the wear of the medial compartment of the knee joint is more common (Cheng *et al.*, 2020). The study found that a small number of patients with VKO had cartilage wear in the lateral compartment (Oh *et al.*, 2018). The results of multiple linear regression analysis showed that heavy labor intensity, absence or insufficiency of lateral meniscus, absence or insufficiency of anterior cruciate ligament, long course of disease and high levels of IL-6, TNF- α and IL-1 β in synovial fluid were independent risk factors for lateral intercompartmental cartilage wear in patients with VKO. In this study, we define mental workers such as technicians, managers and intellectuals as those with light physical labor intensity, and workers, fishermen and herdsman, soldiers and farmers as those with heavy physical labor intensity (Klasan *et al.*, 2020). People with heavy physical labor intensity are engaged in heavy manual labor for a long time, the knee joint has a high load, and the articular cartilage is subjected to high stress load for a long time, so there is a greater risk of cartilage wear in the lateral compartment (Nishida *et al.*, 2017). With the prolongation of the course of disease in patients with VKO, joint protective mechanical factors and nerves are gradually damaged, such as decreased muscle strength, relaxation of valgus and valgus, and loss of proprioceptive sensation, resulting in joint instability affecting the lateral compartment and wear of cartilage in the lateral compartment. In addition, with the prolongation of the course of disease in patients with VKO, the lateral compartment cartilage is prone to degenerative wear and tear under the action of inflammatory mediators and biomechanical changes for a long time (Butt *et al.*, 2021).

The lateral meniscus is a 2 years old crescent-shaped fibrocartilage, which is located on the medial and lateral articular surface of the tibial plateau, covering the lateral tibial plateau. It can increase the stability of the spherical femoral condyle and tibial plateau (Lu *et al.*, 2019). The lateral meniscus bears most of the lateral load, and its effect on the knee joint is much greater than that of the medial meniscus. It is found that the incidence of knee

osteoarthritis increases significantly when the meniscus is absent or incomplete (such as after lateral meniscectomy). In addition, the lateral meniscus often has degenerative wear and tear in patients with inverted knee osteoarthritis, so it can be seen that the integrity of the lateral meniscus and the protection of the external compartment cartilage is very important (Kim *et al.*, 2020). Therefore, patients with inverted knee osteoarthritis with absence or incomplete meniscus are prone to wear and tear of cartilage in the lateral compartment. Anterior cruciate ligament (ACL) is an important stable structure of knee joint, which can limit knee hyperextension, tibial forward movement, internal and external rotation (Lee *et al.*, 2019). It was found that the incidence of lateral compartment cartilage wear in patients with knee osteoarthritis was significantly increased in the absence or insufficiency of anterior cruciate ligament. This may be due to the biomechanical changes and lack of stability of the knee joint in patients with inverted knee osteoarthritis, resulting in injury of the anterior cruciate ligament, which in turn aggravates the biomechanical changes of the knee joint and aggravates the condition of knee osteoarthritis. As a result, the articular cartilage of the lateral compartment is easy to wear (Bloch *et al.*, 2019).

In recent years, with the continuous progress and development of cell culture technology and molecular biology technology, more and more evidence shows that long-term chronic inflammation in the joint, especially chondrocyte inflammation, plays an important role in the occurrence and development of knee osteoarthritis (Filardo *et al.*, 2019). Under the stimulation of adipose factor, inflammatory factor, abnormal mechanical action and other factors, it causes the inflammatory reaction of chondrocytes, which leads to the edema, hypertrophy, senescence and apoptosis of chondrocytes, and then causes the inflammatory reaction of chondrocytes, which eventually leads to knee osteoarthritis. It has been found that pro-inflammatory factors are the key mediators that cause pathophysiological changes in osteoarthritis, in which IL-6, TNF- α and IL-1 β are the main participants. Intra-articular pathogens, autoimmune reaction products, post-traumatic host by-products and debris can stimulate the signal pathways of synoviocytes and chondrocytes to produce cytokines such as IL-6, TNF- α , IL-1 β and proteases, which affect cartilage metabolism, cause progressive destruction of articular cartilage, and then lead to the stability and imbalance of the intra-articular environment, leading to the pathogenesis of knee osteoarthritis. This in turn aggravates the biomechanical changes of the knee joint, leading to the aggravation of knee osteoarthritis and the wear and tear of the articular cartilage of the lateral compartment (Koh *et al.*, 2020).

CONCLUSION

To sum up, heavy labor intensity, absence or insufficiency of lateral meniscus, absence or insufficiency of anterior cruciate ligament, long course of disease and high levels of IL-6, TNF- α and IL-1 β in synovial fluid are independent risk factors for lateral compartment cartilage wear in patients with VKO.

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IRB approval

This research was carried out with the approval of Longyan First Affiliated Hospital of Fujian Medical University

Ethical statement

All applicable international, national, and/or institutional guidelines for the care and use of animals were followed.

Statement of conflict of interest

The authors have declared no conflict of interest.

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