# Original Article

# The advantage and disadvantage of routine X-ray examination and musculoskeletal ultrasound in the diagnosis of the patients with knee osteoarthritis

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Abstract: Objective: This study aimed to compare the advantages and disadvantages of X-ray and musculoskeletal ultrasound in the diagnosis of patients with knee osteoarthritis (KOA). Methods: A total of 60 patients with KOA (120 cases of knees) treated in our hospital were selected as the experimental group. Another 60 healthy individuals (120 cases of knees) with physical examination in our hospital were selected as the control group. X-ray and musculoskeletal ultrasound were performed. The Kazam sonographic evaluation method and the Kellgren-Lawrence radiographic classification system were adopted to grade the level of osteoarthritis in patients from the experimental group. Visual Analogue Scale (VAS) and Western Ontario and McMaster universities (WOMAC) osteoarthritis index were used to assess the clinical manifestation of patients in the experimental group. The correlation between the grading outcomes and the clinical symptoms of patients as well as the diagnostic results from both methods were compared. Results: Knee joints in the control group had none or little effusion in suprapatellar bursa with the smaller anteroposterior diameter of the sonolucent area. The articular cartilage had smooth edges and bilateral symmetry. Knee lesions were observed in the experimental group. The detection rates of musculoskeletal ultrasound were higher than those of X-ray examination (P < 0.05). There was a positive correlation between the grading outcomes of musculoskeletal ultrasound images and VAS and WOMAC index (P < 0.05). There was a positive correlation between the grading outcomes of X-ray results and VAS and WOMAC index (P < 0.05). The correlation coefficient between the outcomes of musculoskeletal ultrasound and X-ray examination was 0.551 (P < 0.05). Conclusion: The musculoskeletal ultrasound was more sensitive in assessing KOA manifestations and could better reflect the pathological changes of soft tissue surrounding the knee joint of KOA patients, which could be used as a KOA diagnostic method.

**Keywords:** Routine X-ray examination, musculoskeletal ultrasound, KOA patients, diagnosis, analysis of advantages and disadvantages

# Introduction

Knee osteoarthritis (KOA) is a common clinical degenerative joint disease characterized by the degeneration of articular cartilage and synovial inflammation. It could lead to pain and dysfunction of joints and total knee arthroplasty in severe cases. The disease has a long course and progressive development, and is a chronic inflammatory disorder. The typical clinical symptoms of patients include subchondral sclerosis or cysts, cartilage destruction, osteophyte, synovial hyperplasia and inflammatory lesions [1, 2]. The elderly population is at high risk of the disease, and the prevalence is much higher

in females than in males. In the elderly population, the incidence rates of the disease are the second highest after the cardiovascular disease. KOA could cause severe damage to the joint functions of the patients. Studies showed that the incidence rates of KOA were positively correlated with the age. With the escalation of population aging in China during recent years, KOA has become a significant factor affecting the quality of life of Chinese residents [3, 4].

Early diagnosis and treatment are of great significance for improving the prognosis and delaying the disease progression of KOA patients. The cause of KOA still remains undefined.

However, studies found that gender, age, obesity, sports injury, geographic location, and other factors are correlated with the occurrence of the disease. The early clinical symptoms of KOA are not obvious and thus are often ignored [5]. In current clinical practice, X-ray examination and MRI scan combined with physical examination are used to diagnose the progression of the disease. As mentioned above, the degeneration of the joint in KOA can cause joint pain, joint swelling and deformities, and limited walking activities among patients. Intermittent pain occurs in the early stage of the disease, and persistent pain occurs in the late stage. The disease progression of the patients could be measured based on the level of joint deformity and pain in clinics. However, this method is less applicable to patients with severe disease conditions [6]. X-ray examination is the most common method in KOA. However, a study showed that X-ray was more cost-effective for the examination of bone tissue but was unable to identify early chronic inflammatory lesions in articular cartilage and synovium [7]. MRI has relatively high sensitivity, specificity and accuracy in detecting the pathological lesion of soft tissue of the knee joints with high spatial resolution. However, due to the high cost of examination, long time consumption, expensive cost of the instruments, high requirement of physicians, and poor generalization, it should not be used as the routine examination method for KOA [8].

Ultrasound detection has the advantages of non-invasiveness, simplicity and rapidity, low cost, high replicability, no radiological hazard, and dynamic imaging. In recent years, it is widely applied in the diagnosis of various bone diseases. In fact, back in 1984, ultrasound was already used for the detection of thickness and morphology of articular cartilage in other countries and was considered as an effective evaluation method for osteoarthritis. However, this technology is still at the initial stage of development in China [9]. Musculoskeletal ultrasound is a type of ultrasound technique that relies on conventional ultrasound equipment and clearly detects lesions in sites such as muscle, soft tissue, and bone. Compared with X-ray and MRI, musculoskeletal ultrasound not only is noninvasive, radiation-free, and contraindicationfree, but also performs real-time dynamic observation of the movement of muscle and

tendon and clearly indicates the pathological lesions in muscle, tendon, ligament and even nervous tissue. This provides the physicians with important diagnostic information that could not be obtained by any other imaging examination methods [10, 11]. This study aimed to compare and analyze the advantages and disadvantages of X-ray and musculoskeletal ultrasound in the diagnosis of KOA so as to provide theoretical basis for the clinical diagnosis and treatment of KOA patients.

### Materials and methods

### General materials

A total of 60 patients (120 cases of knees) clinically diagnosed with KOA and treated in our hospital were selected as the experimental group. Another 60 healthy individuals (120 cases of knees) received physical examination in our hospital during the same period were selected as the control group.

The inclusion criteria were: (1) patients all met the diagnostic criteria of KOA from the American College of Rheumatology and had relevant clinical symptoms such as joint pain, joint swelling and deformities, and limited range of motion; (2) patients were conscious and could cooperate with the study; (3) patients with complete medical records; (4) patients whose Arthroscopy or MRI scan indicated joint degeneration or damage; (5) this study obtained the approval from the hospital ethics committee; (6) all patients signed informed consent.

Exclusion criteria were: (1) patients with mental disorders; (2) those with rheumatoid arthritis, gout arthritis, and other inflammatory joint disease; (3) those with vascular diseases; (4) those with autoimmune diseases; (5) those with metabolic bone diseases; (6) those with tuberculosis or benign tumors; (7) those with diseases affecting vital organs such as heart, brain, kidney, and lung; (8) women during pregnancy or lactation.

# Intervention methods

X-ray examination and musculoskeletal ultrasound were performed respectively in patients of the experimental and control groups.

The detailed procedure for X-ray examination was as following: The patient was in a supine

position with straightened knee joints for examination. The X-ray was taken at the anteroposterior view. The patient was then positioned in a lateral position for the X-ray to be taken at the lateral view. All images were processed by the Workstation. The double-blinded observation and detection of osteophyte, joint space narrowing, and subchondral sclerosis were performed by experienced radiotherapists.

The detailed procedure for musculoskeletal ultrasound was as following: Siemens ACUSON X700 color Doppler ultrasound system was used, with the transducer frequencies of 7.0-18.0 MHz. The patient was in a supine position with straightened knee joints. The physician placed the high-frequency transducer at the position of the suprapatellar bursa at both longitudinal and transverse views. The trochlea of femur and the cartilage of medial and lateral malleolus were examined. Examination of multi-sectional views was required for the medial, lateral and apex sides of the patella. The inner structure of knee joint was examined, and the morphology and echo signals of articular cartilage, articular bones, and subchondral bones were recorded. The patient was then switched to lateral position with straightened knee joints. The presence of cysts at the popliteal fossa was observed, and the medial and lateral condyles of the femur were examined. The collected images were inputted into the Workstation. The outcomes of the double-blinded assessment were performed by experienced radiotherapists.

# Outcome measures and evaluation criteria

Kellgren-Lawrence radiographic classification system: The Kellgren-Lawrence radiographic classification system is a radiological classification of knee osteoarthritis established by J. H. Kellgren and J. S. Lawrence [11]. It classifies the knee osteoarthritis of X-ray results from grade 0 to grade IV based on the severity of the disease. Grade 0 indicates no features of osteoarthritis detected by the X-ray. Grade I indicates doubtful joint space narrowing and possible osteophytes. Grade II indicates clear presence of small marginal osteophytes and possible joint space narrowing in the anteroposterior radiograph. Grade III is characterized by presence of multiple intermediate osteophytes, clear joint space narrowing, and possible subchondral sclerosis. Grade IV is characterized by large number of osteophytes, severe joint space narrowing, and clear subchondral sclerosis and bony deformity of knee joints.

Kazam sonographic evaluation: Kazam sonographic evaluation classifies the progression of diseases into grades 0-IV based on the severity of cartilaginous lesions. Grade 0 indicates normal. Grade I indicates minimal abrasion at cartilage surface. Grade II indicates partial defect in the cartilage. Grade III indicates focal cartilage defect with full thickness. Grade IV indicates the focal cartilage defect with full-thickness and destruction of subchondral bone [12].

Visual Analogue Scale (VAS) index: The VAS is a commonly used method for pain assessment in clinic. It consists of a line of 0-10 cm, in which 0 indicates no pain and 10 indicates the worst possible pain. The patients were asked to mark the pain level based on their experience, and higher mark indicates more severe pain [13].

Western Ontario and McMaster universities (WOMAC) osteoarthritis index: The WOMAC index is commonly used to assess the severity and function of arthritis in clinical practice. This index could be divided into 3 subscales and consists 24 items. The total score equals to the sum of scores from the 3 subscales. Higher score indicates more severe clinical symptoms, functional limitations of joints and restrictions in daily activities [14].

Evaluation criteria for cartilaginous lesions: According to studies, anechoic area of more than 1 mm at joint space indicates joint effusion; more than 2 mm of synovial membrane indicates synovial hypertrophy; less than 2 mm of cortical lesion indicates cortical erosion and more than 2 mm indicates cortical defect [15].

# Statistical analysis

The statistical analysis of collected data was performed using SPSS 20.0 software. For the measurement data expressed in the form of ( $\overline{x}$   $\pm$  sd), the difference between groups was assessed by Student's t test. For the enumeration data expressed in the form of n%, the difference between groups was assessed using Chi-square test. Spearman's rank correlation analysis was performed to evaluate the correlation between the results of ultrasound and various indexes, and P < 0.05 was considered as statistically significant [16].

General clinical data		The experimental group (n = 60)	The control group (n = 60)	t/X²	Р
Gender	Male	34	30	0.536	0.464
	Female	26	30		
Average age (year)		41.29±3.22	41.31±3.19	0.034	0.973
Average weight (kg)		65.49±4.22	65.68±4.11	0.25	0.803
Average BMI (kg/m²)		22.19±3.11	21.98±2.98	0.378	0.706
Education level	Literacy	4	5	0.556	0.415
	Primary school	6	7		
	Junior school	9	10		
	High school and above	41	38		
Marital status	Married	55	53	0.37	0.543
	Not married	5	7		

**Table 1.** Comparison of general clinical data of the two patient groups  $(\bar{x} \pm sd)/[n(\%)]$ 





**Figure 1.** The X-ray image and musculoskeletal ultrasound image of the control group. There was no narrowing of the knee joint space and no obvious inflammatory lesions in the bone (A); the musculoskeletal ultrasound image indicated no effusion in the knee joint and normal cartilage (B).

# Results

Difference in general clinical data from the experimental group and the control group

There was no significant difference in the gender, age, weight, marital status, and education level between the two groups (P > 0.05) (**Table 1**).

The radiological imaging of knee joints of healthy individuals in the control group

The ultrasound images of knee joints in the control group showed no effusion or little effusion in suprapatellar bursa with the anteroposterior diameter of the sonolucent area less than 3 mm. The joint effusion was most clear with knee joints in 30-45 degrees of flexion and the synovial membrane thickness was less

than 2.0 mm. A cross-sectional view of the cartilage in the proximal femur indicated an even distribution of hypoechoic areas with smooth edges, bilateral symmetry and a thickness of about 2 mm. The subchondral bone was indicated with smooth and continuous hyperechoic areas. A longitudinal view of the meniscus indicated presence of inverted triangle with homogeneous echo pattern (Figure 1).

The radiographic imaging of knee joints of KOA patients in

the experimental group

The KOA patients in the experimental group showed degenerative changes of articular cartilage, synovial lesion, suprapatellar bursa effusion, popliteal cyst, subchondral bone destruction, degenerative meniscal tear, joint space narrowing, and other related radiographic characteristics (Figure 2).

Comparison of the values of musculoskeletal ultrasound and routine X-ray in the diagnosis of KOA

Routine X-ray examination and musculoskeletal ultrasound examination were performed in 60 KOA patients (120 cases of knees) in the experimental group. It was found that the detection rates of synovial lesion (75.83%), suprapatellar bursa effusion (77.50%), degeneration of articular cartilage (86.67%), subchondral bone de-

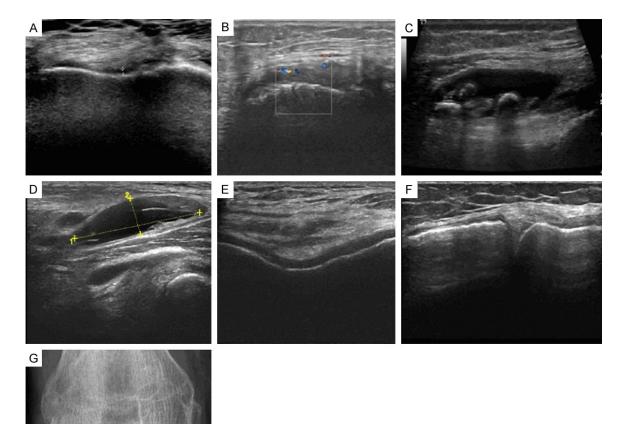


Figure 2. The radiographic imaging of KOA patients in the experimental group indicated thinning of knee articular cartilage (A); knee synovial hyperplasia (B); effusion of suprapatellar bursa effusion (C); knee popliteal cyst (D); abnormal echo of cartilage (E); degenerative meniscus (F); X-ray of knee joint (G).

struction (52.50%), degenerative meniscal tear (34.17%), and popliteal cyst (44.17%) of musculoskeletal ultrasound were higher than those of routine X-ray examination, while the detection rates of joint space narrowing, hyperostosis and osteoporosis of X-ray examination were significantly higher than those of musculoskeletal ultrasound (P < 0.05) (**Table 2**).

Correlation between the grading from musculoskeletal ultrasound and clinical manifestations of KOA patients

VAS, WOMAX index, and Kazam sonographic evaluation were used to evaluate the 60 KOA patients (120 cases of knees) in the experimental group. The correlation analysis indicated that there was a positive correlation between the grading outcomes of musculoskeletal ultrasound images (0-4) and the grading outcomes of VAS and WOMAC index (r = 0.981, r = 0.881, P < 0.05) (**Table 3**).

The correlation between routine X-ray examination and clinical manifestations of KOA patients

The VAS, WOMAX index, and Kellgren-Lawrence radiographic classification system were used to evaluate the 60 KOA patients (120 cases of knees) in the experimental group. The correlation analysis indicated that there was a positive correlation between the grading outcomes of X-ray results (0-4) and grading outcomes of VAS and WOMAC index (r = 0.781, r = 0.722, P < 0.05) (Table 4).

The correlation analysis of the diagnostic outcomes between musculoskeletal ultrasound and routine X-ray examination

A correlation analysis of the diagnostic outcomes was performed between the musculoskeletal ultrasound and routine X-ray examination. The correlation coefficient between the

**Table 2.** The comparison between diagnostic value of musculoskeletal ultrasound and routine X-ray detection for KOA [n (%)]

Pathological lesion	Routine X-ray examination	Musculoskeletal ultrasound	X <sup>2</sup>	P
Synovial lesion	0 (0.00)	91 (75.83)	146.577	< 0.001
Suprapatellar bursa effusion	0 (0.00)	93 (77.50)	151.837	< 0.001
Degeneration of articular cartilage	0 (0.00)	104 (86.67)	183.529	< 0.001
Subchondral destruction	12 (10.00)	63 (52.50)	50.444	< 0.001
Meniscus damage	0 (0.00)	41 (34.17)	49.447	< 0.001
Joint space narrowing	101 (84.17)	83 (69.17)	7.547	0.006
Hyperostosis	93 (77.50)	73 (60.83)	7.815	0.005
Osteoporosis	60 (50.00)	0 (0.00)	80.0	< 0.001
Popliteal cyst	0 (0.00)	53 (44.17)	68.021	< 0.001

**Table 3.** The correlation between grading outcomes of musculoskeletal ultrasound and clinical manifestations of KOA patients

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Items	0 1 2 3		4	r	Ρ		
Case numbers	20	37	23	22	18		
VAS (points)	1.87±0.56	2.76±0.33	3.77±0.44	5.27±0.81	5.98±0.71	0.981	< 0.05
WOMAC (points)	6.98±0.65	10.22±0.45	22.18±1.22	30.18±3.11	37.18±1.78	0.881	< 0.05

**Table 4.** The correlation between the outcomes of routine X-ray detection and clinical manifestations of KOA patients

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Items	0 1 2 3		4	r	Ρ		
Case numbers	50	28	8	24	10		
VAS (points)	3.11±0.32	3.43±0.18	5.21±0.78	5.60±0.56	5.98±0.66	0.781	< 0.05
WOMAC (points)	13.11±2.11	17.89±1.98	30.18±3.22	30.11±2.87	38.17±3.11	0.722	< 0.05

outcomes of musculoskeletal ultrasound and X-ray examination was 0.551, which was statistically significant (P < 0.05) (**Table 5**).

### Discussion

Knee osteoarthritis (KOA), characterized by the degeneration of articular cartilage, subchondral sclerosis, osteophytes at the periphery of joints, synovial hyperplasia, and inflammatory lesions, is a common clinical degenerative joint disease. It can lead to dysfunction and deformity of joints, seriously affecting the health and quality of lives among patients. Studies have shown that the incidence of osteoarthritis is high in population over 60 years old with the incidence rate to be approximately 50%. The incidence rate in population over 65 years old is as high as 80%. However, with the change in lifestyle and diet among residents during recent years, the incidence rate of KOA in young popu-

lation at around 20 years old is also increasing. Knee joint is a common site for the occurrence of osteoarthritis. The articular cartilage of the patient has degeneration and full-thickness cartilage defect, which further affects the subchondral bone, ligaments, articular capsule, surrounding muscle tissue and the synovium. Symptoms such as joint pain and instability occur frequently. With the progression of the disease, patients might even develop ambulation dysfunction, loss of working ability or disability with the progression of the disease [17]. Therefore, early diagnosis and intervention are of great significance for improving the clinical symptoms and quality of life in KOA patients.

The clinical diagnostic criteria for early stages of KOA include two aspects, one is the pain experienced at knee joint, and the other is the joint degeneration or damage measured by the

**Table 5.** The correlation analysis between grading outcomes of musculoskeletal ultrasound and routine X-ray examination

Orania			Ultrasound grading					
Grade		0	1	2	3	4	r	Ρ
Grading outcomes of Routine X-ray	0	20	9	13		8	0.551	< 0.05
	1		28					
	2			8				
	3			2	22			
	4					10		

arthroscopy or MRI scan [18]. In current clinical practice, X-ray examination and MRI are used to diagnose KOA. X-ray has good performance in the detection of osteophyte, abrasion at cartilage surface, joint space narrowing, subchondral sclerosis and cyst formation. However, it was shown that the X-ray could not indicate the articular cartilage clearly and has low sensitivity and specificity in detecting early stages of cartilaginous lesion, leading to poor diagnostic effect [19]. MRI is able to perform comprehensive scan of the anatomical structures of knee joints and articular soft tissue, provides more information of the lesions in knee joints, and has good accuracy and sensitivity in detecting soft tissue. However, MRI is expensive and has high technical requirement for the examiners. Besides, MRI scan is time-consuming, and the instrument is not compatible with grassroots medical institutions. As a result, MRI has little suitability for early screening of KOA [20].

This study evaluated the advantages and disadvantages of X-ray examination and musculoskeletal ultrasound in the diagnosis of KOA patients by setting up two groups. The healthy individuals of control group had narrow joint space, none or little effusion in suprapatellar bursa, and less than 2 mm thickness of synovial membrane. A cross-sectional view of cartilage indicated an even distribution of hypoechoic areas, smooth edges, bilateral symmetry, and homogeneous echo pattern of meniscus. Studies have shown that the color ultrasound detection of healthy knee joint with a high-frequency transducer could show a sharp contrast between the cortical bone and cartilage. In healthy adults, the thickness of articular cartilage was about 2-3 mm. There was little synovial fluid in the suprapatellar bursa. The width of joint space was less than 2 mm. Both healthy tendons and ligaments were indicated with smooth band-like echo with homogeneous pattern and meniscus was indicated with a triangle with homogeneously distributed echo [21, 22]. These are consistent with the results in this study. The measurement of knee joints with inflammatory lesions indicated increased narrowing of joint space with the progression of the disease. The reasons could be that the inflammatory lesions resulted in erosion of the cartilage, and the increased formation of osteophytes resulted in narrowing of joint space, which further affected the joint function.

Routine X-ray examination and musculoskeletal ultrasound examination were performed in 60 KOA patients (120 cases of knees) in the experimental group. It was found that the detection rates of synovial lesion (75.83%), suprapatellar bursa effusion (77.50%), degeneration of articular cartilage (86.67%), subchondral bone destruction (52.50%), degenerative meniscal tear (34.17%), and popliteal cyst (44.17%) of musculoskeletal ultrasound were higher than those of routine X-ray examination, while the detection rates of joint space narrowing, hyperostosis, and osteoporosis of X-ray examination were significantly higher than those of musculoskeletal ultrasound (P < 0.05). Thses findings indicated that there were advantages and disadvantages between the two diagnostic methods. A study of 86 patients with wrist lesions of early rheumatoid arthritis indicated that the detection rate of musculoskeletal ultrasound on bone erosion in the knee joint was 44.19%. significantly higher than that of X-ray (30.23%). The difference was statistically significant [23. 24]. We believed that X-ray had better performance in identifying the skeletal system of the joint and could clearly indicate the structure and calcification of the cortical, medulla and trabecular bone. However, it could only indirectly indicate the structure of articular cartilage, meniscus, subchondral bone marrow edema, effusion, tendon, ligament, and muscle. As a

Table 6. Comparison of the diagnostic value of routine X-ray and musculoskeletal ultrasound in KOA

Lesion	Lesion of soft tissue	Localization of lesion site	Radiation injury	Repeat- ability	Dynamic observation	Average exami- nation cost
Routine X-ray	High sensitivity	Poor	Yes	Poor	Yes	544.19±30.19
Musculoskeletal ultrasound	Low sensitivity	Good	No	Good	No	329.29±20.39

result, this method is less applicable for the early diagnosis of KOA. Musculoskeletal ultrasound could clearly distinguish the cartilage and effusion using high-frequency transducers and indicate the morphology of synovial membrane and change in blood flow, which has great advantages in the evaluation of the lesions of soft tissue. Previous studies indicated that musculoskeletal ultrasound could indicate the severity of the disease through the analysis of synovial hyperplasia and blood flow signals. In general, more severe synovial hyperplasia would result in more intensive blood flow signals, indicating more severe synovitis. The thickness of synovial membrane decreased, and the blood flow signal weakened after treatment. This was consistent with the diagnostic results of the KOA patients after treatment [25, 26].

Finally, the correlation between the diagnostic outcomes of the two methods and the clinical symptoms of KOA patients was analyzed in this study. The results indicated that there was a positive correlation between the grading outcomes of both musculoskeletal ultrasound and X-ray and the clinical manifestations of KOA patients. The reason could be that the increase in the disease severity of KOA was directly reflected by the worsened clinical symptoms of patients. The positive correlation between the grading outcomes of both musculoskeletal ultrasound and X-ray and the clinical manifestations suggests that the state of disease could be determined by a simple physical examination, which provided insight for further treatment.

In conclusion, the musculoskeletal ultrasound had higher sensitivity in the diagnosis of degeneration of articular cartilage, synovial lesion, suprapatellar bursa effusion, popliteal cyst, and other manifestations related to KOA, which showed that musculoskeletal ultrasound could better reflect the pathological changes of soft tissue surrounding the knee joint of KOA patients, localize the sites of lesion and assist the validation of treatment plans. Therefore,

the musculoskeletal ultrasound could be used as one of the diagnostic methods for KOA (Table 6). The innovation of this study is to analyze the correlation between routine X-ray, musculoskeletal ultrasound, VAS score and WOMAC score, which provides a new idea for the clinical symptom assessment and diagnosis of KOA patients. Whether the subsequent diagnosis of KOA can be assisted by X-ray and musculoskeletal ultrasound remains to be further verified. The study has two limitations as following: (1) The sample size was relatively small, leading to a lack of comprehensiveness in the results; (2) No dynamic assessment was performed on the disease state of the patients and no dynamic radiographic imaging results were available for the same patient. Therefore, a follow-up study with a larger sample size was planned to provide a more detailed theoretical basis for the treatment of KOA patients.

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# Disclosure of conflict of interest

None.

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### References

- [1] Pagenstert G, Knupp M, Valderrabano V and Hintermann B. Realignment surgery for valgus ankle osteoarthritis. Oper Orthop Traumatol 2009; 21: 77-87.
- [2] Zhu X, Jiang L, Lu Y, Wang C, Zhou S, Wang H and Tian T. Association of aspartic acid repeat polymorphism in the asporin gene with osteoarthritis of knee, hip, and hand: a PRISMAcompliant meta-analysis. Medicine (Baltimore) 2018; 97: e0200.

- [3] Büchele G, Günther KP, Brenner H, Puhl W, Stürmer T, Rothenbacher D and Brenner RE. Osteoarthritis-patterns, cardio-metabolic risk factors and risk of all-cause mortality: 20 years follow-up in patients after hip or knee replacement. Sci Rep 2018; 8: 5253.
- [4] Kropáčková T, Šléglová O, Růžičková O, Vencovský J, Pavelka K and Šenolt L. Lower serum clusterin levels in patients with erosive hand osteoarthritis are associated with more pain. BMC Musculoskelet Disord 2018; 19: 264.
- [5] Ahn GY, Cho SK, Cha SJ, Nam E, Lee JE, Dreiser RL, Maheu E and Sung YK. Cross-cultural adaptation and validation of the korean version of the functional index for hand osteoarthritis (FIHOA). Int J Rheum Dis 2018; 21: 2095-2103
- [6] Jevotovsky DS, Alfonso AR, Einhorn TA and Chiu ES. Osteoarthritis and stem cell therapy in humans: a systematic review. Osteoarthritis Cartilage 2018; 26: 711-729.
- [7] Matsuzaki T, Alvarez-Garcia O, Mokuda S, Nagira K, Olmer M, Gamini R, Miyata K, Akasaki Y, Su Al, Asahara H and Lotz MK. FoxO transcription factors modulate autophagy and proteoglycan 4 in cartilage homeostasis and osteoarthritis. Sci Transl Med 2018; 10: eaan0746.
- [8] Jeon OH, David N, Campisi J and Elisseeff JH. Senescent cells and osteoarthritis: a painful connection. J Clin Invest 2018; 128: 1229-1237.
- [9] Tack A, Mukhopadhyay A and Zachow S. Knee menisci segmentation using convolutional neural networks: data from the osteoarthritis initiative. Osteoarthritis Cartilage 2018; 26: 680-688.
- [10] Ebell MH. Osteoarthritis: rapid evidence review. Am Fam Physician 2018; 97: 523-526.
- [11] Galuzzi M, Perteghella S, Antonioli B, Tosca MC, Bari E, Tripodo G, Sorrenti M, Catenacci L, Mastracci L, Grillo F, Marazzi M and Torre ML. Human engineered cartilage and decellularized matrix as an alternative to animal osteoarthritis model. Polymers (Basel) 2018; 10: 738.
- [12] Ladny JR, Smereka J, Rodríguez-Núñez A, Leung S, Ruetzler K and Szarpak L. Is there any alternative to standard chest compression techniques in infants? A randomized manikin trial of the new "2-thumb-fist" option. Medicine (Baltimore) 2018; 97: e9386.
- [13] Kho MHT, Chew KS, Azhar MN, Hamzah ML, Chuah KM, Bustam A and Chan HC. Implementing blended learning in emergency airway management training: a randomized controlled trial. BMC Emerg Med 2018; 18: 1.
- [14] Bert J, Kenney J, Sgaglione NA, McClelland S, Brophy R, Toth J, Ruane J, Ali Y, Arquette S, Dasa V and Lopes M. Viscosupplementation for osteoarthritis of the knee: a key opinion leader panel discussion. J Manag Care Spec Pharm 2018; 24: S2-S8.

- [15] Grässel S and Muschter D. Do neuroendocrine peptides and their receptors qualify as novel therapeutic targets in osteoarthritis? Int J Mol Sci 2018; 19: 367.
- [16] Bowman S, Awad ME, Hamrick MW, Hunter M and Fulzele S. Recent advances in hyaluronic acid based therapy for osteoarthritis. Clin Transl Med 2018; 7: 6.
- [17] Bratus-Neuenschwander A, Castro-Giner F, Frank-Bertoncelj M, Aluri S, Fucentese SF, Schlapbach R and Sprott H. Pain-associated transcriptome changes in synovium of knee osteoarthritis patients. Genes (Basel) 2018; 9: 338.
- [18] Bianco D, Todorov A, Čengić T, Pagenstert G, Schären S, Netzer C, Hügle T and Geurts J. Alterations of subchondral bone progenitor cells in human knee and hip osteoarthritis lead to a bone sclerosis phenotype. Int J Mol Sci 2018; 19: 475.
- [19] Rex C. Continuous passive motion therapy after total knee arthroplasty. Nursing 2018; 48: 55-57.
- [20] Karalezli N. Our tenolysis rate after zone 2 flexor tendon repairs and modified Duran passive motion protocol over the past 3 years. J Hand Surg Eur Vol 2019; 44: 867-868.
- [21] Collins KH, Hart DA, Seerattan RA, Reimer RA and Herzog W. High-fat/high-sucrose diet-induced obesity results in joint-specific development of osteoarthritis-like degeneration in a rat model. Bone Joint Res 2018; 7: 274-281.
- [22] Legrand C, Ahmed U, Anwar A, Rajpoot K, Pasha S, Lambert C, Davidson RK, Clark IM, Thornalley PJ, Henrotin Y and Rabbani N. Glycation marker glucosepane increases with the progression of osteoarthritis and correlates with morphological and functional changes of cartilage in vivo. Arthritis Res Ther 2018; 20: 131.
- [23] Lindström E, Rizoska B, Tunblad K, Edenius C, Bendele AM, Maul D, Larson M, Shah N, Yoder Otto V, Jerome C and Grabowska U. The selective cathepsin K inhibitor MIV-711 attenuates joint pathology in experimental animal models of osteoarthritis. J Transl Med 2018; 16: 56.
- [24] Porcheret M, Main C, Croft P and Dziedzic K. Enhancing delivery of osteoarthritis care in the general practice consultation: evaluation of a behaviour change intervention. BMC Fam Pract 2018; 19: 26.
- [25] Liang Y, Chen S, Yang Y, Lan C, Zhang G, Ji Z and Lin H. Vasoactive intestinal peptide alleviates osteoarthritis effectively via inhibiting NFκB signaling pathway. J Biomed Sci 2018; 25: 25
- [26] Maier MW, Hetto P, Raiss P, Klotz M, Bülhoff M, Spranz D and Zeifang F. Cementless humeral head resurfacing for degenerative glenohumeral osteoarthritis fails at a high rate. J Orthop 2018; 15: 349-353.