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Evaluation of the Therapeutic Effect of Contrast-Enhanced Ultrasound on Different Types of Knee Osteoarthritis in the Elderly

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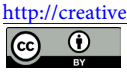

Abstract

Objective: To evaluate the curative effect of the Traditional Chinese Medicine (TCM) external therapy on knee osteoarthritis patients with different TCM constitutions using musculoskeletal ultrasonography and contrast-enhanced ultrasonography, and to explore the application value of contrast-enhanced ultrasonography in knee joint diseases. **Methods:** A total of 57 patients diagnosed with knee osteoarthritis in Shaanxi University of Traditional Chinese Medicine from December 2019 to May 2021 were collected, and they were divided into qi stagnation and blood stasis type group (23 cases) and cold-dampness obstruction type group (34 cases) according to the traditional Chinese medicine method. All patients were given acupuncture combined with TCM fumigation and washing. All patients underwent musculoskeletal ultrasonography and contrast-enhanced ultrasonography before and after treatment, observed and recorded relevant data, and compared the treatment effects between the two groups. **Results:** 85.96% (49/57) of knee osteoarthritis (KOA) patients had suprapatellar bursa effusion, 42.1% (24/57) had iliotibial band bursae effusion, some of which had poor sound transmission, and thickened synovium was seen in most effusions, 33.33% (19/57) had osteophyte formation. Compared with before treatment, the depth of suprapatellar sac effusion in the Qi stagnation and blood stasis type group decreased after treatment ($P < 0.05$). The protrusion height decreased ($P < 0.05$), and the infrapatellar and prefermoral fat pad thickness increased ($P < 0.05$). The contrast-enhanced ultrasonography of the thickened synovial membrane of the knee joint in KOA patients showed different degrees of uniform enhancement, showing slow in and slow out. Compared with the surrounding soft tissue, the arterial phase showed equal enhancement. The enhanced synovium had a clear boundary and a clear boundary with the effusion. In the venous phase, the intensity gradually decreased until clearing. Compared with

before treatment, there was no significant difference in contrast-enhanced ultrasound parameters in the qi stagnation and blood stasis type group after treatment ($P < 0.05$). **Conclusion:** Musculoskeletal contrast-enhanced ultrasonography was used to quantitatively evaluate the efficacy of TCM external therapy on KOA for different TCM constitutions. Dynamic observation of synovial lesions of knee osteoarthritis provides a valuable imaging method for evaluating the efficacy of traditional Chinese medicine.

Keywords

Contrast-Enhanced Ultrasound, External Treatment of Traditional Chinese Medicine, Knee Osteoarthritis, Qi Stagnation and Blood Stasis Type, Cold-Dampness Obstruction Type

1. Introduction

Knee Osteoarthritis (KOA) is a common arthropathy in the elderly, with an incidence of 50% [1]. The deformities and disabilities caused by it seriously affect the quality of life of the elderly. At present, the TCM diagnosis and treatment methods of KOA are mainly acupuncture, traditional Chinese medicine external compress, TCM physiotherapy, and other methods, and their efficacy is accurate and the side effects are low [2]. However, intuitive imaging methods are lacking to quantify their efficacy. Contrast-enhanced ultrasound (CEUS) is an ultrasound technology that has emerged in recent years, using microbubble acoustic contrast agents to infuse microvascular vessels, forming a strong contrast with surrounding tissues, and has been widely used in the diagnosis of lesions in organs such as the liver, heart, and thyroid [3]. The European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) guidelines explicitly use ultrasonography as an effective method of assessing synovial vascularization in rheumatoid arthritis [4], but there have been no studies of the correlation between ultrasonography and KOA lesions. Therefore, this study observes the efficacy of TCM external treatment in elderly KOA patients with different dialectical types, compares the changes of two-dimensional myoskeletal ultrasound and ultrasonography parameters before and after treatment, and aims to explore the clinical application value of ultrasonography in the evaluation of the efficacy of different types of KOA lesions.

2. Materials and Method

2.1. Subjects of Study

From December 2019 to May 2021, 57 cases of patients with knee osteoarthritis were collected, 15 cases were male and 42 cases were female, with an average age of 57.53 ± 7.32 years. According to the Chinese medicine Wang Wen Qing qi, the patients were divided into a qi stagnation blood stasis type group (23 cases)

and a cold and wet paralysis type group (34 cases), both groups were given acupuncture combined with traditional Chinese medicine (TCM) fumigation treatment. Patients are included according to the following criteria: 1) Patients diagnosed with early KOA according to the criteria of the Guidelines for the Diagnosis and Treatment of Osteoarthritis (2018 Edition) [5]; 2) According to the "Consensus of Experts on the Diagnosis and Treatment of Knee Osteoarthritis in Traditional Chinese Medicine (2015 Edition) [6]; Patients who meet the dialectical standards of Chinese medicine qi stagnation blood stasis type or cold and wet paralysis type; 3) No contraindications to ultrasonic angiography. Exclusion criteria: 1) Knee joint with gout, tumors, rheumatoid arthritis, and other connective tissue diseases; 2) Patients with a history of previous surgery on the knee joint; 3) Patients with acute or severe disease of important organs such as heart, brain, and kidneys. All patients signed an informed consent form for ultrasonography to record the changes of ultrasound and angiography parameters of knee muscles and bones by ultrasound and ultrasonography before treatment and after the course of treatment and compared the treatment effect of external treatment in different types of patients.

2.2. Instruments and Methods

2.2.1. Routine Ultrasound

The GE E9 ultrasonic diagnostics are equipped with 9 L and 10 L high-frequency linear array probes at frequencies of 7 - 12 MHz. The patient is in the supine position, the knee joint flexion is 120 degrees, and the horizontal, longitudinal, and sliding scans are performed on the patient's knee joint with a linear array probe to observe the changes in bone and cartilage tissue, surrounding bursal effusion and the thickness of each tendon before and after knee joint treatment, and record the depth of suprapatellar sac effusion, the thickness of the synovial membrane, the thickness of the quadriceps, the thickness of the biceps tendon and patellar tendon, the height of the meniscus protrusion, and the thickness of the infrafemoral fat pad.

2.2.2. Contrast-Enhanced Ultrasound

Scanning the patient's knee joint, selecting the more severe lesion on the side of CEUS, switching the CEUS mode after determining the section, rapidly injecting 2 ml of the acoustic novy contrast agent with the vonovirate through the elbow vein, immediately flushing the tube with 5 ml of saline, observing the enhanced mode, and collecting the image. The time-intensity curve is used to record the peak intensity, peak time, average perfusion time, area under the curve, slope, and other parameters. The changes in parameters before and after treatment in the two groups were observed.

2.3. Other Information

Other Information Record the basic information of the patient: gender, height, weight, body mass index (BMI), time of illness; Image data: K-L grading, etc.

2.4. Statistical Methods

The Statistical Product and Service Solutions [7] SPSS 26.0 software was used for statistical analysis, enumeration data were expressed by case or rate, differences were expressed by chi-square test or Fisher's exact test; measurement data were tested for normality by K-S, normally distributed data were expressed by $\bar{x} \pm s$, and differences were expressed by pairing Sample t-test. $P < 0.05$ was regarded as a statistically significant difference.

3. Results

3.1. Comparison of Basic Data of Two Groups of Patients

There were no statistically significant differences in gender, age, height, weight, BMI, disease duration, and K-L grading between the qi stagnation and blood stasis type group and the cold-dampness obstruction type group ($P > 0.05$), as shown in Table 1.

3.2. Two-Dimensional Musculoskeletal Ultrasonograph

85.96% (49/57) of KOA patients had suprapatellar sac effusion, 42.1% (24/57) had iliotibial band bursae effusion, part of the sound transmission is poor, and a thickened synovial membrane can be seen in part of the effusion. 33.33% (19/57) of patients had osteophyte formation. Compared with before treatment, the depth of suprapatellar sac effusion in the qi stagnation and blood stasis group decreased after treatment ($P < 0.05$). The depth of suprapatellar sac effusion decreased in the cold-dampness obstruction type group ($P < 0.05$). The height of the meniscus protrusion is reduced ($P < 0.05$), and increased infrapatellar and prefemoral fat pad thick ($P < 0.05$). See Table 2.

3.3. Synovial Contrast Ultrasound Comparison

The contrast-enhanced ultrasonography of the thickened synovial membrane of

Table 1. Comparison of basic data of knee osteoarthritis between two groups.

Project	Qi stagnation and blood stasis type group (n = 23)	Cold-dampness obstruction type group (n = 34)	t/x^2	p
Gender (eg, male/female)	8/15	7/27	1.426	0.232
Age (y, $\bar{x} \pm s$)	56.65 ± 7.84	58.12 ± 6.7	−0.735	0.406
Height (cm, $\bar{x} \pm s$)	165.83 ± 6.09	163.26 ± 6.88	1.443	0.692
Weight (kg, $\bar{x} \pm s$)	66.64 ± 12.32	65.36 ± 9.95	0.435	0.067
BMI (kg/m^2, $\bar{x} \pm s$)	24.05 ± 3.26	24.40 ± 3.07	−0.417	0.527
Sick time (y, $\bar{x} \pm s$)	5.37 ± 4.96	5.73 ± 7.08	−0.211	0.074
Right knee (%)	56% (13/23)	58.8% (20/34)	0.03	0.863
K-L Grading ≥ 2 (%)	82.4% (19/23)	79.4% (27/34)	0.585	0.747

Note: △: Compared with before treatment $P < 0.05$.

Table 2. Comparison of musculoskeletal ultrasound parameters before and after treatment between the two groups (mm, $\bar{x} \pm s$).

	Qi stagnation and blood stasis type group (n = 23)		t	P	Cold-dampness obstruction type group (n = 34)		t	P
	Before therapy	After treatment			Before therapy	After treatment		
Suprapatellar sac effusion	5.11 ± 3.00	3.71 ± 2.91△	3.052	0.007	4.54 ± 2.29	3.42 ± 2.25△	2.731	0.011
Synovial thickness	3.84 ± 2.52	3.41 ± 2.55	0.756	0.457	4.16 ± 2.51	3.26 ± 3.07	1.922	0.072
Quadriceps tendon	6.17 ± 0.94	6.55 ± 1.33	−1.388	0.183	6.35 ± 1.30	6.10 ± 0.96	0.810	0.426
Biceps femoris tendon	5.93 ± 0.87	5.99 ± 1.29	−0.221	0.828	3.79 ± 1.00	5.71 ± 1.37	−0.254	0.802
Patellar tendon	3.55 ± 0.55	3.58 ± 0.62	−0.222	0.827	3.69 ± 1.17	3.35 ± 0.33	1.611	0.120
Meniscus protrusion height	2.0 ± 1.78	2.47 ± 2.26	−1.316	0.206	3.17 ± 2.20	2.54 ± 2.25△	2.879	0.008
Infrapatellar fat pad thickness	6.85 ± 1.14	7.38 ± 1.97	−0.974	0.343	6.46 ± 1.42	7.34 ± 1.74△	−2.722	0.012
Anterior thigh fat pad thickness	7.72 ± 2.60	7.62 ± 2.14	−0.069	0.945	6.90 ± 2.02	7.88 ± 2.28△	−2.655	0.014

Note: △: Compared with before treatment $P < 0.05$.

the knee joint in KOA patients showed different degrees of uniform enhancement, showing slow in and slow. In the arterial phase, it is isoenhanced compared with the surrounding soft tissue, and the enhanced synovium has a clear boundary and is clearly demarcated from the effusion. The intensity of the venous phase gradually decreases until washout. Compared with before treatment, there was no significant difference in contrast-enhanced ultrasound parameters between the qi stagnation and blood stasis type group after treatment ($P > 0.05$). In the cold-dampness paralysis group, the peak intensity decreased and the area under the curve decreased, $P < 0.05$ (See Figure 1 and Table 3).

4. Discussion

KOA is a chronic degenerative bone and joint disease caused by cartilage degeneration and bone hyperplasia of the knee joint. Clinically, it mainly manifests as knee joint pain and different degrees of dysfunction, some joint swelling, and fluid accumulation, which seriously affects the physical and mental health of middle-aged and elderly people. In traditional Chinese medicine, KOA is called "crane knee wind", or "knee arthralgia". The dialectical classification of knee arthralgia includes liver and kidney deficiency syndrome, damp-heat arthralgia syndrome, qi and blood deficiency syndrome, cold-damp arthralgia syndrome, and qi stagnation and blood stasis syndrome. This study focuses on the analysis of the most common syndromes of Qi stagnation and blood stasis and cold-dampness obstruction. Both of the above belong to the category of knee arthralgia complex constitution. Qi stagnation and blood stasis are caused by stagnation of blood due to poor Qi movement. Clinical manifestations are dark color, mysterious pulse, chest tightness and sighing, stomach and abdominal pain, belching, introverted personality, melancholy, and narrow-mindedness. Obstruction of cold-dampness is mostly due to the deficiency of qi and blood in the

Table 3. Comparison of contrast-enhanced ultrasound parameters of knee osteoarthritis synovium before and after treatment ($\bar{x} \pm s$).

	Peak intensity (dB)	AUC	Time to peak (s)	Mean perfusion time (s)	Wash in slope (dB/s)
Qi stagnation and blood stasis type group (n = 23)					
Before therapy	6.37 ± 5.06	328.16 ± 239.90	27.92 ± 13.90	62.14 ± 5.51	0.98 ± 0.62
After treatment	4.44 ± 2.10	154.52 ± 77.40	32.01 ± 30.53	70.40 ± 1.77	0.58 ± 0.37
t	−1.095	−1.461	0.000	1.826	−0.73
P	0.273	0.144	1.000	0.068	0.465
Cold-dampness obstruction type group (n = 34)					
Before therapy	7.61 ± 4.84	287.46 ± 164.09	24.07 ± 8.48	60.74 ± 10.60	0.81 ± 0.53
After treatment	4.58 ± 5.03△	127.36 ± 92.01△	32.38 ± 17.63	65.97 ± 5.47	0.49 ± 0.53
t	8.39	2.804	1.273	−1.370	1.092
P	0.000	0.038	0.259	0.229	0.325

Note: △: Compared with before treatment $P < 0.05$.

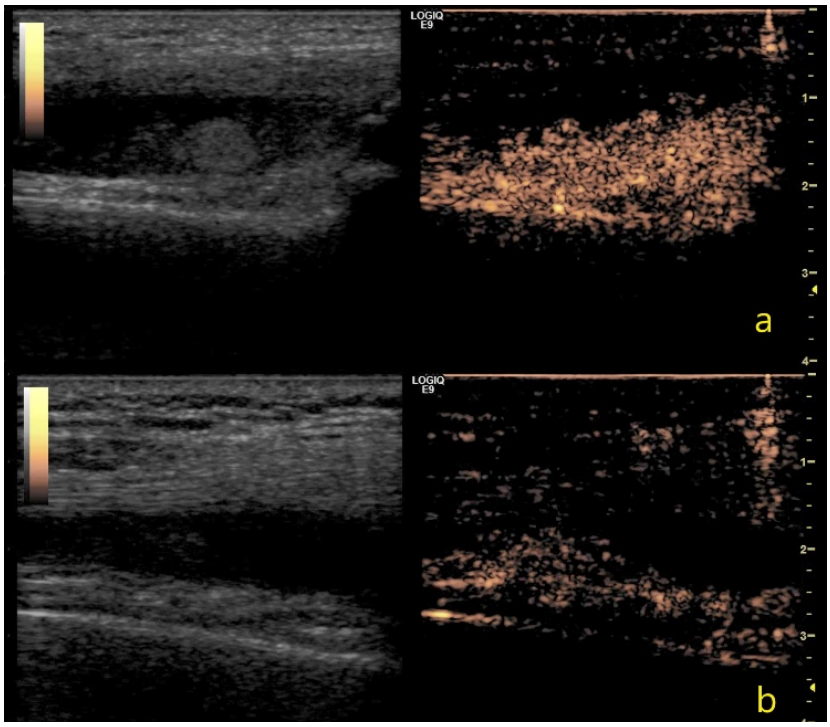

Figure 1. Real-time double-frame contrast-enhanced ultrasound images of the knee joint synovium in the cold-dampness obstruction type group. Note: (a) shows the two-dimensional and contrast-enhanced ultrasound images before treatment; (b) shows the two-dimensional and contrast-enhanced sonograms after treatment.

body, strain, and the evil of cold and dampness invades and obstructs the meridians of the knee, causing the qi and blood to run poorly. The clinical manifesta-

tions are: A fat tongue, white and greasy coating, and a pulse that is tight and slow.

At present, the commonly used methods for the treatment of KOA include injection of sodium hyaluronate into the joint cavity of western medicine, acupuncture and moxibustion of traditional Chinese medicine, fumigation and washing of traditional Chinese medicine, and other external treatment methods. External treatment of traditional Chinese medicine has been widely accepted by the majority of middle-aged and elderly patients because of its obvious effect, safety, and no side effects [8]. The course of senile KOA is prolonged, and multiple evaluations are required during the treatment process. The Western Ontario and McMaster Universities Arthritis Index (WOMAC) score is a commonly used clinical scoring method, but it is highly subjective. Conventional X-rays can show bone lesions, but it is difficult to show soft tissue lesions such as synovium and joint capsule. In recent years, musculoskeletal ultrasound technology has progressed rapidly, which can display the sonographic changes of cortical bone and intra-articular soft tissue in real-time. Contrast-enhanced ultrasound can further image microvascular blood perfusion [9]. The degree of intra-articular synovial inflammation was quantitatively assessed and highly consistent with pathological changes [10]. In this study, through quantitative analysis, musculoskeletal ultrasonography and contrast-enhanced ultrasonography were used to observe the changes before and after treatment in elderly patients with different TCM dialectical types of knee osteoarthritis. The results shown are compared to those before treatment. After treatment, the suprapatellar sac effusion in the qi stagnation and blood stasis group was significantly reduced. In the cold-damp block type group, the suprapatellar sac effusion and the height of the meniscus were significantly reduced and the thickness of the infrapatellar fat pad and the prefemoral fat pad were significantly increased. The peak intensity and area under the curve of the knee joint synovium were significantly reduced by contrast-enhanced ultrasound, indicating that the blood perfusion in the synovium was reduced, and the inflammatory activity was controlled. The above phenomenon shows that acupuncture combined with traditional Chinese medicine fumigation and washing method has a curative effect in the treatment of knee osteoarthritis in two different types of people, and the curative effect of cold-dampness obstruction type is more significant. Two-dimensional musculoskeletal ultrasound showed that there was no significant difference in synovial thickness between the two groups before and after treatment ($P > 0.05$). The results of contrast-enhanced ultrasound showed that the synovial inflammation of the knee joint was improved in the cold-dampness obstruction type group, which indicated that contrast-enhanced ultrasound was more sensitive than musculoskeletal ultrasound in evaluating the efficacy of the knee joint, and could accurately assess the degree of synovial inflammation in knee osteoarthritis.

CEUS can quantitatively analyze and dynamically observe the changes in the synovial micro-blood flow of the knee joint, effectively diagnose and evaluate the degree of knee joint synovial lesions, and provide accurate imaging information

for the evaluation of the efficacy of the knee joint, important clinical application.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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