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Correlation between musculoskeletal ultrasound signs of gouty arthritis and disease activity

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Gouty arthritis is an extremely painful condition that involves small joints and causes tissue stiffness and joint dysfunction in patients. Musculoskeletal ultrasound (MSUS) offers significant advantages over conventional examinations such as X-ray, computed tomography (CT) and magnetic resonance imaging (MRI) in obtaining images of bones and soft tissues. Here, we analyzed the correlation between musculoskeletal ultrasound signs of gouty arthritis and disease activity. Eighty-nine patients with gouty arthritis who were diagnosed and treated in Affiliated Nanhua Hospital, University of South China, Hengyang, China, between November 2019 and December 2021 were involved in this retrospective research. The patients were devided into Group H (DAS$>$3.2, n=41) and Group L (2.6$<$DAS$\leq$3.2, n=48) according to the disease activity scores (DASs). All patients underwent musculoskeletal ultrasound and were assessed for disease activity. Pearson analysis was employed to analyze the correlation between musculoskeletal ultrasound manifestations and disease activity. Patients with moderate to high disease activity showed significantly higher musculoskeletal ultrasound scores and DAS results than those with low disease activity (P <0.05). Synovial hyperplasia score, blood flow signal score, joint effusion score, bone erosion score, and total musculoskeletal ultrasound score were all positively correlated with disease activity (r=0.811, 0.814, 0.837, 0.788, 0.976, all P <0.05). Gouty arthritis musculoskeletal ultrasound findings are positively correlated with disease activity. Thus, the manifestations of musculoskeletal ultrasound demonstrate a good potential to provide informative evidence for the assessment of disease activity in patients with gouty arthritis.

Keywords: Blood flow signal score, Bone erosion score, Joint effusion score, Joint pain, Synovial hyperplasia score

Gouty arthritis is a metabolic disease associated with the consumption of excessive food and alcohol[1] and is characterised by hyperuricemia and the deposition of inflammatory monosodium urate (MSU) crystals in synovial membranes and other tissues, accompanying extreme pain.Inadequate management will damage the bones and lead to functional impairment[2,3]. Epidemiological statistics show that gouty arthritis is more prevalent in men over 40 years of age and is associated with a 38% increased risk of cardio-vascular disease-related death, 55% of coronary heart disease-related death and 28% of death from any cause[4]. The clinical diagnosis and treatment of gouty arthritis are complicated by multiple comorbidities, medical factors including 'difficult-to-treat' hyper-uricemia, and the associated pain and dysfunction may considerably reduce patients' quality of life and jeopardise their health[5,6].

Ultrasound provides high sensitivity and specificity for the diagnosis of gouty arthritis. However, traditional ultrasound beams fail to penetrate the bones due to their high density, which requires high-frequency ultrasound for musculoskeletal examination. Musculoskeletal ultrasound allows the observation of synovial thickening and fluid accumulation in the joint cavity by ultrasound techniques[7,8]. It can examine various skeletal joints such as the shoulder, elbow, hip, knee and ankle joints, observe muscle damage, detect local redness or dislocation and determine muscle inflammation, which provides an improved assessment of the structure and function of the joints[9,10]. The Disease Activity Score (DAS28) is currently used in scientific research and clinical practice to provide an overall assessment of arthritis disease activity. There is little knowledge available related to the association between musculoskeletal ultrasound findings in gouty arthritis and disease activity. Hence, this study, we analyzed the correlation between musculoskeletal ultrasound signs of gouty arthritis and disease activity.

Materials and Methods

Participants

Eighty-nine patients with gouty arthritis who were diagnosed and treated in our hospital between November 2019 and December 2021 were involved in this retrospective research. The patients were devided into group H (DAS$>$3.2, n=41) and group L (2.6$<$DAS$\leq$3.2, n=48) according to the disease activity scores (DASs)[22]. The study was approved by the ethics committee of our hospital. The study was in accordance with the Declaration of Helsinki, and

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written informed consent was provided by all eligible patients.

Inclusion and exclusioncriteria

Inclusion criteria: (i) Patients met the Gout Clinical Index and were diagnosed with gouty arthritis by relevant tests; (ii) Patients were adults regardless of gender and had a normal cognitive function to cooperate with the study; and (iii) Clinical data were complete.

Exclusion criteria: (i) Other osteoarthritis; (ii) major diseases such as dry neuropathy or autoimmune system diseases; (iii) pregnant or breastfeeding women; (iv) secondary gout caused by medications or blood disorders; and (v) The patient has recently taken anti-inflammatory drugs or is undergoing related treatments.

Examination methods

All patients underwent a musculoskeletal ultrasound examination and received DAS assessment.All examinations were performed by two highly qualified doctors without knowledge of the patient's condition. A Philips EPIQ 5 colour Doppler ultrasound instrument with a 12 MHz probe was used for musculoskeletal ultrasound.

Musculoskeletal ultrasound

The patient's swollen and painful joints were scanned, and a full cross-sectional and longitudinal view of each joint was obtained, including examination of the metatarsal, ankle, knee and wrist joints for gout. Patients were examined in the supine position for the knee joint, in the bent knee position for the ankle and toe metatarsal joints, in the sitting position with the arms down for the shoulder joint, and with the arms naturally extended on the examination bed for the wrist, elbow and meta-carpophalangeal joints[11]. The probe frequency was adjusted according to joint size, and synovial hyperplasia, blood flow signal, joint effusion and bone erosion were recorded for each joint musculoskeletal ultrasound semi-quantitative system and graded and scored according to criteria.

Disease activity score (*DAS*)

Venous blood was collected from patients on admission, and C-reactive protein levels were determined using a particle-enhanced immunoturbidimetric assay to calculate the DAS28 score[22].

Grouping criteria

Patients with a DAS28 score below 2.6 were considered to be in remission, those with a score above 2.6 and below 3.2 were of low disease activity, those with a score above 3.2 and below 5.1 were of moderate disease activity, and those with a score above 5.1 were of high disease activity.Patients with a DAS28 score of moderate to high disease activity were included in Group H, and those with a DAS28 score of low disease activity were included in Group L.

Outcome measures

Musculoskeletal ultrasound scoring criteria

The synovial hyperplasia score, blood flow signal score, joint effusion score and bone erosion score are each scored from 0-3. The presence of synovial hyperplasia with normal blood flow was scored as 0. The presence of synovial hyperplasia with a thickness of less than 2 mm, with fewer than three punctate flow signals, was scored as 1. The presence of synovial hyperplasia with a thickness between 2 and 4 mm, with less than half the area of fused blood flow signal, was scored as 2. The presence of synovial hyperplasia with a thickness greater than 4 mm, with the presence of fused blood flow signal in more than half the area was scored as 3. The total score was calculated.

The disease activity score (DAS28) scale was used, with a total score of 0-10.The higher the score the greater the disease activity of the patient.

Statistical analysis

GraphPad Prism 8 was used for image processing, and SPSS 26.0 software was used to collate and statistically analyse the data.Measurement data were expressed as ($\bar{x} \pm s$) and tested by t-test for statistical differences.Count data were expressed as a rate (%), and a chi-square test x2 was used to compare any statistical differences.Pearson correlation analysis was used for correlation analysis. Statistical significance was indicated by $P < 0.05$.

Results and Discussion

Baseline patient profiles

There were 28 males and 13 females in Group H, aged 20-85 (45.45±15.61) years, with a BMI of 23.16±2.84 kg/m^2, duration of illness 1-7 (3.41±1.24) years, SBP of 113.15±5.14 mmHg, DBP of 73.41±7.41 mmHg, HR of 78.45±4.45 beats per min, 25 cases of diabetes mellitus, 31 cases of hypertension, and a blood uric acid of 495.41±99.48 mmol/L. There were 32 males and 16 females in Group L, aged 20-85 (45.56±16.13) years, with a BMI of 23.04±2.91 kg/m^2, duration of illness 1-7

(3.35±1.38) years, SBP of 113.49±5.32 mmHg, DBP of 73.53±7.52 mmHg, HR of 78.37±4.61 beats per min, 22 cases of diabetes mellitus, 33 cases of hypertension, and a blood uric acid of 495.77±100.31 mmol/L. The two arms were well-balanced in terms of baseline patient profiles (P >0.05). (Table 1)

Musculoskeletal ultrasound results

In Group H, the synovial hyperplasia score was (2.11±0.73), the blood flow signal score was (2.01±0.64), the joint effusion score was (2.08±0.62), the bone erosion score was (1.91±0.71), and the total score was (7.98±1.79). In Group L, the synovial hyperplasia score was (1.65±0.32), the blood flow signal score was (0.83±0.54), the joint effusion score was (0.78±0.52), the bone erosion score was (0.75±0.51), and the total score was (3.41±0.82). Patients with moderate or high disease activity exhibited significantly higher musculoskeletal ultrasound scores than patients with low disease activity (P <0.05). (Table 2)

Disease activity

Patients in Group H had a DAS28 score (7.48±1.14), and patients in Group L had a DAS28 score (2.81±0.45).

Correlation analysis

Synovial hyperplasia score, blood flow signal score, joint effusion score, bone erosion score, and total musculoskeletal ultrasound score were all positively correlated with disease activity (r=0.811, 0.814, 0.837, 0.788, 0.976, all P <0.05). (Table 2)

Table 1 — Baseline patient profiles

	Group H (n=41)	Group L (n=48)	*t*	*P*
Gender				
Male	28	32	-	-
Female	13	16	-	-
Age (year)				
Range	20-85	20-85	-	-
Mean	45.45±15.61	45.56±16.13	0.033	0.974
BMI (kg/m^2)	23.16±2.84	23.04±2.91	0.196	0.845
Duration of disease (year)				
Range	1-7	1-7	-	-
Mean	3.41±1.24	3.35±1.38	0.214	0.831
SBP (mmHg)	113.15±5.14	113.49±5.32	0.305	0.761
DBP (mmHg)	73.41±7.41	73.53±7.52	0.076	0.940
HR (beats/min)	78.45±4.45	78.37±4.61	0.083	0.934
Complications				
Diabetes	25	22	-	-
Hypertension	31	33	-	-
Blood uric acid (mmol/L)	495.41±99.48	495.77±100.31	0.017	0.986

Table 2 — Musculoskeletal ultrasound results

DAS	Group H (n=41)	Group L (n=48)	*t*	*P*
Synovial hyperplasia score	2.11±0.73	1.65±0.32	3.947	<0.001
Blood flow signal score	2.01±0.64	0.83±0.54	9.435	<0.001
Joint effusion score	2.08±0.62	0.78±0.52	10.759	<0.001
Bone erosion score	1.91±0.71	0.75±0.51	8.940	<0.001
Total score	7.98±1.79	3.41±0.82	15.858	<0.001

The pathogenesis of gout includes impaired purine metabolism, reduced renal uric acid excretion, elevated blood uric acid levels, and deposition of monosodium urate (MSU) crystals in the joints and soft tissues. It causes fusion, fibrosis and even ossification of the joint space and joint surfaces in patients, ultimately leading to joint dysfunction or deformity. The clinical presentation is progressive and may be associated with polyarticular episodes involving the wrist and prolonged duration of arthritis, leading to an unclear diagnosis[12,13].

To improve the diagnosis of the disease, this study focused on the analysis of the relationship between musculoskeletal ultrasound findings and disease activity in gouty arthritis. The DAS28 score is calculated from physical examination and subjective assessment and is a valid measure of arthritic disease activity. Musculoskeletal ultrasound allows visualization of intra-articular and bony destruction, synovial hyperplasia and joint effusion, and sensitive detection of inflammatory soft tissue lesions and bone lesions[14,15]. In the present study, patients with moderate to high disease activity showed significantly higher musculoskeletal ultrasound scores and DAS results than those with low disease activity (P <0.05). Synovial hyperplasia score, blood flow signal score, joint effusion score, bone erosion score, and total musculoskeletal ultrasound score were all positively correlated with disease activity (r=0.811, 0.814, 0.837, 0.788, 0.976, all P <0.05). This suggests that musculoskeletal ultrasound scores can accurately reflect the degree of disease activity in patients with gouty arthritis, i.e., Higher the disease activity in patients with gouty arthritis, the more severe was the joint inflammation. The associated inflammatory factors accumulate and infiltrate at the site of joint inflammation, resulting in the thickening of the synovial membrane of the affected joints, increased joint fluid accumulation, promoting an inflammatory response and clearer deterioration of the bone destruction visible on ultrasound, which is consistent with the findings of previous studies. One study involving 60 patients with gout found that ultrasound of the musculoskeletal system clearly demonstrated

synovial hyperplasia, tenosynovitis and soft tissue swelling, bursal ossification, bone surface erosion, gout stones and blood flow and inflammation over the periosteum, which may constitute the basis for the diagnosis and management of gouty arthritis. The advantages of ultrasound include high safety, non-invasiveness, simplicity and low financial burden, and can identify early deposits of MSU crystals in certain joint structures. However, conventional ultrasonography only demonstrates structural lesions in the patient's joints and fails to accurately diagnose bone infiltration. For example, X-ray plain scanning can show osteoporosis and bone destruction in arthritis but yield little differential diagnostic value[16]. Musculoskeletal ultrasound is indicative of the main pathological factor causing bone destruction, i.e., abnormal proliferation of blood vessels within the joint.Clinical studies have reported that most gouty joints display increased blood flow and clear tissue layers in tendons and tendon sheaths on musculoskeletal ultrasound in patients with inflammation, and therefore the degree of inflammation in gouty arthritis can be understood by assessing local blood flow[17,18]. It can also sensitively detect inflammatory soft tissue lesions and bone lesions with the advantage of good reproducibility and sensitivity, and may guide puncture and local injection therapy into the joint cavity to assess the presence of synovial inflammation. As an example, monosodium urate deposits on the synovial surface usually appear as punctate hyperechoic clusters on ultrasound. As the crystal cluster grows, it produces a mixed high-low echogenic gout stone image. Since bone erosion is primarily caused by gout stones, the borders of areas of bone erosion are free of proliferative blood flow signals, resulting in clear boundaries[19]. The relevant literature shows that musculoskeletal ultrasound offers accurate imaging of joint lesions and soft tissues by mechanical scanning, and that the frequency of the probe can be adjusted to the patient’s lesion. It enables observation of lesions in patients’ joint structures and also reflects the degree of bone infiltration, which can provide more comprehensive information for disease diagnosis[20,21]. Combined with the results of this study, it can be hypothesized that musculoskeletal ultrasound can be used as a criterion for disease activity index and provide diagnostic value for gouty arthritis.

The limitation of the current study is the inconsistent definition of certain criteria. It has been suggested that the DAS28 score may underestimate disease activity, which could lead to bias and missed diagnoses. Moreover, the current study was conducted in the same centre with a small sample size. In addition, this study did not specifically address the sensitivity and specificity of musculoskeletal ultrasound or the value of diagnostic assessment for the management or care of gouty patients. Thus, future studies with larger sample size are required for further verification.

Conclusion

In the above study, Gouty arthritis musculoskeletal ultrasound findings were found positively correlated with disease activity. Thus, the manifestations of musculoskeletal ultrasound demonstrate a good potential to provide informative evidence for the assessment of disease activity in patients with gouty arthritis.

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