Risk factors for the formation of double-contour sign and tophi in gout

Chao Sun, Xuan Qi, Yu Tian, Lixia Gao, Hongtao Jin and Huifang Guo

Abstract

Background: This study aimed to confirm the diagnostic accuracy of ultrasound (US) on gout and explore the potential risk factors for double-contour sign and tophi formation in gout patients.

Methods: The US analyses were performed on all knee, ankle, and first metatarsophalangeal (MTP 1) joints to reveal the type and location of lesions. While a questionnaire and blood biochemical index were used to explore the potential risk factors for double-contour sign and tophi in gout, the SPSS17.0 software was used for statistical analysis in the present study.

Results: Totally, 117 gout patients with 702 joints (38 lesions in knee joint, 93 lesions in ankle joint, and 112 lesions in MTP 1 joint) were enrolled in current analyses. Double-contour sign and joint effusion were the two most outstanding lesion manifestations in knee joints and ankle joints. Tophi and double-contour sign were the two most outstanding lesion manifestations in TMP 1 joints. Moreover, factors including uric acid (UA) level and the highest blood UA were potential risk factors of the double-contour sign, while age and history of US were potential risk factors for tophi.

Conclusion: US was effective on the joints of gout patients. There was US sensitivity for tophi and double-contour sign in MTP 1 joints. The double-contour sign was a potential specific manifestation in knee joints and ankle joints. Furthermore, UA and highest blood UA level were potential risk factors for double-contour sign, while age and US history were potential risk factors for tophi.

Keywords: Gout, Ultrasound, Double-contour sign, Tophi, Risk factor, Questionnaire

Introduction

Gout is an inflammatory disorder characterized by hyperuricemia and the deposition of monosodium urate (MSU) crystals [1]. It is due to elevated levels of uric acid (UA) in the blood [2]. A high level UA accumulation in joints, tendons, and surrounding tissues can induce episodic gout flares, gouty arthropathy, and tophi formation [3]. Gout affects about 2% of the Western population at some point in their lives [4]. As the most common cause of inflammatory arthritis, gout has already caused a great social burden to human in recent decades [5]. Thus, it is necessary to develop novel strategies for gout treatment.

The investigation of useful risk factors is essential for gout treatment [6]. Epidemic study shows that hypertension, renal insufficiency, hypertriglyceridemia, hypercholesterolemia, hyperuricemia, diabetes, obesity, and early menopause are all higher risk for gout [7, 8]. Actually, the accurate diagnosis is critical for revealing appropriate risk factors of gout [9, 10]. In clinical practice, various strategies have been successfully used to detect gout including ultrasonography (US), magnetic resonance imaging (MRI), computed tomography (CT), and X-ray [11, 12]. However, the differential diagnosis between gout and other causes of arthritis can be challenging [13]. Owing to these limitations, recent study shows that the high frequency US has higher diagnostic coincidence efficiency in gout tophus than those of X-ray, CT, and MRI [14]. Based on the US detection, the joint and tendon subclinical involvement are proved to be risk factors of gouty arthritis [15]. US double-contour sign is a specific manifestation of urate deposition in gouty
arthritides [16, 17]. The American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR)-gout have already clarified the association between US and double-contour sign [18]. Zhu et al. indicated that double-contour sign increased the sensitivity of sonography for detection of urate deposits in gout [19]. Based on an US pilot study in daily clinical practice, Slot et al. has demonstrated that the double-contour sign is a consistent finding in MTP joints in gout patients [20]. Despite of that, as a deposit of UA crystals, tophi is an outcome measure for chronic gout [21]. The development of gouty tophi can limit joint function and cause bone destruction, leading to noticeable disabilities, especially when gout cannot successfully be treated [22]. Thus, the prediagnosis of clinical sign including double-contour or tophi is important for gout therapy [23]. Although double-contour sign and tophi are the two reliable evidence for gout formation under US detection [24], little is known with the independent predictive risk factors for these evidence. Thus, an investigation based on US detection to explore the potential risk factors for double-contour sign and tophi formation in gout patients is needed.

Based on a newly designed questionnaire and US investigation, the present study aimed at investigating the risk factors for double-contour sign and tophi formation in gout patients. Meanwhile, the diagnostic accuracy of US on gout patients was further confirmed. By revealing the potential factors affecting the deposition of urate, we hoped to enhance the prediagnosis rate of gout in clinical practice.

Methods

Patients

Between September 2015 and September 2016, patients with gout who present to the rheumatology department of the Second Hospital of Hebei Medical University were recruited in the present study. The inclusion criteria were (1) primary gout arthritis and (2) in accordance with gout diagnostic criteria of the American Society for Rheumatology (ACR). All the patients conformed to the criteria for the classification of the acute arthritis of primary gout [25]. Patients with rheumatoid arthritis, reactive arthritis, psoriatic arthritis, spinal arthritis, or other inflammatory arthritis were excluded. Ethical approval for the present study was obtained from the Second Hospital of Hebei Medical University ethics committee. Meanwhile, the informed consent was obtained from all participants.

Questionnaire index

All gout patients were investigated with a unified questionnaire. The questionnaire parameters included (1) gender, age, height, and weight; (2) the duration of disease; (3) the frequency of gout attacks over the past 1 year; (4) the highest blood UA level, the usual blood UA level, and the detection frequency of blood UA; (5) usual eating habits; (6) medication history; (7) the history of uric acid-lowering drugs; (8) complications (such as coronary heart disease, diabetes, chronic kidney disease, hyperlipidemia); (9) the history of known tophi, kidney stones, or articular US; (10) whether there is a long-term treatment plan for gout; (11) knowledge of gout; and (12) knowledge of the high purine food. Then, the body mass index (BMI) was calculated by a same physician. The BMI is defined as the body mass divided by the square of the body height and is universally expressed in kg/m² [26]. In the present study, the BMI of 18.5–24 kg/m² represented normal, 24–28 kg/m² represented overweight, and greater than 28 kg/m² was considered as obese.

Biochemical index analysis

A total of 3 ml fasting venous blood was obtained from all participants and then was analyzed using the Roche automatic biochemical analyzer (cobas 8000, Roche Diagnostics Products (Shanghai) Co., Ltd.). The blood urea nitrogen (BUA), creatinine (CREA), and UA were detected using Berthelot’s enzymic colorimetric method [27–29], The total cholesterol (TC) was detected by HMMPS method (cholesterol oxidase) based on total cholesterol assay kit (YZB/JAP 1794-2008, Wako Pure Chemical Industries, Ltd.). The total triglycerides (TG) was detected by glycerine phosphate oxidase- peroxidase (GPO-PAP) method based on TG assay kit (TR7971, Randox Laboratories Ltd). All the operation of the assay kits were strictly according to the manufacturer’s instruction.

Ultrasound investigation

The representative US images of each individual element lesion presented in the longitudinal and transverse scans from each patient were collected to observe the pathological changes of joint effusion, synovial hyperplasia, synovitis, bone erosion, gout, and double-contour sign. The detailed US examinations were as follows: knee (hyaline cartilage of the femoral condyles; patellar tendon, including both proximal and distal insertion; femoral bone profile; operated with 4–13 MHz linear array probe), ankle (Achilles tendon), and foot (first metatarsophalangeal joint (MTP 1) for hyaline cartilage, bone profile, periarticular tissue). These anatomical areas were selected because of their accessibility by US and their frequent involvement in patients with gout. Based on the full digital color Doppler ultrasound diagnostic instrument (ESAOTE MyLab 90, Genoa, Italy), all the US investigations were
performed by the same doctor who had received a formal musculoskeletal US training.

Statistical analysis

The SPSS17.0 software (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis in the present study. The distribution of the quantitative data was represented by mean ± standard deviation. The normality test was performed by the Shapiro-Wilk method. The means in two groups were compared with *t* test if the data was conformed to normal distribution; if not, the Mann-Whitney *U* test was used [30]. The differences of qualitative data between groups were compared with the chi-square test. The analyses of risk factors for double-contour sign and tophi formation were performed using logistic binary regression. Bilateral *P* < 0.05 was considered as statistically significant.

Results

Baseline characteristics

A total of 117 gout patients were enrolled in this study (114 males and 3 females, average age 40.32 ± 11.93 years). The average BMI was 28.34 ± 5.38 kg/m². There were 81 patients with acute stage and 36 patients with intermittent period. The US detection was performed on a total of 234 knee joints, 234 ankle joints, and 234 MTP 1 joints (Table 1). The results showed that there were 38 lesions (16.2% of 234 knees) in knee joints, 93 lesions (39.7% of 234 ankles) in ankle joints, and 112 lesions (47.9% of 234 MTP 1) in MTP 1 joints.

Lesions examination of joints

The pathological manifestations of all kinds of joint (knees, ankles, and MTP 1) were explored by US examination (Table 2). The results showed that double-contour sign (30 joints) and joint effusion (17 joints) were the two most outstanding manifestations of knees in gout patients. Meanwhile, double-contour sign (44 joints) and joint effusion (42 joints) were the two most outstanding manifestations of ankles in gout patients. Furthermore, the tophi (78 joints) and double-contour sign (64 joints) were the two most outstanding manifestations of MTP 1 in gout patients. The representative US images for double-contour sign and tophi are shown in Figs. 1 and 2, respectively.

Risk factors analysis of double-contour sign

All the parameters in the current questionnaire were included in the risk factor investigation. The significance test of double-contour sign showed that UA level (*P* < 0.01), peak blood UA (*P* < 0.01), and disease duration (*P* < 0.01) were associated with the occurrence of double-contour sign (Table 3). Then, the logistic regression analysis of risk factors was performed on double-contour sign based on the significance test. The results showed that UA (*P* = 0.011; OR = 1.006; 95% CI = 1.001–1.010), highest blood UA (*P* = 0.014; OR = 7.570; 95% CI = 1.511–37.930), drug intervention history in the intermittent period (*P* = 0.041; OR = 3.468; 95% CI = 1.036–10.876), and history of US (*P* = 0.003; OR = 8.234; 95% CI = 1.117–60.710) were potential independent risk factors for the double-contour sign (Table 4).

Risk factors analysis of tophi

The significance test of double-contour sign and tophi is listed in Table 5. The results showed that the UA level (*P* = 0.007), frequency of UA or renal function examination (*P* = 0.002), and ever done a joint US (*P* < 0.01) were associated with the occurrence of tophi. The logistic regression analysis of risk factors was performed on tophi in gout patients based on the significance test. The risk factor investigation showed that age (mean age of patients with tophi 42.640 ± 12.112; mean age of patients without tophi 36.980 ± 10.940; *P* = 0.008; OR = 1.070; 95% CI = 1.018–1.124) and history of US (*P* = 0.006; OR = 26.801; 95% CI = 2.529–284.051) were potential independent risk factors for tophi (Table 6).

Discussion

Gout is characterized with deposition of urate including double-contour sign and tophi [31]. The risk factors that participate in the process of urate crystal formation are vital for the prediagnosis and treatment of gout [32]. To reveal the US diagnostic effect and potential risk factors affecting the deposition of urate, a study was performed based on US and questionnaire investigation. Totally, 117 gout patients with 702 joints were enrolled in current analyses. In those 702 joints, there were 38 lesions (16.2% of 234 knees) in knee joints, 93 lesions (39.7% of 234 ankles) in ankle joints, and 112 lesions (47.9% of 234 MTP 1) in MTP 1 joints. Double-contour sign and joint effusion were the two most outstanding lesion manifestations in knee joints and ankle joints. Meanwhile, tophi and double-contour sign were two most outstanding lesion manifestations in MTP 1 joints. Based on the questionnaire and blood biochemical index
detection, the logistic regression analyses showed that UA, highest blood UA, drug intervention history in the intermittent period, and history of US were potential risk factors of the double-contour sign, while age and history of US were potential risk factors for tophi.

Urate deposition is closely related to the structural joint damage in gout patients [33]. US can reflect the concurrent validity of urate deposition change [34]. Naredo et al. indicated that US bilateral assessment might be valid for diagnosing gout with acceptable sensitivity and specificity [35]. Due to the benefits of safe, non-invasive, free of ionizing radiation, less expensive, and multiple-target assessment in real time, US is the optimal tool for urate deposition monitoring in gout patients [36]. In this study, the US detection rate of joint lesions in 234 knee joints, 234 ankle joints, and 234 MTP 1 joints was 16.2%, 9.7%, and 47.9%, respectively. These results showed that US could reveal lesions in all three kinds of joints in gout patients. Interestingly, the occurrence rate of lesion in MTP 1 joints was significantly higher than that in knee joints and ankle joints in the current study. Pineda et al. showed that the double-contour sign was found in almost 25% of MTP 1 joints (higher than any other kinds of joints) of gout patients [37]. Previous studies indicate that the double-contour sign and tophi are the two classical manifestations of urate deposition in joints of gout patients [16, 17, 38]. However, based on a meta-analysis of the diagnostic accuracy for US, Young et al. showed that US signs of tophi and the double-contour sign were not sensitive in gout patients [39]. Singh and Dalbeth even doubt that the double-contour sign was not specific for gout but for calcium pyrophosphate crystal deposition or other arthropatitis [17]. Thus, although US is optimal tool for urate deposition monitoring, the US diagnostic sensitivity and specificity for tophi and the double-contour sign in gout patients is controversial. In the present study, US examination showed that the double-contour sign was one of

Table 2 The pathological manifestations of knees, ankles and MTP 1 joints in gout patients

| Area       | Hypodermic edema | Joint effusion | Tenosynovitis | Synovial hyperplasia | Synovitis | Tophi | Double-contour sign | Bone erosion | Tendon sheath effusion | Crystal deposition |
|------------|-------------------|----------------|---------------|----------------------|-----------|-------|---------------------|--------------|-----------------------|------------------|
| Right knee | 0                 | 11             | 0             | 0                    | 1         | 7     | 16                  | 0            | 0                     | 0                |
| Left knee  | 0                 | 6              | 0             | 0                    | 1         | 4     | 14                  | 0            | 0                     | 0                |
| Right ankle| 18                | 20             | 3             | 2                    | 6         | 6     | 23                  | 0            | 0                     | 0                |
| Left ankle | 17                | 22             | 1             | 1                    | 4         | 7     | 21                  | 0            | 1                     | 1                |
| Right MTP 1| 0                 | 1              | 0             | 1                    | 15        | 36    | 33                  | 17           | 0                     | 3                |
| Left MTP 1 | 1                 | 2              | 0             | 0                    | 11        | 42    | 31                  | 19           | 0                     | 1                |

MTP 1 first metatarsophalangeal joint

Fig. 1 The ultrasound image for double-contour sign in gout patients. The white arrow represented the signal of double-contour sign in gout patients.

Fig. 2 The ultrasound image for tophi in gout patients. The red signal represented the tophi in gout patients.
the most outstanding lesion manifestations in both knee joints and ankle joints, while the tophi and double-contour sign were the two most outstanding lesion manifestations in TMP 1 joints. Based on those results, we speculated that there might be an US sensitivity for tophi and double-contour sign in MTP 1 joints. Furthermore, the double-contour sign might be the specific manifestation in knee joints and ankle joints, which was different from the results of Singh and Dalbeth [17]. The reason for this difference might be the larger sample size of knee and ankle joints enrolled in the present study. However, a further investigation is needed to confirm the results obtained in this study.

Table 3 The significance test of different parameters on double-contour sign in gout patients

| Parameters                  | Groups          | Without double-contour sign | With double-contour sign | P value |
|-----------------------------|-----------------|-----------------------------|--------------------------|---------|
| Age*                        |                 | 37.510 ± 11.709             | 42.640 ± 11.694          | 0.020   |
| BUN (mmol/L)                |                 | 5.094 ± 1.461               | 5.368 ± 1.719            | 0.458   |
| CREA (μmol/L)               |                 | 75.672 ± 17.683             | 78.345 ± 19.149          | 0.429   |
| UA (μmol/L)*                |                 | 443.640 ± 114.603           | 518.120 ± 131.620        | 0.002   |
| TC (mmol/L)                 |                 | 4.781 ± 1.178               | 4.823 ± 1.450            | 0.646   |
| TG (mmol/L)                 |                 | 2.049 ± 1.401               | 2.179 ± 1.644            | 0.916   |
| FBG (mmol/L)                |                 | 5.217 ± 0.708               | 5.315 ± 1.004            | 0.511   |
| Sex                         | Female          | 3                            | 0                        | 0.180   |
|                             | Male            | 50                           | 64                       |         |
| BMI                         | Normal          | 7                            | 11                       | 0.598   |
|                             | Overweight      | 22                           | 21                       |         |
|                             | Obesity         | 24                           | 32                       |         |
| Duration                    | ≤ 1 year        | 23                           | 4                        | < 0.001 |
|                             | 1–5 years       | 21                           | 35                       |         |
|                             | ≥ 5 years       | 9                            | 25                       |         |
| Gout attack in 1 year       | 0–2 times       | 29                           | 13                       | < 0.001 |
|                             | 3–6 times       | 20                           | 27                       |         |
|                             | 7–12 times      | 4                            | 24                       |         |
| Peak blood UA               | 421–539         | 19                           | 5                        | < 0.001 |
|                             | ≥ 540           | 34                           | 59                       |         |
| UA level                    | ≤ 421           | 13                           | 3                        | < 0.001 |
|                             | 421–539         | 20                           | 15                       |         |
|                             | ≥ 540           | 20                           | 46                       |         |
| Frequency of UA or renal function examination | Regularly checked | 13 | 5 | 0.053 |
|                             | Occasionally checked | 18 | 26 | |
| Eating habits               | Strict diet     | 14                           | 17                       | 0.967   |
|                             | Avoid the high purine diet as much as possible, but not strictly controlled | 23 | 29 | |
|                             | No control over diet | 16 | 18 | |
| Medication during the interval | Insist on taking | 15 | 5 | 0.009 |
|                             | Without medications | 29 | 41 | |
|                             | Occasional medications | 8 | 17 | |

UA uric acid, CHD coronary heart disease, CKD chronic kidney disease, US ultrasound. P < 0.05 was considered as significantly different. t test
In gout patients, UA level, double-contour sign, and tophi as well as ankle musculoskeletal examination have high diagnostic value in clinical practice [40]. The interaction between UA level and other risk factors in the development of gout has been proved in the previous study [41]. Although the increased UA level is a major risk factor for gout, Kumar et al. showed that serum UA level did not confirm or exclude gout; many people did not develop gout, and during acute attacks, serum levels might be normal [42]. A biochemical analyses in previous report showed that the UA concentration in the knee joint of a gout patient was consistently less than 5 mg/dL (297.6 μmol/L), but the US confirmed a resemblance of the double-contour sign typical of UA deposits [43]. Moreover, many researchers believe that serum UA levels cannot be considered a sensitive marker for double-contour sign during the diagnosis of gout [44, 45]. Actually, the logistic regression analyses in this study showed that UA and highest blood UA were both risk factors for double-contour sign. Furthermore, recent data suggest that the prevalence of gout is increased with age both in men and women [46]. A previous logistic regression analysis shows that age is one of the risk factors associated with tophi formation in gout [23]. A meta-analysis of cigarette smoking on gout occurrence shows that age is an influence factor for the occurrence of gout [47]. Although tophi are an important manifestation in gout, the study focused on relation between age and tophi formation is rare. In this study, the occurrence of tophi formation in low age group (mean age 36.980 ± 10.940) was significantly lower than the high age group (mean age 42.640 ± 12.112). Thus, based on the logistic regression investigation, we speculated that the risk of tophi formation might increase with the age in gout patients. Interestingly, the risk factor analyses in the current study showed

| Variables | P | OR  | 95% CI      |
|-----------|---|-----|-------------|
| Age       | 0.067 | 1.051 | 0.997–1.108 |
| UA (μmol/L) | 0.011 | 1.006 | 1.001–1.010 |
| Duration of gout | 0.062 | 2.322 | 0.958–5.625 |
| Gout attacks over the past 1 year | 0.067 | 2.063 | 0.951–4.474 |
| The highest UA level | 0.014 | 7.570 | 1.511–37.930 |
| Peak blood UA level | 0.937 | 0.962 | 0.366–2.529 |
| Drug intervention history in the intermittent period | 0.041 | 2.046 | 1.036–5.876 |
| History of US | 0.039 | 8.234 | 1.117–60.710 |
| Constants | < 0.001 | | |

UA uric acid, OR odds ratio, CI confidence interval. P < 0.05 was considered as significantly different

### Table 5 The significance test of different parameters on tophi in gout patients

| Parameters | Groups | Without double-contour sign | With double-contour sign | P value |
|------------|--------|-----------------------------|--------------------------|---------|
| Age*       | 36.980 ± 10.940 | 42.640 ± 12.112 | 0.011 |
| BUN (mmol/L) | 5.043 ± 1.380 | 5.383 ± 1.743 | 0.372 |
| CREA (μmol/L) | 77.488 ± 22.947 | 76.888 ± 14.758 | 0.331 |
| UA (μmol/L)* | 478.167 ± 145.745 | 488.704 ± 117.178 | 0.678 |
| TC (mmol/L) | 4.828 ± 1.400 | 4.789 ± 1.296 | 0.618 |
| TG (mmol/L) | 1.991 ± 1.578 | 2.208 ± 1.515 | 0.125 |
| FBG (mmol/L) | 5.225 ± 0.674 | 5.303 ± 1.002 | 0.751 |

Sex
- Female: 1, 2: 1.000
- Male: 47, 67: 0.233

BMI
- Normal: 10, 8: 0.372
- Overweight: 19, 24: 0.059
- Obesity: 19, 37: 0.007

Duration
- ≤ 1 year: 16, 11: 0.059
- 1–5 years: 22, 34: 0.007
- ≥ 5 years: 10, 24: 0.007

Gout attack in 1 year
- 0–2 times: 24, 18: 0.019
- 3–6 times: 17, 30: 0.591
- 7–12 times: 7, 21: 0.591

Peak blood UA
- ≥ 540: 11, 13: 0.059
- ≤ 540: 37, 56: 0.059

UA level
- ≥ 421: 12, 4: 0.007
- < 421: 37, 56: 0.007

Frequency of UA or renal function examination
- Regularly checked: 14, 4: 0.002
- Occasionally checked: 15, 29: 0.002

Eating habits
- Strict diet: 16, 15: 0.286
- Avoid the high purine diet as much as possible, but not strictly controlled: 21, 31: 0.286

Medication during the interval
- No control over diet: 11, 23: 0.286
- Insist on taking medications: 14, 6: 0.002
- Without medications: 24, 46: 0.002
- Occasional medications: 8, 17: 0.002
that the patients who had US history might have a lower occurrence of tophi formation than patients without US history. We speculated that a potential threptic effect of US operation or patient itself raises awareness of the prevention for pre-existing diseases might be the reasons. Unfortunately, there is no such report on US history decreasing the formation of tophi. Thus, a further investigation to confirm the effect of US history on tophi formation is needed. However, there were still some limitations in the current study such as small sample size and lack of subsequent verification test.

### Table 5 The significance test of different parameters on tophi in gout patients (Continued)

| Parameters       | Groups       | Without double-contour sign | With double-contour sign | P value |
|------------------|--------------|-----------------------------|--------------------------|---------|
| Hypertensive     | No           | 35                          | 53                       | 0.631   |
|                  | Yes          | 13                          | 16                       |         |
| CHD              | No           | 48                          | 64                       | 0.149   |
|                  | Yes          | 0                           | 5                        |         |
| Diabetes         | No           | 47                          | 66                       | 0.884   |
|                  | Yes          | 1                           | 3                        |         |
| CKD              | No           | 45                          | 67                       | 0.677   |
|                  | Yes          | 3                           | 2                        |         |
| Other diseases   | No           | 29                          | 43                       | 0.835   |
|                  | Yes          | 19                          | 26                       |         |
| Hyperlipidemia   | No           | 43                          | 66                       | 0.364   |
|                  | Yes          | 5                           | 3                        |         |
| Kidney stones    | Yes          | 12                          | 13                       | 0.782   |
|                  | No           | 30                          | 37                       |         |
| Tophi            | Yes          | 10                          | 16                       | 0.140   |
|                  | No           | 18                          | 13                       |         |
| Ever done a joint US | Done | 11                          | 1                        | < 0.001 |
|                  | Never done   | 37                          | 66                       |         |
| Whether there is a long-term treatment plan for gout | Yes | 21                          | 15                       | 0.011   |
|                  | No           | 27                          | 54                       |         |
| Understand gout  | Understand   | 14                          | 10                       | 0.050   |
|                  | A little      | 26                          | 35                       |         |
|                  | Not understand| 8                           | 23                       |         |
| Knowledge of high purine food | Fully understand | 17                          | 15                       | 0.083   |
|                  | A little      | 25                          | 33                       |         |
|                  | Unknown       | 6                           | 19                       |         |

UA uric acid, CHD coronary heart disease, CKD chronic kidney disease, US ultrasound. P < 0.05 was considered as significantly different.

**Table 6 Logistic regression analysis of risk factors for tophi in gout patients**

| Variables                                      | P   | OR   | 95% CI   |
|------------------------------------------------|-----|------|----------|
| Age                                           | 0.008|1.070|1.018–1.124|
| Gout attacks over the past 1 year              | 0.385|1.332|0.697–2.548|
| Drug intervention history in the intermittent period | 0.422|1.367|0.638–2.928|
| Joints US history                             | 0.006|26.801|2.529–284.051|
| Whether there is a long-term treatment plan    | 0.512|1.414|0.502–3.982|
| Blood UA level                                | 0.068|2.111|0.946–4.712|
| Frequency of UA or renal function test         | 0.330|1.426|0.699–2.910|
| Constants                                      | < 0.001|     |          |

UA uric acid, OR odds ratio, CI confidence interval. P < 0.05 was considered as significantly different.

### Conclusions

In conclusion, the diagnostic accuracy of US on the joints of gout patients might be ideal. There might be an US sensitivity for tophi and the double-contour sign in MTP 1 joints, while the double-contour sign might be the specific manifestation in knee joints and ankle joints. Furthermore, UA and peak blood UA level might be the potential risk factors for double-contour sign, while age and US history might be the potential risk factors for tophi in gout.

### Abbreviations

ACR: American College of Rheumatology; BMI: Body mass index; BUA: Blood urea nitrogen; CREA: Creatinine; CT: Computed tomography; EULAR: European League Against Rheumatism; GPO-PAP: Glycerine phosphate oxidase-peroxidase; MRI: Magnetic resonance imaging; MSU: Monosodium urate; MTP 1: First metatarsophalangeal joint; TC: total cholesterol; TG: Total triglycerides; UA: Uric acid; US: Ultrasound.

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### Authors’ contributions

CS drafted the manuscript. XQ performed the statistical analysis. YT acquired the data. LG analyzed and interpreted the data. HJ obtained the funding. HG conceived and designed the research and revised the manuscript for important intellectual content. All authors read and approved the final manuscript.

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### Availability of data and materials

Not applicable.

### Ethics approval and consent to participate

The ethical approval for the present study was obtained from the Second Hospital of Hebei Medical University Ethics Committee.

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.
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