Original Article

# Burden and distribution of monosodium urate deposition in patients with hyperuricemia and gout: a cross-sectional Chinese population-based dual-energy CT study

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**Background:** To investigate the distribution and burden of monosodium urate (MSU) deposition in hyperuricemia and gout patients with dual-energy computed tomography (DECT).

**Methods:** A total of 1,936 consecutive patients from January 1, 2009, to September 15, 2017, underwent DECT examinations in Jinling Hospital. Of these, 1,294 patients were excluded due to other clinical diagnoses (n=1,041), inappropriate locations (n=82), poor-quality images (n=105), training cases (n=30) and duplicated data (n=36). Finally, 642 patients were included in this study. We retrospectively analyzed 1,127 DECT examinations in 642 consecutive patients (hyperuricemia group, n=121; gout group, n=521) and recorded the volume and number of MSU deposits. For each anatomical location, we recorded MSU deposition in the soft tissue and joint cavity. MSU deposition was analyzed and compared between groups. For normally distributed data, independent sample t-tests were used for comparison between the two groups. The independent samples nonparametric test was used to analyze nonnormally distributed data.

**Results:** (I) The burden of MSU deposition in the gout group {volume [0.14 (0.04–1.36)] and numbers [10.00 (5.00–19.00)]} was significantly higher than that {volume [0.08 (0.02–0.47), P=0.003] and numbers [9.50 (2.00–16.00), P=0.01]} in the hyperuricemia group. (II) The burden of MSU deposition in the knees {volume [0.24 (0.01–1.79), P=0.002] and quantity [6.00 (2.00–12.00), P=0.04]} and feet {volume [0.10 (0.04–0.66)] and number [9.00 (5.00–15.00)]} was significantly higher in the gout group than those {knees: the volume [0.03 (0.00–0.27), P=0.002] and the quantity [4.00 (0.00–9.00), P=0.04]; feet: the volume [0.07 (0.02–0.19), P=0.003)] and number [8.00 (2.25–12.00), P=0.04]} in the hyperuricemia group, respectively. (III) In the hyperuricemia group, the volume of MSU deposition was significantly higher in the soft tissues of the knee (0.022±0.042) and ankle (0.062±0.305) than in those (knee: 0.001±0.005, P=0.02; ankle: 0.027±0.234, P=0.02) in the joint cavity.

**Conclusions:** Although subclinical urate deposition can occur in patients with asymptomatic hyperuricemia, the burden of urate deposition is greater in patients with symptomatic gout, and the distribution is more pronounced in the foot/knee. Thus, more effective patient management and monitoring can be achieved by measuring the burden of MSU deposits in the patient's feet/knees. These data suggest

that a threshold for urate crystal volume at typical sites may be required before symptomatic disease develops.

**Keywords:** Monosodium urate (MSU); dual-energy computed tomography (DECT); gout; hyperuricemia

Submitted Nov 02, 2022. Accepted for publication Apr 30, 2023. Published online May 24, 2023.
doi: 10.21037/qims-22-1208
**View this article at:** https://dx.doi.org/10.21037/qims-22-1208

## Introduction

Gout is the most common form of inflammatory arthritis (1), with a prevalence of 1.1% among adults in China (14.66 million people) and 3.9% among adults in the US (9.2 million people) (2,3). Both the prevalence and incidence of gout seem to be rising across the globe (4). Gout is more prevalent in men than in women, with increasing age, and in some ethnic groups (5). Gout is caused by the deposition of monosodium urate (MSU) crystals in articular and non-articular structures (6). Hyperuricemia is the most important risk factor for gout (7,8). In clinical practice and research, hyperuricemia (blood urate concentration over the saturation threshold) is typically reported when serum urate (sUA) is higher than or equal to 0.42 mmol/L (7 mg/dL) (6). Elevated levels of sUA greater than 6.0 mg/dL can cause crystallization of MSU deposits and eventually trigger gout in some patients (9,10). While hyperuricemia is a known cause of gout, many patients with hyperuricemia do not develop gout (11). To date, it is not fully understood why some patients with asymptomatic hyperuricemia (i.e., hyperuricemia in the absence of gout) develop symptomatic gout. Sedimentary sites may play a role; for example, deposition around the joints may not lead to clinically significant diseases (12). The quantity of urate crystal deposition may also affect the development of symptomatic disease (12). Nevertheless, the mechanism and location of MSU crystal deposition in gout have received little attention from the scientific community until now. Therefore, the main purpose of this study was to determine whether the distribution and burden of MSU deposits are related to the activity of the disease so that we can decrease the occurrence of gout and improve the management of clinical gout. Moreover, we innovatively divide a single joint into distinct segments (soft tissue and joint cavity). In this way, systemic MSU deposition in gout patients can be measured more precisely.

For decades, the gold standard for the diagnosis of gout has been the identification of MSU crystal deposits in the synovial fluid of the affected joint using polarized light microscopy (13,14). Joint aspiration can be a painful, invasive process (15), which not all health care providers are able to perform. Dual-energy computed tomography (DECT) scans are a noninvasive technique that may be an alternative diagnostic tool, especially in patients with more established gout (16), as DECT scans have excellent reliability (17). Due to its high sensitivity and specificity for gout diagnosis, DECT has been incorporated into the new 2015 classification criteria for gout developed in collaboration by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR). DECT is an advanced imaging method that allows for specific detection and volume measurement of urate deposits in gout patients and has also shown efficacy in burden quantification and treatment monitoring (18-20). Although DECT has been proven to be useful in detecting articular MSU detection in gout patients in some studies (21,22), no study has been reported to use DECT to compare the distribution and burden of MSU deposits in patients with hyperuricemia and gout.

Therefore, we aimed to investigate the distribution and burden of MSU crystal deposition in Chinese patients with asymptomatic hyperuricemia and symptomatic gout with DECT. We present this article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-22-1208/rc).

## Methods

### *Study population*

This retrospective study was approved by the institutional review board of Jinling Hospital, Medical School of Nanjing University. Written informed consent was waived for this retrospective analysis. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). We recruited a retrospective cohort of gout and hyperuricemia patients who underwent DECT at Jinling

 

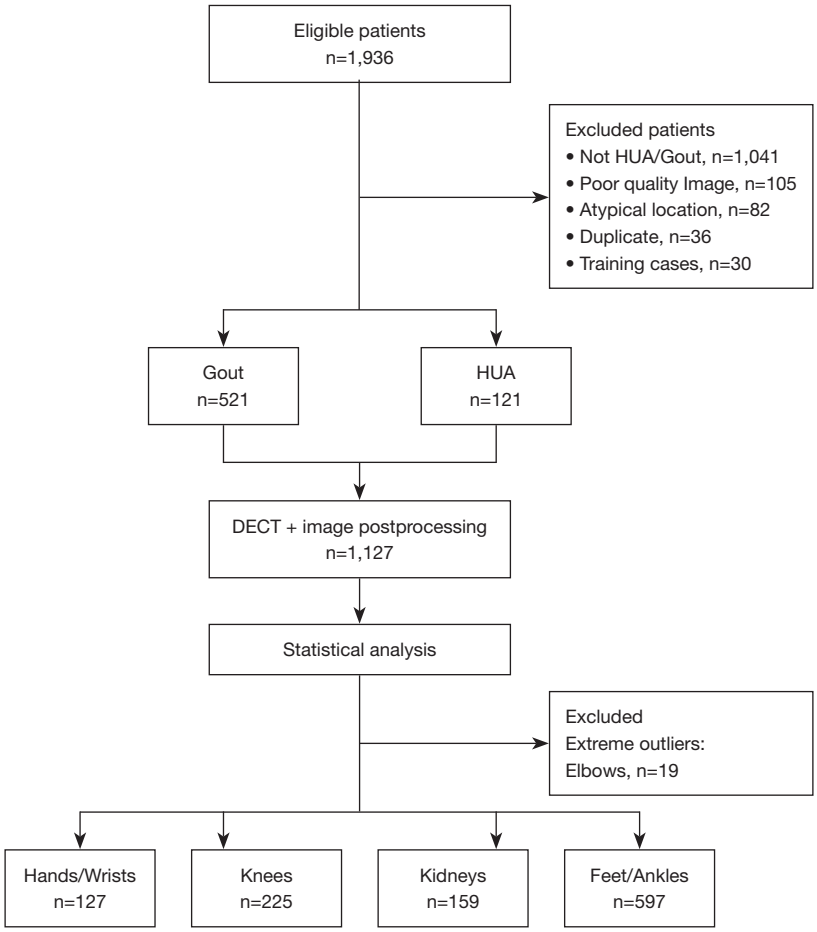


**Figure 1** Patient flow, a large cohort Chinese population-based DECT study. HUA, hyperuricemia; DECT, dual-energy computed tomography.

Hospital from January 1, 2009, to September 15, 2017. A total of 1,936 consecutive patients were included in the study. Inclusion criteria were patients who had undergone a multisite DECT scan and were clinically diagnosed with gout and hyperuricemia. Of these, 1,294 patients were excluded due to other clinical diagnoses, which were neither gout nor hyperuricemia (n=1,041), poor quality images (n=105), atypical MSU deposition site (n=82), training cases (n=30) and duplicated data (n=36).

Two experienced observers (CXT and XYZ with 8 and 5 years of experience in DECT interpretation) assessed image quality by consensus using a five-stage system (23): Grade 1: nondiagnostic; Level 2: limited due to distortion, blur, and motion artifacts; Level 3: adequate and diagnosable, but minimal distortion, blur, and motion artifacts; Grade 4: good, diagnosable, no artifacts; and Level 5: excellent, diagnosable, no artifacts. A patient who had a score no less than 3 was included in further quantitative analysis. Finally, 642 patients (male: 94.4%; mean age: 44±16 years) were included. The flowchart of this study is provided in *Figure 1*. Additionally, the demographics and comorbidities from the patients' medical histories were recorded from the patients' medical records.

### *Subdivision distribution of MSU deposits in joints*

Gout flares can occur in the joints or periarticular tissues (6) (e.g., bursae, tendons, and entheses). A joint can be further subdivided into the constituent bones of the joint, the joint cavity, and the soft tissue surrounding the joint. DECT software has a mechanism to avoid false-positive detection of beam hardening by excluding MSU pixels within a

 

certain distance of cortical bone. Given the known artifacts and shortcomings of the DECT technique, it is doubtful that cortical MSU deposition can be reliably measured. Therefore, cortical bone was ignored in this study when subdividing sites, and cortical bone deposits were not included in subsequent analyses. Finally, cortical bone was excluded in the division of joint sites, and each measured bone joint was divided into two distinct parts (soft tissue and joint cavity).

Among the 642 enrolled patients, each had at least two sites of DECT. A total of 127 patients had scans of their hands (125 had scans of both wrists and two had scans of one hand); 225 patients had knee scans (220 on both knees and 5 on one); foot scans were performed on 597 patients (591 patients had both feet and 6 patients had one foot). Thus, a total of 1,885 joints (i.e., two joints on both hands) of DECT films were included in the subsequent analysis. For each anatomical site, for example, there were 113 patients with gout and 14 patients with hyperuricemia out of 127 patients who had DECT on their hands.

### *DECT scans*

DECT examinations were performed in 59% (380/642) of patients on the first-generation dual-source CT system (Somatom Definition or Definition FLASH, Siemens Healthcare, Erlangen, Germany), while the remaining 41% of patients underwent DECT examination on a second-generation dual-source CT system (Somatom Definition or Definition FLASH, Siemens Healthcare) within 1 week of clinical diagnosis. Given the differences between different scanning devices, to ensure the generalization and credibility of the images, we preprocessed the images with voxel standardization and gray standardization to reduce the influence caused by the difference in image acquisition parameters.

Each patient underwent at least 2 of the 10 anatomical locations for DECT scans: hands/wrists, elbows, knees, feet/ankles, and kidneys (one for each side). All scans were performed with the same imaging protocols except for tube voltage (kV) and effective tube current (mAs). The scanning parameters were as follows: tube voltage of (sn)140/80–100 KVp, effective tube currents of 40/170 mAs and 37/157 mAs in the first generation and the second generation dual-source CT for upper extremity; 55/234 mAs /240/120 mAs for knees and 250/125 mAs for feet/ankles, 95/404 mAs/153/120 mAs for kidney. Technical features included a slice thickness of 0.6 mm, a field of view of 120 and a slice interval of 0.3 mm. Bone and soft tissue window algorithm images were obtained in the axial plane with additional sagittal and coronal reconstructed images.

### *Image postprocessing and image analysis*

Postprocessing and image interpretation were performed with a commercial software program (Syngo.via, VB10, Siemens Healthineers) to create material-selective images to perform postprocessing, where MSU depositions were color-coded as green, cortical bone was color-coded as blue and trabecular bone was color-coded as purple. Prior to the beginning of the study, 30 training cases (15 gout cases and 15 control cases) were used to familiarize the observer with the Gout DECT software. These 30 training cases were excluded from the final analysis. When the observer measured the volume of MSU crystal deposition, artifacts such as nail beds, skin, submillimeter, motion, and beam hardening were removed manually because they are easy to identify (24).

Each case was double-read by two musculoskeletal radiologists with 5 and 8 years of experience who had the same training to identify artifacts on DECT in gout patients. For the three cases in which a discrepancy existed, agreement was reached by consensus. Therefore, ultimately, there was no variation between the observers. Artifacts were defined by the criteria listed in a previous study (24); these criteria are based on observations from previous studies (22,24-26).

For the evaluation of interobserver agreement, two radiologists (CXT and XYZ with 8 and 5 years of experience in DECT interpretation) who were blinded to all clinical features, including gout status and sUA results, recorded the sites, numbers and volume of urate deposition using DECT software in 100 randomly selected cases independently. Then, one radiologist (XYZ) evaluated the remaining cases. The volume and number of MSU deposits on DECT were recorded for specific anatomical locations (hands/wrists, feet/ankles, knees, elbows, and kidneys) and different parts of each anatomical location (the surrounding soft tissues and the joint cavity). The numbers of MSU deposits were recorded; one separated MSU deposit or multiple deposits with a continuous border on the DECT was regarded as one, or else they were defined as two or more. Representative cases are shown in *Figure 2*.

### *Statistical analysis*

All statistical data were analyzed using SPSS V.23 (SPSS,

 

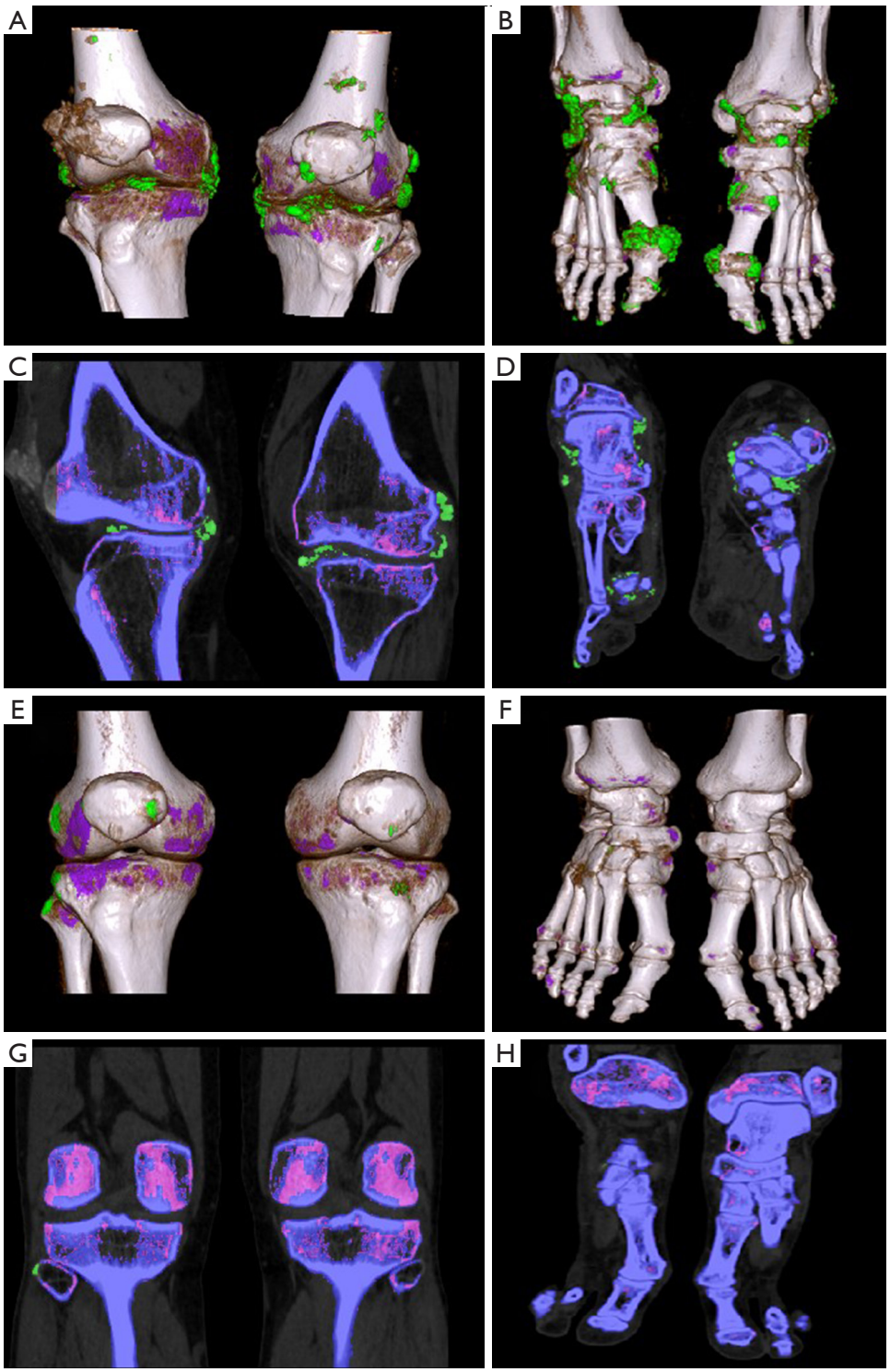


**Figure 2** Dual-energy CT image examples. (A) Gout patient, urate volume of the knees is 17.59 $cm^3$. (B) Gout patient, urate volume of the feet/ankles is 29.39 $cm^3$. (C,D) The MPR figures of the corresponding locations of panels A and B. (E) Hyperuricemia patient, urate volume of the knees is 1.75 $cm^3$. (F) Hyperuricemia patient, urate volume of the feet/ankles is 0.42 $cm^3$. (G,H) MPR figures of the corresponding locations of panels (E) and (F). (A-D) are from the same gout patient, while (E-H) are from the same hyperuricemia patient. Green indicates urate; blue indicates cortical bone; purple indicates trabecular bone. CT, computed tomography; MPR, multiplanar reconstruction.

 

**Table 1** Clinical features of the participants in this study

| Characteristic | Asymptomatic hyperuricemia (n=121) | Symptomatic gout (n=521) | P value |
|---|---|---|---|
| Age (years) | 38±16 | 47±16 | <0.001 |
| Sex (male) | 108 [89] | 497 [95] | 0.02 |
| Chronic kidney disease | 5 [4] | 89 [17] | 0.48 |
| Ischemic heart disease | 1 [0.8] | 9 [2] | 0.40 |
| Heart failure | 0 [0] | 3 [0.6] | 0.70 |
| Diuretic use | 1 [0.8] | 6 [1.2] | 0.17 |
| ULT* | 38 [31] | 216 [41] | 0.28 |
| Duration of ULT (months) | 0.5±4.8 | 1.0±4.0 | 0.32 |
| Serum urate (μmol/L) | 499.5±123.8 | 515.6±143.8 | 0.25 |
| Serum creatinine (μmol/L) | 83±36 | 88±45 | 0.005 |

Unless specified, data are presented as the mean ± SD if normally distributed. Categorical variables were expressed as numbers [frequencies or percentages]. *, includes allopurinol and probenecid. ULT, urate-lowering therapy; SD, standard deviation.

Chicago, IL, USA) software. The Kolmogorov-Smirnov test was used to assess the normality of quantitative data. Continuous variables that conformed to the normal distribution were expressed as the mean ± standard deviation (SD), and continuous variables that did not conform to the normal distribution were expressed as the median P50 (P25, P75). The unpaired *t*-test for normal continuous variables or Mann-Whitney U test for skewed continuous variables were used for comparisons between 2 groups. Categorical variables were expressed as frequencies or percentages with differences analyzed using the chi-squared test or Fisher's exact test, as appropriate. For normally distributed data, independent sample *t*-tests were used for comparisons between two groups. The independent samples nonparametric test was used to analyze nonnormally distributed data. Reliability was assessed using agreement statistics to obtain intraclass correlation coefficients (ICCs). With regard to the calculation of the consistency analysis between readers, the study used kappa values to calculate the consistency of the sites, using the correlation coefficient within the group (ICC) to calculate the consistency of numbers and volumes. The 95% confidence intervals are presented. All tests were two tailed, and P<0.05 was considered statistically significant.

In these enrolled patients, the data were analyzed to exclude extreme abnormal statistics. Finally, the elbow part (n=19) was excluded due to extreme anomaly statistics and was not included in subsequent analyses. The missing data, such as the body mass index (BMI) value of asymptomatic hyperuricemia patients in *Table 1*, did not affect the results or conclusions of the study. Since they did not affect the results, the data column has been removed from *Table 1*. The flowchart of this study is provided in *Figure 1*.

## Results

### *Patient characteristics*

A total of 121 patients (males: 89%; mean age: 38±16 years) with hyperuricemia and 521 patients (males: 95%; mean age: 47±16 years) with gout were included in this study. Detailed clinical features of the participants can be seen in *Table 1*.

### *DECT urate deposition analysis*

#### Interreader agreement

The level of agreement between the two observers in measuring the sites of MSU deposition with DECT was moderate (k=0.63). The level of agreement between the two observers in measuring the volume and number of MSU deposits with DECT was high. The ICCs were 0.945 (in volume) and 0.996 (in quantity).

#### Comparison of MSU deposits between the gout and hyperuricemia groups

Overall, the volume [0.14 (0.04–1.36), P=0.003] and number [10.00 (5.00–19.00), P=0.01] of MSU deposits in

 

**Table 2** Volume and number of MSU deposition in the asymptomatic hyperuricemia and symptomatic gout patient groups

| Location | Asymptomatic HUA (n=121) | Symptomatic gout (n=521) | P value |
|---|---|---|---|
| DECT MSU volume, $cm^3$ | | | |
| Average value | 0.08 (0.02–0.47) | 0.14 (0.04–1.36) | 0.003 |
| Anatomical locations | | | |
| Hands/wrists (n=127) | 0.00 (0.00–0.01) | 0.01 (0.00–0.09) | 0.02 |
| Knees (n=225) | 0.03 (0.00–0.27) | 0.24 (0.01–1.79) | 0.002 |
| Kidneys (n=159) | 0.00 (0.00–0.00) | 0.00 (0.00–0.00) | 0.22 |
| Feet/ankles (n=597) | 0.07 (0.02–0.19) | 0.10 (0.04–0.66) | 0.003 |
| DECT MSU number, n | | | |
| Average value | 9.50 (2.00–16.00) | 10.00 (5.00–19.00) | 0.01 |
| Anatomical locations | | | |
| Hands/wrists (n=127) | 0.00 (0.00–0.25) | 1.00 (0.00–7.00) | 0.06 |
| Knees (n=225) | 4.00 (0.00–9.00) | 6.00 (2.00–12.00) | 0.04 |
| Kidneys (n=159) | 0.00 (0.00–0.00) | 0.00 (0.00–0.00) | 0.22 |
| Feet/ankles (n=597) | 8.00 (2.25–12.00) | 9.00 (5.00–15.00) | 0.04 |

Data are shown as the median (interquartile range). The elbow part (n=19) was excluded due to extreme outliers and was not included in subsequent analyses. MSU, monosodium urate; HUA, hyperuricemia; DECT, dual-energy computed tomography.

the gout group were significantly higher than the volume [0.08 (0.02–0.47), P=0.003] and number [9.50 (2.00–16.00), P=0.02] in the hyperuricemia group (*Table 2*).

The burden of MSU deposition in the knees and feet was significantly higher in the gout group than in the hyperuricemia group. The volume [0.24 (0.01–1.79), P=0.002] and quantity [6.00 (2.00–12.00), P=0.04] of knee MSU deposition in the gout group were significantly higher than those in the hyperuricemia group [0.03 (0.00–0.27), P=0.002] and the quantity [4.00 (0.00–9.00), P=0.04]. The volume of foot MSU deposition was 0.10 (0.04–0.66) in the gout group and 0.07 (0.02–0.19) in the hyperuricemia group, P=0.003, and the number of foot MSU was 9.00 (5.00–15.00) in the gout group and 8.00 (2.25–12.00) in the hyperuricemia group, P=0.04 (*Table 2*). In the hands/wrists, the volume of MSU deposition was significantly higher in the gout group than in the hyperuricemia group (P=0.02), but there was no significant difference in the amount of MSU deposition between the two groups (P=0.06). The volume and number of MSU deposits in the kidneys between the gout and hyperuricemia groups were not statistically significant (P=0.22) (*Table 2*).

### Distribution of MSU deposition in soft tissue and joint cavity

There was no significant difference in the amount of MSU deposition in soft tissues and joint cavities among the gout groups (hands, knees, and feet) (all P>0.05) (*Table 3*). In the hyperuricemia group, the burden of volume of MSU deposition was significantly higher in the soft tissues than in the joint cavity of the knees (P=0.02, P=0.007) and ankles (P=0.02, P=0.01) (*Table 3*).

## Discussion

Our study explored the burden and distribution of MSU deposition in symptomatic gout and asymptomatic hyperuricemia with DECT. We observed the following important results: (I) the overall burden of MSU deposition in the gout group was significantly higher than that in the hyperuricemia group. (II) The burden of MSU deposition in the knees and feet was significantly higher in the gout group than in the hyperuricemia group. (III) In the hyperuricemia group, the volume burden of MSU deposition was significantly higher in the soft tissues than in

 

**Table 3** The distribution and burden of volume (units: $cm^3$) of MSU deposition in the symptomatic gout group and the asymptomatic hyperuricemia group

| Location | Soft tissue (n=1,885) | Joint cavity (n=1,885) | P value |
|---|---|---|---|
| Gout group | | | |
| Hands/wrists (n=113) | | | |
| Left | 0.216±1.308 | 0.110±0.757 | 0.33 |
| Right | 0.148±0.726 | 0.021±0.122 | 0.14 |
| Knees (n=183) | | | |
| Left | 0.367±1.368 | 0.275±2.045 | 0.82 |
| Right | 0.434±1.464 | 0.349±1.987 | 0.49 |
| Feet/ankles (n=484) | | | |
| Left | 0.294±1.478 | 0.185±1.280 | 0.38 |
| Right | 0.260±1.303 | 0.271±1.996 | 0.95 |
| HUA group | | | |
| Hands/wrists (n=14) | | | |
| Left | 0.012±0.045 | 0.000±0.000 | 0.55 |
| Right | 0.019±0.048 | 0.000±0.000 | 0.13 |
| Knees (n=41) | | | |
| Left | 0.022±0.042 | 0.001±0.005 | 0.02 |
| Right | 0.022±0.045 | 0.000±0.000 | 0.007 |
| Feet/ankles (n=112) | | | |
| Left | 0.062±0.305 | 0.027±0.234 | 0.02 |
| Right | 0.088±0.535 | 0.015±0.149 | 0.01 |

Unless specified, data are presented as the mean ± SD if normally distributed. The elbow part was excluded due to extreme outliers and was not included in subsequent analyses. MSU, monosodium urate; HUA, hyperuricemia; SD, standard deviation.

the joint cavity of the knees and ankles.

Gout is the most common inflammatory arthritis and is increasing in prevalence and incidence in many countries worldwide (27,28). Burden quantification and treatment monitoring are key in the effective care of patients with gout (29). DECT is the most sensitive and specific imaging modality for diagnosis, burden quantification, and treatment monitoring in patients with gout (29). Previous research (12) has compared the frequency and volume of DECT urate deposits between asymptomatic hyperuricemia and symptomatic gout, and the results are consistent with our study: although subclinical urate deposits can occur in asymptomatic hyperuricemia, these deposits are more frequent and larger in symptomatic gout patients. However, to date, no studies have further explored the distribution of MSU crystal deposits in these two groups of patients. Our study compared the distribution and burden of urate deposition on DECT in asymptomatic hyperuricemia and symptomatic gout. Our findings show that patients with diagnosed symptomatic gout have a higher MSU deposition burden than asymptomatic HUA patients, especially in the foot/ankle and knee, suggesting an association between MSU burden and disease activity, which is also consistent with recent studies (2,30) that the total amount of crystal deposition was positively correlated with gout attack. This also reminds us that DECT can be used to better monitor and manage patients with hyperuricemia in our clinical work. We should pay more attention to the burden of MSU deposition in asymptomatic hyperuricemia patients, which may be helpful in predicting disease activity. Is there a quantified threshold at which the burden of MSU deposits reaches a certain threshold that causes clinically

 

asymptomatic hyperuricemia to develop into symptomatic gout? Is the distribution of MSU deposition also an influencing factor (the critical value of qualitative change required by the burden of different sites is different)? What are the underlying reasons for this distribution? This study is a preliminary study, and further research is needed.

Based on our large sample size, MSU deposition in the feet and knees of patients with symptomatic gout is more frequent than that in patients with hyperuricemia (12). This implies that the distribution of MSU deposits in the knees and feet is more discriminative for patients with hyperuricemia and those with gout. Perhaps the deposition in these areas is more clinically indicative. Therefore, clinicians should pay more attention to the follow-up and observation of the knees and feet of patients. Gout presents as intermittent episodes of severely painful arthritis (gout flares) caused by the innate immune response to deposited MSU crystals (6). The central strategy for effective management of gout is long-term urate-lowering therapy to reverse hyperuricemia, which leads to the dissolution of MSU crystals and long-term prevention of gout flares (6). While the use of DECT for the diagnosis of clinically evident tophaceous gout is usually not necessary, it provides value in the quantification of disease burden and evaluation of treatment response (29). The current clinical literature also suggests DECT as a clinical outcome for gout management (30). On the one hand, with DECT, individualized treatment plans could be developed based on the patient's unique urate burden, so more effective management and monitoring of gout patients can be achieved by measuring the burden of MSU deposits in the patient's feet/knees. On the other hand, for asymptomatic hyperuricemia patients with MSU deposits, measuring the burden of MSU deposits in the feet/knees by DECT can accurately prevent, diagnose, and treat potential gout in time.

In the hyperuricemia group, the MSU deposits in the soft tissue of the knee and foot/ankle were both significantly higher than those in the joint cavity. This means that in practice, it will be more clinically meaningful to observe the soft tissue changes and structural functions of these key locations (knees, feet, and ankles) in patients with hyperuricemia. Research on soft tissue changes in these areas should also be more in depth, which is not only conducive to refined clinical management but may also reveal the deeper mechanisms and reasons behind the progression of hyperuricemia to gout.

The results of this study indicate that there may be a correlation between the burden of MSU deposition and disease activity and that gout patients have a higher burden of deposition in the feet and knees than hyperuricemia patients. This suggests that the MSU deposition burden in the feet and knees may be more closely related to the disease activity, thus narrowing the scope of clinical detection (the detection of multiple parts of the body to a specific site: the foot/knee). This is also consistent with previous studies (6,31) showing that the lower extremities (feet, ankles, and knees) are preferentially affected during gout attacks, with the first metatarsophalangeal joint being characteristic of involvement.

In conclusion, this study has the following clinical value. First, monitoring and warning of gout in asymptomatic hyperuricemia patients in time: MSU deposition burden in specific sites (feet/knees) in asymptomatic hyperuricemia patients can help to better warn of the occurrence of gout. Second, better management of gout patients is needed. This study provides a more accurate measurement site (foot/knee) for the evaluation of the therapeutic effect of gout patients by using DECT, which not only reduces the radiation dose of patients (avoiding the measurement of multiple parts of the body) but also reduces the economic burden of patients, with better clinical and economic effects. Last, but not least, it is well known that gout patients typically have attacks in the first metatarsophalangeal joint of the foot, but for those patients who have had foot surgery, metal artifacts are too heavy, and image quality is poor, making it difficult to obtain a good imaging diagnosis. For these patients, this study found that MSU deposition in the knees and feet had the same obvious detection results, and clinicians could perform DECT measurement of the knees for patients after foot surgery instead, which could achieve the same clinical effect and better image quality.

To the best of our knowledge, this is the largest sample study to estimate the burden of MSU deposition distribution using DECT. However, we must acknowledge that our study has several limitations. The main limitation of this study is a selection bias of anatomical regions and patients. The purpose of this study was to explore the systemic distribution of MSU deposition in patients with gout and hyperuricemia. However, we did not systematically investigate all parts of the body but selected several representative sites. In our institution, a four-limb and kidney DECT protocol was performed in patients with gout and hyperuricemia. First, systemic investigation involves too much radiation for the patient, which may not meet the standards of institutional ethical review. In

 

addition, the economic and social burden of doing so is heavier. Moreover, this study was a retrospective study, and the included consecutive patients may not have had systematic general examinations. Therefore, the inclusion criteria for this study were adjusted to consecutive patients who underwent DECT examination of multiple sites (at least two sites of the whole body). However, the lack of systematic investigation may lead to selection bias, which may affect the reproducibility and credibility of the data. DECT software has a mechanism to avoid false-positive detection of beam hardening by excluding MSU pixels within a certain distance to the cortical bone. Given the known artifacts and flaws of DECT technology, we doubt that cortical MSU deposition can be reliably measured. Therefore, we ignored the deposition of the cortex when subdividing the site, which can lead to the data we present being incomplete. In addition, not all regions were imaged in all patients. This fact must be considered for the analysis, especially when comparing the tophus volume of different anatomical regions. Furthermore, selection bias may be present in our study because our study enrolled patients from a single hospital.

In addition, our study is retrospective; thus, many variables were missing. Moreover, the accuracy of DECT differs for different anatomical locations, and the sample size of some anatomical locations is small. Thus, it is important to collect more anatomical locations to observe MSU distribution. For the first time, we divided a single joint with bone erosion into different parts (soft tissue and joint cavity), but whether DECT can fully and accurately distinguish the distribution of MSU in different components lacks corresponding clinical application, and further data support and verification are needed.

## Conclusions

In conclusion, this cross-sectional retrospective study showed the systemic distribution and burden of urate deposition in symptomatic gout and asymptomatic hyperuricemia with the DECT technique. Although subclinical urate deposition can occur in patients with asymptomatic hyperuricemia, the burden of urate deposition is heavier in patients with symptomatic gout, and the distribution is more pronounced in the foot/knee. Thus, more effective patient management and monitoring can be achieved by measuring the burden of MSU deposits in the patient's feet/knees. These data suggest that a threshold for urate crystal volume at typical sites may be required before symptomatic disease develops. These findings encourage the study of MSU deposition in specific sites (knee, foot, and ankle) reaching a certain threshold, which may have clinical implications for the progression of hyperuricemia to gout, revealing the mechanism by which asymptomatic hyperuricemia develops into symptomatic gout to prevent, diagnose and treat gout in a more targeted and timely manner.

## Acknowledgments

*Funding:* This study was supported by The National Key Research and Development Program of China (No. 2022YFC2010004 to LJZ).

## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-22-1208/rc

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-22-1208/coif). LJZ reports receiving grant from The National Key Research and Development Program of China (No. 2022YFC2010004 to LJZ). The other authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the institutional ethics board of Jinling Hospital, Medical School of Nanjing University. Written informed consent was waived for this retrospective analysis.



 

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**Cite this article as:** Zhang XY, Tang CX, Zhou F, Lin PH, Yin CQ, Gao QY, Zhou LL, Zhou CS, Lu GM, Zhang LJ. Burden and distribution of monosodium urate deposition in patients with hyperuricemia and gout: a cross-sectional Chinese population-based dual-energy CT study. Quant Imaging Med Surg 2023;13(7):4380-4391. doi: 10.21037/qims-22-1208

 