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# What is the diagnostic value of dual-energy computed tomography in patients with clinical diagnosis of gout?

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## Abstract

**Objectives:** To investigate the frequency of monosodium urate (MSU) crystal deposits on dual-energy computed tomography (DECT) in patients with clinical diagnosis of gout and the factors associated MSU crystal positivity.

**Methods:** This study was conducted in patients with clinical diagnosis of gout who underwent DECT. Clinical features were compared between patients with positive and those with negative DECT results. A logistic regression analysis was performed to determine the factors associated with MSU crystal positivity on DECT.

**Results:** A total of 148 patients with clinical diagnosis of gout were included, and MSU crystal deposition on DECT was observed in 64 patients (43.3%). The patients with positive DECT results were more likely to have renal insufficiency, longer disease duration, and higher serum urate level than those with negative. In the multivariable analysis, first gout attack (odds ratio 0.462; 95% confidence interval 0.229–0.931,  $p = 0.031$ ) was associated with a less likely MSU crystal deposit-positive DECT result. In the subgroup analysis of patients with first attack, serum urate level > 8 mg/dL was associated with DECT positivity.

**Conclusion:** Of the patients with clinical diagnosis of gout, those with renal insufficiency, longer disease duration, and high serum urate level were more likely to be positive of gout on DECT. First gout attack was associated with less likely to be positive for MSU crystal on DECT. Thus, performing DECT scan in the selected patients who had characteristics that highly probability of DECT positivity could increase positive predictive value.

**Keywords:** Monosodium urate, Gout, Dual-energy computed tomography, Diagnostic imaging

## Introduction

Gout is caused by the deposition of monosodium urate (MSU) crystals in the joints, cartilage, and soft tissues. It is the most common inflammatory arthritis in the West, and its prevalence is constantly increasing in Korea [1]. An important test in diagnosing gout is to check for MSU crystals under polarizing microscopy through joint fluid aspiration in the affected joint [2]. However, in the case of the first metatarsal joint, puncture is not easy thus it may be difficult to confirm the presence of MSU crystals under polarizing microscopy. Furthermore, an

experienced inspector is required to detect MSU crystals under polarizing microscopy [3].

When the presence of MSU crystal deposits cannot be confirmed by synovial fluid examination, imaging could be used as a diagnostic tool in patients with suspected gout. Plain radiographs showed punched-out erosions with overhanging or sclerotic margins and tophi as ill-defined mass lesions in chronic gout [4]. However, findings from plain radiographs are often normal, and the sensitivity of plain radiography for gout diagnosis is only 30% [5]. Recently, the use of ultrasonography in the diagnosis of gout has been increasing. The presence of MSU crystal deposits is suggested by the double-contour sign, tophus, and snowstorm appearance [6]. In addition, cortical bone erosion characterized by punched-out

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lesions can be detected on ultrasonography [7]. However, ultrasonography highly depends on operator experience and patient factors, including obesity or the involved joint. Conventional computed tomography and magnetic resonance imaging can demonstrate erosion or tophi in gout, but these findings are not specific to gout [8].

Dual-energy computed tomography (DECT), which has been widely used in recent years, is a computerized tomography test that does not use a contrast agent. It is a noninvasive test that can identify soft tissues and MSU crystals using tissue-specific image attenuation. Its known sensitivity and specificity are 78–89% and 93–100%, respectively [9–11]. Patients with short disease duration, with first gout attack, and taking uric acid-lowering drugs are known to most likely have false-negative test results for gout. In addition, in gout patients without tophi, the sensitivity of DECT is lower than in patients with tophi [12–15]. Thus, a negative result is difficult to interpret in patients with suspected gout.

Research is limited on whether clinical manifestations differ between positive and negative MSU crystals on DECT in patients with clinical diagnosis of gout, and on factors associated with the positive DECT results. Therefore, in this study, we aimed to examine the clinical characteristics of patients with positive MSU crystals on DECT in comparison with patients with negative MSU crystals and the factors associated with DECT positivity.

## Materials and methods

### Study population

In this retrospective cohort study, we reviewed the electronic medical records of patients who underwent DECT because of episode of inflammatory arthritis or tendinitis possibly caused by gout but could not undergo synovial fluid aspiration at Seoul Veterans Hospital, Seoul, South Korea, between January 2013 and March 2020. Clinical diagnosis of gout was on the basis of the 1977 or 2015 gout classification criteria [16, 17]. First, in accordance with the 2015 ACR/EULAR classification criteria, patients with a score of  $\geq 8$  excluding DECT results were included as clinical diagnosis of gout cases. Among the patients with scores  $< 8$ , those who met at least 6 or more of the 12 items of the 1977 ACR criteria were classified as having clinical diagnosis of gout. Patients taking urate-lowering agents (including allopurinol, febuxostat, or benzbromarone) were excluded from the analysis. From the medical records, the following data were collected: (1) demographic information, including age and sex; (2) data on accompanying medical conditions such as hypertension, diabetes mellitus, renal insufficiency (defined as an estimated glomerular filtration rate of  $< 60$  mL/min/1.73 m<sup>2</sup> obtained using the Chronic Kidney Disease Epidemiology Collaboration equation), cardiovascular disease, and alcohol intake; (3) affected joint,

number of attacks, and disease duration; and (4) laboratory data, including serum urate levels and glomerular filtration rate.

This study was approved by the institutional review board of the Seoul Veterans Hospital, Seoul, Korea (IRB No. BOHUN 2020–07–012-001). The requirement for informed consent was waived owing to the retrospective nature of the study.

### DECT imaging scans

All of the patients underwent DECT of the painful joint under the clinical suspicion of gout attack. A dual-source DECT scanner (Somatom Definition Flash, Siemens Healthcare) with 80/Sn140 kV and 250 mAs for one tube and the other automatically adjusted to maintain a 2:1 ratio. All the datasets were reconstructed using a bone algorithm to 0.75-mm slices with a 0.5-mm increment. Post-processing was performed using a commercial software program (“gout,” Syngo CT Workplace, Siemens Medical System). The MSU crystals were shown in green (Fig. 1a and b).

Erosion was defined as cortical disruption in any two planes (Fig. 1c and d). A musculoskeletal radiologist evaluated the DECT images and recorded the locations of the urate depositions.

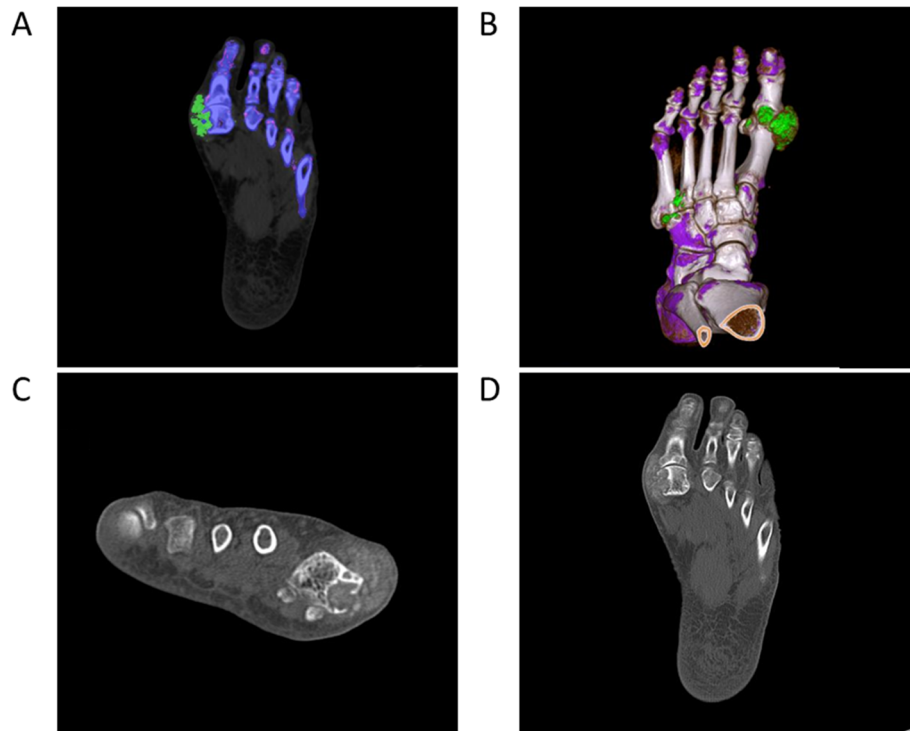
### Statistical analyses

The chi-square and Fisher exact tests were used for comparisons of categorical data between the 2 groups according to DECT results. Continuous values were expressed median (interquartile range) using the Mann-Whitney *U* test for comparing 2 groups of patients according to DECT results. A logistic regression analysis with a backward elimination procedure was performed to identify the factors associated with DECT positivity. Variables with *P* values  $< 0.2$  in the univariate analysis were selected for the multivariable analysis. The SPSS 20.0 software (SPSS Inc., Chicago, IL, USA) was used for all the statistical analyses.

## Results

### Comparison of the MSU crystal deposit-positive and MSU crystal deposit-negative DECT groups

A total of 148 patients with clinical diagnosis of gout who underwent DECT were included. Among 148 included patients, 132 met the 2015 ACR/EULAR classification criteria excluding DECT results and 16 met the 1977 ACR criteria. Sixty-four patients had a first gout attack. Table 1 shows the baseline clinical characteristics and laboratory data of the included patients. Among the 148 patients, 64 had positive and 84 had negative DECT results for MSU crystal deposits. The mean age and sex distribution were similar between the 2 groups. No significant difference in the presence of comorbidities,



**Fig. 1** Dual-energy computed tomography (DECT) images. A) Color mapping showing uric acid deposits (green) in the periarticular tissues of the first MTP joint. B) Three-dimensional DECT image with color mapping showing tophi (green) in the first MTP joint. C, D) Two-dimensional CT image showing high-attenuation tophi associated with erosions in the first MTP joint

including hypertension, diabetes mellitus, and cardiovascular disease, were found between the 2 groups. However, the patients with MSU crystal deposit-positive DECT results were more likely to have renal insufficiency (29/64, 45.3% vs. 20/84, 23.8%;  $P = 0.006$ ) and longer gout disease durations (38.5 months [3.3–120 months] vs. 5 months [1.3–33.3 months];  $P < 0.001$ ). Furthermore, among the patients with the MSU crystal deposit-positive DECT results, the proportion of those who had a first attack was lower (21/64, 32.8% vs. 43/84, 51.2%;  $P = 0.025$ ) than that among the patients with MSU crystal deposit-negative DECT results. The serum urate level was higher in the patients with positive than in those with negative DECT results for MSU crystal deposits. Among 16 patients who did not meet the 2015 gout classification criteria, 5 showed positive DECT result and met the 2015 ACR/EULAR classification criteria. Of 64 patients with positive DECT results, 60 started receiving urate-lowering agents after undergoing DECT.

#### Factors associated with DECT positivity

Table 2 shows the factors associated with DECT positivity. In the univariate analysis, age (odds ratio [OR] 1.043, 95% confidence interval [CI] 1.008–1.078,  $p = 0.016$ ), renal insufficiency (OR 2.651, 95% CI 1.313–5.356,  $p =$

0.007), first gout attack (OR 0.446, 95% CI 0.237–0.914,  $p = 0.026$ ), and serum urate level  $> 8$  mg/dL were significantly associated with DECT positivity. In the multivariable analysis, first attack (OR 0.462, 95% CI 0.229–0.931,  $p = 0.031$ ) was associated with DECT positivity.

#### Comparison of the MSU crystal deposit-positive and MSU crystal deposit-negative DECT groups in first attack

Next, we focused the patients with first episode of inflammatory arthritis or tendinitis. Among the 64 patients with a first gout attack, 21 showed DECT-positive results for MSU crystal deposits (Table 3). Similarly to the total group, the frequencies of renal insufficiency and serum urate level were higher in the patients with positive than in those with negative DECT results for MSU crystal deposits. Erosion on DECT was detected in 38.1% (8/21) of the patients with positive and in 2.3% (1/43) of the patients with negative DECT results for MSU crystal deposits ( $P < 0.001$ ).

#### Factors associated with DECT positivity in the first gout attack

Table 4 shows the factors associated with DECT positivity in the first attack group. In the univariate analysis, serum urate level  $> 8$  mg/dL was significantly associated with DECT positivity (OR 3.472, 95% CI 1.128–10.685,

**Table 1** Baseline characteristics of the patients with clinical diagnosis of gout

Variable	DECT (+) (n = 64)	DECT (-) (n = 84)	p
Age (years)	71 (68.3–74)	71 (62.3–74)	0.122
Male sex	63 (98.4)	80 (95.2)	0.390
Comorbidity			
Hypertension	43 (67.2)	47 (56.0)	0.165
Diabetes mellitus	12 (18.8)	19 (22.6)	0.567
Renal insufficiency	29 (45.3)	20 (23.8)	0.006
Cardiovascular disease	15 (23.4)	18 (21.4)	0.771
Alcohol intake	4 (6.2)	11 (13.1)	0.172
Disease duration (months)	38.5 (3.3–120)	5 (1.3–33.3)	< 0.001
Frequency of attack			
First attack	21 (32.8)	43 (51.2)	0.025
Three or more attacks/year	11 (17.2)	11 (13.1)	0.488
Symptomatic joints			
First MTP	44 (68.8)	54 (64.3)	0.569
Midfoot	11 (17.2)	18 (21.4)	0.520
Ankle	8 (9.8)	8 (10.8)	0.828
Knee	1 (1.6)	3 (3.6)	0.634
Hand	0 (0)	5 (6.0)	0.070
Uric acid (mg/dL)	8.7 (7.7–9.5)	8.1 (6.8–9.1)	0.013
GFR (ml/min/1.73m <sup>2</sup> )	58 (49–68.8)	67 (55–85.8)	0.005

Values are presented as number (%), or median (interquartile range)  
 DECT dual-energy computed tomography, MTP metatarsophalangeal, GFR  
 Glomerular Filtration Rate

$p = 0.030$ ). In addition, age and renal insufficiency showed a tendency of association with DECT positivity. In the multivariable analysis, serum urate level > 8 mg/dL (OR 3.180, 95% CI 1.004–10.076,  $p = 0.049$ ) were associated with DECT positivity.

## Discussion

In the present study, MSU crystals were detected in 43.2% of the patients with clinical diagnosis of gout by DECT. The characteristics of the patients with MSU crystal deposit-positive DECT results showed higher frequency of renal insufficiency, longer disease duration, and higher serum urate level than those with MSU crystal deposit-negative DECT results. First gout attack was associated with a less likely MSU crystal deposit-positive DECT result.

According to the European League Against Rheumatism guideline, an effort to confirm the diagnosis of gout on the basis of the presence of MSU crystals is required [18]. However, there is a limitation in performing joint fluid aspiration in small joints, including the first metatarsophalangeal joint. Clinical diagnosis of gout without joint aspiration could be uncertain, and the effort to search for MSU crystal deposition using imaging continues to be necessary. DECT scan is a noninvasive test to confirm the presence of MSU crystals. The known specificity of DECT is 93–95% [19, 20]; thus, positive DECT results can be used in gout diagnosis. Furthermore, three-dimensional DECT color imaging of the MSU crystal could improve adherence to treatment with urate-lowering agents [21, 22]. However, the sensitivity is relatively low [15, 23], and the possibility of false-negative results should be considered. In a previous study, DECT showed high sensitivity in gout patients with tophi but low sensitivity in those without

**Table 2** Factors associated with dual-energy computed tomography positivity

	Univariate			Multivariable		
	OR	CI	P	OR	CI	P
Age	1.043	1.008–1.078	0.016	1.030	0.994–1.069	0.106
Male sex	3.150	0.343–28.888	0.310			
Hypertension	1.612	0.819–3.171	0.167			
Diabetes mellitus	0.789	0.4351–1.774	0.567			
Renal insufficiency	2.651	1.313–5.356	0.007	2.110	0.994–1.069	0.055
Cardiovascular disease	1.122	0.515–2.445	0.771			
Disease duration	1.004	1.000–1.008	0.049			
Alcohol intake	0.442	0.1134–1.460	0.181			
First MTP joint involvement	1.222	0.612–2.441	0.570			
First attack	0.446	0.237–0.914	0.026	0.462	0.229–0.931	0.031
Three or more attacks/year	1.377	0.556–3.413	0.489			
Uric acid > 8 mg/dL	1.776	0.892–3.537	0.028			

OR odds ratio, CI Confidence interval, MTP metatarsophalangeal

**Table 3** Baseline characteristics of the patients with clinical diagnosis of gout (first attack)

Variable	DECT (-) (n = 43)	DECT (+) (n = 21)	p
Age (years)	71 (59–74)	72 (68.5–80.5)	0.149
Male sex	41 (95.3)	21 (100)	1.000
Comorbidity			
Hypertension	23 (53.5)	15 (71.4)	0.170
Diabetes mellitus	9 (20.9)	6 (28.6)	0.540
Renal insufficiency	10 (23.3)	10 (47.6)	0.048
Cardiovascular disease	10 (23.3)	4 (19.0)	1.000
Alcohol intake	6 (14.0)	2 (9.5)	1.000
Disease duration	2 (2–4)	2 (2–4.5)	0.457
First MTP	29 (67.4)	13 (61.9)	0.661
Uric acid	7.6 (6.4–8.5)	8.6 (7.4–9.5)	0.045
GFR	72 (33–86)	60 (49–74)	0.078
Erosion	1 (2.3)	8 (38.1)	< 0.001

Values are presented as number (%), or median (interquartile range)  
 DECT dual-energy computed tomography, MTP metatarsophalangeal, GFR Glomerular Filtration Rate

tophi [15]. In addition, another study reported various sensitivity rates (35.71–92.86%) according to the first attack and early- and late-stage gout [14]. This indicates that the crystal size affects the sensitivity of DECT. In the present study, the proportion of positive MSU crystal deposition on DECT was 43.2%, which is a relatively low value. As > 40% of the patients we included were having their first gout attack, the crystal size might not be large enough to be detected on DECT. On the other hand, although we included patients with clinical diagnosis of gout, some of them might not have true gout. Thus, interpreting whether negative DECT results indicate a false negative or no gout is difficult, and the diagnostic role of DECT is limited. Thus, performing DECT seems useful in patients with a high probability of positive DECT results.

In the present study, the frequencies of renal insufficiency and serum urate level were higher in the patients with MSU crystal-positive than in those with MSU crystal-negative DECT results. The association of renal insufficiency and gout is well known. Among the patients with gout, approximately 20% had a chronic kidney disease (CKD) [24], and gout is associated with a higher risk of CKD [25]. Furthermore, recently, urate-lowering therapy has been found to be beneficial to renal function [26]. As two-thirds of urate is excreted by the kidney [27], patients with renal insufficiency might have a higher possibility of having a MSU crystal deposit in the affected joint.

A previous study reported that DECT positivity is associated with gout attack frequency [13]. In addition, short-term gout, especially the first attack, showed 35.7% sensitivity [14]. In the present study, the patients having their first attack showed 32.8% positive rate, and first attack was associated with a less likely MSU crystal-positive DECT result. Previous studies have reported that patients with asymptomatic hyperuricemia also showed 15–24% positive rate of DECT [28, 29]. Although the positive rates in patients having their first attack were slightly higher than those in asymptomatic hyperuricemia, the diagnostic role of DECT is limited in patients having their first gout attack. Thus, DECT might not be recommended in patients with a first attack. However, in the 2020 American College of Rheumatology guideline, patients with a first attack with CKD stage ≥3 or uric acid level > 9 mg/dl are recommended to start urate-lowering therapy [30]. Indeed, in the subgroup analysis, the patients with a first attack and positive DECT results showed higher frequency of renal insufficiency and higher serum urate levels than those with negative results. Thus, in the first attack, performing a DECT scan in patients with hyperuricemia or CKD could increase the positive predictive value. In addition, the frequency of erosion was 38.1% in the patients with MSU crystal

**Table 4** Factors associated with dual-energy computed tomography positivity (first attack)

	Univariate			Multivariable		
	OR	CI	p	OR	CI	p
Age	1.058	0.998–1.121	0.057	1.052	0.992–1.115	0.089
Hypertension	2.174	0.709–6.666	0.174			
Diabetes mellitus	1.511	0.456–5.009	0.500			
Renal insufficiency	3.000	0.988–9.111	0.053			
Cardiovascular disease	0.776	0.212–2.846	0.703			
Disease duration	0.997	0.950–1.047	0.905			
Alcohol intake	0.649	0.119–3.529	0.617			
First MTP joint involvement	1.222	0.612–2.441	0.570			
Uric acid > 8 mg/dL	3.472	1.128–10.685	0.030	3.180	1.004–10.076	0.049

OR odds ratio, CI Confidence interval, MTP metatarsophalangeal

deposits in the first gout attack. In a previous study, DECT demonstrated a high reproducibility for joint erosion. The erosion was positively correlated with MSU crystal volume and indicated a high disease severity that might require intensive urate-lowering therapy [31]. Thus, in selective patients with a suspicious first gout attack, including hyperuricemia or CKD, performing DECT could provide more information about erosion and MSU crystal deposition.

The present study has some limitations. The presence of MSU crystals could not be confirmed on polarizing microscopy; thus, we could not evaluate the sensitivity or specificity of DECT for the diagnosis of gout in our cohort. Furthermore, false-positive or false-negative DECT results are also possible. Second, because of the single-center retrospective design of the study, the generalizability of the study results is limited. For example, the ages of the included patients were older than the expected age for gout.

## Conclusion

The positivity rate by DECT was 43.2% in the patients with clinical diagnosis of gout and decreased more in the patients having their first gout attack. Positive DECT results were more frequently observed in patients with chronic kidney disease and hyperuricemia. When DECT demonstrates negative MSU crystal finding, diagnostic role of DECT is limited. Thus, performing DECT in selected patients with characteristics that have high probability of DECT positivity could increase the diagnostic value of DECT.

## Abbreviations

CKD: Chronic kidney disease; CI: Confidence interval; CT: Computed tomography; DECT: Dual-energy computed tomography; MSU: Monosodium urate; OR: Odds ratio

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## Authors' contributions

JSL contributed to data acquisition, data analysis and interpretation, article writing. WJS contributed to study design and article review. All authors take full responsibility for the integrity of the study and approved the final version of the manuscript.

## Authors' information

Not applicable.

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## Availability of data and materials

Not applicable.

## Declarations

### Ethics approval and consent to participate

This study was approved by the institutional review board of the Seoul Veterans Hospital, Seoul, Korea (IRB No. BOHUN 2020-07-012-001).

### Consent for publication

Not applicable.

### Competing interests

The authors declare that they have no competing interests.

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