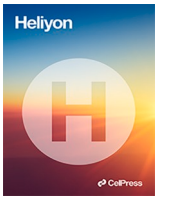
Heliyon 10 (2024) e24548

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

Detection of monosodium urate depositions and atherosclerotic plaques in the cardiovascular system by dual-energy computed tomography

Haolin Ren [a,b], Hang Qu [a], Yong Zhang [a], Yue Gu [a], Yi Zhao [a], Wenjuan Xu [a], Mingsheng Zhou [c], Wei Wang [a,*]

[a] Department of Medical Imaging, Affiliated Hospital of Yangzhou University, Yangzhou, China
[b] Graduate School of Dalian Medical University, Dalian, China
[c] Department of Physiology, Shenyang Medical College, Shenyang, China

A B S T R A C T

Aim: The study aimed to explore the relationship between urate deposition and surrounding atherosclerotic plaques, and to confirm the contribution of urate deposition to the development of coronary atherosclerosis.
Methods and results: The present study employed Dual-energy CT (DECT) material separation technology through calcium score scan to access the presence of MSU crystal deposition in coronary atherosclerotic plaques in patients with clinically suspected coronary heart diseases undergoing DECT. DECT showed that among 872 patients, 441 had plaques in coronary arteries; the incidence of plaque was 50.6 %. The patients were divided in the atherosclerotic plaque vs. non-plaque groups. There were significant differences in age, sex, blood pressure, blood glucose, serum creatinine, and history of gout and hyperuricemia between the plaque and non-plaque groups (all $P < 0.05$). Among the patients with coronary plaques, there were 348 patients (78.9 %) with simple atherosclerotic plaque (AP), 8 (1.8 %) with simple urate depositions (UD), and 85 (19.3 %) with urate depositions and atherosclerotic plaques (UDAP). The multivariable analysis showed that urate deposition was independently associated with plaques after adjustment for age, sex, blood pressure, blood glucose, serum creatinine, history of gout, and history of hyperuricemia (OR = 13.69, 95% CI: 7.53–22.95, $P = 0.035$). UPAP patients had significantly higher coronary calcium scores than AP patients [210.1 (625.2) AU vs 58.2 (182.5) AU, $P < 0.001$] Urate deposition (16.7 mm^3) positively correlated with plaque calcification (73.8 mm^3) in UPAP patients ($r = 0.325$, $P < 0.001$).
Conclusion: Patients with gout or a history of hyperuricemia were more likely to exhibit UDAP. Urate deposition was independently associated with plaques.

1. Introduction

Coronary atherosclerotic disease is the major cause of death worldwide [1–3]. Most myocardial infarctions are caused by the erosion or rupture of coronary plaques [4–6]. About 2/3 of cases of myocardial infarctions and sudden cardiac deaths result from plaque rupture [7,8]. With the development of high-performance image technologies, including invasive and noninvasive coronary angiography, coronary plaques can easily be detected. Still, we know little about the nature and features of coronary plaque, such as plaque components and architecture. Indeed, the physical and chemical characteristics of plaque are important factors determining the stability and rupture of coronary artery plaques [6,9]. Plaque instability is caused by the complex interplay among structural plaque features, local hemodynamic forces, and biological processes acting on the plaque surface. Thus, the identification of physical characteristics and chemical composition of the plaque by imaging may help physicians to predict plaques at high risk of major adverse

* Corresponding author.
E-mail address: waywang1@163.com (W. Wang).

https://doi.org/10.1016/j.heliyon.2024.e24548
Received 2 May 2023; Received in revised form 18 December 2023; Accepted 10 January 2024
Available online 17 January 2024
2405-8440/© 2024 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

cardiovascular events [5].

Gout is a risk factor for cardiovascular diseases (CAD) [10–19]. Hyperuricemia associated with gout causes a systemic inflammation that may lead to monosodium urate (MSU) deposition in various tissues and organs in the body; for example, the most common urate deposition is observed in musculoskeletal joints, leading to inflammatory arthritis [20]. Early studies revealed that MSU deposition can be detected in aortic aneurysms and coronary plaques from endarterectomy specimens [21]. Conventional imaging techniques cannot distinguish monosodium urate deposition from atherosclerotic plaque.

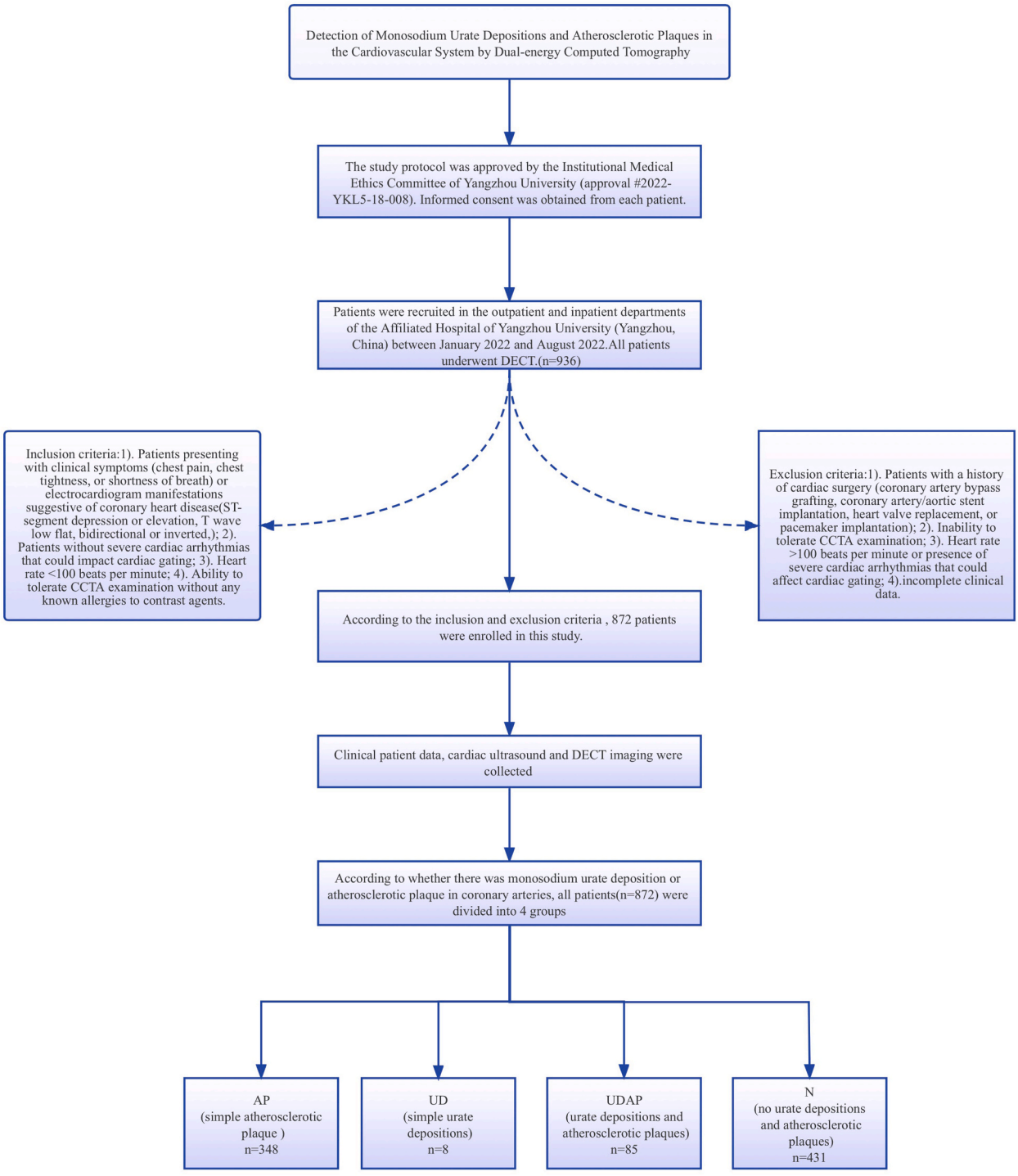


Fig. 1. Flow chart.

Dual-energy computed tomography (DECT) imaging allows the identification of the material characterization based on the principle that materials have a specific X-ray absorption spectrum of atomic elements at two different energy levels [22]. DECT can detect MSU deposition in kidney stones, which are much larger than coronary plaques and likely with higher MSU concentration. Some studies have attempted to detect urate deposition in coronary plaque using DECT without definite proof. Recently, several articles reported that DECT detects coronary MSU plaque in patients with gout or hyperuricemia [23–25]. MSU deposition is closely associated with coronary artery diseases [23], but there are few clinical studies about urate deposition plaque in coronary heart diseases [23,24].

Therefore, the present study aimed to employ Dual-energy CT (DECT) material separation technology to explore the relationship between urate deposition in coronary plaques and surrounding atherosclerotic plaques, and to confirm the contribution of urate deposition to the development of coronary atherosclerosis.

2. Methods

2.1. Participants

Patients with clinically suspected coronary heart diseases were recruited in the outpatient and inpatient departments of the Affiliated Hospital of Yangzhou University (Yangzhou, China) between January 2022 and August 2022.

2.1.1. Inclusion criteria

1). Patients presenting with clinical symptoms (chest pain, chest tightness, or shortness of breath) or electrocardiogram manifestations suggestive of coronary heart disease (ST-segment depression or elevation, T wave low flat, bidirectional or inverted); 2). Patients without severe cardiac arrhythmias that could impact cardiac gating; 3). Heart rate <100 beats per minute; 4). Ability to tolerate CCTA examination without any known allergies to contrast agents.

2.1.2. Exclusion criteria

1). Patients with a history of cardiac surgery (coronary artery bypass grafting, coronary artery/aortic stent implantation, heart valve replacement, or pacemaker implantation); 2). Inability to tolerate CCTA examination; 3). Heart rate >100 beats per minute or presence of severe cardiac arrhythmias that could affect cardiac gating; 4). incomplete clinical data.

The study protocol was approved by the Institutional Medical Ethics Committee of Yangzhou University (approval #2022-YKL5-18-008). Informed consent was obtained from each patient.

2.2. Study design

The patients underwent coronary DECT to evaluate monosodium urate deposition and atherosclerotic plaque in coronary arteries, and the patients agreed to undergo DECT and signed informed consent before the examination (Fig. 1).

The criteria for the clinical diagnosis of myocardial ischemia was defined as a typical history of angina pectoris and/or ECG signs of

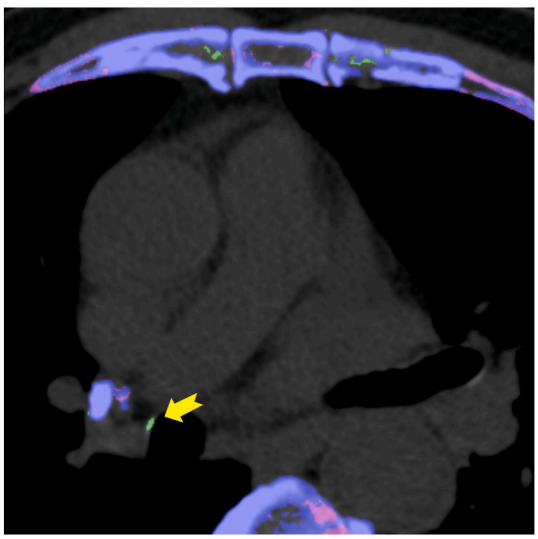


Fig. 2. Several artifacts of cardiac DECT. The green pixels were bronchial calcification.

ischemic ST-T depression. The inclusion criteria for DECT examination were patients with clinically suspected myocardial ischemia and heart rate (HR) < 100 beats/min. The lesions with a diameter of <2 mm were not classified as positive findings of MSU plaque because such a small signal may be produced by other deposits in skin or vessels during DECT examination, which is difficult to distinguish from true MSU deposits. According to the American College of Radiology/European League Against Rheumatism guidelines, nail bed deposits, submillimeter deposits, skin deposits, and deposits obscured by motion, beam hardening, vascular artifacts, artifacts on rib cartilage, and bronchial calcifications [26] were not classified as positive findings in the present study [27] (Fig. 2).

2.2.1. Endpoint

The primary endpoint of the study was the presence of atherosclerotic plaques. The secondary endpoint of the study was the coexistence of atherosclerotic plaques and urate deposition.

2.2.2. Data collection

The following clinical patient data were collected or measured in the outpatient and inpatient clinics of the hospital: sex, age, body mass index (BMI), blood pressure, history of angina pectoris, ECG sign of myocardial ischemia, history of gout, history of hyperuricemia, and fasting plasma levels of cholesterol, triglycerides, fasting blood glucose, creatinine, C-reactive protein (CRP), and neutrophils.

2.2.3. Cardiac ultrasound

Two physicians with extensive experience of 10 and 14 years in cardiac ultrasound (US) examined all patients. They used an Eagus R9ultrasonic machine (Mindray, China) with a 1.5–4 MHz probe. All US results were evaluated by two independent physicians who were blinded to clinical data. A consensus was reached regarding the images from some doubtful cases.

2.2.4. Cardiac DECT

All patients underwent DECT with two energies at 90 kV of tube A and 150 kV of tube B, with a pitch of 0.15. A non-contrast electrocardiography-gated computed tomography (CT) examination with standardized scan parameters was performed using a 256-slice dual-source CT (SOMATOM Force; Siemens) with a rotation time of 0.25 s, and prospective electrocardiography triggering for HRs <100 bpm. Axial images were reconstructed with 1.0-mm slice width, increment of 0.5, and a medium-smooth convolution kernel (Qr36). The parameters of the gout algorithm were a resolution of 5, a minimum value of 150 HU, an iodine ratio of 1.33, and an air distance of 5.

2.2.5. Detection of plaques in the cardiovascular system

According to the location of the plaque, coronary artery plaques were divided into the right coronary artery, left main artery, circumflex artery, and left anterior descending artery plaques. Calcified plaques and Agatston units (AU) were calculated in the original CT scanning images, while urate deposits were recognized in color-coded DECT images.

2.2.6. Identification of MSU deposition in the cardiovascular system

The original images from Digital Imaging and Communications in Medicine (DICOM) were imported into the Syngovia workstation. The MSU deposition was evaluated using the embedded software, where the pixels in green were defined as “MSU deposition”,

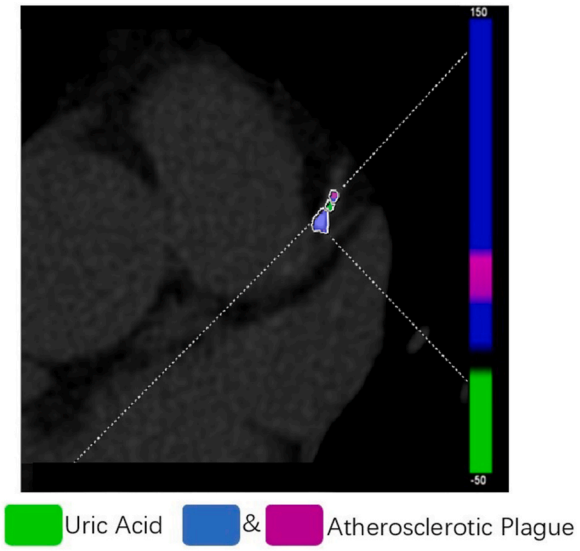


Fig. 3. Quantification of uric acid deposition and atherosclerotic plaque volume.

and the blue and purple pixels were defined as "atherosclerotic plaque" [22]. The plaque volume was calculated by multiplying sectional areas of all layers by layer thickness (1 mm). The regions of interest (ROIs) were drawn by two independent radiologists (Fig. 3). Two radiologists with rich experience of 8 and 10 years in gout imaging and cardiovascular imaging by DECT evaluated and scored the DECT images in consensus. They were blind to clinical and medical history, and the plaque volume was taken as an average value of the two reviewers' measurements.

2.3. Statistical analysis

Statistical analyses were conducted using SPSS 25.0 (IBM, Armonk, NY, USA). Categorical data were presented as n (%) and analyzed using the chi-square test. Continuous data were presented as means (standard deviation) and analyzed using Student's t-test. Univariable and multivariable regression analyses were determined to examine the factors associated with plaques. Comparison of calcium score between patients with gout and controls, as well as comparison of calcium score between DECT-positive and DECT negative patients, was performed with a 2-tailed *t*-test. Spearman rank sum was used to analyze the correlation between uric acid crystal volume and surrounding atherosclerotic plaque volume. Two-tailed P-values <0.05 were considered statistically significant.

3. Results

3.1. Characteristics of the patients

According to the inclusion criteria, 936 participants were enrolled and underwent a DECT examination of the coronary arteries. And accroding to the exclusion criteria, 64 patients were excluded and 872 patients were enrolled in this study.

Among the 872 patients, 441 patients were found to have plaques in the coronary arteries or aorta, with a plaque detection rate of 50.6 %, including 348 patients with simple atherosclerotic plaque (AP), 8 patients with simple urate deposition (UD), and 85 patients with atherosclerotic plaque and urate coexisting plaque (UDAP) (Table 1 and Fig. 4) (A1. The presence of a plague at the beginning of the left anterior descending coronary artery and the corresponding DECT shows the coexistence of urate deposition (yellow arrow) and atherosclerotic plaque (white arrow). A2. The corresponding positions of the original images are represented by arrows, respectively. B1-2. The plaque was seen in the distal right coronary artery in the transverse position, and the corresponding DECT showed the coexistence of urate deposition (yellow arrow) and atherosclerotic plaque (white arrow).). Among the 441 patients with artery plaque, 85 had MSU deposition, accounting for 19.3 % of the total number of plaques. These results suggested that MSU is more likely to deposit in atherosclerotic lesions. Furthermore, we analyzed the location of urate deposition in the coronary artery. Among the 85 patients with atherosclerotic plaque and urate deposition, we found 116 urate deposits, including 57 (49.1 %) in the left anterior descending arteries, 44 (37.9 %) in the right coronary artery, and 15 (12.9 %) in the left circumflex coronary artery (some patients had urate depositions in multiple coronary arteries).

3.2. Clinical characteristics in patients with plaques

The patients were divided in the atherosclerotic plaque vs. non-plaque groups. The clinical characteristics of the patients are presented in Table 1. There were significant differences in age, sex, blood pressure, blood glucose, serum creatinine, and history of gout and hyperuricemia between the plaque and non-plaque groups (all $P < 0.05$), while other clinical parameters showed no significant

Table 1
Characteristics of the patients.

	Plaque group (n = 441)	Non-plaque group (n = 431)	P
Age	69(14)	61(18)	0.001
Sex			0.004
Male	65.3 %	45 %	
Female	34.6 %	55 %	
Body mass index (kg/m^2)	24.50 (3.89)	24.85 (4.19)	0.578
Blood uric acid (mmol/L)	336.4 (129.3)	311.4 (116.4)	0.131
Blood pressure (mmHg)			
Systolic blood pressure	155 (40)	140 (33)	0.001
Diastolic blood pressure	90 (20)	87 (29)	0.001
Blood glucose (mmol/L)	6.33 (2.78)	5.86 (1.77)	0.033
Serum creatinine (μmol/L)	69.7 (21.9)	64.0 (28.4)	0.011
Triglyceride (mmol/L)	1.51 (1.41)	1.41 (1.07)	0.313
Total cholesterol (mmol/L)	4.10 (1.44)	4.2 5 (1.31)	0.628
C-reactive protein (mg/L)	1.35 (3.72)	1.79 (3.26)	0.337
Neutrophil ($\times 10^9$/L)	3.81 (1.83)	3.63 (1.49)	0.210
History of gout	12.2 %	8.8 %	0.002
History of hyperuricemia	28.1 %	18.3 %	0.001
Urate deposition			0.001
Yes	85	8	
No	356	423	

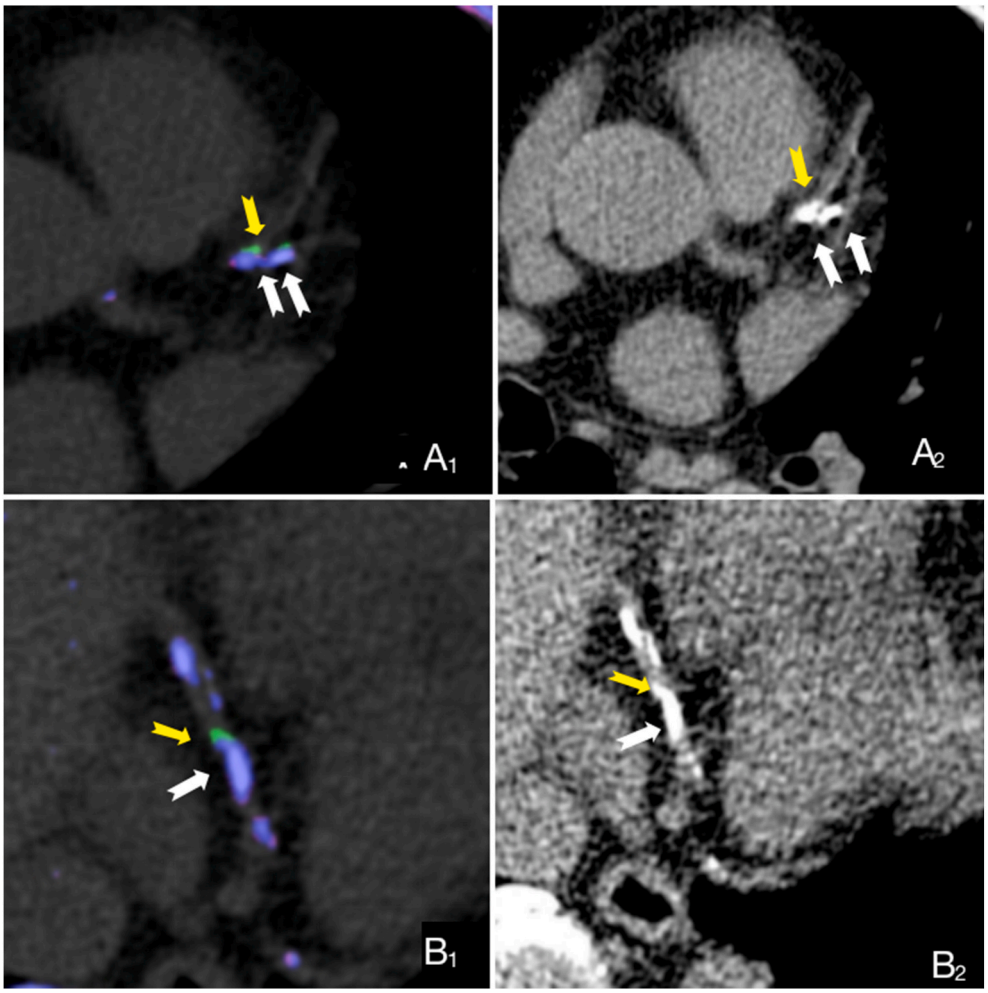


Fig. 4. Urate deposition of DECT in the cardiovascular system (the basic information of the patient is shown in Table 1). A1. The presence of a plague at the beginning of the left anterior descending coronary artery and the corresponding DECT shows the coexistence of urate deposition (yellow arrow) and atherosclerotic plaque (white arrow). A2. The corresponding positions of the original images are represented by arrows, respectively. B1-2. The plaque was seen in the distal right coronary artery in the transverse position, and the corresponding DECT showed the coexistence of urate deposition (yellow arrow) and atherosclerotic plaque (white arrow).

difference (Table 1).

In addition, the multivariable analysis showed that urate deposition was independently associated with plaques after adjustment for age, sex, blood pressure, blood glucose, serum creatinine, history of gout, and history of hyperuricemia (OR = 13.69, 95%CI: 7.53–22.95, P = 0.035) (Table 2).

Table 2
Multivariable logistic regression analysis.

	OR (95%CI)	P
Unadjusted model		
Urate deposition		
Yes	15.23 (8.792–27.795)	0.024
No	REF	
Adjusted model[a]		
Urate deposition		
Yes	13.69 (7.528–22.953)	0.035
No	REF	

[a] Adjusted for age, sex, blood pressure, blood glucose, serum creatinine, history of gout, and history of hyperuricemia.

3.3. Subgroup analysis of the plaque group

The patients with plaques were divided into the AP and UDAP + UD groups. Compared with the AP group, the UDAP + UD group showed a higher frequency of gout (25.71 % vs. 10.42 %, P = 0.001) and hyperuricemia (P = 0.001). There were no differences between the two groups regarding the other characteristics (Table 3).

3.4. Correlations between urate deposition and calcification around plaque

Both atherosclerosis and urate deposition are prone to induce calcification. The mean coronary calcium score among UPAP was significantly higher than the calcium score among AP [210.1 (625.2) AU vs 58.2 (182.5) AU, P < 0.001]. Spearman rank sum correlation analysis was used to analyze the relationship between uric acid deposition and plaque calcification in UPAP patients. Urate deposition volume is 16.7 (22.15) mm^3, and calcification volume around plaque is 73.8 (125.65) mm^3 in UPAP patients. MSU deposition volume were positive correlated with calcification volume around plaque (r = 0.325, P < 0.001).

4. Discussion

This study presents a novel perspective on the deposition of MSU in the cardiovascular system. The results indicate that patients with a history of hyperuricemia or gout have a higher likelihood of MSU deposition in their atherosclerotic plaques. Furthermore, a strong correlation was observed between MSU deposition and atherosclerotic plaques with larger volumes and higher calcification. Regarding function, patients with MSU deposition in atherosclerotic plaques exhibited a slightly decreased cardiac ejection fraction than those without MSU deposition.

This study considered MSU deposits (green pixels) adjacent to calcifications as artifactual when they were <2 mm in size. Despite the presence of heavy calcifications, large deposits of MSU were observed frequently in control patients. In coronary calcium scoring (thicker collimation and 3-mm reconstructions), calcification involving less than three adjacent pixels is usually considered an artifact. Due to the higher resolution of the DECT protocol and the more advanced CT system (SOMATOM Force; Siemens), a threshold of less than two pixels was selected for artifacts. Even though this distinction may appear arbitrary, the present study and Klauser et al. [23,28] experience showed that a two-mm threshold is appropriate for distinguishing true MSU deposits from artifacts. Even though cardiovascular motion, beam hardening, and partial volume effects may cause substantial artifacts, the present study was not limited by these limitations. Artifacts related to motion would be expected to produce blurred areas of colorization corresponding to areas of maximum motion, not the well-defined color-coded regions corresponding to vascular plaques observed here. Images might show streaks if dual-energy results are related to beam hardening. Findings related to partial volume effects might be expected to outline the periphery of plaques. These features were not observed here either. MSU deposits were also concentrated in areas of vascular plaque rather than dispersed along vessel walls, as one might expect from artifacts. Most importantly, the cadaver studies by Klauser et al. [23,28] confirmed that DECT did identify true areas of MSU deposits [23,28].

Gout is a kind of metabolic disease. In recent years, along with the improvement of living standards and changes in diet, the content of serum MSU in the population has been increasing [10]. At present, most studies on gout using DECT focus on peripheral joints, such as the metatarsophalangeal joint, knee joint, sacroiliac joint, and wrist joint, and there are few studies on the deposition of MSU crystals in the cardiovascular system [23–25]. Several clinical studies confirmed a correlation between gout and the incidence of CVD [10–19]. Although gout is an independent high-risk factor for CVD, the effect of hyperuricemia on CVD is still conflicting. Some authors believe that there is a correlation between serum MSU acid and atherosclerosis [14,29,30], but some authors reported the opposite [31,32]. Colantonio et al. [33] confirmed a linear relationship between increased serum MSU and poor prognosis after acute myocardial infarction. Several mechanisms for the transport of MSU into coronary plaque have been suggested, one of which is that the elevated SUA levels increase platelet adhesion, promote the production of cytokines, lead to vasoconstriction and endothelial

Table 3
Subgroup analysis of the plaque group.

	AP (n = 348)	UDAP + UD (n = 93)	P
Sex, Male (%)	65.2	54.8	0.081
Age (years)	68.0 ± 10.5	70.5 (12.0)	0.431
Body Mass Index (kg/m^2)	24.26 ± 3.45	24.3 (3.2)	0.514
Serum uric acid level (mmol/L)	336.9 ± 89.0	325.6 (112.1)	0.455
Gout (%)	10.42	25.71	0.001*
Hyperuricemia (%)	27.08	42.85	0.001*
Blood pressure (mmHg)			
Systolic pressure	160 (39)	155 (47)	0.683
Diastolic pressure	90 (20)	90 (20)	0.993
Serum glucose (mmol/L)	6.04 (2.24)	6.53 (2.55)	0.482
Serum creatinine (μmol/L)	65.9 (23.3)	69.8 (15.0)	0.596
Triglyceride (mmol/L)	1.50 (1.17)	1.53 (1.66)	0.747
Total cholesterol (mmol/L)	4.13 (1.37)	4.11 (1.45)	0.418
Serum C-reactive protein (mg/L)	1.24 (4.62)	1.13 (1.74)	0.155
Serum neutrophils ($\times 10^9$/L)	3.62 (1.75)	3.59 (1.49)	0.44

dysfunction, and then form necrotic cores and make plaques unstable and even promote their progression [34–36]. In hyperuricemia, reactive oxygen species (ROS) are produced simultaneously with the formation of uric acid by xanthine oxidases. Intracellular uric acid has also been reported to promote the production of ROS. ROS and intracellular uric acid regulate several intracellular signaling pathways, and alterations in these pathways may result in the development of atherosclerotic lesions [36]. Patetsios et al. [21] qualitatively and quantitatively measured the components of atherosclerotic plaques and found that the levels of uric acid, cholesterol, and xanthine oxidase in atherosclerotic plaques increased in carotid endarterectomy specimens but not in non-atherosclerotic control specimens, which supported the pathophysiological role of MSU in atherosclerosis. In a study in 2019, Klauser et al. [23] first proposed that there could be MSU deposition in the coronary arteries and proved this view by autopsy. Then, in 2020, Feuchtner et al. [24] also proved that there was MSU deposition in the coronary arteries by establishing a model of MSU deposition in the coronary artery.

According to DECT, this study made a noninvasive visualization and quantitative study of urate deposition in the cardiovascular system, which can provide a novel value of diagnosis and treatment for the clinic. The proportion of MSU deposition in people with plaques is about 21.1 %. In addition, since the DECT scanning mode does not significantly increase the dose line exposed by the patient [37,38], this study also clarified that the presence of MSU in atherosclerotic plaques in the cardiovascular system could not be predicted by relying solely on the basic and clinical data of the patients. Therefore, if DECT can be routinely used in the physical examination of high-risk populations (such as a personal or family history of gout, hyperuricemia, and known coronary heart disease), it can provide guidance value for clinical treatment. It can also roughly estimate the incidence of atherosclerosis caused by urate deposition in the population.

A total of 93 patients had MSU deposition in this study. After excluding patients with incomplete clinical data, the lack of a significant difference in serum uric acid levels between UDAP and AP patients could be attributed to the chronic nature of MSU deposition and atherosclerotic plaque formation. A single blood test may not accurately reflect the overall condition of the patient. Therefore, this study investigated the patients' prior history of hyperuricemia and gout and found that patients with such a history were more likely to develop MSU deposition in their atherosclerotic plaques. Hyperuricemia is defined as a serum urate level of 6.8 mg per deciliter (404 μmol per liter) or more [3]. In future studies, drugs should be administered to patients with a history of gout or hyperuricemia, followed by a DECT evaluation of the volume of urate deposition post-treatment for hyperuricemia. Therefore, we should continue to explore the causal relationship between patient data and clinical outcomes.

There are several limitations to this study. First, the latest generation of DECT (SOMATOM Force, Siemens) has been used in this study, and the temporal and spatial resolution of the scanned image has reached the best. However, limited by the hardware performance, this scanning scheme still has requirements for the HR of patients. According to this study, when the HR of patients is < 120 bpm, the image can meet the needs of DECT post-processing and diagnosis. Still, at present, there is no clear "gold standard" for the scanning scheme and post-processing scheme of DECT in the cardiovascular system. The parameters and post-processing scheme of this scan were based on the experience and research of Klauser et al. [23] and Feuchtner et al. [24]. Second, we cannot verify the sensitivity and specificity of DECT detection of MSU deposition in atherosclerotic plaque, though Klauser suggested that the 2-mm threshold was appropriate to discriminate true MSU deposits from artifacts [28]. Further studies are needed to investigate the correlation between the pixels identified by DECT and the pathological findings from polarizing microscopy. Moreover, the percentage and reasons for any discrepancies between DECT and polarizing microscopy should be the next study focus.

5. Conclusion

This study used DECT to detect MSU deposition in atherosclerotic plaques. Patients with gout or hyperuricemia are more likely to display MSU deposition. The clinical significance of the coexisting plaque should be investigated by future clinical studies. DECT may provide a relatively simple method for detecting and identifying coronary MSU deposition at risk for cardiovascular diseases.

Funding

Dr Wang received a restricted grant in support of the Key Discipline Program of Strengthening Health Project by Science &Technology and Education of the "Thirteenth Five-Year Plan" in Yangzhou City (ZDXK201806).

Data availability

The data associated with our study have not been deposited in a publicly available repository. The data generated during the current study can be made available on reasonable request.

CRediT authorship contribution statement

Haolin Ren: Writing – review & editing, Writing – original draft, Project administration, Conceptualization. **Hang Qu:** Writing – original draft, Conceptualization. **Yong Zhang:** Formal analysis, Data curation. **Yue Gu:** Formal analysis, Data curation. **Yi Zhao:** Writing – original draft, Formal analysis. **Wenjuan Xu:** Writing – original draft, Data curation. **Mingsheng Zhou:** Writing – review & editing, Writing – original draft, Formal analysis. **Wei Wang:** Writing – review & editing, Writing – original draft, Project administration, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] S. Priori, C. Blomström-Lundqvist, A. Mazzanti, N. Blom, M. Borggrefe, J. Camm, et al., ESC guidelines for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: the task force for the management of patients with ventricular arrhythmias and the prevention of sudden cardiac death of the European society of cardiology (ESC). Endorsed by: association for European paediatric and congenital cardiology (AEPC), Eur. Heart J. 36 (41) (2015) 2793–2867, 2015.

[2] M. Patel, J. Calhoon, G. Dehmer, J. Grantham, T. Maddox, D. Maron, et al., ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2017 appropriate use criteria for coronary revascularization in patients with stable ischemic heart disease: a report of the American College of cardiology appropriate use criteria task force, American association for thoracic surgery, American heart association, American society of echocardiography, American society of nuclear cardiology, society for cardiovascular angiography and interventions, society of cardiovascular computed tomography, and society of thoracic surgeons, J. Am. Coll. Cardiol. 69 (17) (2017) 2212–2241.

[3] N. Dalbeth, A. Gosling, A. Gaffo, A. Abhishek, Gout, Lancet (London, England) 397 (10287) (2021) 1843–1855.

[4] P. Libby, J. Buring, L. Badimon, G. Hansson, J. Deanfield, M. Bittencourt, et al., Atherosclerosis, Nature Rev. Disease Primers. 5 (1) (2019) 56.

[5] G. Figtree, P. Adamson, C. Antoniades, R. Blumenthal, M. Blaha, M. Budoff, et al., Noninvasive plaque imaging to accelerate coronary artery disease drug development, Circulation 146 (22) (2022) 1712–1727.

[6] Y. Asada, A. Yamashita, Y. Sato, K. Hatakeyama, Pathophysiology of atherothrombosis: mechanisms of thrombus formation on disrupted atherosclerotic plaques, Pathol. Int. 70 (6) (2020) 309–322.

[7] H. Huikuri, A. Castellanos, R. Myerburg, Sudden death due to cardiac arrhythmias, N. Engl. J. Med. 345 (20) (2001) 1473–1482.

[8] M. Haukilahti, L. Holmström, J. Vähätalo, T. Kenttä, J. Tikkanen, L. Pakanen, et al., Sudden cardiac death in women, Circulation 139 (8) (2019) 1012–1021.

[9] J. Willerson, P. Golino, J. Eidt, W. Campbell, L. Buja, Specific platelet mediators and unstable coronary artery lesions. Experimental evidence and potential clinical implications, Circulation 80 (1) (1989) 198–205.

[10] G.G. Teng, L.W. Ang, K.G. Saag, M.C. Yu, J.M. Yuan, W.P. Koh, Mortality due to coronary heart disease and kidney disease among middle-aged and elderly men and women with gout in the Singapore Chinese Health Study, Ann. Rheum. Dis. 71 (6) (2012) 924–928.

[11] H.J. Janssens, E.H. van de Lisdonk, H. Bor, H.J. van den Hoogen, Janssen M. Gout, Just a nasty event or a cardiovascular signal? A study from primary care, Fam. Pract. 20 (4) (2003) 413–416.

[12] E. Krishnan, J.F. Baker, D.E. Furst, H.R. Schumacher, Gout and the risk of acute myocardial infarction, Arthritis Rheum. 54 (8) (2006) 2688–2696.

[13] M.A. De Vera, M.M. Rahman, V. Bhole, J.A. Kopec, H.K. Choi, Independent impact of gout on the risk of acute myocardial infarction among elderly women: a population-based study, Ann. Rheum. Dis. 69 (6) (2010) 1162–1164.

[14] C. Kuo, L. See, S. Luo, Y. Ko, Y. Lin, J. Hwang, et al., Gout: an independent risk factor for all-cause and cardiovascular mortality, Rheumatology 49 (1) (2010) 141–146.

[15] A. Gelber, M. Klag, L. Mead, J. Thomas, D. Thomas, T. Pearson, et al., Gout and risk for subsequent coronary heart disease. The Meharry-Hopkins Study, Arch. Intern. Med. 157 (13) (1997) 1436–1440.

[16] L.E. Clarson, P. Chandratre, S.L. Hider, J. Belcher, C. Heneghan, E. Roddy, et al., Increased cardiovascular mortality associated with gout: a systematic review and meta-analysis, Eur. J. Prev. Cardiol. 22 (3) (2015) 335–343.

[17] E. Roddy, W. Zhang, M. Doherty, Concordance of the management of chronic gout in a UK primary-care population with the EULAR gout recommendations, Ann. Rheum. Dis. 66 (10) (2007) 1311–1315.

[18] E. Roddy, C.D. Mallen, S.L. Hider, K.P. Jordan, Prescription and comorbidity screening following consultation for acute gout in primary care, Rheumatology 49 (1) (2010) 105–111.

[19] L.E. Clarson, S.L. Hider, J. Belcher, C. Heneghan, E. Roddy, C.D. Mallen, Increased risk of vascular disease associated with gout: a retrospective, matched cohort study in the UK clinical practice research datalink, Ann. Rheum. Dis. 74 (4) (2015) 642–647.

[20] S. Lim, N. Lu, A. Oza, M. Fisher, S. Rai, M. Menendez, et al., Trends in gout and rheumatoid arthritis hospitalizations in the United States, 1993-2011, JAMA 315 (21) (2016) 2345–2347.

[21] P. Patetsios, M. Song, W. Shutze, C. Pappas, W. Rodino, J. Ramirez, et al., Identification of uric acid and xanthine oxidase in atherosclerotic plaque, Am. J. Cardiol. 88 (2) (2001) 188–191. A6.

[22] T.R. Johnson, Dual-energy CT: general principles, AJR Am. J. Roentgenol. 199 (5 Suppl) (2012) S3–S8.

[23] A.S. Klauser, E.J. Halpern, S. Strobl, J. Gruber, G. Feuchtner, R. Bellmann-Weiler, et al., Dual-energy computed tomography detection of cardiovascular monosodium urate deposits in patients with gout, JAMA Cardiol 4 (10) (2019) 1019–1028.

[24] G.M. Feuchtner, F. Plank, C. Beyer, C. Schwabl, J. Held, R. Bellmann-Weiler, et al., Monosodium urate crystal deposition in coronary artery plaque by 128-slice dual-energy computed tomography: an ex vivo phantom and in vivo study, J. Comput. Assist. Tomogr. 45 (6) (2021) 856–862.

[25] S. Barazani, W. Chi, R. Pyzik, H. Chang, A. Jacobi, T. O'Donnell, et al., Quantification of uric acid in vasculature of patients with gout using dual-energy computed tomography, World J. Radiol. 12 (8) (2020) 184–194.

[26] M. Károlyi, B. Szilveszter, M. Kolossváry, R. Takx, C. Celeng, A. Bartykowszki, et al., Iterative model reconstruction reduces calcified plaque volume in coronary CT angiography, Eur. J. Radiol. 87 (2017) 83–89.

[27] M. Gamala, S.P. Linn-Rasker, M. Nix, B.G.F. Heggelman, J.M. van Laar, P.C.M. Pasker-de Jong, et al., Gouty arthritis: decision-making following dual-energy CT scan in clinical practice, a retrospective analysis, Clin. Rheumatol. 37 (7) (2018) 1879–1884.

[28] E. Halpern, G. Feuchtner, A. Klauser, Identification of cardiovascular monosodium urate crystal deposition in patients with gout using dual-energy computed tomography-reply, JAMA Cardiol. 5 (4) (2020) 486–487.

[29] K. Lottmann, X. Chen, P. Schädlich, Association between gout and all-cause as well as cardiovascular mortality: a systematic review, Curr. Rheumatol. Rep. 14 (2) (2012) 195–203.

[30] A. Mandurino-Mirizzi, S. Cornara, A. Somaschini, A. Demarchi, M. Galazzi, S. Puccio, et al., Elevated serum uric acid is associated with a greater inflammatory response and with short- and long-term mortality in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. Nutrition, metabolism, and cardiovascular diseases, Nutr. Metabol. Cardiovasc. Dis. 31 (2) (2021) 608–614.

[31] J. Moriarity, A. Folsom, C. Iribarren, F. Nieto, W. Rosamond, Serum uric acid and risk of coronary heart disease: atherosclerosis Risk in Communities (ARIC) Study, Ann. Epidemiol. 10 (3) (2000) 136–143.

[32] B. Culleton, M. Larson, W. Kannel, D. Levy, Serum uric acid and risk for cardiovascular disease and death: the Framingham Heart Study, Ann. Intern. Med. 131 (1) (1999) 7–13.

[33] L. Colantonio, R. Reynolds, T. Merriman, A. Gaffo, J. Singh, T. Plante, et al., Higher serum urate levels are associated with an increased risk for sudden cardiac death, J. Rheumatol. 48 (11) (2021) 1745–1753.

[34] X. Li, X. Meng, Y. He, A. Spiliopoulou, M. Timofeeva, W.Q. Wei, et al., Genetically determined serum urate levels and cardiovascular and other diseases in UK Biobank cohort: a phenome-wide mendelian randomization study, PLoS Med. 16 (10) (2019) e1002937.

[35] Z. Liu, T. Chen, H. Niu, W. Ren, X. Li, L. Cui, et al., The establishment and characteristics of rat model of atherosclerosis induced by hyperuricemia, Stem Cell. Int. 2016 (2016) 1365257.

[36] Y. Kimura, D. Tsukui, H. Kono, Uric acid in inflammation and the pathogenesis of atherosclerosis, Int. J. Mol. Sci. 22 (22) (2021).
[37] R. Ghasemi Shayan, M. Oladghaffari, F. Sajjadian, M. Fazel Ghaziyani, Image quality and dose comparison of single-energy CT (SECT) and dual-energy CT (DECT), Radiol. Res. Practice 2020 (2020) 1403957.
[38] J.R. Grajo, M. Patino, A. Prochowski, D.V. Sahani, Dual energy CT in practice: basic principles and applications, Appl. Radiol. (2016) 6–12.