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Subclinical carotid atherosclerosis in gouty patients: relation to musculoskeletal ultrasonographic findings and serum sclerostin level

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ABSTRACT

Objectives. To detect subclinical carotid atherosclerosis in gout patients and its relation to musculoskeletal ultrasound (MSK US) manifestations and serum sclerostin (SCL) levels.

Patients and methods. Thirty Egyptian gouty patients were classified into two groups: Group A included 15 patients with diagnostic MSK US manifestations of gout (double contour sign), and Group B included 15 patients without MSK US findings. MSK US was done for both knees and the first MTP joints. Carotid duplex ultrasonography was done to evaluate carotid intima-media-thickness (CIMT) and serum SCL level was measured in all patients by ELISA technique.

Results. Gouty patients with MSK US findings had a significantly higher increase in serum SCL levels than those without MSK US findings ($p < 0.01$). Group A patients had a significantly greater CIMT than patients of group B ($p < 0.01$). Serum uric acid and SCL levels were found to be significantly positively correlated. The ROC curve revealed that the optimal SCL cutoff value for detecting positive MSK US findings in gout patients was >25.05 ng/ml. At this level, there was a significant difference between the patients with a CIMT >0.9 mm and the patients with a CIMT ≤0.9 mm ($p < 0.05$).

Conclusions. Patients with MSK US manifestations of gout are more liable to have subclinical carotid atherosclerosis than patients without these manifestations. SCL at a certain level >25.05 ng/ml in gout patients might predispose patients to radiographic findings of MSK US of gout and subclinical atherosclerosis.

Keywords: gout, carotid atherosclerosis, ultrasound, sclerostin, uric acid

Abbreviations (in alphabetical order):

ACR – American College of Rheumatology
BMI – Body mass index
CBC – Complete blood picture
CCA – common carotid arteries
CIMT – Carotid intima-media thickness
CRP – C-reactive protein
CV – Cardiovascular
CVD – Cardiovascular disease
DC – Double contour
DECT – Duel energy computed tomography
ESR – Erythrocyte sedimentation rate
EULAR – European League Against Rheumatism
HBA1c – Glycosylated hemoglobin
HDL – high-density lipoprotein cholesterol
IL-1 – Interleukin 1
LDL – low-density lipoprotein cholesterol
MSK US – musculoskeletal ultrasound
MSU – Monosodium urate
OPG – Osteoprotegrin
SCL – Sclerostin
sUA – Serum uric acid
TNF-α – tumor necrosis factor α
ULT – Urate lowering therapy

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INTRODUCTION

Monosodium urate (MSU) crystals in joints and extra-articular tissues are the basis of the inflammatory conditions of gout. The value of gout prevalence ranged from less than 1% to 6.8% with males having a higher prevalence than female [1].

Subclinical carotid atherosclerosis has been found to be dominant in gout patients with the prevalence ranged from approximately 29.1 to 59.2% [2].

Although, Calabuig et al. (2020) revealed an association between carotid atherosclerosis and ultrasonographic manifestations of MSU deposition in gouty patients [3]. According to Andrés et al. (2017), there is no association between subclinical atherosclerosis and gout's clinical manifestations [4].

Musculoskeletal ultrasonography has a well-established role in the diagnosis of gout. The American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) developed the gout classification criteria, which involve MSK ultrasonography. Its role in monitoring gout has been shown [5].

Aggregates, double contour (DC) sign and tophi are considered typical US abnormalities of MSU crystal deposits [6].

In patients with gout, tophi has been closely related to the pathophysiology of bone erosions. Osteoprotegerin (OPG), RANKL, and SCL levels were all linked to periarticular bone loss. It was suggested that SCL and OPG might stimulate compensatory processes at sites of MSU crystal deposition in gout [7].

SCL (soluble glycoprotein) is synthesized mainly by osteocytes and by nonmineralized cells under pathological conditions. One of the essential components of bone formation is SCL, which naturally inhibits the canonical Wnt pathway [8].

As far as we know, no prior research has shown any relationship between MSK US findings of gout and serum SCL levels; however, Zou et al. (2019) reported that higher Dickopff-1 and RANKL levels were associated with MSK US manifestations such as DC sign and tophi in gouty patients [9].

Moreover, there is a great debate regarding the association of SCL with carotid atherosclerosis, and no previous study has revealed the association between carotid intima-media thickness (CIMT) and SCL in patients with gout. Some studies [10-11] have shown a positive correlation between them, while others have shown a negative correlation [12-13].

This study aimed to detect subclinical carotid atherosclerosis in gout patients and its relation to MSK US manifestations and serum SCL levels.

MATERIALS AND METHODS

A cross-sectional study was conducted on 30 gouty patients aged more than 18 years old who were referred to our department in our university for further assessment. The diagnosis of these patients was done based on the ACR/ EULAR classification criteria for gout [5].

Two patient groups were classified: Fifteen patients with diagnostic MSK US manifestations of gout (DC sign) in Group A and fifteen patients without MSK US manifestations in Group B.

The Research Ethics Committee at our faculty gave ethical approval for the study. No. FMASU MD 187 /2021. Written informed consent was applied to all participants after receiving details about the objective of the study

Patients aged less than 18 years or patients with metabolic syndrome [14], rheumatoid arthritis, osteoarthritis, other rheumatic diseases, or acute gout attack at the time of examination were excluded. Additionally, patients with known atherosclerotic cardiovascular (CV) clinical complications such as coronary heart disease and stroke; patients with impaired renal function; or with a family history of cerebrovascular stroke, myocardial infarction, and sudden death before the age of 55 years for males and 65 years for females [15], or with hyperuricemia secondary to psoriasis, malignancy, radiotherapy, or chemotherapy were excluded.

Full assessment

Patients' full history taking with special emphasis on age, gender, smoking status, dietary intake of high-purine foods, arthritic manifestations, other comorbidities (particularly prior major CV events), use of urate-lowering treatment (ULT) (especially allopurinol or febuxostat), disease duration, and gout flare frequency was taken. Full clinical examination with special emphasis on the neck examination, carotid pulsations, neck veins, and thyroid, chest, cardiac, and abdominal examinations were performed. Skin and joint examinations were performed to detect tophi, erythema, swelling, warmth, tenderness, effusion, and range of motion of the affected joints.

Laboratory studies

Complete blood picture (CBC), serum creatinine, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), glycosylated hemoglobin (HbA1c), serum uric acid (sUA), total cholesterol, triglycerides (TGs), high-density lipoprotein cholesterol (HDL) and low-density lipoprotein cholesterol (LDL) levels were measured.

Measurement of serum SCL: The samples were obtained from the patients after appropriate disinfection. Centrifugation of the tubes was done at 3,000 RPM (for 20 min), after which the supernatant was collected without sediment and was stored at -80°C Then, assessment of SCL was done by the en-

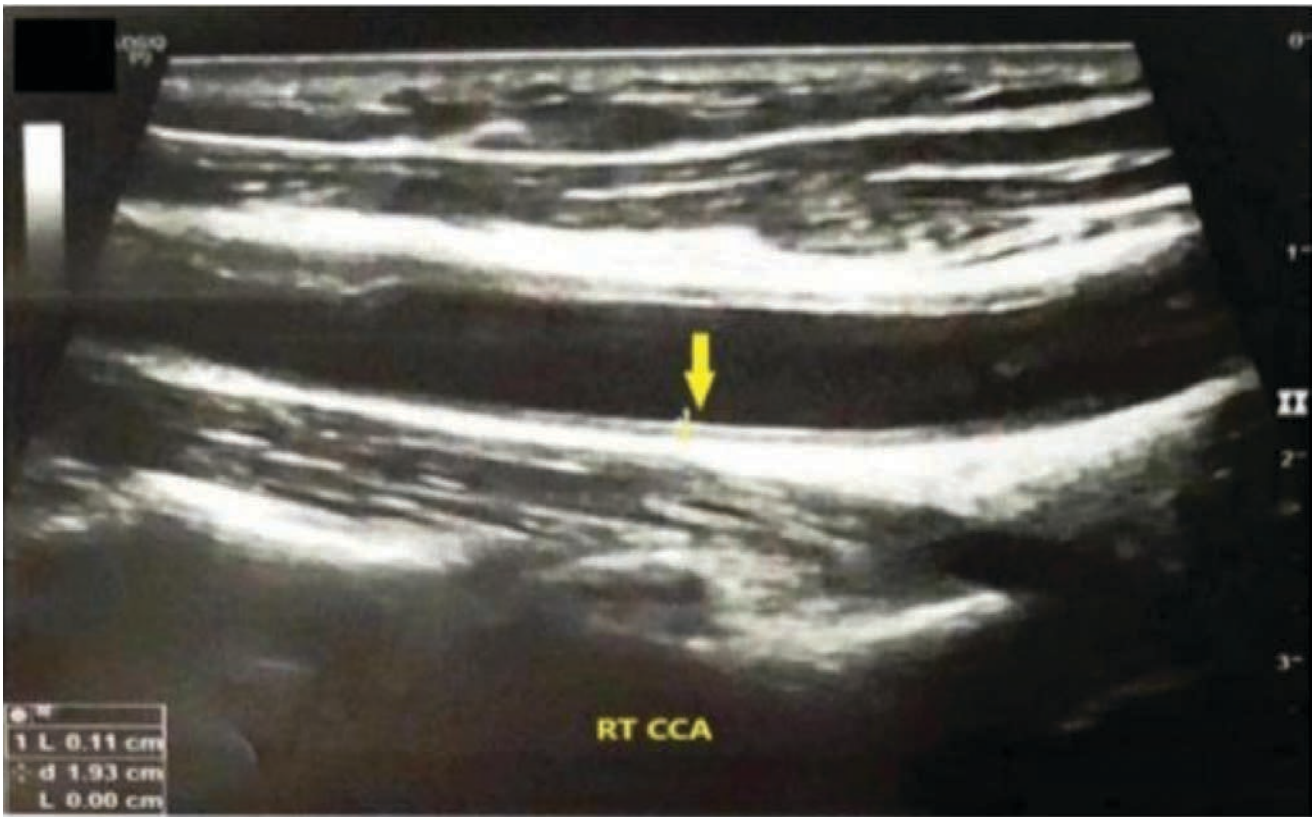


FIGURE 1. Ultrasound grayscale showing intima-media thickness of the right common carotid artery measuring 1.1 mm. Arrow: refers to intimal-media thickness, RT CCA: right common carotid artery.

zyme-linked immunosorbent assays (ELISAs). The measurements were done according to the manufacturer's instructions using ELISA kits (Enanhu Dist, Jiaxing, Zhejiang, China) from the Bioassay Technology Laboratory Company (BT LAB).

Musculoskeletal ultrasonography

Musculoskeletal ultrasonography was done by a General Electric system (Logiq P5 R4.0.) using a multifrequency linear transducer probe (3-12 MHz) (General Electric, Milwaukee, Wisconsin, USA). Ultrasound was made according to the EULAR guidelines following OMERACT definitions[16]. Greyscale and power Doppler imaging were performed for bilateral 1st MTPs and knees in both longitudinal and transverse views to detect DC sign, gouty tophus, aggregates, bone erosion, synovial hypertrophy (SH), and synovial effusion (SE).

Duplex ultrasonography

Duplex ultrasonography was performed for both common carotid arteries (CCAs) using a GE, LOGIQ P9 R3 machine (Republic of Korea) with a L6-12-RS probe. Special emphasis was placed on the CIMT following the technique proposed by the American Society of Echocardiography using 4–12 MHz multifrequency high-resolution B-mode ultrasonography to measure the maximum CIMT from the CCA, and the mean of 2 measurements was recorded[17]

The CCAs on the left and right were scanned independently. A 10 mm longitudinal section was studied at 1 cm from the carotid bifurcation and a value greater than 0.9 mm was considered abnormal [18]

The CIMT was assessed by a trained investigator as the area between the lumen-intima line and the media-adventitia line in a region free of plaques [18] (Figure 1).

Statistical analysis

Data analysis was done using IBM SPSS Statistics (Version. 23.0, IBM Corp, USA, 2011). Quantitative parametric data are expressed as the mean ± SD and range, nonparametric data are expressed as the median (interquartile range), and qualitative variables are expressed as percentages. For statistical comparisons, the chi-square test, independent t-test, Fisher exact test, and Mann-Whitney test were used. The best cut-off point for the studied marker was assessed using the receiver operating characteristic (ROC) curve. Correlation analysis was done using Spearman correlation coefficients. $P < 0.05$ was considered significant (S) and $p < 0.01$: was considered highly significant (HS).

RESULTS

Demographic and clinical data

Thirty gouty patients referred to our department's outpatient clinic participated in this study. Two

TABLE 1. Comparison between Group A and Group B regarding demographic, clinical, and laboratory data

		Group A	Group B	t /Z/ χ^2	p-value
		No. = 15	No. = 15		
Gender	Female	7 (46.7%)	9 (60.0%)	0.536	0.464
	Male	8 (53.3%)	6 (40.0%)		
Age (years)	Mean ± SD	48.07 ± 6.11	46.27 ± 6.91	-0.756	0.456
	Range	39 – 58	37 – 57		
BMI (kg/m²)	Mean ± SD	29.72 ± 2.23	29.10 ± 2.28	-0.751	0.459
	Range	24.62 – 32.87	24.11 – 32.05		
Smoking	No	10 (66.7%)	14 (93.3%)	3.333	0.068
	Yes	5 (33.3%)	1 (6.7%)		
Disease duration (months)	Median (IQR)	24 (12 – 48)	12 (8 – 24)	-2.384.	**0.017***
	Range	12 – 72	6 – 36		
Joint tenderness	1st MTP	7 (46.7%)	6 (40.0%)	0.136	0.713
		8 (53.3%)	9 (60.0%)		
Urate lowering treatment (ULT)	No	4 (26.7%)	4 (26.7%)	0.917#	0.632
	Allopurinol	9 (60.0%)	7 (46.7%)		
	Febuxostat	2 (13.3%)	4 (26.7%)		
ULT duration (months)	Median (IQR)	3 (3 – 6)	6 (3 – 7)	-1.148	0.251
	Range	2 – 7	2 – 9		
Haemoglobin (g/dl)	Mean ± SD	12.83 ± 1.19	12.45 ± 1.24	-0.842	0.407
		9.7 – 14.2	10.4 – 15.7		
Platelet (10^3/cm)	Mean ± SD	259.73 ± 71.81	309.40 ± 64.43	1.994	0.056
	Range	112 – 406	186 – 408		
ESR (mm/hr)	Median (IQR)	20 (15 – 30)	20 (10 – 22)	-0.545	0.586
	Range	9 – 90	5 – 40		
CRP (mg/l)	Median (IQR)	6 (4 – 7)	6 (4 – 6.1)	-0.590	0.555
		3 – 53	2 – 6.8		
Serum creatinine (mg/dl)	Mean ± SD	0.89 ± 0.19	0.85 ± 0.23	-0.523	0.605
	Range	0.6 – 1.2	0.5 – 1.2		
Uric acid level (mg/dl)	Mean ± SD	7.87 ± 1.23	7.13 ± 0.80	-1.948	0.061
	Range	6.6 – 11	6.1 – 9		
Total cholesterol (mg/dL) (≤200)	Mean ± SD	226.20 ± 16.85	227.47 ± 36.36	0.122	0.903
	Range	201 – 272	153 – 313		
HDL(mg/dl) (≥ 40)	Mean ± SD	44.13 ± 7.19	48.73 ± 9.41	1.504	0.144
	Range	29 – 55	37 – 74		
LDL (mg/dl) (≤ 100)	Mean ± SD	143.47 ± 21.68	130.93 ± 21.21	-1.600	0.121
	Range	110 – 185	103 – 177		
Triglycerides (mg/dl) (≤ 150)	Mean ± SD	184.60 ± 57.31	182.33 ± 45.38	-0.120	0.905
	Range	102 – 277	101 – 237		

*. : χ^2: Chi-square test; t: Independent t-test, #: Z: Mann-Whitney test, CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate, LDL: low-density lipoprotein, BMI: body mass index, HDL: high-density lipoprotein, *: p-value < 0.05: significant*

groups of patients were classified; Group A consisted of 15 patients with diagnostic MSK US manifestations of gout (DC sign) and Group B consisted of 15 patients without MSK US manifestations.

Among all the patients, 16 (53.3%) out of the 30 patients were females, while 14 (46.7%) patients were males, with a mean age of 48.07 ± 6.11 (39-58) years for patients in group A and 46.27 ± 6.91 (37-57) years for group B patients.

No significant differences were found in terms of age, gender, body mass index (BMI), smoking status, joint complaints, ULT, or ULT intake duration among the patients of the two groups (Table 1).

Laboratory data

No significant differences in terms of ESR, CRP, hemoglobin level, platelets, serum creatinine, sUA, total cholesterol, HDL, LDL, and TGs were found among the two groups (p >0.05). Regarding the disease duration, a longer disease duration was found in group A patients than in group B patients with a significant difference between them (p <0.05) (Table 1).

The serum SCL level concentration ranged from 27.42 – 194.3 ng/ml with a median of 57.3 ng/ml for patients in group A and it ranged from 14.68-46.76 ng/ml with a median of 18.84 ng/ml for group B patients. Patients of group A had a significantly greater SCL concentration than patients of group B] p<0.01[(Figure 2).

MSK US examination

Positive radiographic findings of MSK US were observed in group A. These findings included DC signs, tophi, aggregates, and erosions (Figures 3 and 4). Table 2 gives a thorough explanation of the MSK US findings' topographic distribution.

The best cut-off point for the serum SCL for detecting gouty patients with positive findings in MSK US using receiver operating characteristic (ROC) analysis was found to be >25.05 ng/ml (sensitivity 100%, and specificity 93.33%). The area under the curve (AUC) was 0.982 and the accuracy of the test was 98.2% (Figure 5).

TABLE 2. Musculoskeletal ultrasound findings among group A patients

		Group A
		No. = 15
Right knee	Double contour	14 (93.3%)
	Tophus	0 (0.0%)
	Aggregate	7 (46.7%)
	Erosion	7 (46.7%)
	Enthesopathy	6 (40.0%)
	SE	13 (86.7%)
	SH	7 (46.7%)
	PD	3 (20.0%)

		Group A
		No. = 15
Left knee	Double contour	13 (86.7%)
	Tophus	2 (13.3%)
	Aggregate	1 (6.7%)
	Erosion	7 (46.7%)
	Enthesopathy	4 (26.7%)
	SE	7 (46.7%)
	SH	5 (33.3%)
	PD	4 (26.7%)
Right first MTP	Double contour	13 (86.7%)
	Tophus	2 (13.3%)
	Aggregate	10 (66.7%)
	Erosion	9 (60.0%)
	Enthesopathy	0 (0.0%)
	SE	9 (60.0%)
	SH	9 (60.0%)
	PD	3 (20.0%)
Left First MTP	Double contour	11 (73.3%)
	Tophus	0 (0.0%)
	Aggregate	5 (33.3%)
	Erosion	4 (26.7%)
	Enthesopathy	0 (0.0%)
	SE	10 (66.7%)
	SH	10 (66.7%)
	PD	1 (6.7%)

SE: synovial effusion, MTP: metatarsophalangeal joint, SH: synovial hypertrophy, PD: power Dopple

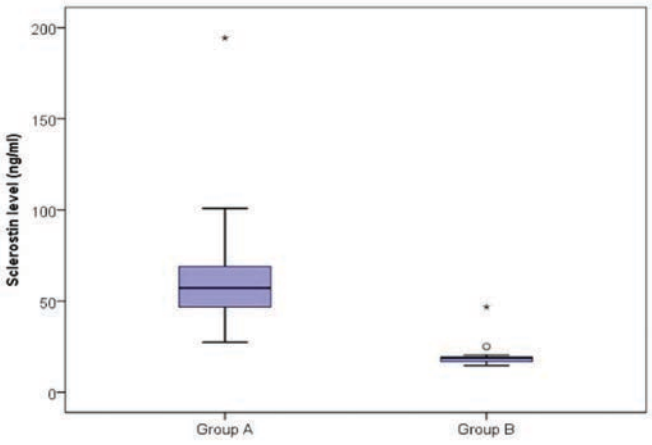


FIGURE 2. Comparison between Group A and Group B regarding sclerostin level

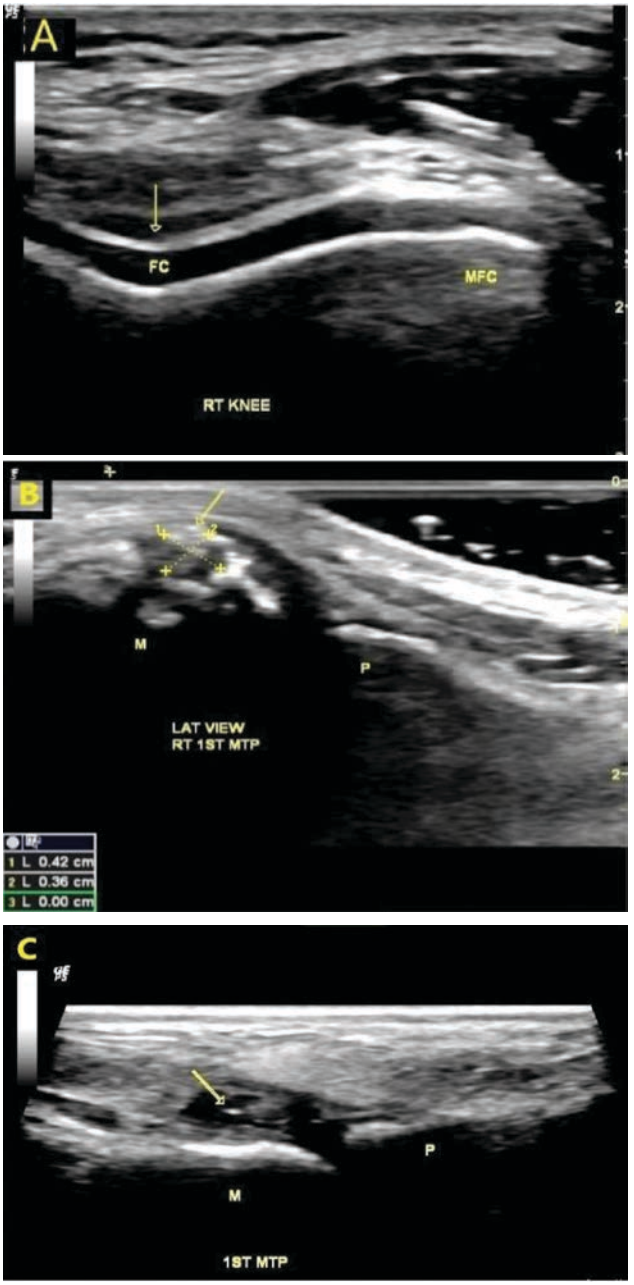


FIGURE 3. Ultrasound grayscale. A: DC sign over the femoral cartilage of the RT knee, B: Tophus measuring (42×36 mm) with underlying erosion at the right 1st MTP. C: Aggregate at the 1st MTP joint. 1st MTP: first metatarsophalangeal joint, M: metatarsal bone, MFC: medial femoral cartilage

Carotid duplex ultrasonography

Regarding CIMT, 15 (50%) out of 30 patients had an increased CIMT >0.9 mm, and 15 (50%) had a CIMT ≤0.9 mm.

The mean CIMT was 1.02 ± 0.15 mm for Group A patients and 0.82 ± 0.18 mm for Group B patients. The CIMT of group A was statistically significant greater than that of group B]p <0.01[. Carotid plaque (>1 mm) was detected in two (13.3%) patients out of 15 in group A while no plaques were detected in patients in group B.

Patients with a serum SCL level >25.05 ng/ml showed a statistically significant increase in CIMT >0.9 mm than patients with a SCL level ≤25.05 ng/ml (Table 3).

TABLE 3. Comparison between serum sclerostin and increased CIMT in gouty patients

		CIMT ≤0.9 mm	CIMT > 0.9 mm	χ^2	p-value
		No. = 15	No. = 15		
Serum Sclerostin (ng/ml)	≤25.05 ng/ ml	10 (66.7%)	4 (26.7%)	4.821	**0.028***
	>25.05 ng /ml	5 (33.3%)	11 (73.3%)		

**: Significant; χ^2: Chi-square test. CIMT: carotid intima-media thickness*

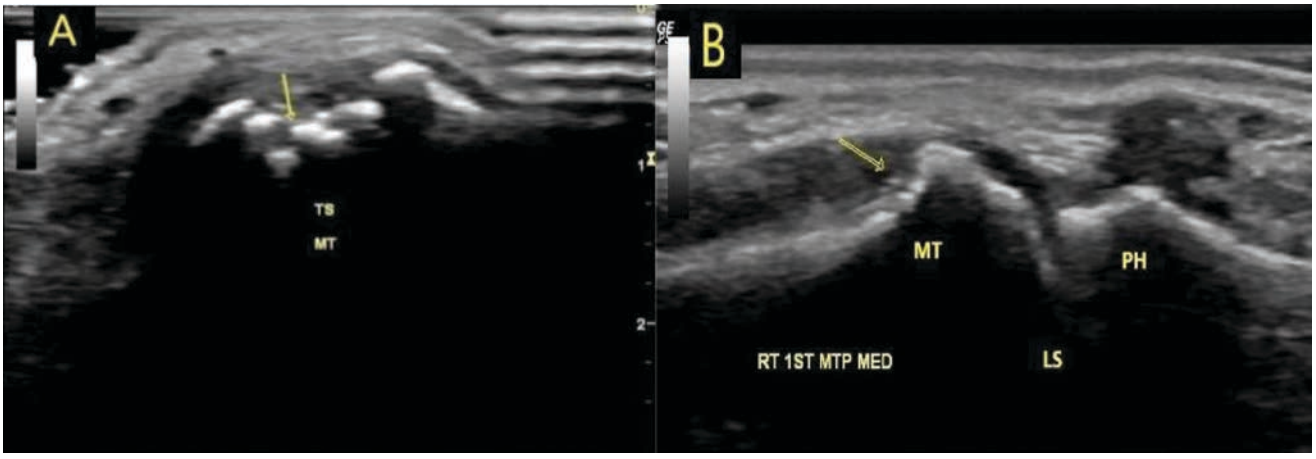
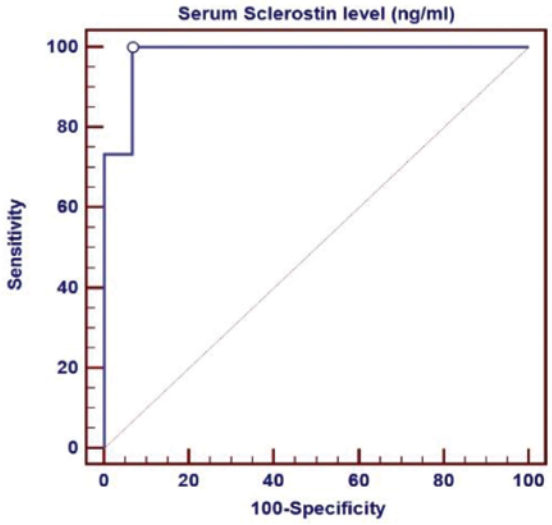


FIGURE 4. Ultrasound gray scale showing Bone Erosions. A: shows erosion in the metatarsal bone by transverse view. B: shows erosions in the metatarsal bone by longitudinal view. Arrow refers to erosion, MT: metatarsal bone, TS: transverse view, PH: Phalanx, RT1st MTP: right first metatarsophalangeal joint, LS: Longitudinal view



Variables	Cut off point	AUC	Sensitivity	Specificity	+PPV	-NPV	Accuracy
Sclerostin level (ng/ml)	>25.05	0.982	100.00	93.33	93.7	100.0	98.2 %

FIGURE 5. Receiver operating characteristic curve for serum sclerostin level to detect gouty patients with positive findings in Musculoskeletal ultrasound. PPV: positive predictive value, NPV: negative predictive value, AUC: area under curve

Correlation studies

Correlation studies of uric acid levels, serum SCL, and CIMT with other studied parameters among all the studied patients revealed a statistically significant positive correlation between the serum SCL and uric acid levels (r= 0.487, p= 0.006**). There was a significant positive correlation between CIMT and disease duration (r= 0.377, p= 0.040*), and no correlation between CIMT and the serum SCL was detected (r= 0.272, p= 0.146) (Table 4).

TABLE 4. Correlation of uric acid, sclerostin, and CIMT with other studied parameters among all the studied patients

	Uric acid level (mg /dl)		**Sclerostin level (ng/ml)**		**CIMT (mm)**	
	r	**p-value**	**r**	**p-value**	**r**	**p-value**
Uric acid level (mg /dl)	–	–	0.487	**0.006****	0.185	0.328
Sclerostin level (ng/ml)	0.487	**0.006****	–	–	0.272	0.146
CIMT (mm)	0.185	0.328	0.272	0.146	–	–
Disease duration (months)	0.086	0.651	0.262	0.163	0.377	**0.040***

*P-value > 0.05: Nonsignificant; *: Significant; **: Highly significant, r: Spearman correlation coefficient.CIMT: carotid intima-media thickness*

DISCUSSION

In chronic gout patients, MSU crystals are deposited in joints and around synovial membranes, eroding and destroying bone by decreasing osteoblastic activity and increasing osteoclastic activity, leading to serious complications such as erosive gouty arthritis and cardiovascular diseases (CVDs) [19].

MSK US has been widely used for both medical purposes and research as it is less expensive, safer, and free of radiation. In addition, it can be used repeatedly within a short period for disease monitoring[5].

Assessments of the carotid arteries and joints using ultrasound are beneficial in detecting MSU crystal deposits in joints and discovering subclinical atherosclerosis, thus significantly improving risk assessment for CVDs in gout patients [20].

As far as we know, this could be the first study to detect subclinical carotid atherosclerosis in gout patients and its relation to MSK US manifestations and serum SCL levels.

Our findings support the usefulness of the US in determining crystal burden for predicting CV outcomes in gout patients. In our study, we found that sonographic MSU crystal deposition manifestations (such as DC signs, aggregates, tophi, and bone erosion) were associated with an increase in CIMT. Although there is a relationship between gout and CVD, the underlying mechanism is still unknown.

De Oliveira et al (2022) explained the two major causes likely underlying this CV risk: hyperuricemia and inflammation. However, the main suspect linking gout and CVDs is inflammation [21].

In agreement with our results, Calabuig et al (2021) revealed a significant association between subclinical inflammation and ultrasonographic crystal deposition and with carotid atherosclerosis in 103 gout patients [22].

In accordance with our results, Hammer et al. (2022) reported that increased MSU crystal deposition in gouty patients, as assessed by MSK US, was associated with increased inflammatory markers, increased CIMT, and the presence of atherosclerotic plaques suggesting that crystal depositions might be related to subclinical carotid atherosclerosis, as shown in our results [23].

The confirmed presence of deposits by MSK US, along with the increased CIMT recognized in this study, could permit an early ULT beginning when the diagnosis is ultimately established. However, other experts recommended delaying the beginning of ULT until reaching a certain severity of the disease [24].

Our study revealed that, in gout patients, serum SCL levels were significantly higher in patients with MSK US manifestations than in those without.

There are no prior studies establishing the relationship between MSK US manifestations and SCL levels in the study of various gout-related bone remodeling markers. However, Harre et al (2011) revealed that the tophus in gouty patients expresses cytokines linked to bone resorption, such as interleukin 1 (IL-1), and tumor necrosis factor α (TNF-α). These inflammatory cytokines in the tophus may encourage SCL production, hence promoting osteoclast differentiation [25].

We can determine the bone erosive effect of MSU crystals on the joints and blood vessels by measuring SCL in patients with gout via MSK US findings. Chhana et al (2016) revealed a possible role of SCL, RANKL, and OPG in facilitating bone erosion related to tophus [7].

Zou et al (2019) also reported that increased Dickkopf-1 (another WNT pathway inhibitor, SCL) and RANKL levels were associated with MSK US manifestations, such as DC and tophi, in gout patients, and these manifestations were alleviated by ULT. Consequently, MSK US may be a beneficial tool for evaluating bone remodeling and observing the response to treatment [9].

In our study, we found that there was no correlation between the serum SCL and CIMT in gout patients. In agreement with our study, some studies have found no correlation between serum SCL and CIMT in axial spondyloarthritis patients [26], in rheumatoid arthritis patients [27], or in the follow-up of the general population [28-29].

In contrast, some studies have shown a positive correlation between them in diabetic patients [30,31], while others have shown a negative correlation in chronic kidney disease patients [32] and with type 2 diabetic postmenopausal women [13].

The explanation of lacking the correlation in our study might be due to age, race, ethnicity, small sample size, study design, and analytical methods.

However, we found that patients with a serum SCL level >25.05 ng/ml had a statistically significant increase in CIMT >0.9 mm than patients with a SCL level ≤ 25.05 ng/ml.

This can be explained by the fact that SCL inhibits the β-catenin-dependent Wnt signaling pathway, which regulates many processes complicated in vascular calcification and atherosclerosis. It has a role in the migration and proliferation of VSMCs, endothelial dysfunction, and intimal thickening. It also facilitates the differentiation of progenitors and VSMCs into an osteo/chondrogenic phenotype. The resultant osteoblast-like cells enhance the activity of alkaline phosphatase, which induces the process of vascular tissue mineralization. Accordingly, SCL is considered an indicator of subclinical vascular diseases [33].

In contrast, many studies have shown that SCL may guard against the development of vascular complications as in patients with diabetes, probably by decreasing the β-catenin upregulation in the vascular cells [13].

In addition, in our study, we found that the longer the course of the disease was, the greater the CIMT was, indicating that the longer the disease course was, the more serious the degree of atherosclerosis was.

The current study has several strengths. This is the first study to assess the relationship between serum SCL level and carotid atherosclerosis with MSK US manifestations in gout patients. Moreover, by using the US to assess the joints and carotid arteries, we could reveal the subclinical characteristics of these patients. We were able to determine the SCL level at which the gout patients might be at risk of various MSK US manifestations and subclinical carotid atherosclerosis through further studies to determine whether the SCL can be used as a prognostic factor or not.

Limitations of this study include the small sample size and its cross-sectional design, which lead to an inadequate power to express potential causal relationships. Additionally, a single measurement for parameters, including inflammatory markers, serum SCL, MSK US, and carotid ultrasonographic variables was taken. These data may not exactly reveal changes in parameters over time or the consequence of cumulative burden associated with exposure time.

Recommendations of our study are first, screening for serum SCL is helpful in gout patients; second, the interventional studies to determine the effect of ULT on MSK US findings and accelerated atherosclerosis in gout patients are recommended. Last, lifestyle modifications such as exercise, quitting smoking, weight reduction, and control of hypertension help reduce complications of the disease and atherosclerosis.

CONCLUSIONS

Patients with MSK US manifestations of gout are more liable to have subclinical carotid atherosclerosis than patients without these manifestations. SCL at a certain level >25.05 ng/ml in gout patients might predispose patients to radiographic findings of MSK US of gout and subclinical atherosclerosis.

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