An ultrasound-based femoral artery calcification score

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ABSTRACT

Objective: Duplex ultrasound (US) of the lower extremities is commonly used to assess patients with lower extremity atherosclerosis. Arterial calcification can often be visualized in these images; however, efforts to quantify its extent have been limited. We, thus, sought to develop a new scoring system to measure calcification on duplex US studies of the femoral artery and correlate it with standard computed tomography (CT)-based methods. We then made preliminary attempts to correlate US-based femoral artery calcification scores with limb-specific outcomes in patients with peripheral arterial disease.

Methods: Patients who underwent CT evaluation of the lower extremities and arterial duplex US of either lower extremity within 6 months of each examination were included in the study. CT-based calcium scores of the femoral artery were generated using calcium scoring software. To determine the US score, five standard arterial segments (ie, common femoral artery, proximal superficial femoral artery [SFA], mid-SFA, distal SFA, and above the knee popliteal artery) were scored using a scale of 0 to 2 (0, a completely normal vessel segment; 1, a vessel with hyperechoic irregularities of the vessel wall; and 2, clear anechoic shadowing). The available scores were then averaged to yield a single femoral calcium score for each leg. Predictors of femoral calcification scores were then assessed and compared with the CT-based methods. The correlation between the US- and CT-based femoral calcification was assessed, and then the association between the US-based femoral calcification score and limb outcomes was evaluated.

Results: A total of 113 patients met the inclusion criteria and were included in the final analysis. US-based calcification scores were increased in patients with diabetes, renal failure, and the presence of chronic limb threatening ischemia similar to CT-based femoral calcification. The US- and CT-based calcification scores showed a moderate to strong correlation ($r = 0.64$). An elevated US-based femoral artery calcification score was associated with decreased amputation-free survival.

Conclusions: A novel US-based method shows promise as a simple method for quantifying the extent of femoral artery calcification in patients with peripheral arterial disease. The US-based method correlates with standard CT-based methods. Preliminary studies show that it could be useful for predicating outcomes for patients with peripheral arterial disease. (J Vasc Surg Cases Innov Tech 2024;10:101381.)

Keywords: Arterial calcification; Calcium scoring; Computed tomography angiography; Duplex ultrasound; Peripheral arterial disease

Arterial calcification is frequently seen on radiographs and computed tomography (CT) scans of the lower extremities as bright opacities within the vessel wall. When quantified, higher calcification levels are associated with an increased risk of major amputation and death and worse outcomes after endovascular interventions.[1-3] Documentation of the extent of calcification has recently been incorporated into the Global Limb Anatomic Staging System as a marker of increased amputation risk.[4,5] In addition, increased pedal artery calcium scores are associated with decreased healing potential.[4,5] The methods for assessing the extent of vascular calcification, however, remain cumbersome, typically involving the use of semiautomated algorithms based on non–contrast-enhanced CT scans or visual scoring of plain radiographs of the foot.[6,7] Such studies are not commonly used for serial surveillance of patients after endovascular or open intervention. In addition, although such methods can be useful, these limitations have prevented their widespread adoption.

One imaging method commonly used to assess the extent of occlusive disease in patients with peripheral arterial disease (PAD) is arterial duplex ultrasound (US).[8] The findings from the assessment of arteries using duplex US correlate highly with those from other imaging methods, including CT and digital subtraction angiography.[8,9] Duplex US provides both anatomic detail and hemodynamic information that can guide procedures without the use of radiation or iodinated contrast agents. Although evidence of calcification is commonly noted on routine US evaluations of lower extremity arteries, the development of robust methods for assessing its extent has been limited, and efforts to link US-based calcification scores with outcomes have not been undertaken.[8,10,11] We, thus, sought to develop a standardized method of quantifying calcification on routine US images of the femoropopliteal artery, assess its correlation with CT-based methods, and determine whether

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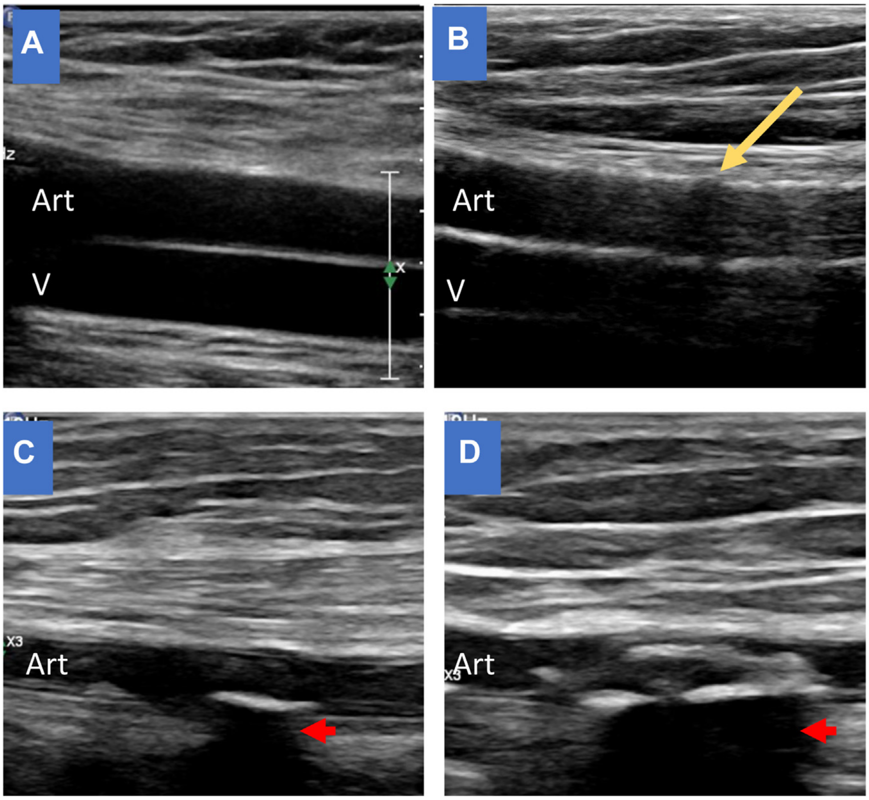


Fig 1. Ultrasound (US) images and scoring system for arterial calcification. **A,** Score of 0: US scan showing no echogenic shadowing or intimal irregularity. **B,** Score of 1: US scan showing discontinuous hyperechoic wall irregularities (*yellow arrow*). **C,D,** Score of 2: US images showing distinct anechoic shadowing (*red arrows*). *Art,* Artery; *V,* vein.

elevated US-based calcium scores correlate with poor limb outcomes similar to the correlation with CT-based calcium scoring methods.

METHODS

Patient population. Patients who underwent lower extremity arterial duplex US and CT angiography within 6 months of each examination were identified through a search of the medical records database under an institutional review board exempt protocol. The list of patients was generated by the institution's Joint Data Analytics Team through a search of all medical records between 2012 and 2020. The electronic medical records were reviewed for demographic and cardiovascular risk factors, including hypertension, renal disease, diabetes, hypercholesterolemia, smoking history, age, and sex. All patients underwent diagnostic imaging for known or suspected lower extremity arterial disease. Patients who had previously undergone lower extremity bypass procedures or amputations were excluded from further analysis.

US calcium scoring. To assess lower extremity calcification on arterial duplex US, we developed a visual scoring system. The femoropopliteal artery segment was divided into five regions: common femoral, proximal superficial femoral (SFA), mid-thigh SFA, distal SFA, and above the knee popliteal arteries. Using B-mode images in the longitudinal orientation, the arteries were assigned a score of 0 if no wall heterogeneity or anechoic shadowing was observed (Fig 1, *A*), a score of 1 if evidence was present of wall heterogeneity without anechoic shadowing (Fig 1, *B*), and a score of 2 if clear anechoic shadowing was present (Fig 1, *C and D*). The five US scores were then averaged to yield a single score between 0 and 2 for each femoropopliteal segment. Only imaging studies with at least three clearly visualized femoral segments were used for the present study.

CT calcium scoring. Quantification of calcification on non–contrast-enhanced CT scans was performed in a standard manner using calcium scoring software as previously reported.[1] To calculate the femoropopliteal calcium score, automated image analysis was performed using Syngo software (Siemens Healthineers) on virtual non–contrast-enhanced CT scans derived from images acquired using dual energy. On cross-sectional images through the lower extremities, areas of calcification along the femoropopliteal segment

Table I. Baseline characteristics of total patient population stratified by median ultrasound (US) calcium score

Characteristic	Total (n = 113)	US calcium score		*P* value
		Less than median (n = 56)	Greater than median (n = 57)	
US calcium score	1.14 (0-2.0)	0.27 (0-0.8)	1.4 (1-2)	NA
Age, years	67.7 ± 13.9	65.7 ± 14.7	69.7 ± 13.2	.18
Male sex	61 (54)	26 (48)	33 (58)	.44
Diabetes mellitus	71 (63)	26 (47)	43 (75)	.003[a]
Tobacco use	93 (82)	41 (75)	50 (88)	.09
HCL	85 (75)	35 (64)	48 (84)	.02[a]
HTN	97 (86)	44 (80)	51 (90)	.19
Renal disease	34 (30)	9 (17)	23 (40)	.01[a]
CLTI	66 (58)	31 (56)	35 (61)	.6

CLTI, Chronic limb threatening ischemia; *HCL*, hypercholesterolemia; *HTN*, hypertension; *NA*, not applicable.
Data presented as median (range), mean ± standard deviation, or number (%).
[a]Statistically significant.

with a cross-sectional area >1 mm^2 and a density of >130 Hounsfield units were identified automatically. Regions of interest along the artery segment were manually selected and labeled. Measurements were started at the top of the femoral head and ended at the tibial plateau. The calcium scores were determined according to the method described by Agatston et al.[12] The calcium values for each artery segment were summed to derive a single combined femoropopliteal calcium score. The laterality of the extremity was chosen by the availability of the US images. If bilateral US images were available, both extremities were scored, and the extremity with the higher calcium score was selected. For each patient, a single calcium score was derived for the entire vessel segment.

Follow-up. The outcomes were determined from a review of the medical records and included amputation and death. The outcomes were assessed at 6 months and 1 year after the US examination was performed based on patient follow-up in the outpatient setting and a review of the medical records.

Statistical analysis. The demographic and cardiovascular risk factor data for the patient population are expressed as the mean ± standard deviation or numbers and percentages. The US- and CT-based calcium scores are expressed as the median and range. Correlations between the US- and CT-based scoring were calculated using GraphPad software (GraphPad Software Inc). Receiver operating characteristic curves were generated to identify the inflection points in the US-based scoring. Interobserver agreement in the US-based calcium scores was calculated using correlation analysis in GraphPad. Logistic regression was performed using dichotomized US and CT scores to assess how these variables predicted for major amputation and death.

RESULTS

A total of 113 patients met the inclusion criteria and were included in the analysis. The average age for the total population was 67.7 years, and 54% were men. The average US-based calcification score for this population of patients with PAD was 1.14 ± 0.35 (range, 0-2; median, 1.2). Compared with the patients with US-based femoropopliteal calcification scores in the bottom half of the study population, those in the top half were more likely to have diabetes, hyperlipidemia, or renal disease. However, age, male sex, and hypertension were not different between the two groups. Tobacco use was greater for the patients with higher US-based calcium scores. However, the difference did not reach statistical significance ($P = .09$; Table I).

The average CT-based calcification score was 2259 ± 3008 (range, 0-14,632; median, 1077). Similar to US-based scoring, the patients with CT-based femoropopliteal calcification scores in the upper half were more likely to have diabetes, hyperlipidemia, and renal disease, although age, male sex, and hypertension were not different between the two groups. Tobacco use again showed a trend toward a greater prevalence in the top half of the study population, and this approached, but did not reach, statistical significance (Table II).

We next sought to determine whether our US-based scoring system correlated with standard the CT-based scoring methods. We first tested whether our scoring system could be used consistently between investigators. For 22 randomly selected scans, the interobserver variability between two investigators was assessed using Spearman's correlation, which demonstrated a high degree of agreement. The Spearman correlation coefficient was 0.92 ($P < .0001$. We next plotted the US-based femoropopliteal calcification scores vs CT-based femoropopliteal calcification scores and found a moderate correlation ($r = 0.64$; Fig 2).

Table II. Baseline characteristics of patients stratified by median computed tomography (CT)-based calcium score

Characteristic	CT calcium score		*P* value
	Less than median (n = 56)	Greater than median (n = 57)	
CT calcium score	272 (0-1024)	4330 (1116-14,631)	NA
Age, years	64.9 ± 12.6	70.5 ± 13.2	.13
Male sex	27 (48)	32 (56)	.5
Diabetes mellitus	26 (46)	43 (75)	.02[a]
Tobacco use	41 (73)	50 (88)	.06
HCL	36 (65)	49 (86)	.001[a]
HTN	44 (79)	51 (89)	.1
Renal disease	8 (14)	24 (42)	.002[a]
CLTI	30 (54)	36 (63)	.3

CLTI, Chronic limb threatening ischemia; *HCL,* hypercholesterolemia; *HTN,* hypertension; *NA,* not applicable.
Data presented as median (range), mean ± standard deviation, or number (%).
[a]Statistically significant.

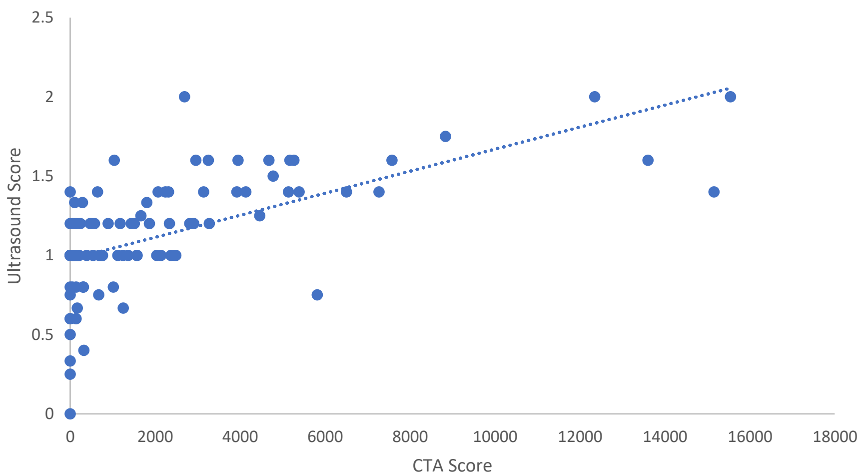


Fig 2. Correlation between computed tomography (CT)-based and ultrasound (US)-based femoropopliteal calcification scores. The correlation was moderately strong between the two scores ($r = 0.64$). *CTA,* Computed tomography angiography.

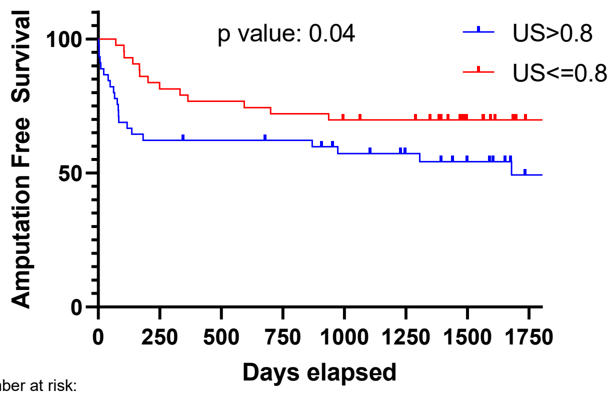
We also performed Kaplan-Meier analysis to determine whether patients with increased US calcium scores had an increased risk of amputation or death. The Kaplan-Meier analysis demonstrated that patients with US calcium scores >0.8 had worse amputation-free survival ($P = .04$; Fig 3).

To determine whether other factors could play a role in predicting for amputation-free-survival, we studied 100 patients with 6-month follow-up data documented in their medical records. An unadjusted, univariable analysis revealed that only a calcium score >0.8 predicted for amputation (odds ratio, 3.4; 95% confidence interval, 1.2-10.5; $P = .04$). Diabetes, tobacco use, hyperlipidemia, hypertension, and renal disease were not associated with amputation-free survival at 6 months (Table III).

DISCUSSION

In this preliminary study, we demonstrate that an US-based scoring system for femoral artery calcification is moderately correlated with standard CT-based methods. It can be performed on routine arterial duplex US studies, and higher scores are associated with increased amputation or death for patients with PAD. Future efforts to integrate calcium scoring systems into patient care pathways could allow for more personalized decision making for patients with PAD.

Prior efforts to quantify lower extremity calcification have involved visual assessment of plan radiographs or quantified scoring of CT using dedicated algorithms.[1,13,14] Although these methods have proved reliable, neither is used routinely in the care of patients with lower extremity occlusive disease. Duplex US is not only used for initial



Number at risk:

US<=0.8	43	36	34	32	30	29	19	12
US>0.8	45	29	28	27	23	20	16	10

Fig 3. Kaplan-Meier analysis results of amputation-free survival for patients with ultrasound (US)-based scores >0.8 compared with patients with US-based scores of ≤0.8.

Table III. Unadjusted odds ratios for major amputation or death stratified by risk factor and ultrasound (US) calcium score at 6 months

Variable	OR (95% CI)	*P* value
Diabetes mellitus	1.9 (0.7-6.5)	.3
Tobacco use	1.4 (0.4-6.7)	.8
HCL	1.9 (0.5-8.7)	.5
HTN	2.1 (0.3-41)	.8
Renal disease	2.0 (0.7-5.5)	.3
US calcium score >0.8	3.4 (1.2-10.5)	.04[a]
US calcium score ≥1.4	3.8 (1.3-10.9)	.06

CI, Confidence interval; *HCL,* hypercholesterolemia; *HTN,* hypertension; *OR,* odds ratio.
[a]Statistically significant.

assessment but also for interval surveillance and long-term follow-up of patients after lower extremity endovascular interventions, making it an ideal method for quantifying femoral calcification over time. Previously, Okuno et al[15] described an angiogram-based femoral calcium score that relies on measuring the length of calcification >5 or <5 cm and involvement of one or both sides of the artery wall. The method can predict the loss of patency after endovascular femoropopliteal interventions.[15] Several groups have reported on US-based methods to specifically quantify medial artery calcification. Although these methods have not been correlated with CT-based calcium scores, they appear to correlate with radiograph-based medial calcification and predict for complications in patients with diabetes. Such methods require consistent US imaging approaches with standardized protocols, and we were unable to confirm the interobserver reproducibility of such efforts.[7,10]

The present scoring system evolved during the course of the study owing to a lack of correlation when using more finely adjusted scales. Our original method involved scoring vessels for calcification using a 0 to 4 scale. However, the interobserver variation was high and ambiguity was present in the middle of the scale, resulting in poor reproducibility. A binary 0 to 1 scoring system was also evaluated; however, this did not provide sufficient differentiation between patients with mild vs extensive calcification. Thus, the correlation with CT scores was poor. The final scoring system involving a 0 to 2 scale averaged for five sections of artery proved more reproducible and allowed for greater correlation with CT-based calcium scores. Our current study involves a small cohort of 100 patients, and although all risk factors showed a positive correlation with poor outcomes, only US-based femoral calcium scores >0.8 showed statistical significance in predicting amputation or death at 6 months.

The present study has several limitations that suggest methods to improve future calcium scoring using US. First, US scans were not obtained using a standard protocol; thus, not all arterial segments could be assessed in each leg. Future efforts to standardized scanning protocols could decreased variability and improve the correlation with CT-based methods. Only patients with at least three visualized segments were used in this study. The risk factors for increased US femoral artery calcification were similar to those for CT-based methods, suggesting that the systems can be used interchangeably. However, our analysis only showed a moderate correlation with CT-based calcium scoring, and further methods to refine the scoring system are warranted. It is likely that low levels of medial calcification, typically scored as "1" on US are more easily identified on CT, and this will be a limitation of these methods. We have not attempted to correlate the extent of calcification with the amount of occlusive disease, and it is possible, if not likely, that the relationship between higher femoral calcium scores and worse outcomes could be due to this. Femoral calcium could be serving as a surrogate marker for the extent of occlusive disease in this segment; however, prior work from several groups, including our own, has suggested that the effects of calcification on poor outcomes are independent of the atherosclerotic burden. Future work to define the individual contributions and relationships between atherosclerotic plaque, femoral calcification, and limb events is warranted. In the present study, we did not assess tibial or pedal calcification. Future efforts will investigate the comparative effects of calcium scores in each of these regions with outcomes. Finally, a much larger study population will be needed to accurately assess the predicative value of calcification on the long-term outcomes of patients with PAD.

Duplex US imaging can be limited by many factors, including physician or technician expertise and patient body habitus. In the present study, there was variability in US imaging and some views were of higher quality than others, leading to possible inaccuracies in scoring. In US views with poor depth or technique, it is difficult to distinguish artifact from true anechoic shadowing. Such discrepancies would likely be improved with a standardized US protocol performed by skilled ultrasonographers. The results of the present study could also have been influenced by the specific patient population, because only those patients with more significant lower extremity arterial disease would be likely to undergo both CT angiography and lower extremity arterial duplex US within 6 months of each imaging study. Additionally, we did not assess the WIfI (wound, ischemia, foot infection) score and, thus, were unable to include the score in our statistical analysis.

CONCLUSIONS

We have developed a standardized scoring system for femoral artery calcification based on duplex US. The method correlates moderately with CT-based methods, and our preliminary analysis suggests that it can predict for poor outcomes for patients with PAD. Future work to standardize femoral imaging protocols for calcium scoring are needed, as are larger and longer term studies to assess its applicability in our PAD patient population.

DISCLOSURES

None.

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