Tibial scoring as a predictor for amputation-free survival in critical limb ischemic patients

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Background/aim
Evaluating the risk of amputation in patients with peripheral arterial disease (PAD) is essential. A critical Limb Ischemic patient (CLI) is known as end stage of PAD. Creating novel approaches to pinpoint high-risk patients would allow for targeted treatments and support specialized clinical trials focused on limb preservation. This study's objective is to evaluate tibial adversity and scoring for risk of lower extremity amputation in critical limb ischemic patients (CLI).
Patients and methods
This study is a prospective study carried out on 30 patients with symptomatic lower extremity PAD in Al-Zahraa University Hospital from February 2023 to January 2024 interval. All patients were assessed by hemodynamics study and multislice noncontrast CT and tibial angioplasty according to inclusion and exclusion criteria. The patients followed up at day 1 and 3 and 6 months.
Results
Patients with CLI exhibited significant high ($p < 0.05$) tibial artery calcification scores, which were linked to increased limb ischemia levels, with high risk for amputation compared to traditional risk factors. 26 patients were amputation free rate and only 4 patients were done major amputation. Nonmodifiable risk factors correlated with elevated tibial artery calcification scores.
Conclusions
The present study indicated that tibial scoring independently predicts the risk of lower extremity amputation, even when considering other risk factors in patient with CLI. Increasing calcium scores are associated with greater PAD severity.

Keywords:
Tibial, artery, calcification, critical, limb, ischemia

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Introduction

Peripheral artery disease (PAD) is one of the most common atherosclerotic morbidities worldwide, surpassed only by coronary artery and cerebrovascular disease. Symptomatic PAD in the lower limb presents as either intermittent claudication or critical limb ischemia (CLI) [1].

CLI is defined by ongoing rest pain lasting a minimum of 14 days and/or the presence of tissue damage, such as ulcers or gangrene, in the lower extremities. This condition is both limb-threatening and potentially life-threatening, representing the advanced stage of PAD and affecting about 10% of PAD patients. CLI is associated with a grim prognosis, with only half of the patients managing to preserve their limbs within a year of diagnosis [1]. Numerous studies have employed various devices to address the significant challenge posed by calcium presence. Atherectomy devices, scoring, and cutting balloons have been used to enhance outcomes and patency rates but with limited success [2].

The tibial artery calcification (TAC) score measures the amount of plaque – a mix of fat and calcium – within the tibial artery. This plaque, a waxy substance, does not directly appear in computed tomography (CT) scans. However, over time, calcium deposits leave detectable traces inside the artery [3]. The innermost layer of the artery becomes calcified and this can be identified by CT scans in a manner similar to how radiographs reveal bones [4].

Plaque buildup can obstruct arteries, slowing blood flow and preventing adequate oxygen levels from reaching certain areas of the heart. Moreover plaque deposits can also lead to blood clots, potentially triggering heart attacks [5]. The coronary artery calcification score provides an indirect measure of plaque burden in the coronary arteries, making calcium scoring a valuable tool for predicting the likelihood of future heart attacks, strokes, and PAD [6].

This study aims to evaluate compound tibial adversity and risk stratification for CLI patients undergoing endovascular revascularization. The goal is to maintain patency rates and reduce the risk of major lower extremity amputations, which are associated with significant morbidity and mortality.

Patients and methods

Patients

The present study enrolled 30 patients with CLI. The patients were recruited from the Vascular Clinics of Al-Zahraa University Hospital from February 2023 to January 2024. All patients were assessed using a hemodynamics study and multislice noncontrast CT and tibial angioplasty according to inclusion and exclusion criteria. The patients followed up at day 1 and 3 and 6 months.

Inclusion criteria

Patients aged 20–80, with hyperlipidemia, smokers, Rutherford 4–5 criteria, type 3 diabetes and good femoral pulse.

Exclusion criteria

Patients under 20, those with iliac and SFA lesions, long lesions requiring bypass, congestive heart failure, Rutherford 6 criteria, type 2 diabetes, and chronic renal disease with creatinine levels above 1.7.

Ethical approval

The study followed the Declaration of Helsinki principles and received approval from the Ethical Committee of the Faculty of Medicine at Al-Azhar University in Cairo, Egypt, under approval number 1503/2023. Informed written consent was obtained from each participant before they were included in the study.

Methods

All patients underwent tibial balloon angioplasty, and TAC was measured by noncontrast CT. Patient outcomes were assessed presurgery and on the first day, 3 and 6 months postsurgery.

Clinical assessment

Patients were evaluated and grouped based on PAD symptoms such as claudication, rest pain due to ischemia, and ulcers. A comprehensive medical history was recorded, focusing on vascular risk factors like smoking, hyperlipidemia, hypertension, and diabetes. Pulse examinations and noninvasive arterial Doppler tests were performed. The results from physical examinations and Doppler tests were used to classify the degree of limb ischemia according to the Rutherford criteria.

Laboratory investigations

Venous blood samples were drawn from the participants in the morning after a fasting period of about 12 h. Laboratory tests were applied by the Laboratory Unit of Al-Zahraa University Hospital to assess fasting blood glucose, Glycated hemoglobin (HbA1C), serum cholesterol, triglycerides, urea and creatinine. Diabetic was considered according to fasting blood glucose level of more than 110 mg/dl and HbA1C of more than 7%. Hyperlipidemia was considered according to the significant increases in levels of total cholesterol and triglycerides with levels greater than 240 mg/dl [7]. Renal patients with creatinine levels between 1 and 1.7 mg/dl were included in the study, while patients greater than 1.7 mg/dl and blood urea level above 100 mg/dl were excluded from our study [8].

Cardiac assessment

Cardiac patients were assessed by ECG and echocardiography in 2B mode (Mindray, Shenzhen, China), ejection fraction (EF) (55–70%). Ischemic Heart disease (IHD) and congestive heart failure (CHF) patients with EF<30 %, were not fit for surgery and were excluded from our study [9].

Noncontrast computed tomography imaging

Patients underwent noncontrast CT scans of the lower limbs using a single 16-slice CT scanner. Calibration was performed before surgery and again on the first day after surgery, as well as at 3 and 6 months, following standardized protocols. These scans utilized the MX8000 IDT from Philips Medical, Cleveland, Ohio, USA.

Tibial artery calcium scoring

Calcium scoring was conducted using specialized software that analyzed cross-sectional images of the lower limbs to identify calcified areas in the tibial arteries. The regions examined included the infrapatellar area, distal popliteal, anterior tibial, posterior tibial, and peroneal arteries. Measurements began at the base of the patella and extended to the widest part of the tibial and fibular malleoli at the ankle, covering the lower half of the popliteal artery and the full length of the three tibial arteries. The calcium scores from these regions were aggregated to produce a single TAC score for each patient. TAC scores above 400 indicated a high risk for amputation and cardiovascular disease, scores between 101 and 400 indicated moderate risk, and scores between 0 and 100 indicated mild risk.

Follow-up protocol

Patient outcomes were assessed through interviews conducted during regular clinical follow-ups. Patients with CLI were monitored at least once a month until their symptoms resolved, complete healing occurred, or amputation was required. Additional data were collected from institutional board chart reviews and follow-up surveys conducted by phone. Follow-up evaluations were conducted on the first day postsurgery and at 3 and 6 months.

Sample size calculation

The sample size was estimated owing to an earlier study as references by Das and Mitra [10] and Kaplan *et al.* [11]. Accordingly, the minimal permissible sample size for each test is 10 specimens as the effect size was 1.92 with 80% power and 0.05 type I error probability. The independent *t* test was accomplished by using P.S. power 842.

Statistical analysis

Data analysis was performed using SPSS, version 23.0 (SPSS inc: Chicago, Illinios, USA). Quantitative data were expressed as mean±SD and ranges for parametric distributions and compared using an independent *t* test between two groups and an analysis of variance test between more than two groups. Qualitative variables were presented as counts and percentages and compared using χ^2 test. The normality of the data was evaluated using the Kolmogorov–Smirnov and Shapiro–Wilk tests. A *P* value of less than 0.05 was considered statistically significant.

Results

The data presented in Table 1 demonstrates that there is an insignificant difference in the amputation-free rate compared to the nonamputation rate according to the Rutherford criteria 5, with a *P* value greater than 0.05, using the independent *t* test.

Table 2 shows that the highest mean value of duplex ultrasound measurements is observed in amputation-free patients compared to those who underwent amputation in pre and post 1 day, 3 and 6 months of operation with a *P* value less than 0.001.

Table 3 indicates a significantly higher frequency of patients achieving amputation-free status compared to those who underwent amputation, based on CT angiography after 6 months postoperative, with a *P* value less than 0.001, using χ^2 test, while insignificant changes were recorded in CT angiography preoperative.

According to ankle peak systolic velocity measurements, there is a significant difference

Table 1 Comparison between amputation-free rate and nonamputation according to Rutherford criteria 5 in all patients

	Amputation-free rate		
Rutherford criteria 5	Free (*N*=26)	Non (*N*=4)	*P* value
Mean±SD	4.27±0.78	3.50±0.58	0.069
Range	3-5	3-4	

Insignificant difference at *P* value more than 0.05, using independent *t* test

Table 2 Comparison between amputation-free rate and nonamputation at different time intervals after 1 day, 3 and 6 months according to duplex

Duplex (cm/sec)	Mean±SD	Range
Preoperative	$37.53±4.99^{a}$	28–45
Postoperative D1	$46.70±7.21^{b}$	31–58
Postoperative M3	$47.43±7.58^{b}$	30–56
Postoperative M6	$46.77±7.75^{b}$	30–59

All data with a different superscript letters (a, b) in the same column were significantly changed at *P* value less than 0.05, using analysis of variance test.

Table 3 Comparison between amputation-free rate and nonamputation according to computed tomography angio in preoperative and post 6 months of operative

	Amputation-free rate		
CT angio	Free (*N*=26)	Non (*N*=4)	*P* value
CT angio pre			
ATA	11 (42.3)	1 (25.0)	0.158
ATA and PTA	3 (11.5)	2 (50.0)	
PTA	12 (46.2)	1 (25.0)	
CT angio post (6 months)			
Occluded	0	1 (25.0)	0.000*
Occluded PTA	1 (3.8)	2 (50.0)	
Patent	25 (96.2)	1 (25.0)	

*Significant difference at *P* value less than 0.05, using χ^2 test.

Table 4 Comparison between preoperative and postoperative according to ankle peak systolic velocity in all patients

APSV (cm/sec)	Preoperative	Postoperative (6 months)	*P* value
Mean±SD	0.52±0.09	0.64±0.08	0.046*
Range	0.4–0.7	0.5–0.8	

APSV, ankle peak systolic velocity. *Significant difference at *P* value less than 0.05, using independent *t* test.

Table 5 Comparison between amputation-free rate and nonamputation according to calcium scoring in preoperative and postoperative at day 1, 3 and 6 months

	Amputation-free rate		
Calcium scoring (HU)	Free (*N*=26)	Non (*N*=4)	*P* value
Preoperative			
Mean±SD	38.81±4.01	29.25±0.96	0.001*
Range	30–45	28–30	
Postoperative D1			
Mean±SD	48.92±4.66	32.25±0.96	0.001*
Range	41–58	31–33	
Postoperative M3			
Mean±SD	49.92±4.26	31.25±0.96	0.001*
Range	44–56	30–32	
Postoperative M6			
Mean±SD	49.23±4.71	30.75±0.96	0.001*
Range	41–59	30–32	
Amount of change			
Mean±SD	10.42±2.37	1.50±0.58	0.001*
Range	3–14	1–2	

HU, Hounsfield unit. *Significant difference at *P* value less than 0.05, using independent *t* test.

between preoperative and postoperative, as shown in Table 4, with a *P* value greater than 0.05, using an independent *t* test.

Table 5 reveals the highest mean value of calcium scoring in patients who are amputation-free compared to those who are not with a *P* value less than 0.001 in preoperative and postoperative at day 1 and 3 and 6 months, using independent *t* test. This suggests that calcium scoring is a predictor of amputation-free survival in patients with CLI.

Kaplan–Meier analysis of our data, conducted over a follow-up period of 6 months with a mean observation time of 5.77 months (95% confidence interval: 5.53–6.00), reveals that the cumulative overall survival rate at 6 months for amputation-free patients with CLI was 86.7%, while the amputation rate was 13.3%, as illustrated in Fig. 1.

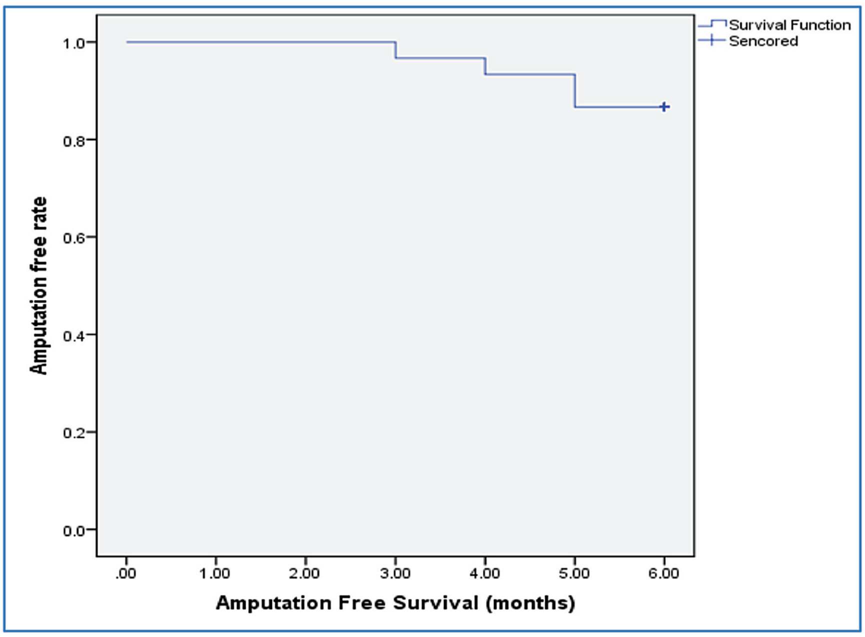
Figure 2 shows noncontrasted multislice CT showing a patient without calcification (a) and with significant TAC (b). Arrows identify calcified tibial arteries. TAC is strongly associated with the stage of lower extremity vascular disease and the near-term risk of major amputation.

Figure 3 shows representative cases of minimal (a), intermediate (b), and extensive (c) TAC. Patients with minimal tibial calcification did not require amputation, while one in seven patients presenting with ischemic symptoms and moderate and extensive calcification underwent major amputation.

Discussion

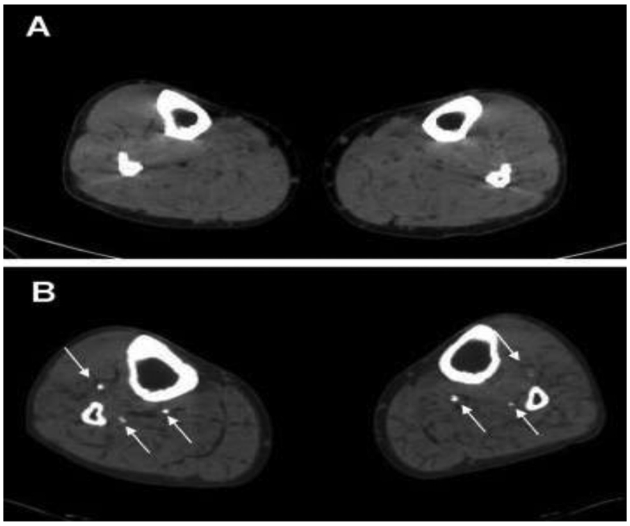
The present study aims to evaluate compound tibial adversity and risk stratification for CLI patients undergoing endovascular revascularization. Moreover, to maintain patency rates and reduce the risk of major lower extremity amputations, which are associated with significant morbidity and mortality. However, the present study demonstrates that multislice noncontrast CT scans are highly effective

Figure 1



Kaplan–Meier curve showing amputation-free survival in critical limb ischemic patients.

Figure 2



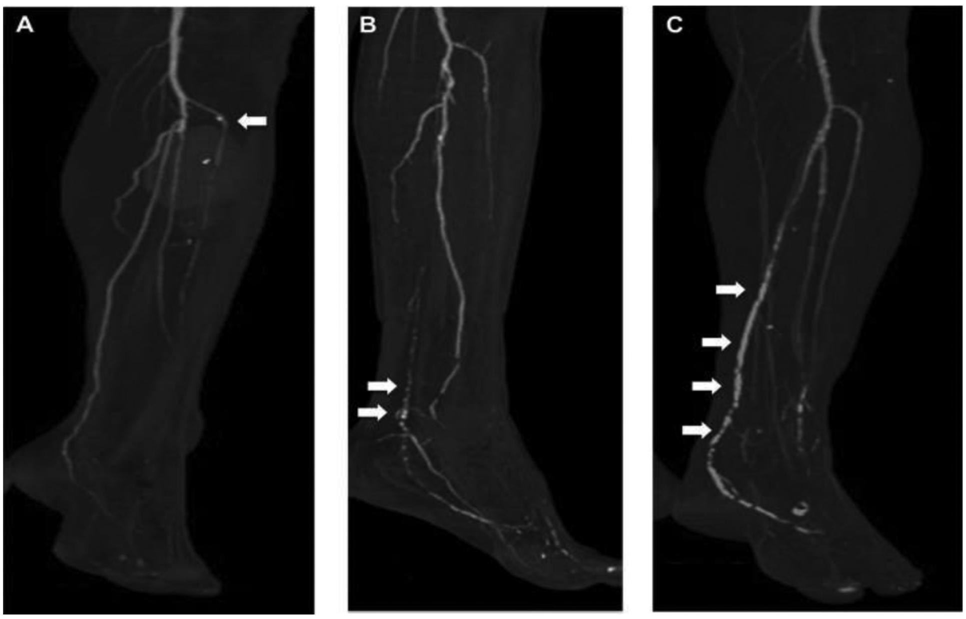
Noncontrasted multislice computed tomography showing a patient without calcification (a) and with significant tibial artery calcification (b). Arrows identify calcified tibial arteries.

in measuring the amount of calcification in the tibial arteries, which are the arteries in the lower legs. This measurement is referred to as the TAC score. Moreover, the higher TAC scores are strongly linked to more severe vascular disease in the lower extremities and a greater near-term risk of major amputation. This association remains significant even after considering traditional risk factors and the ankle–brachial index (ABI), which is a common but indirect measure of blood flow to the feet. Notably, none of the patients without tibial calcification required an amputation, whereas, among patients with ischemic symptoms and TAC score near 400, one in seven underwent major amputation. This suggests that measuring tibial artery calcium could be crucial for identifying patients at different levels of risk and tailoring treatments specifically to help preserve their limbs [12].

On the other hand, while an abnormal ABI can predict the likelihood of death from all causes and cardiovascular-specific issues, it does not correlate well with the symptoms patients experience. It can also provide misleading results, particularly in patients with calcified vessels, such as those with diabetes. Moreover, the ABI is not a reliable indicator of whether a forefoot amputation will heal properly. Our findings imply that the TAC score could be especially beneficial for patients who already have known vascular disease. It might offer a more precise tool for assessing risk in these patients. For instance, patients with low or normal TAC scores might be safely managed with standard medical treatments, while those with higher TAC scores might need more intensive medical therapy, custom footwear, and more frequent foot examinations. This scoring system could also be very useful in selecting participants for clinical trials that aim to prevent amputation [13].

To align with methods used for scoring coronary calcium, we did not differentiate between intimal and medial calcification. While some studies suggest

Figure 3



Representative cases of minimal (a), intermediate (b), and extensive (c) tibial artery calcification (TAC). The arrows indicate calcification.

that medial calcification is a stronger predictor of cardiovascular events than intimal calcification, our inability to distinguish between these types did not diminish the predictive power of the TAC score. However, comparing a total calcification score with one focused solely on medial calcification could provide further insights into the pathophysiological significance of these different types of calcification [14,15].

The progression of CLI is not well understood. Traditionally, it was thought that PAD progresses linearly from mild claudication (pain during walking) to severe claudication, then to rest pain, and finally to ulceration or tissue loss. However, recent observations suggest that many patients with CLI do not follow this sequential progression. Prior studies indicate that more than half of CLI patients were asymptomatic 6 months before their diagnosis, suggesting a rapid progression for many [16].

Our data support this finding, revealing that many patients with high TAC scores showed minimal symptoms of lower extremity vascular disease. This indicates that high TAC scores could be present even in patients who do not yet exhibit severe symptoms. Therefore, further research is needed to determine if these patients with high TAC scores and minimal symptoms are at a greater risk of developing CLI.

Additionally, our study assessed various limb salvage efforts, such as endovascular revascularization, wound care, and other treatments provided to patients. It is important to note that the TAC scores were not known to the physicians who recommended amputation, meaning these scores did not influence their clinical decisions [17].

Conclusion

Patients with CLI have high mortality rates and face a significant risk of lower extremity amputation. Increasing calcium scores are associated with greater PAD severity. The TAC score independently predicts the risk of lower extremity amputation, even when considering other risk factors.

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Conflicts of interest

There are no conflicts of interest.

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