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CLINICAL INVESTIGATION ARTERIAL INTERVENTIONS

Prediction of Limb Salvage Following Percutaneous Vascular Intervention Using a Composite Tibial Artery Perfusion Score

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Abstract
Purpose To assess a novel tibial artery perfusion score (TPS) for predicting limb salvage in critical limb ischemia (CLI) patients undergoing percutaneous vascular intervention (PVI).
Patients and Methods A consecutive cohort of 115 CLI patients undergoing PVI in 144 limbs from 2011 to 2016 was analyzed. TPS comprised a 27-point scale based on: (1) patent tibial vessels following PVI, (2) severity of calcification of the tibial arteries, (3) presence of an intact pedal arch following intervention, (4) whether or not revascularization was direct or indirect based on the target angiosome, (5) presence of angiosome blush at the completion of index intervention. Limbs were stratified into (1) High [21–27 points], (2) Medium [13–20 points], and (3) Low [0–12 points] TPS. Predictive value of TPS was evaluated using logistic regression and Cox proportional hazards models.
Results The median follow-up was 15.7 months (range 0.4–69.9 months). Limb salvage in High, Medium, and Low TPS groups was 90.6%, 85.9%, and 55.6%, respectively, as freedom from the composite outcome: (1) limb complication resulting in death, (2) tibial bypass surgery, (3) above-the-knee amputation, or (4) below-the-knee amputation in patients without supratibial disease at the time of PVI. TPS was significantly associated with limb salvage defined as freedom from both the composite outcome and major amputation.
Conclusions Based on this preliminary investigation, TPS was associated with limb salvage in CLI limbs, particularly in high-risk limbs. Further validation in a prospective cohort may identify patients with high-risk limbs in need of closer surveillance and earlier reintervention.
Level of Evidence Level IV, case series.

Keywords Tibial artery perfusion score (TPS) · Limb ischemia · High-risk population · Vascular intervention

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Introduction

The annual incidence of peripheral arterial disease (PAD) is estimated to be 2–3%, affecting more than 200 million people worldwide [1, 2]. Approximately 11% of patients with PAD develop critical limb ischemia (CLI), which has an incidence rate of 0.3–0.4% per year [1, 2]. CLI represents the most severe form of PAD and is associated with a high risk of amputation or death [3, 4]. The 1-year survival can be as low as 75%, and 25% of those who survived will require major amputation [5]. The 5-year survival for CLI patients is only 40–50% [6–11].

Endovascular or surgical revascularization remains the only reliable way for limb salvage for patients with CLI [12, 13]. In the recent years, endovascular techniques for treating CLI have improved significantly and have been increasingly used as a first-line strategy for treating an increasing number of CLI patients [4, 14, 15]. However, the extent to which angiographic increases in tibial blood flow improve wound healing and limb salvage is incompletely understood [4, 16]. More importantly, no current classification system relies entirely on intra- or perioperative parameters to stratify prognosis for CLI patients undergoing endovascular revascularization [16].

The purpose of this study was to assess a novel composite tibial artery perfusion score (TPS) for predicting limb salvage rates in CLI patients undergoing percutaneous vascular intervention (PVI), using parameters which are intended to be readily obtainable at the time of percutaneous revascularization.

Materials and Methods

Patient Selection

The study was conducted after institutional review board approval and was in compliance with the Health Insurance Portability and Accountability Act. Patients were identified using the division's quality improvement database (HI-IQ; Conexsys, Inc, Lincoln, Rhode Island). Patients with CLI who underwent PVI interventions by interventional radiology were identified over a 5-year period (2011–2016). PVI included tibial angioplasty, with additional stent and/or atherectomy when failure of angioplasty occurred. The indication for tibial intervention is $>$ 50% stenosis in the infragenicular vessels. Failure of angioplasty was defined as occlusive dissection flap or $>$ 30% residual stenosis. Tibial stents and tibial atherectomy were used in a highly selective fashion. We used short (28–35 mm) everolimus-eluting stents (Abbott Vascular, Santa Clara, CA) (diameters 3.0–3.5 mm) as a bail-out strategy when failure of angioplasty occurred in the proximal tibial regions such as the tibioperoneal trunk (7/144 limbs). This bail-out strategy was seldom used. We used orbital atherectomy (1.25 mm microcrown, Cardiovascular Systems Inc., Minneapolis, MN) selectively when patients with heavily calcified tibial arteries failed angioplasty or required target lesion revascularization within 3 months for restenosis (4/144 limbs). We did not use drug-eluting balloons in the tibial vessels as there were not available at the time of the study. Direct revascularization was always attempted first leaving indirect revascularization as a second option after unsuccessful attempt at direct revascularization. However, attention was always prioritized to the vessel supplying the angiosome where the patient harbors the wound. The goal was not to revascularize as many tibial vessels as possible but to create sufficient blood supply to the foot to achieve limb salvage. For example, if a foot could be well perfused by creating two vessel runoff, our practice was not to attempt to revascularize a third tibial vessel. Hemodynamically significant ($>$ 50% stenosis) proximal disease (aortoiliac and/or femoropopliteal) was also treated with PVI concurrent to the tibial revascularization procedure. Patients who underwent isolated aortoiliac and/or femoropopliteal interventions were excluded.

Calculation of Tibial Perfusion Score

To derive TPS, point allocation was performed through a series of scatter plots (not shown) with each domain and points assigned according to optimal distributions to enable discrimination between limbs. The results of these iterative scatter plots led to TPS being calculated on a 27-point scale based on: (1) number of patent tibial arteries following intervention (0–8 pts), (2) severity of calcification of the tibial arteries (0–7 pts), (3) presence of an intact pedal arch following intervention (0–4 pts), (4) whether or not revascularization was direct or indirect based on the target angiosome (0–4 pts), (5) presence of angiosome blush during PVI (0–4 pts). Calcification of the tibial arteries was assessed on frontal, ipsilateral oblique and lateral views routinely acquired during the procedure. Assessment of pedal arch patency was made a binary decision (patent versus not) due to our goal to derive the most parsimonious model. The scoring criteria for each category of the TPS are illustrated in Table 1. Limbs were stratified into three prognostic groups based on TPS: (1) High (21–27 points), (2) Medium (13–20 points), and (3) Low (0–12 points). The cutoff values for the different TPS categories were chosen based on plotting percentage of patients reaching outcomes on the y-axis and TPS score on the x-axis (Supplementary Figure 1). Tibial artery patency (TAP) was scored as High (3 vessels patent), Medium (2 vessels patent), and Low (0–1 vessel patent).

Outcomes

Limb salvage was defined as freedom from a composite outcome (CO): (1) limb complication resulting in death, (2) tibial bypass surgery, (3) above-the-knee amputation, or (4) below-the-knee amputation following intervention in cases where supratibial disease was absent at the time of intervention. Intervention was deemed a clinical success if none of the above criteria was met. Limb complication resulting

Table 1 Tibial artery perfusion score (TPS) classification system

Category	Score	Description
Number of patent tibial arteries following intervention	8	3 tibial arteries fully intact
	7	2 tibial arteries fully intact
	5	1 tibial artery fully intact
	0	0 tibial arteries fully intact
Tibial artery calcification	7	No fluoroscopically visible tibial calcification
	5	Calcification confined to one side of tibial vessel and discontinuous
	3	Circumferential but discontinuous calcification
	0	Circumferential, continuous calcification
Presence of intact pedal arch following intervention	4	Presence of intact pedal arch following intervention
	0	Absence of intact pedal arch following intervention
Percutaneous revascularization technique	4	Direct percutaneous revascularization
	0	Indirect percutaneous revascularization
Presence of angiosome blush during intervention	4	Presence of angiosome blush during intervention
	0	Absence of angiosome blush during intervention

in death was only counted as an event when the death directly resulted from a limb complication. Criterion (4) of the CO was limited to cases where supratibial disease was absent at the time of intervention because patients with supratibial disease who would otherwise have undergone an above-the-knee amputation but instead received a below-the-knee amputation after intervention were considered success rather than failure. In addition, two secondary outcomes defining limb salvage were also evaluated: freedom from major amputation (satisfaction of criteria 3 and 4 above) and target vessel revascularization (TLR). All patients were seen within 2 weeks of PVI in the interventional radiology clinic. Primary unassisted patency was assessed on duplex ultrasound at follow-up or repeat angiography during subsequent interventions. Our postoperative care includes antiplatelet medication for 3 months if a stent was placed and statin/beta blocker/ACE inhibitor therapy in perpetuity. Patients were followed at 3-month intervals for the 1st year after PVI and 6-month intervals thereafter. Duplex ultrasound was performed at each visit with selective use of pulse volume recordings.

Statistical Analysis

Calculation of percentages, means, ranges were performed on the data using spreadsheet software (Excel 2010; Microsoft, Redmond, Washington). Logistic regression and Cox proportional hazards model were performed to assess the efficacy of TPS and TAP in predicting limb salvage (i.e., freedom from CO, major amputation or TLR). Variables significant on univariate analysis were entered into the multivariate analysis. An event occurred if one of the outcomes in CO was reached before the last follow-up. Otherwise, the data point was censored in the Cox regression analysis. Statistical analyses were conducted using IBM SPSS Statistics for Windows version 24 (IBM Corporation, Armonk, New York) and JMP version 12.2.0 (SAS Institute Inc, Cary, North Carolina).

Results

A total of 115 CLI patients undergoing PVI of 144 limbs (including patients undergoing PVI of both limbs, in a staged fashion as two or more separate procedures) were analyzed. The mean age was 70 years. There were 66 males and 49 females. The median follow-up was 15.7 months (range 0.4–69.9 months). Patient demographics, comorbidities, and PVI procedures are listed in Table 2. Of 115 patients included in this study, thirty-two (27.8%) patients had history of prior amputation, and 29 (26.6%) patients had history of prior revascularization. Seventy-six patients (52.8%) had concurrent femoropopliteal interventions.

Out of the total 144 limbs, 46.5% (n = 67) were treated with PTA alone, 6.9% (n = 10) PTA and atherectomy, 31.3% (n = 45) PTA and stent, 14.6% (n = 21) PTA, stent and atherectomy, and 0.7% (n = 1) PTA and thrombectomy. Eighty-three (57.6%) limbs were treated once, 39 (27.1%) two times, and 22 (15.3%) more than two times. Seventy-six (52.8%) limbs had concurrent fem-pop intervention, but this was not significantly different among the different TPS groups ($p = 0.52$). The total number of PVI procedures for the entire cohort during the study period was 232, yielding a mean of 1.6 PVI procedures/limb and 2.0 PVI procedures/patient.

Table 2 Baseline characteristics of the overall cohort according to tibial perfusion score (TPS)

	TPS				p
	Low (n = 27)	Medium (n = 64)	High (n = 53)	Overall (n = 144)	
Age, years (mean ± SD)	72 ± 13	72 ± 12	66 ± 11	70 ± 12	0.03
Gender (male)	17(63.0%)	34(53.1%)	35(66.0%)	86(59.7%)	0.34
Ethnicity (Caucasian)	11(40.7%)	27(42.2%)	27(50.9%)	65(45.1%)	0.56
Body mass index, kg/m^2 (mean ± SD)	29 ± 8	27 ± 8	27 ± 6	28 ± 7	0.68
Comorbidity					
DM	21(77.8%)	41(64.1%)	34(64.2%)	96(66.7%)	0.40
HTN	19(70.4%)	48(75.0%)	42(79.2%)	109(75.7%)	0.67
HCL	14(51.9%)	32(50.0%)	25(47.2%)	71(49.3%)	0.91
CAD	8(29.6%)	20(31.3%)	20(37.7%)	48(33.3%)	0.69
CVA	3(11.1%)	10(15.6%)	6(11.3%)	19(13.2%)	0.74
CHF	7(25.9%)	9(14.1%)	8(15.1%)	24(16.7%)	0.36
Chronic A-Fib	10(37.0%)	6(9.4%)	8(15.1%)	24(16.7%)	0.01
ESRD	14(51.9%)	18(28.1%)	17(32.1%)	49(34.0%)	0.09
Current dialysis	14(51.9%)	17(26.6%)	16(30.2%)	47(32.6%)	0.06
Smoking (current/former)	10(37.0%)	37(57.8%)	41(77.4%)	88(61.1%)	< 0.01
Drug					
ACEI/ARB	11(40.7%)	25(39.1%)	18(34.0%)	54(37.5%)	0.79
β-Blocker	18(66.7%)	41(64.1%)	30(56.6%)	89(61.8%)	0.60
Statin	17(63.0%)	39(60.9%)	31(58.5%)	87(60.4%)	0.92
ASA 81 mg	14(51.9%)	37(57.8%)	37(69.8%)	88(61.1%)	0.23
ASA 325 mg	3(11.1%)	5(7.8%)	5(9.4%)	13(9.0%)	0.87
Plavix	10(37.0%)	28(43.8%)	23(43.4%)	61(42.4%)	0.82
Prior amputation	8(29.6%)	21(32.8%)	16(30.2%)	45(31.3%)	0.94
Prior revascularization	11(40.7%)	23(35.9%)	22(41.5%)	56(38.9%)	0.81
Laterality (right)	15(55.6%)	29(45.3%)	32(60.4%)	76(52.8%)	0.25
2nd limb involved	5(18.5%)	10(15.6%)	14(26.4%)	29(20.1%)	0.34
Rutherford score					0.06
4	0	10(17.0%)	11(20.8%)	21(14.6%)	
5	27(100.0%)	52(81.3%)	42(79.2%)	121(84.0%)	
6	0	2(3.1%)	0	2(1.4%)	
Concurrent femoropopliteal revascularization	15(55.6%)	32(50.0%)	29(54.7%)	76(52.8%)	0.52
Type of intervention					0.84
PTA	14(51.9%)	28(43.8%)	25(47.2%)	67(46.5%)	
PTA + atherectomy	3(11.1%)	3(4.7%)	4(7.5%)	10(6.9%)	
PTA + stent	7(25.9%)	20(31.3%)	18(34.0%)	45(31.3%)	
PTA + stent + atherectomy	3(11.1%)	12(18.8%)	6(11.3%)	21(14.6%)	
PTA + thrombectomy	0	1(1.6%)	0	1(0.7%)	
Total tibial IR interventions					0.08
1	11(40.7%)	37(57.8%)	35(66.0%)	83(57.6%)	
2	13(48.1%)	16(25.0%)	10(18.9%)	39(27.1%)	
> 2	3(11.1%)	11(17.2%)	8(15.1%)	22(15.3%)	

TPS tibial artery perfusion score; *SD* standard deviation; *DM* diabetes mellitus; *HTN* hypertension; *HCL* hypercholesterolemia; *CAD* coronary artery disease; *CVA* cerebrovascular accident; *CHF* chronic heart failure; *A-Fib* atrial fibrillation; *ESRD* end-stage renal disease; *ACEI/ARB* angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers; *ASA* aspirin; *PTA* percutaneous transluminal angioplasty; *IR* interventional radiology

Limb salvage defined as freedom from composite outcome in High, Medium, and Low TPS groups was achieved in 90.6% (48/53 limbs), 85.9% (55/64 limbs), and 55.6% (15/27 limbs). Limb salvage defined as freedom from major amputation in High, Medium, and Low TPS groups was achieved in 94.3% (50/53 limbs), 90.6% (58/64 limbs), and 74.1% (23/27 limbs). Among comorbid risk factors, patients within the Low TPS group had higher prevalence of chronic atrial fibrillation (37.0%, $p = 0.005$).

Within High, Medium, and Low TAP groups, limb salvage defined as freedom from CO was achieved in 96.2% (25/26 limbs), 82.0% (41/50 limbs), and 76.1% (51/67 limbs) (Fig. 1). Limb salvage defined as freedom from major amputation in High, Medium, and Low TAP groups was achieved in 96.2% (25/26 limbs), 92.0% (46/50 limbs), and 83.6% (56/67 limbs). Univariate logistic regression analysis of factors associated with limb salvage defined as freedom from CO is shown in Supplementary Table 1. On multivariate logistic regression analysis, after adjusting for significant factors on univariate logistic regression analysis, Medium (OR 4.2; 95% CI 1.5–12.1; $p = 0.008$) and High TPS (OR 6.9; 95% CI 2.1–23.1; $p = 0.002$) compared to Low TPS were significantly associated with limb salvage (Table 3). Univariate Cox proportional hazards analysis of factors associated with CO is shown in Supplementary Table 2. Kaplan–Meier curves comparing the different TPS categories are shown in Fig. 2. On multivariate Cox regression analysis, Medium (HR 0.3; 95% CI 0.1–0.6; $p = 0.003$) and High TPS (HR 0.2; 95% CI 0.1–0.5; $p = 0.003$) compared to Low TPS were significantly associated with decreased risk of clinical failure (Table 4). Logistic regression and Cox proportional hazards analyses of factors associated with limb salvage defined as freedom from major amputation are shown in Supplementary Tables 3 and 4. On multivariate Cox regression analysis, Medium (HR 0.3; 95% CI 0.1–0.9; $p = 0.03$) and High TPS (HR 0.2; 95% CI 0.1–0.7; $p = 0.013$) compared to Low TPS were significantly associated with decreased risk of clinical failure. Kaplan–Meier curves comparing the different TPS categories are shown in Supplementary Figure 2. When limb salvage was defined as freedom from TLR, High (OR 3.3; 95% CI 1.2–8.8; $p = 0.017$) compared to Low TPS was significantly associated with limb salvage on univariate logistic regression analysis, while Medium compared to Low TPS was not ($p = 0.207$); on univariate Cox regression analysis, High (HR 0.3; 95% CI 0.2–0.7; $p = 0.006$) compared to Low TPS was significantly associated with decreased risk of clinical failure, while Medium compared to Low TPS was not ($p = 0.116$). To identify any factor that could be driving the composite endpoint, univariate logistic regression and Cox proportional hazards analyses of TPS compared to each of its components are shown in Supplementary Tables 5 and 6. TPS was more significantly associated with CO, major amputation or TLR, and freedom from these outcomes than any of its component variables on Cox and logistic regression analysis, respectively. For CO or major amputation as outcome, the most significant component driving TPS was an intact pedal arch following intervention. For TLR as outcome, the most significant component driving TPS was tibial artery calcification. Duration of primary unassisted patency (mean ±

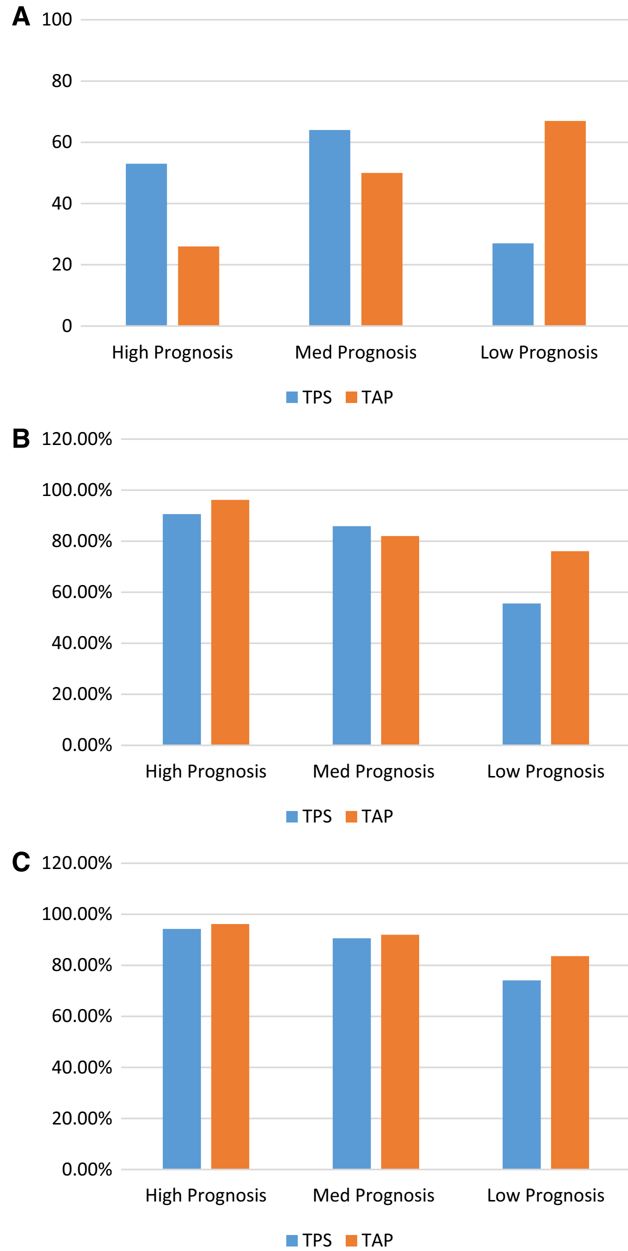

Fig. 1 Stratified by the TPS system and by TAP alone. (**A**) The number of patients in each risk group, (**B**) freedom from composite outcome rate, and (**C**) freedom from major amputation rate in each risk group. *TPS* tibial perfusion score; *TAP* tibial artery patency

Table 3 Factors associated with freedom from composite outcome on multivariate logistic regression

Variable	Odds ratio (95% CI)	*p* value
TPS		
Low	1.00(Reference)	
Medium	4.19(1.45–12.09)	< 0.01
High	6.88(2.05–23.08)	< 0.01
Chronic A-Fib		
No	1.00(Reference)	
Yes	0.47(0.16–1.43)	0.18
ESRD		
No	1.00(Reference)	
Yes	0.44(0.18–1.10)	0.08
Dialysis		
No	1.00(Reference)	
Yes	1.07(0.19–6.21)	0.94

TPS tibial artery perfusion score; *A-Fib* atrial fibrillation; *ESRD* end-stage renal disease

Table 4 Multivariate Cox proportional hazards analyses to predict independent predictors of composite outcome

Variable	HR (95%CI)	*p* value
TPS		
Low	1.00(Reference)	
Medium	0.26(0.11–0.63)	< 0.01
High	0.17(0.06–0.48)	< 0.01
Chronic A-Fib		
No	1.00(Reference)	
Yes	2.07(0.84–5.09)	0.11
ESRD		
No	1.00(Reference)	
Yes	2.06(0.93–4.53)	0.07
Dialysis		
No	1.00(Reference)	
Yes	1.18(0.28–4.96)	0.82

TPS tibial artery perfusion score; *A-Fib* atrial fibrillation; *ESRD* end-stage renal disease

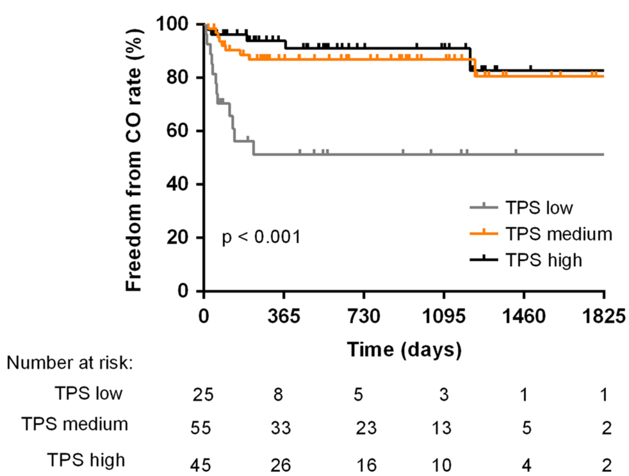

Fig. 2 Comparison of freedom from composite outcome among 3 TPS groups. *CO* composite outcome; *TPS* tibial artery perfusion score

SD) for TPS Low, Medium, and High groups were 448 ± 707, 820 ± 845, and 1033 ± 883 days ($p = 0.014$).

Discussion

Since CLI was defined in 1982, multiple classification schemes have been proposed to classify risk of adverse events and to assess the risk–benefit of various forms of revascularization treatments [16]. Accurate risk stratification is crucial in identifying patients who require earlier intervention, more aggressive management, and closer surveillance. However, because of the rapid development of revascularization techniques and change in presenting patient demographics, the traditional classification systems, such as the Fontaine and Rutherford System, fail to accurately assess outcomes in patients with CLI. The Society of Vascular Surgery (SVS) proposed a Lower Extremity Threatened Limb Classification system, commonly known as the Wound, Ischemia, and foot Infection (WIfI) classification to allow risk stratification and outcome analyses of various forms of therapy for patients with CLI [16]. However, the WIfI classification is complex and can be especially challenging to implement into everyday clinical practice. The WIfI system comprises 64 permutations of different outcomes based on its scoring criteria, and its accuracy for risk stratification remains controversial [11, 17–19]. In addition, no current classification system exists specifically for patients who undergo PVI. In this study, we proposed the tibial artery perfusion score (TPS) as a means for stratifying risks in patients with CLI undergoing PVI. In TPS, we used readily measurable variables that are indirect correlates of perfusion with intention of deriving a scoring system that has practical value in everyday clinical practice in the care of patients with CLI. We found that TPS was associated with limb salvage in CLI limbs, particularly in high-risk limbs.

Recent studies have demonstrated the clinical importance of tibial artery patency (TAP) for patients with CLI. TAP is a simple dichotomous outcome that denotes the patency of the tibial artery. In a randomized controlled clinical trial comparing drug-eluting stent (DES) ($n = 82$) versus bare metal stent (BMS) ($n = 79$) for tibial angioplasty in CLI, Rastan et al. showed that TAP at 1 year was 80.6% versus 55.6%, and the event-free survival rates after a follow-up of 1016 days were 65.8% and 44.6% for patients who received DES and BMS, respectively [20, 21]. In addition, several retrospective studies have also shown a correlation between TAP and clinical outcomes [20, 22–24]. In our study, decreasing TPS was associated with clinical failure (i.e., reaching CO) substantially more than decreasing TAP (OR 2.95, $p = 0.001$ versus OR 2.04, $p = 0.035$). Furthermore, decreasing TPS was associated with major amputation, while decreasing TAP was not (OR 2.54, $p = 0.023$ versus OR 2.23, $p = 0.066$). In particular, TPS performed better than TAP in patients with the worst prognosis in terms of scoring criteria (55.6% vs. 76.1% limb salvage rate). One explanation for this is that TPS is a more detailed scoring system than TAP.

WIfI was proposed as a risk stratification scheme to guide clinical decisions while accounting for the multifactorial nature of CLI [16]. Among a few studies that attempted to validate WIfI, a recent study by Robinson et al. of 257 patients with 280 threatened limbs showed that increasing WIfI stage was associated with decreased 1-year limb salvage rate (96%, 84%, 90%, and 78% for WIfI stages I, II, III, and IV, respectively, $p = 0.003$) [3]. Along with the study by Robinson et al., a few other studies showed that although WIfI stage 1 patients clearly had the most favorable outcomes and stage IV patients the poorest outcomes, the patients with stages II and III had similar outcomes [3, 17–19]. In our study, the patients who were classified as having High, Medium, and Low prognoses according to the TPS system achieved 93.3%, 85.2%, and 57.7% 1-year limb salvage, respectively. The limb salvation rates of High, Medium, and Low prognoses stratified by TPS correspond to WIfI stages I, II/III, and IV, respectively. Similar to TAP, our preliminary data suggests that the WIfI classification system may be less able than TPS to identify patients with the worst prognosis (57.7% vs. 78% limb salvage rate). This could be attributed to the fact that WIfI requires subjective factors that are not directly related to treatment of CLI, such as severity of the wound and degree of infection, whereas TPS relies more on objective measures that are easily obtainable during or immediately post PVI. Although direct visualization of wounds can be helpful, it is often not practical during the procedure. Compared to WIfl which has 64 permutations of different outcomes based on its scoring system, TPS was derived from the most parsimonious model with the fewest number of variables that have the highest predictive value. Thus, TPS may be simpler to implement clinically, and its accuracy in risk stratification could be advantageous over the current standard WIfI system. TPS can be an important tool to guide clinical decision making. For example, in elderly patients with multiple comorbidities, the benefit of treating an occluded peroneal artery in the presence of patent anterior and posterior tibial arteries is likely low. High-risk patients (i.e., low TPS score) will require closer follow-up. In addition, restoration of flow may be too resource intensive in these patients and other options such as surgical bypass should be considered.

We acknowledge several limitations besides the retrospective nature of the study and selection bias as only patients suitable or selected for PVI were included in the study. First, the TPS was scored by a single reader in our study. Although the criteria are well defined and objective, the potential for inter- or intra-observer variability was not evaluated. Second, each limb was assumed as an independent event for the purpose of statistical analysis. Third, Rutherford score was not included in the multivariate analyses since the majority of the patients had a Rutherford score of 5. Fourth, several other important variables such as the TransAtlantic inter-Society Consensus (TASC) classification of vessel lesions, preoperative ankle-brachial index (ABI), and preoperative transcutaneous oxygen pressure (TcPO2) were not routinely collected. Similarly, outcomes such as time to wound healing and the postoperative change in ABI were not recorded. Fifth, TPS could not be directly compared with WIfl score due to the complex nature of the WIfl scoring system as described above. Finally, our study cohort is relatively small. In the design of the TPS, we initially conducted an exploratory multivariate analysis and excluded several variables from the final score methodology which we initially anticipated could be predictive of limb salvage outcomes, such as cardiac ejection fraction. It is possible that these variables may have been predictive of limb salvage in a larger patient cohort. Furthermore, introduction of new technologies during the 5 years of the study could have influenced results. Larger prospective studies are required to validate TPS.

Conclusion

Based on this preliminary investigation, TPS was associated with limb salvage in CLI limbs, especially in high-risk limbs. Further validation in a prospective cohort is warranted to identify patients with high-risk limbs in need of closer surveillance and earlier reintervention.

Compliance with Ethical Standards

Conflict of interest Timothy W.I. Clark has received royalties and consulting fees (Bard, Teleflex, Merit Medical) and received funding for research unrelated to this study from Surmodics (Eden Prairie, Minnesota). The other authors do not have a conflict of interest.

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