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The relationship between the Global Limb Anatomic Staging System (GLASS) and midterm outcomes of retrograde tibiopedal access after failure of antegrade recanalization for chronic limb threatening ischemia.

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Title: The relationship between the Global Limb Anatomic Staging System (GLASS) and midterm outcomes of retrograde tibiopedal access after failure of antegrade recanalization for chronic limb threatening ischemia.

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What this paper adds?

The current study explored the relationship between the Global Limb Anatomic Staging System (GLASS) and midterm outcomes of retrograde tibiopedal access, after failed recanalization of infrainguinal chronic total occlusions (CTOs) using the antegrade approach, in patients with chronic limb threatening ischemia (CLTI). In comparison to GLASS I, GLASS III anatomy was associated with a significantly worse limb based patency (LBP), limb salvage, amputation free survival (AFS), and overall survival. As continuous validation of the GLASS is required, the current data analysis demonstrated that GLASS may be a useful predictor of midterm limb- and survival-related outcomes of this approach and would help the initial decision making.

Abstract:

Objective: To examine the relationship between the Global Limb Anatomic Staging System (GLASS) and midterm limb- and survival-related outcomes of retrograde tibiopedal access, after failed recanalization of infrainguinal chronic total occlusions (CTOs) using the antegrade approach, in patients with chronic limb threatening ischemia (CLTI).

Methods: This prospective, observational study was conducted between January 2017 and April 2019, and included 213 patients (29 GLASS I, 53 GLASS II, and 131 GLASS III lesions) with infrainguinal CTO in whom a percutaneous tibiopedal access was attempted as a consequence of failed recanalization using an antegrade approach. Multivariable Cox proportional hazard regression was performed to assess possible predictors of midterm clinical outcomes. Kaplan-Meier survival curves were used to estimate limb based patency (LBP), limb salvage, amputation free survival (AFS), and overall survival.

Results: The study reported access, crossing, and treatment success of 92.5%, 89.2%, and 89.2% of all tibiopedal access attempts, respectively. In comparison to GLASS I, GLASS stage III was associated with significantly worse midterm LBP (p= .005), overall survival (p= .037), limb salvage (p= .021), and AFS (p <.001).

Conclusion: Retrograde tibiopedal access for recanalization of infrainguinal CTOs in patients with CLTI is associated with high access, crossing, and treatment success, and low complication rates. The study suggests that GLASS stage may be a useful predictor of midterm limb- and survival-related outcomes of this approach. In comparison to GLASS I, GLASS III anatomy is associated with a significantly worse LBP, limb salvage, AFS, and overall survival.

Keywords: Retrograde access, tibiopedal access, GLASS, limb based patency, chronic limb threatening ischemia, access site complications.

Introduction

Chronic limb threatening ischemia (CLTI) is a severe degree of peripheral arterial disease (PAD) that includes a broad and heterogeneous group of patients with varying degrees of ischemia sufficient to cause rest pain, impair wound healing, and increase amputation risk.[1]

Endovascular revascularization is an established approach for limb salvage, however, constitutes a real challenge in the presence of widespread multilevel disease associated with long, calcified, chronic total occlusions (CTOs) as frequently encountered in patients with CLTI.[2-4]

Moreover, the traditional antegrade ipsilateral or contralateral femoral approach fails to cross CTO lesions in up to 20% of infrainguinal endovascular interventions, with a consequent increased risk of major amputations and death.[5-7]

The retrograde approach via many distal access sites has been used to overcome antegrade recanalization failures, particularly in patients with poor surgical options.[8]

The novel Global Limb Anatomic Staging System (GLASS) represents an integrated limb-based scheme that is proposed to better define the evidence based revascularization strategies in CLTI, in contrast to the current poorly correlated lesion-based classification systems. However, it requires validation across different practice settings.[1]

The purpose of the present study was to examine to the relationship between GLASS and midterm limb- and survival-related outcomes of retrograde tibiopedal access, after failed recanalization of infrainguinal chronic total occlusions (CTOs) using the antegrade approach, in patients with chronic limb threatening ischemia (CLTI).

Methods

This prospective, observational study was conducted between January 2017 and April 2019 in a single tertiary referral university hospital. It included all consecutive patients presenting with intermediate and advanced limb-threatening ischemia (WIfI stages 2-4) associated with significant perfusion deficits (WIfI ischemia grades 2-3), according to Wound, Ischemia, and foot Infection (WIfI) classification system,[9] due to an infrainguinal CTO in whom a percutaneous retrograde tibiopedal access was attempted immediately after failed recanalization using an antegrade approach. There were no specific exclusion criteria. This study comprised 213 patients (213 limbs), including 92 with rest pain and 121 with tissue loss.

The Institutional Review Board approved the study protocol developed in accordance with the Declaration of Helsinki. All patients provided written informed consent for the study enrollment and planned revascularization procedure.

Patient evaluation

All patients underwent physical examination, clinical risk assessment, ankle brachial index (ABI)/toe brachial index (TBI) measurements, and preoperative diagnostic imaging by duplex ultrasound (DUS) examination and computed tomography angiography (CTA), in order to plan the access and treatment strategy.

The anatomic pattern of arterial disease was retrospectively defined according to GLASS, by two investigators (HA, AE) involved in patient care, who blindly reviewed the pre- procedural CTA, further confirmed by the interventional angiography, to reach an inter observer agreement regarding the target arterial path (TAP) defined as the optimal IP arterial pathway to restore in-line pulsatile flow to the

foot being either the least diseased or an angiosome based vessel.[1] Then, the GLASS stage (I-III) was determined based on the scoring system for both femoropopliteal (FP), infrapopliteal (IP) grades (0- 4).

Calcification of target lesions was quantified according to the Peripheral Artery Calcium Scoring System (PACSS).[10]

All patients followed best medical treatment (BMT) protocol, including statins, aspirin 75 mg/d, and they were given clopidogrel 300 mg as a loading dose the day before the procedure.

Procedure description

Patients were treated according to the standard of care at our hospital by experienced vascular surgeons. All procedures were performed under local or regional anesthesia in a hybrid operating room equipped with a digital angiographic system (Artis zee; Siemens Healthineers, Erlangen, Germany).

The antegrade approach, using either the ipsilateral or contralateral common femoral artery, to the target lesion was initially attempted in all patients. After sheath insertion, 5000 IU bolus of heparin was administered intra-arterial, with an additional 2500 IU given for procedures longer than 1 hour. Once re-entry into the distal true lumen was unsuccessful via an antegrade approach, attention was directed towards a retrograde tibiopedal approach guided by fluoroscopy or DUS according to the surgeon discretion.

A patent and as healthy as possible segment of the target IP vessel was chosen to be the point of access. The leg was adequately positioned to maximize the exposure of the target vessel being accessed, as described previously.[11,12]

After successful retrograde puncture, a .018-inch guidewire (V-18 Control; Boston Scientific, Marlborough, MA, USA) was inserted through the needle. Then, .018 platform support (TrailBlazer, Medtronic Inc., Santa Rosa, CA, USA; CXI, Cook Medical, Bloomington, IN, USA) or balloon (Pacific Plus, Medtronic Inc.) catheter was advanced over the guidewire in a sheathless manner to minimize trauma to the access artery. Contrast medium was injected through the catheter to confirm intraluminal position.

Retrograde negotiation of the CTO lesion was performed, using the combination of guidewire and support/balloon catheter. In case of failure of retrograde wire crossing, a reversed controlled antegrade retrograde tracking (CART)[11,13] and/or double balloon technique [6] was adopted. Once the dissection membrane was disrupted, guidewire was advanced from either the antegrade or retrograde direction.

Once the guidewire had passed the CTO and entered the proximal true lumen as confirmed by contrast injection, it was snared from above through a 5-Fr Judkins Right 4.0 or Bern catheter (Boston Scientific) to allow externalization of the guidewire out of the antegrade sheath. Afterwards, a balloon was inserted via the antegrade sheath through the occlusion to enable reversing the guidewire so that its soft tip directed downward, then balloon angioplasty (.035 Admiral Xtreme; .018 Pacific Plus, Medtronic) was accomplished in the standard antegrade fashion. Stenting (EverFlex, Medtronic) was reserved for flow limiting dissections or residual stenosis >30%.

Hemostasis of the distal puncture site was secured by manual compression for 5-10 minutes, inflation of a blood pressure cuff 10 mm Hg more than the systolic blood pressure for 5 minutes, and/or prolonged low-pressure balloon inflation at the site of

puncture. All patients received lifelong aspirin 75 mg/d plus clopidogrel 75 mg/d for at least one month.

Follow-up protocol

All patients underwent DUS examination the day after the procedure to assess patency of the treated lesion(s) and possible access site complications. Afterwards, they were scheduled for routine follow-up visits comprising both physical and DUS examination at our outpatient clinic every 3 months for the first year and yearly thereafter. A further follow-up was then tailored for each patient.

Outcome measures

Short-term outcome measures were: (a) access success, defined as the ability to gain percutaneous entry into a tibiopedal artery in the desired location with subsequent intraluminal guidewire delivery; (b) crossing success, defined as the ability to pass a guidewire through the proximal boundary of an infrainguinal CTO via a tibiopedal access; (c) treatment success, defined as residual diameter stenosis of less than 30% at the end of the procedure as demonstrated on completion angiography; (d) immediate technical failure (ITF), defined as failure to cross the target lesion or to establish the predetermined TAP;[1] and (e) procedural complications, defined and categorized according to SIR criteria.[14]

Midterm outcome measures were: (a) limb based patency (LBP), defined as continued patency of the entire TAP from groin to ankle with absence of anatomic (occlusion, critical stenosis >70%, or reintervention affecting any portion of the defined TAP), and hemodynamic failure (significant drop in ABI ≥.15/TBI ≥.10 or stenosis >50% in the TAP in the presence of recurrent or unresolved clinical symptoms as rest pain,

worsening or persistent tissue loss);[1] (b) assisted primary patency; (c) secondary patency; (d) limb salvage; (e) amputation free survival (AFS); and (f) overall survival.

Statistical analysis

Descriptive statistics were used; with continuous variables expressed as mean ± standard deviation (SD) and/or median and interquartile range (IQR), and categorical variables as frequency and percentage. Categorical variables were compared using the chi square test or Fisher's exact test, while continuous variables were compared using Student's t-test or analysis of variance (ANOVA). Multivariable Cox proportional hazard regression was performed, including patient and lesion characteristics with a p value <.05 in univariable analysis, using a stepwise approach, to assess possible predictors of midterm clinical outcomes, and results were presented as hazard ratio (HR) and 95% confidence interval (CI). Kaplan-Meier survival curves were used to estimate patency rates, limb salvage, AFS, and overall survival, reported as proportion ± standard error (SE), and the GLASS stages were compared using the log-rank test. Post-hoc power analysis, using G*Power 3.0.10 (Franz Faul, University of Kiel, Germany), of the study sample size yielded a statistical power of .90. A p value <.05 was considered the threshold of statistical significance. Statistical analysis was performed using SPSS 24.0 (IBM Corp, Armonk, NY, USA), and MedCalc 16.8 (MedCalc Software, Ostend, Belgium).

Results

Between January 2017 and April 2019, 1237 patients with intermediate and advanced limb-threatening ischemia underwent endovascular recanalization of an infrainguinal CTO using the conventional antegrade approach. Among them, 213 patients (213 limbs, 17.2%), including 29 GLASS I, 53 GLASS II, and 131 GLASS III lesions,

underwent attempts for retrograde tibiopedal access immediately after failed recanalization using the antegrade approach, and those constituted our study cohort.

There were no statistically significant differences among the GLASS stages regarding baseline patients' demographics, clinical presentation, and lesion characteristics except for lesion length ($p < .001$) (Tables 1 and 2).

The most common indication for retrograde approach was failure to cross the occlusion from antegrade, as encountered in 96 patients (45.1%). Twenty two tibiopedal access site complications were reported, with vessel spasm at the distal access site (13/213 patients, 6.1%) being the most commonly encountered one. Further procedural details are highlighted in Table 3.

Access success was obtained in 197 patients (197/213, 92.5%). The target vessel puncture was unsuccessful in 16 cases with subsequent failure of intraluminal wire delivery, and that was attributed to severe calcification at the target access site.

Crossing success was reported in 96.4% (190/197) of successful retrograde access cases. For the remaining 7 cases, failure was owing to an inability to traverse the occlusion (3 patients), or enter the proximal true lumen (4 patients), with a subsequent procedure abortion.

The treatment applied after successful guidewire crossing and entrance into the proximal true lumen was standard balloon angioplasty in 116 patients (61.7%), while stenting was deemed necessary in 72 patients (38.2%). Treatment success was obtained in all cases in which wire crossing was achieved. Post-operatively, the mean ABI/TBI increased significantly from $.39 \pm .13$ to $.82 \pm .07$ ($p < .001$).

ITF was encountered in 23 cases (23/213, 10.8%), including 16 failed access, and 7 failed crossing. Twenty cases (87%) occurred in GLASS III anatomy, while the remaining 3 cases (13%) occurred in GLASS II anatomy. Those cases underwent either distal bypass (12 patients) in case of good life expectancy, surgical risk, and autogenous conduit or major amputation (11 patients) if any of the former factors were not fulfilled.

All patients were followed up for a mean period of 29.2 ± 4.0 months. The primary (LBP), assisted primary, and secondary patency rates were 50.4% ± 3.8%, 65.9% ± 3.6%, and 73.3% ± 3.3% at 12 months, and 35.8% ± 4.2%, 56.9% ± 3.9%, and 68.8% ± 3.5% at 24 months, respectively (Fig. 1).

During the follow-up period, 27 patients (12.7%) were lost to follow-up, 57 patients (26.8%) died, and 63 patients (29.6%) underwent major amputation. Kaplan-Meier analysis yielded an overall survival of 79.3% ± 2.8%, and 71.8% ± 3.2%, limb salvage rate of 71.0% ± 3.4%, and 64.8% ± 3.7%, and AFS of 52.6% ± 3.5%, and 40.2% ± 3.5% at 12 and 24 months, respectively.

Compared to GLASS stage I, GLASS stage III was associated with significantly worse midterm LBP (GLASS III, 33.0% vs GLASS I, 47.3%; p= .005), overall survival (65.7% vs 85.1%; p= .037), limb salvage (60.8% vs 79.7%; p= .021), and AFS (30.0% vs 66.3%; p <.001) (Fig. 2).

Multivariable Cox regression analysis revealed that diabetes, tissue loss, moderate to severe calcification, single runoff vessel, and GLASS stage III were significantly associated with loss of LBP. Moreover, smoking, tissue loss, moderate to severe calcification, single runoff vessel, and GLASS stage III were independently related to worse AFS. Presentation with tissue loss, WIfI stage III-IV, and GLASS stage III

were independent predictors of major amputation, while diabetic patients with single runoff vessel, and GLASS stage III were independently related to overall mortality (Table 4).

Discussion

In 1988, Tønnesen et al[15] were the first to report retrograde puncture of the popliteal artery under fluoroscopy with the patient in prone position. Two years later, Lyer et al[16] reported successful retrograde recanalization of an occluded PTA using a cut down at the level of the ankle in two cases. Since then, this approach has undergone an enormous evolution and nowadays, almost every infrainguinal arterial segment can be accessed percutaneously in retrograde fashion while the patient in supine position.[6,17,18]

There are several proposed advantages of retrograde approach compared to the standard antegrade one that may contribute to its high success rate. First, the distal cap of CTO lesion is often soft and thin in contrast to the hard fibrotic proximal cap, thus increasing the likelihood of successful lesion crossing via the retrograde approach.[19] Second, it provides more control and pushability of the wire through the occlusion due to proximity to the target lesion.[20] Third, there is less tendency of the guidewire to divert into collaterals, as they are usually pointing in a craniocaudal direction opposite to that of the wire, thus maintaining a straight path inside the main vessel.[3,6,21]

Both fluoroscopy and DUS can be used to guide retrograde access. Fluoroscopy is preferred in obese patients, presence of leg edema, and when accessing heavily calcified or deep vessels as proximal ATA and PA. However, it typically requires complex positioning of the x-ray tube and image intensifier, and stable position of the foot. On the other hand, DUS has the advantages of minimizing the contrast medium

dosage and radiation exposure. However, it requires special experience as visualization of tip of micropuncture needle (unless echogenic) is difficult.[3,11,17]

In a systematic review comprising 1168 below the knee (BTK) attempts in 19 studies, access, crossing, and treatment success were obtained in 94%, 86%, and 84% of all attempts, respectively.[8] This is in accordance with results of the current study.

Considering that 17.2% (213/1237) of CLTI patients with infrainguinal CTOs treated at our institution experienced failed antegrade approach, then only 10.8% (23/213) experienced failed retrograde access/crossing, this implies that only 1.9% (23/1237) of CTO lesions cannot be endovascularly treated.

In the current study, Kaplan-Meier estimates demonstrated primary patency rate of 50.4%, and 35.8%, and AFS of 52.6%, and 40.2% at 12, and 24 months, respectively. In a series of 579 retrograde attempts, Schmidt et al[4] reported primary patency rate of 36.0%, and 21.5%, and AFS of 78.4%, and 66.6% at 12, and 24 months, respectively. The discrepancy of AFS between the two studies may be attributed to the unique study population in this study with severe co-morbidities, late presentation with severe infection and major tissue loss.

Complications were reported in 10.3% of tibio-pedal access attempts, and vessel spasm was encountered in 6.1% of cases. Schmidt et al[4] reported 17.7% access site complications, with vessel spasm in 14.8% of cases. On the other hand, Welling et al[8] reported 4.1% access site complications among 1168 BTK puncture attempts, and the most common was vessel perforation (1.1%).

Patients with GLASS II anatomy reported ITF and 1 year-LBP rates of 5.7% and 59%, respectively, while those with GLASS III reported 15.3% and 41%,

respectively. This is in accordance with the Global Vascular Guidelines, regarding the 1 year-LBP but not the ITF, that estimated ITF and 1 year-LBP rates of <20% and 50-70% for GLASS II, and >20% and <50% for GLASS III anatomy, respectively.[1]

On multivariable Cox regression analysis, GLASS stage III was an independent predictor of loss of LBP, worse AFS, major amputation, and overall mortality.

Although recent studies, including the present one, demonstrated that GLASS stage was a useful predictor of both limb- and survival-related outcomes following endovascular revascularization in patients with CLTI,[22,23] others reported contradictory results concerning wound healing,[24] and LBP of tibial interventions.[25] Therefore, further validation and refinement of the GLASS is clearly demanded in larger multicenter contemporary studies.

Limitations of this study include: a) it is a single-center, single-arm study, with moderate number of patients, and relatively short follow up period, b) the GLASS calcifications and inframalleolar modifiers were not used in this study, c) no drug coated balloons (DCBs), atherectomy devices, or re-entry catheters were used in this study, d) lack of evaluation of wound healing and interval to wound healing, and e) no independent core lab assessment of the angiographic images was performed. However, authors do believe that this study provides high-level scientific data as it includes all CLTI comers with no exclusion criteria regarding patient co-morbidities or lesion characteristics, thus represents a real world experience. Also, an advantage of this single-center study is to exclude any confounding variables that may arise when patients are treated at different hospitals.

Conclusion

According to this analysis of single-center data, retrograde tibiopedal access for recanalization of infrainguinal CTOs in patients with CLTI is associated with high access, crossing, and treatment success, and low complication rates. In comparison to GLASS I, GLASS III anatomy is associated with a significantly worse LBP, limb salvage, AFS, and overall survival. The study suggests that GLASS stage may be a useful predictor of midterm limb- and survival-related outcomes of this approach. These results, perhaps, would warrant a modified intervention or treatment regimen for GLASS III patients.

Conflict of interest statement: None.

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Figures legends:

- Figure 1. Cumulative Kaplan-Meier estimate of primary (solid line), assisted primary (dashed line), and secondary (dotted line) patency rates in patients following retrograde tibiopedal access for chronic limb threatening ischemia (CLTI).
- Figure 2. Relationship between Global Limb Anatomic Staging System (GLASS) and midterm clinical outcomes following retrograde tibiopedal access for chronic limb threatening ischemia (CLTI). (A) Limb based patency (LBP), (B) Limb salvage, (C) Amputation free survival (AFS), and (D) Overall survival.

Table 1. Demographics and clinical characteristics of the study cohort.

	Overall n= 213	GLASS I n= 29	GLASS II n= 53	GLASS III n= 131	*P*
Age, years Mean ± SD Range Median (IQR)	 65.2 ± 6.2 53-79 65 (10)	 65.3 ± 8.1 53-79 65 (14)	 64.6 ± 5.3 55-73 65 (9)	 65.4 ± 6.1 55-79 65 (10)	.74
Male gender	163 (76.5)	20 (69.0)	38 (71.7)	105 (80.2)	.28
Diabetes	157 (73.7)	19 (65.5)	41 (77.4)	97 (74.0)	.50
Hypertension	68 (31.9)	8 (27.6)	17 (32.1)	43 (32.8)	.86
CAD	44 (20.7)	5 (17.2)	12 (22.6)	27 (20.6)	.85
Previous stroke/TIAs	19 (8.9)	3 (10.3)	6 (11.3)	10 (7.6)	.70
Current smoking	103 (48.4)	12 (41.4)	27 (50.9)	64 (48.9)	.70
CKD (eGFR <60 mL/min/1.73 m^2)	36 (16.9)	4 (13.8)	10 (18.9)	22 (16.8)	.84
COPD	30 (14.1)	4 (13.8)	9 (17.0)	17 (13.0)	.78
Dyslipidemia	56 (26.3)	7 (24.1)	14 (26.4)	35 (26.7)	.96
Obesity (BMI >30 kg/m^2)	24 (11.3)	5 (17.2)	8 (15.1)	11 (8.4)	.24
Rutherford Stage Stage 4 Stage 5-6	 92 (43.2) 121 (56.8)	 11 (37.9) 18 (62.1)	 20 (37.7) 33 (62.3)	 61 (46.6) 70 (53.4)	.45
WIfI stage II III IV	 71 (33.3) 103 (48.4) 39 (18.3)	 10 (34.5) 16 (55.2) 3 (10.3)	 22 (41.5) 22 (41.5) 9 (17.0)	 39 (29.8) 65 (49.6) 27 (20.6)	.43

Continuous data are presented as the means ± standard deviation (SD) and/or median and interquartile range (IQR); categorical data are given as the counts (percentage).

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; TIAs, transient ischemic attacks; WIfI, Wound Ischemia foot Infection.

Table 2. Lesion characteristics of the study group.

	Overall n= 213	GLASS I n= 29	GLASS II n= 53	GLASS III n= 131	*P*
Nature of lesion					
De novo lesion	177 (83.1)	25 (86.2)	42 (79.2)	110 (84.0)	.40
Restenotic/occlusive lesion	25 (11.7)	2 (6.9)	6 (11.3)	17 (13.0)	
In-stent restenosis/occlusion	11 (5.2)	2 (6.9)	5 (9.4)	4 (3.0)	
Lesion length, cm					
Mean ± SD	27.0 ± 7.5	18.1 ± 0.9	22.3 ± 1.1	30.9 ± 6.9	<.001
Range	17-40	17-20	20-24	22-40	
Median (IQR)	23 (13)	18 (2)	23 (2)	34 (14)	
Calcification (PACSS)					
Grade 0	76 (35.7)	8 (27.6)	16 (30.2)	52 (39.7)	.088
Grade 1/2	43 (20.2)	5 (17.2)	7 (13.2)	31 (23.7)	
Grade 3/4	94 (44.1)	16 (55.2)	30 (56.6)	48 (36.6)	
Runoff vessels					
1	97 (45.5)	11 (37.9)	25 (47.2)	61 (46.6)	.86
2	70 (32.9)	10 (34.5)	16 (30.2)	44 (33.6)	
3	46 (21.6)	8 (27.6)	12 (22.6)	26 (19.8)	

Continuous data are presented as the means ± standard deviation (SD) and/or median and interquartile range (IQR); categorical data are given as the counts (percentage).

Abbreviations: GLASS, Global Anatomic Staging System; PACSS, Peripheral Artery Calcium Scoring System.

Table 3. Procedural details of the study group.

Indication (N=213)	
Failure to enter/identify occlusion	48 (22.5)
Failure to cross occlusion	96 (45.1)
Failure to re-enter true lumen distal to occlusion	44 (20.7)
Guidewire perforation	25 (11.7)
Access vessel (N=213)	
Proximal anterior tibial artery	29 (13.6)
Distal anterior tibial /Dorsalis pedis artery	75 (35.2)
Posterior tibial artery	103 (48.4)
Peroneal artery	6 (2.8)
Access vessel diameter, mm	
Mean ± SD	2.8 ± 0.7
Range	2-4
Median (IQR)	3 (1.5)
Access guidance (N=213)	
Fluoroscopy	137 (64.3)
Ultrasound	76 (35.7)
Access configuration (after successful access, N=197)	
Guidewire/Support catheter	135 (68.5)
Guidewire/Balloon catheter	62 (31.5)
Crossing technique (after successful access, N=197)	
Retrograde guidewire crossing	126 (63.9)
Reversed CART technique	49 (24.9)
Double balloon technique	22 (11.2)
Intervention method (after successful crossing, N=190)	
Balloon angioplasty	116 (61.1)
Stenting	74 (38.9)
Hemostasis method (after successful access, N=197)*	
Manual compression	121 (61.4)
Blood pressure cuff	47 (23.9)
Balloon inflation	36 (18.3)
Hemostasis time, minutes	
Mean ± SD	12.4 ± 5.7
Range	5-30
Median (IQR)	11 (7)
Procedure time, minutes	
Mean ± SD	102.0 ± 14.4
Range	80-150
Median (IQR)	102.5 (16)
Fluoroscopy time, minutes	
Mean ± SD	49.0 ± 10.7
Range	30-65
Median (IQR)	52.5 (20)
Contrast volume, mL	
Mean ± SD	40.5 ± 16.3
Range	20-100
Median (IQR)	40 (30)
Access complications	

Spasm	13 (6.1)
Hematoma	5 (2.3)
Thrombosis	1 (.50)
Occlusion	1 (.50)
AV fistula	2 (.90)

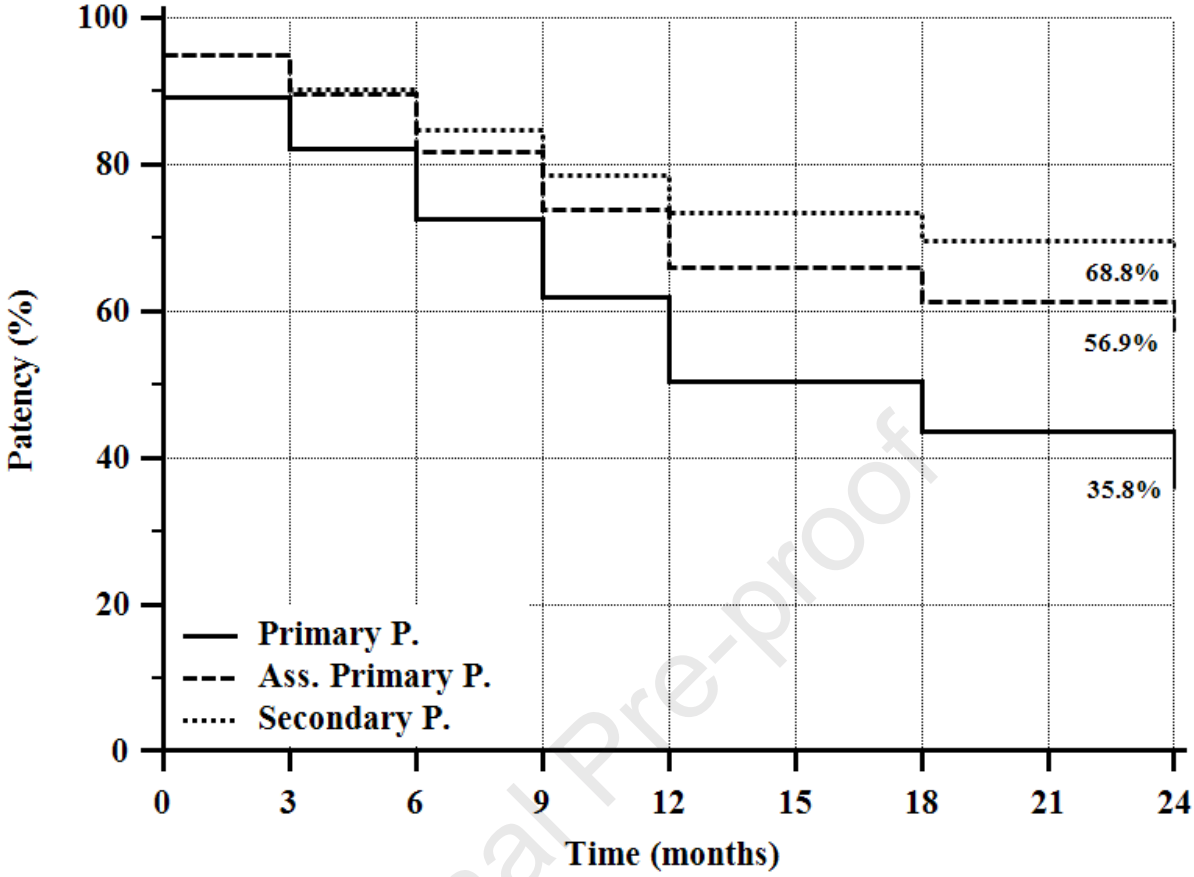
Continuous data are presented as the means ± standard deviation (SD) and/or median and interquartile range (IQR); categorical data are given as the counts (percentage).

*Total exceeds 100% due to cases in which multiple methods were used.

Table 4. Relationship between baseline patient and lesion characteristics and midterm clinical outcomes using Cox proportional hazards regression analysis.

	Univariable analysis		Multivariable analysis	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Loss of LBP				
Diabetes	2.80 (1.50-5.22)	.001	1.98 (1.05-3.73)	.035
Smoking	1.54 (1.05-2.25)	.028		
Dyslipidemia	1.52 (1.03-2.24)	.034		
Rutherford category 5-6	2.06 (1.33-3.20)	.001	1.67 (1.05-2.64)	.030
WIfI stage III	2.04 (1.19-3.49)	.010		
WIfI stage IV	2.49 (1.38-4.49)	.003		
PACSS grade 1/2	2.14 (1.19-3.85)	.011		
PACSS grade 3/4	1.96 (1.19-3.24)	.009	1.60 (1.07-2.40)	.024
Runoff vessels no. 1	3.51 (2.00-6.15)	<.001	3.36 (2.22-5.10)	<.001
GLASS stage III	2.26 (1.24-4.13)	.008	2.27 (1.49-3.45)	<.001
Major amputation/overall mortality				
Smoking	1.74 (1.21-2.50)	.003	1.68 (1.16-2.42)	.006
Rutherford category 5-6	2.27 (1.52-3.40)	<.001	2.12 (1.40-3.22)	<.001
PACSS grade 3/4	1.70 (1.11-2.60)	.015	1.71 (1.17-2.49)	.005
Runoff vessels no. 1	1.79 (1.10-2.92)	.020	1.46 (1.02-2.10)	.038
GLASS stage III	3.47 (1.75-6.88)	<.001	3.13 (2.07-4.73)	<.001
Major amputation				
Rutherford category 5-6	1.97 (1.14-3.40)	.015	2.07 (1.20-3.59)	.010
WIfI stage IV	2.86 (1.43-5.73)	.003	1.87 (1.09-3.19)	.023
PACSS grade 3/4	1.89 (1.04-3.45)	.038		
GLASS stage III	2.97 (1.18-7.48)	.022	2.09 (1.21-3.62)	.009
Overall mortality				
Diabetes	2.84 (1.29-6.24)	.010	2.56 (1.16-5.63)	.021
Runoff vessels no. 1	1.99 (0.99-3.40)	.056	2.06 (1.21-3.51)	.009
GLASS stage III	2.78 (1.00-7.71)	.051	2.14 (1.18-3.91)	.013

Abbreviations: CI, confidence interval; GLASS, Global Anatomic Staging System; HR, hazard ratio; LBP, limb based patency; PACSS, Peripheral Artery Calcium Scoring System; WIfI, Wound Ischemia foot Infection.



Primary P.	213	163	128	87	59	59	39	39	22
Ass. Prim. P.	213	179	147	111	87	87	69	69	54
Secondary P.	213	180	153	120	100	100	83	83	72