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Original Article

Wound outcomes and factors associated with wound healing after first-time femoropopliteal artery intervention in patients with ischemic tissue loss

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ABSTRACT

Background/objective: This study's goal is to describe wound outcomes at 2 years following intervention for atherosclerotic femoropopliteal lesions in patients with ischemic tissue loss.
Methods: A retrospective review of 135 first-time endovascular procedures for chronic femoropopliteal atherosclerotic lesions related to ischemic tissue loss was performed. The final wound outcomes were categorized according to the initial wound healing, recurrence and the need of major/minor amputation.
Results: At 2-years of follow up, 76 limbs (56.3%) showed complete wound healing without recurrence, however, wound development occurred at other sites on the same foot following complete primary healing in 11 limbs (8.1%). Tolerable wounds persisted or wounds recurred at the same site in 30 limbs (22.2%), and 18 limbs (13.3%) needed major amputations. Independent factors that prevented wound healing without recurrence at 2 years were renal insufficiency (HR = 0.225, 95% C.I. = 0.091–0.556, p = 0.001), ankle pressure < 50 mmHg or flat forefoot PVR (HR = 0.328, 95% C.I. = 0.124–0.867, p = 0.025) and functional performance < 4 metabolic equivalents (MET) (HR = 0.150, 95% C.I. = 0.063–0.360, p < 0.001).
Conclusion: Wound outcome classifications showed detailed information regarding clinical outcomes in patients with ischemic tissue loss. Renal insufficiency, ischemia grade 3 and poor functional performance were independent risk factors that prevented wound healing.

1. Introduction

Critical limb-threatening ischemia (CLTI) is associated with a high risk of lower limb amputation and substantial mortality.[1,2] Arterial revascularization in CLTI has been evaluated with various endpoints including those related to anatomical factors and clinical outcomes. Anatomical endpoints assessed for CLTI include primary patency and restenosis. Clinical endpoints commonly include overall survival, limb salvage rate, amputation-free survival (AFS), and wound healing.[3,4]

Most large-scale studies use AFS as a decisive clinical endpoint; other research has reported results detailing wound outcomes in patients with tissue loss.[3,5–11] However, descriptions of detailed wound outcomes are important for assessing and gauging treatment results for patients with CLTI, because traditional parameters, such as limb salvage and AFS, are not sufficient for estimating treatment benefits.[3] Most patients with ischemic tissue loss can avoid major amputations if appropriate conservative management is performed.[12–14] In addition, amputation is a clinician-driven outcome; the decision and timing of amputation are both physician and patient driven.[15] Furthermore, the survival of patients with CLTI is largely determined by their comorbidities, not by the intervention results.[16–19] Therefore, evaluating the efficacy of treatment based on all-cause mortality and major amputation outcomes can have consequences on understanding and evaluating treatment outcomes. When limbs are salvaged in CLTI, ischemic wound recurrence or persistent wounds need to be classified into appropriate categories as they fall outside the category of complete healing without recurrence.

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In this study, we sought to describe detailed wound outcomes along with conventional endpoints at 2 years after intervention for atherosclerotic femoropopliteal lesions with or without below-the-knee interventions in patients with ischemic tissue loss. Furthermore, we investigated factors that prevented wound healing without recurrence and limb salvage at 2 years following the intervention.

2. Methods

A retrospective review of prospectively collected data was conducted on patients who underwent first-time endovascular treatment of the femoropopliteal artery for ischemic tissue loss between May 2010 and Feb 2018. The patients with TASC (Trans-Atlantic Inter Society Consensus) A–C lesions were managed according to the “endovascular-first” policy at our hospital. For those with D lesions, patients with good performance status and good saphenous vein quality (diameter >2.5 mm) received vein bypass surgery first, while other patients with D lesions were managed with the “endovascular-first” policy. During the above period, 138 first bypass surgeries using saphenous vein graft for chronic atherosclerotic femoropopliteal lesions were performed on 138 limbs in 121 patients. Among the 1053 limbs that underwent interventions for chronic femoropopliteal lesions during study period, limbs with claudication (n = 541), rest pain (n = 101) and reintervention (n = 159) were excluded. Among the 252 limbs that underwent interventions to treat de novo chronic femoropopliteal lesions due to ischemic tissue loss, we excluded patients with vasculitis (n = 2), those that experienced technical failure (n = 7) and major tissue loss (extending above the trans-metatarsal level) which inevitably necessitated major amputations (n = 8). Patients that refused initial wound management procedures such as debridement or minor amputation (n = 16) and those that did not have sufficient wound follow-up data at 2-years after procedures (n = 84) were excluded. Finally, 135 first-time procedures on 135 limbs from 112 patients for de novo chronic femoropopliteal atherosclerotic steno-occlusive disease with sufficient 2-year follow-up data were included in this study. Arterial revascularization was not attempted in patients who were completely bedbound and below-the-knee amputation was recommended for patients in whom adequate wound closure utilizing a skin flap or negative pressure wound therapy failed following forefoot amputation.

We reviewed demographic data, comorbidities, details of endovascular therapy procedures, and clinical outcomes. In addition, cardiac ejection fraction and patient functional performances before the development of tissue loss were included as variables. All patients who had successful endovascular interventions received dual antiplatelet therapy. Patients underwent routine clinical follow-up evaluations, including ankle–brachial index (ABI) measurements, duplex scan or computed tomography (CT) angiography at 1, 3, and 6 months post procedure and every 6 months thereafter. Primary patency of femoropopliteal artery was defined as treated vessel without a significant stenosis (a peak systolic velocity ratio >2.4 on duplex scan and >50% stenosis on angiography). Secondary patency of femoropopliteal artery was defined patency of the target lesion after treatment of a re-occlusion of the index lesion.

Wound status was investigated retrospectively, and limbs were categorized by the final wound status at the 2-year follow-up. Ischemic wounds were graded using the Society for Vascular Surgery wound, ischemia, and foot infection (WIfI) classification at initial presentation. Wound healing was defined as complete epithelization of an ischemic wound on the target limb that persisted for at least 14 days.[4] Wound outcomes were categorized as follows: Group A, wound healing without recurrence; Group B, wound occurrence at other sites on the same foot following complete healing with or without minor amputation; Group C, tolerable persisting wounds or wound occurrence at the original site with or without minor amputation; and Group D, major amputation needed. Renal insufficiency was defined as a serum creatinine level ≥ 1.5 mg/dl or renal replacement therapy requirements. Outcome

Table 1
Patient characteristics.

Characteristics	Patients (n = 112)
Age ≥ 70 years	68 (60.7%)
Mean	70.8 ± 8.8
Range	45–86
Male	83 (74.1%)
Prevalence of comorbidities	
Diabetes mellitus	77 (68.8%)
Hypertension	87 (77.7%)
Current or Ex-smoker	73 (65.2%)
Ischemic heart disease	30 (26.8%)
Medical treatment	10 (8.9%)
PCI	16 (14.3%)
Coronary bypass	4 (3.6%)
Stroke	28 (25.0%)
Renal insufficiency	50 (44.6%)
On renal replacement	37 (33.0%)
Not on renal replacement	13 (11.6%)
Ejection fraction	
≥ 50%	74 (66.1%)
< 50%	38 (33.9%)
Functional performance	
≥ 4MET	68 (60.7%)
< 4MET	44 (39.3%)

PCI, percutaneous coronary intervention, MET, metabolic equivalents.

Table 2
Wound stage according to WIfI classification, lesion characteristics and procedural details.

Characteristics	Limbs (n = 135)		
WIfI grade	Wound	0	- (0%)
		1	37 (27.4%)
		2	85 (63.0%)
		3	13 (9.6%)
	Ischemia	0	41 (30.4%)
		1	31 (23.0%)
		2	26 (19.3%)
		3	37 (27.4%)
	Foot infection	0	25 (18.5%)
		1	74 (54.8%)
		2	32 (23.7%)
		3	4 (3.0%)
WIfI clinical stage of major limb amputation		1	14 (10.4%)
		2	30 (22.2%)
		3	35 (25.9%)
		4	56 (41.5%)
TASC			
A/B	25 (18.5%)/49 (36.3%)		
C/D	39 (28.8%)/22 (16.3%)		
Runoff n.			
> 1	54 (40.0%)		
≤ 1	81 (60.0%)		
Concomitant procedure			
Iliac angioplasty	35 (25.9%)		
BTK angioplasty	100 (74.1%)		
Type of F–P procedures			
POBA	56 (41.5%)		
DCB	34 (25.2%)		
POBA + BMS	4 (3.0%)		
DCB + BMS	34 (25.2%)		
DES	3 (2.2%)		
Supera stent	3 (2.5%)		
Atherectomy	1 (0.7%)		

TASC, Trans-Atlantic Inter Society Consensus; BTK, below-the-knee.
POBA, plain old balloon angioplasty; DCB, drug-coated balloon; BMS, bare metal stent; DES, drug-eluting stent; WIfi grade, Society for Vascular Surgery wound, ischemia, and foot infection grade.

Table 3
Wound outcome after intervention (N = 135).

A. Wound classification at 2 years after intervention

Wound category		Limb no.
A	**Complete healing without recurrence with or without minor amputation**	76[a] (56.3%)
B	**Occurrence of wound at other sites of the same foot after complete healing with or without minor amputation**	11[b] (8.1%)
C	**Tolerable persisting wound or recurrent wound at the same site with or without minor amputation**	30[c] (22.2%)
D	**Below-the-knee (BK) amputation needed**	18[d] (13.3%)

[a] Toe amputation or debridement, 73; Transmetatarsal amputation, 3
[b] Toe amputation or debridement, 11; Transmetatarsal amputation, 0
[c] Toe amputation or debridement, 29; Transmetatarsal amputation, 1
[d] BK amputation performed, 13; BK amputation refused, 5

B. Wound classification in survival and death groups at 2 years after intervention

Wound Category	Limb no.		Wound Category	Limb no.	
Survival (N = 87)	**A**	54[a] (62.1%)	**Death (N = 48)**	**A**	22[a] (45.8%)
	B	5[b] (5.7%)		**B**	6[b] (12.5%)
	C	19[c] (21.8%)		**C**	11[c] (22.9%)
	D	9[d] (10.3%)		**D**	9[d] (18.8%)
	Total	87 (100%)		**Total**	48 (100%)

Survival group:
[a] Toe amputation or debridement, 52; Transmetatarsal amputation, 2
[b] Toe amputation or debridement, 5; Transmetatarsal amputation, 0
[c] Toe amputation or debridement, 18; Transmetatarsal amputation, 1
[d] BK amputation performed, 7; BK amputation refused, 2

Death group:
[a] Toe amputation or debridement, 21; Transmetatarsal amputation, 1
[b] Toe amputation or debridement, 6; Transmetatarsal amputation, 0
[c] Toe amputation or debridement, 11; Transmetatarsal amputation, 0
[d] BK amputation performed, 6; BK amputation refused, 3

Table 4
Treatment outcomes according to conventional outcome endpoint (N = 135).

	1-year	2-year
Primary patency[a]	82.4%	70.2%
Secondary patency[a]	90.1%	88.3%
Limb salvage	87.4%	86.7%
Survival	81.9%	64.4%
AFS	72.1%	57.8%

AFS, amputation-free survival.
[a] Femoropopliteal artery.

variables included classifications based on detailed wound outcomes, limb salvage, patient survival, and AFS.

The risk factor analysis for complete wound healing without recurrence and limb salvage at 2-year was performed. The univariate analysis of categorical variables was performed with a Chi-square test. Only the variables determined to be statistically significant by univariate analysis were used subsequently in the multivariate analysis which utilized a logistic regression model with binary variables. The results were reported as hazard ratios (HR) with 95% confidence intervals. A p-value <0.05 was considered statistically significant. The Kaplan–Meier method was used to calculate primary patency, secondary patency, limb salvage, patient survival, and AFS. All statistical analyses were performed using SPSS Statistics for Windows, version 21.0 (IBM Co., Armonk, NY, USA).

The study protocol was developed in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (No. DSMC 2019-07-008). The requirement of for informed consent was waived due to the retrospective nature of study.

3. Results

3.1. Patient population, lesions, and procedural characteristics

Patient characteristics are shown in Table 1. Among 112 patients (74.1% male; age 70.8–8.8 years; range, 45–86 years), 68.8% had diabetes and 44.6% had renal insufficiency. Anatomic characteristics and procedural details of the 135 limbs are shown in Table 2. Iliac angioplasty and BTK angioplasty as a concomitant procedure was performed in 25.9% and 74.1% of patients, respectively.

3.2. Intermediate–term outcomes according to wound classification and survival

At 2 years following the procedures, 76 limbs (56.3%) were categorized as group A (wound healing without recurrence) and 11 limbs (8.1%) as group B (wound occurrence at other sites on the same foot with or without minor amputation). Wounds that persisted or occurred at the original site in 30 limbs (22.2%) were categorized as group C. Eighteen limbs (13.3%) that needed major amputations were categorized as group D. For these 18 patients, BTK amputations were performed in 13 limbs while 5 patients (or their families) refused the amputation (Table 3–A). When divided into groups based on those who survived (survival group) versus those that died (death group), wound outcomes according to detailed wound classifications are presented in Table 3–B. Treatment outcomes according to conventional endpoints such as patency, limb salvage rates, patient survival, and AFS are summarized in Table 4.

3.3. Influencing factors on wound healing without recurrence at 2-years

Table 5–A shows the univariate analysis results of factors related to complete wound healing without recurrence at 2 years. This analysis showed that renal insufficiency, ischemia grade 3 (ankle pressure < 50 mmHg or flat forefoot PVR according to WIfI classification), an ejection fraction < 50% and functional performance < 4 MET correlated with non-healing or wound recurrence. The independent risk factors that prevented wound healing without recurrence at 2 years, according to the binary logistic regression model for the multivariate analysis (Table 5–B), were renal insufficiency (HR = 0.225, p = 0.001), ischemia grade 3 (HR = 0.328, p = 0.025), and functional performance < 4 MET (HR = 0.150, p < 0.001).

3.4. Influencing factors on limb salvage at 2-years

Table 6–A show the results of the univariate analysis of factors related to limb loss at 2 years. The univariate analysis showed that WIfI stage 4, ischemia grade 3, and functional performance < 4 MET correlated with the need for major amputation. The independent risk factors for major amputation at 2 years, according to the binary logistic regression model for multivariate analysis (Table 6–B),

Table 5
Factors related to complete wound healing without recurrence at 2 years following the intervention (N = 135).

A. Univariate analysis of factors

Variables	No (%)		p-value
	Complete wound healing w/o recurrence	Wound recurrence or persisting wound or limb loss	
Age ≥ 70 years	43 (58.9%)	39 (62.9%)	0.635[a]
Female	18 (24.7%)	18 (29.0%)	0.567[a]
Hypertension	57 (78.1%)	49 (79.0%)	0.893[a]
Diabetes mellitus	48 (65.8%)	46 (74.2%)	0.288[a]
Current smoker or Ex-smoker	47 (64.4%)	43 (69.4%)	0.541[a]
Ischemic heart disease	17 (23.3%)	22 (35.5%)	0.119[a]
Stroke	18 (24.7%)	17 (27.4%)	0.715[a]
Renal insufficiency	24 (32.9%)	37 (59.7%)	0.002[a]
TASC C or D	33 (45.2%)	28 (45.2%)	0.996[a]
WIfI stage 4	25 (34.2%)	31 (50.0%)	0.064 [a]
Iliac artery stenosis/occlusion	22 (30.1%)	13 (21.0%)	.226[a]
Tibial runoff ≤ 1	39 (53.4%)	42 (67.7%)	0.091[a]
BTK treatment	46 (63.0%)	43 (69.4%)	0.439[a]
Ankle pressure < 50 mmHg or flat forefoot PVR[b]	12 (16.4%)	25 (40.3%)	0.002[a]
Ejection fraction < 50%	18 (24.7%)	27 (43.5%)	0.02 [a]
Functional performance < 4 MET[c]	14 (19.2%)	42 (67.7%)	< .001[a]
Paclitaxel-delivery treatment	21(28.8%)	20 (32.3%)	0.660[a]
Use of stenting	22(30.1%)	22(35.5%)	0.509[a]
Death	21 (28.8%)	27 (43.5%)	0.074[a]

TASC, Trans-Atlantic Inter Society Consensus; BTK, below-the-knee; PVR, pulse volume recording; MET, metabolic equivalents; WIfi grade, Society for Vascular Surgery wound, ischemia, and foot infection grade
[a] Chi-square test
[b] In severe arterial calcification precluding reliable ankle pressure
[c] Unable to walk ≥ 2 blocks (160 m) on level ground without stopping or Unable to perform daily activities independently

B. Multivariate analysis of factors by binary logistic regression model

Variables	p-value	HR (95% CI)
Renal insufficiency	0.001	0.204 (0.079–0.525)
Ankle pressure < 50 mmHg or flat forefoot PVR	0.023	0.309 (0.112–0.853)
Ejection fraction < 50%	0.733	0.851 (0.338–2.146)
Functional performance < 4 MET	< .001	0.104 (0.041–0.260)

PVR, pulse volume recording; MET, metabolic equivalents.

were ischemia grade 3 (HR = 3.897, p = 0.048) and functional performance < 4 MET (HR = 11.001, p < 0.003).

4. Discussion

During the last few years, the treatment of femoropopliteal occlusive disease has undergone a paradigm shift towards an aggressive endovascular therapeutic approach.[20–26] Especially for patients with CLTI, the main evidence supporting various endovascular treatments includes information on acceptable limb salvage and AFS.[27] In this study, we focused on the detailed outcomes of ischemic wounds other than conventional endpoints. Whether or not major amputation is performed at the end of follow-up, does not provide sufficient data on treatment benefits in those who experience ischemic tissue loss. In this study, classifying the wound outcomes provided additional information regarding the practical benefits that can be achieved following intervention.

In practice, treatment of CLTI is determined by considering not only the severity of the lesion, but also various risk factors of the patients. These risk factors subsequently have an effect on various clinical outcomes. One of the advantages of endovascular treatment is that it can be performed in frail patients with high limb salvage rate, which has helped in expanding the treatment indication. One recent review showed that the estimated 1-year major amputation rates were 0%, 8%, 11%, and 38%, for WIfI stage I–IV, respectively.[28] Our outcomes showed comparable results (Appendix I). In this study, we were able to achieve a high limb salvage rate and an acceptable patency rate in patients with various risk factors; however, wound recurrence or unhealed wounds remained a significant problem after treatment.

Wound outcome classifications as an ultimate clinical parameter have not been described in many studies.[5,9,10,14,27] By definition, in order to achieve clinical success in patients with ischemic tissue loss, improvement requires downgrading by at least 1 Rutherford category. To accurately assess this, wound healing needs to be an absolute indicator.[4] However, approximately 20% of the limbs remained unhealed or recurred at the original site (category C). In the analysis, 53.3% (16/30) and 63.3% (19/30) of patients in category C were found to have poor functional performance (< 4MET) and renal insufficiency, respectively. Most risk factors such as diabetes and renal insufficiency are uncorrectable, and therefore the microvascular insufficiency associated with these conditions continuously prohibits wound healing.

Many risk factors associated with patency, limb salvage, and wound healing have been identified in previous studies. Black et al showed that insulin-dependent diabetes, poor runoff in the foot, and renal insufficiency were predictive of endoluminal failure following intervention.[29] Renal insufficiency affects endovascular lesions by promoting calcification and leading to small arterial disease.[30] Renal insufficiency has been shown consistently to have an adverse effect on percutaneous intervention and open revascularization.[30] Tibial runoff has been discussed in many previous studies with regard to both endoluminal treatments and open surgery.[31–36] In this study, poor tibial runoff was not shown to have a statistically significant influence on wound healing (p = 0.091). In the subgroup analysis, BTK intervention in those with poor runoff did not have a significant impact on limb salvage or wound healing (Appendix II). The efficacy and indication for BTK interventions combined with femoropopliteal interventions are still unclear.[33–35] On the other hand, in a study by Smolock et al., no significant

Table 6
Risk factors related with limb loss at 2 year after intervention (N = 135).
A. Univariate analysis of risk factors of limb loss.

Variables	No (%)		p-value
	Limb salvage	Limb loss	
Age ≥ 70 years	73 (62.4%)	9 (50.0%)	0.316[a]
Female	34 (29.1%)	2 (11.1%)	0.153[b]
Hypertension	93 (79.5%)	13 (72.2%)	0.485[a]
Diabetes mellitus	82 (70.1%)	12 (66.7%)	0.769[a]
Current smoker or Ex-smoker	77 (65.8%)	13 (72.2%)	0.591[a]
Ischemic heart disease	32 (27.4%)	7 (38.9%)	0.315[a]
Stroke	28 (23.9%)	7 (38.9%)	0.178[a]
Renal insufficiency	51 (43.6%)	10 (55.6%)	0.342[a]
TASC C or D	51 (43.6%)	10 (55.6%)	0.342[a]
WIfI stage 4	41 (35.0%)	15 (83.3%)	< .001[a]
Iliac artery stenosis/occlusion	30 (25.6%)	5 (27.8%)	0.847[a]
Tibial Runoff ≤ 1	68 (58.1%)	13 (72.2%)	0.256[a]
BTK treatment	76 (65.0%)	13 (72.2%)	0.545[a]
Ankle pressure < 50 mmHg or flat forefoot PVR[c]	24 (20.5%)	13 (72.2%)	< .001[a]
Ejection fraction < 50%	36 (30.8%)	9 (50.0%)	0.107[a]
Functional performance < 4 MET[d]	40 (34.2%)	16 (88.9%)	< .001[b]
Paclitaxel-delivery treatment	37 (31.6%)	4 (22.2%)	0.584[b]
Use of stenting	40 (34.2%)	4 (22.2%)	0.422[b]
Death	39 (33.3%)	9 (50.0%)	0.169[a]

TASC, Trans-Atlantic Inter Society Consensus; BTK, below-the-knee; PVR, pulse volume recording; MET, metabolic equivalents; WIfi grade, Society for Vascular Surgery wound, ischemia, and foot infection grade
[a]Chi-square test
[b]Fisher's exact test
[c]In severe arterial calcification precluding reliable ankle pressure
[d]Unable to walk ≥ 2 blocks (160 m) on level ground without stopping or unable to perform daily activities independently

B. Multivariate analysis of risk factors for limb loss by binary logistic regression model

Variables	p-value	HR (95% CI)
WIfI stage 4	0.089	3.761 (0.815–17.342)
Ankle pressure < 50 mmHg or flat forefoot PVR	0.048	3.897 (1.012–15.013)
Functional performance < 4 MET	0.003	11.001 (2.275–53.190)

PVR, pulse volume recording; MET, metabolic equivalents. WIfi grade, Society for Vascular Surgery wound, ischemia, and foot infection grade.

benefits were observed after concomitant tibial interventions in terms of limb salvage, AFS, freedom from recurrent symptoms, or clinical success.[36] Although BTK interventions are justified in CLTI, whether their effects have a significant impact on clinical success in intermediate or long term should be the focus of future studies.

A number of studies have used major lower limb amputation as a surrogate for CLTI.[37] It is known that the risk of amputation is high in CLTI patients, even after successful revascularization.[38] The rates of amputation at 4 years were 35.3%, and 67.3% for Rutherford class 5, and class 6, respectively.[39] Initial presentation of gangrene, dialysis dependence, diabetes, and TASC D lesions were predictive factors for major amputations.[40] In addition, patients' comorbidities were independently associated with an increased risk of amputation following revascularization for CLTI.[41] Multiple studies evaluated the prognostic value of the WIfI classification and some showed that the risk of amputation increased with a higher WIfI grade.[42,43] WIfI stage 4 showed a tendency towards an association with poor outcomes but did not reach statistical significance in this study. Statistical significance of ischemia grade 3 on wound healing and limb salvage in this study is consistent with other studies showing that limb perfusion is a key factor in predicting amputation risk.[42] Poor performance revealed a significant relationship with non-healing of wounds and limb loss. Technical feasibility and risk estimation systems are only part of process in treatment choices for patients with CLTI. Vascular surgeons should determine the optimal treatments based on a comprehensive review of the patients baseline condition. A patient's baseline performance status should be the most important factor for surgeons to consider.

This study has several limitations. First, the initial wound data and follow-up wound data were not available in many cases due to the retrospective design. Second, it is hard to define the term, "tolerable persisting wound" objectively. In this study, those lesions generally showed some improvement overtime and appeared to have healing potential without further amputations; however, those wounds persisted without complete healing. More aggressive treatments such as forefoot amputation at a more proximal level other than conservative management could be a possible option in those cases. Third, the sample size was not sufficient to achieve conclusive results, and in particular, this study was based on data from different treatment modalities.

In conclusion, more than half of treated limbs remained healed without recurrence at 2-years after endovascular treatment; however, wound recurrence or unhealed wounds remained a significant problem after treatment. Renal insufficiency, ischemia grade 3 and poor functional performance were significant independent risk factors that prevented wound healing without recurrence at 2 years.

Authorship

Young-Nam Roh: Study design, data collection, data analysis, data interpretation, preparation of manuscript, literature analysis.
Hyun Yong Lee: Data collection.
Ui Jun Park: Data collection, data analysis.
Hyoung Tae Kim: Data collection, data analysis.

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Declaration of competing interest

None.

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None.

Appendix I. Limb loss rate according to WIfI stage (N = 135)

		Stage I (n = 14)	Stage II (n = 30)	Stage III (n = 35)	Stage IV (n = 56)
No. of limb loss	**Amputation, performed**	–	–	2	11
	Amputation, refused	–	–	1	4
Limb loss, %		0%	0%	8.6%	26.8%

Appendix II. Effect of BTK intervention on wound outcome in patients with poor tibial runoff (no. of tibial runoff ≤ 1) at 2-year after intervention (N = 81)

	Limbs with no. of tibial runoff ≤ 1		p-value
	BTK intervention, performed (n = 57)	BTK intervention, not performed (n = 24)	
Complete wound healing w/o recurrence, n (%)	29 (50.9)	10 (41.7)	0.449[a]
Limb salvage, n (%)	48 (84.2)	20 (83.3)	1.000[b]

[a]Chi-square test.
[b]Fisher's exact test.

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