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Predictors and outcomes of restenosis following tibial artery endovascular interventions for critical limb ischemia

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Objective: **Restenosis following tibial artery endovascular interventions (TAEIs) is thought to be benign but is not well characterized. This study examines the consequences and predictors of recurrent stenosis of TAEIs for critical limb ischemia.**

Methods: **All TAEIs for critical limb ischemia performed between 2004 and 2010 were retrospectively reviewed. Restenosis was detected by noninvasive imaging and angiography when indicated. Restenoses were identified and the limb outcomes recorded. Tibial reinterventions were performed only for persistent, worsening, or recurrent tissue loss or rest pain with evidence of recurrence on duplex ultrasound or hemodynamic imaging. The χ^2 test and logistic regression were applied as indicated. One-year patency rates were calculated using the Kaplan-Meier method.**

Results: **A total of 235 limbs in 210 patients were treated for critical limb ischemia (70% tissue loss, 30% rest pain). Tissue loss included gangrene (49%) and ulcers (51%), and involved the forefoot (80%), the heel (14%), or both (6%). Seventy-eight percent of limbs had Trans-Atlantic InterSociety Consensus C/D lesions, with mean preoperative runoff score of 12. Interventions were isolated tibial (45%) or multilevel (55%) (including tibial). Mean postoperative runoff score improved to 6.6, but restenosis occurred in 96 limbs (41%) at a mean of 4 months. The 1-year primary patency was 59% with a mean follow-up of 9 months. Restenosis presented with a persistent wound (32%), worsened wound (42%), rest pain (16%), or no symptoms (10%). A repeat TAEI was performed in 42 (44%), major amputation in 26 (27%), open bypass in 20 (21%), and observation in eight (8%). The overall amputation rate was 13%, but limb loss was significantly higher in patients with restenosis (n = 26 [27%]) than in patients with no restenosis (n = 5 [4%]; $P < .001$). Patients with restenosis and tissue loss were more likely to have presented with gangrene (63% vs 38%; $P = .0003$) but had comparable wound distribution (P = NS). There was a trend toward a higher restenosis rate in patients with renal insufficiency (odds ratio, 5.57; $P = .08$), but this was unaffected by diabetes, statin therapy, or smoking (P = NS). The rate of repeat intervention after the first reintervention was 36%, with an 87% overall limb salvage rate.**

Conclusions: **TAEIs can be used successfully to treat patients with critical limb ischemia with acceptable limb salvage rates. Special attention should be given to patients with extensive tissue loss or gangrene because they are at risk for early restenosis and subsequent limb loss. Strict wound and hemodynamic surveillance, wound care, and timely reinterventions are crucial to achieve successful outcomes in this patient population. Amputation or alternative revascularization options, when feasible, should be considered in patients with restenosis and tissue loss given the high rate of limb loss with tibial reinterventions. (J Vasc Surg 2013;57:692-9.)**

Tibial artery endovascular interventions (TAEIs) have become a first line-approach of revascularization in many centers in patients with tibioperoneal occlusive disease.[1-5] Several studies have shown the efficacy and procedural safety of TAEI for the treatment of critical limb ischemia (CLI).[1,6-9] Low patency rates after endovascular interventions, especially in infrapopliteal arteries, and high restenosis rates have been uniformly noted, with a high rate of restenosis and requirement for reinterventions.[3,4,9-13] Tibial restenosis and reinterventions have been traditionally considered to be benign and successful, without significant consequences on limb outcomes.[14] This perception may be based on the ease of reinterventions, as lesions typically regress back to their baseline angiographic presentation without any disease extension or loss of outflow vessels.[6-8,12,13,15] However, the impact of tibial restenosis and reinterventions in patients with CLI has not been well characterized. This study sought to examine the consequences and predictors of recurrent stenosis of TAEI in the setting of CLI and its effect on wound healing and limb salvage.

METHODS

Patient population. All patients who underwent TAEI between September 2004 and May 2010 were retrospectively identified from a prospectively maintained registry, and patient characteristics, comorbidities, interventions, and complications were recorded. Patients were treated for rest pain (Rutherford class 4) and/or tissue

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loss (Rutherford classes 5 and 6). Patients who presented with acute ischemia were excluded from the study. Patients who experienced restenosis and underwent reintervention were identified. Clinical outcomes, including patency rates, limb salvage, and wound healing, were determined. Each preprocedural and postprocedural angiogram was reviewed to assess baseline and postprocedural popliteal-tibial runoff score. Except for our standard follow-up protocol, there were no set revascularization protocols within our group for patients presenting with CLI. Hence, treatment biases were based on individual surgeon practices and as such reflect real-world clinical practice.

Endovascular intervention and reinterventions. All endovascular interventions were performed by vascular surgeons with patients under local anesthesia and moderate conscious sedation, using fixed imaging in hybrid operating rooms or interventional radiology suites. The majority of the interventions (79%) were performed through contralateral retrograde common femoral access, whereas ipsilateral antegrade common femoral and left transbrachial access was used selectively. Interventions were performed after systemic heparinization (100 U/kg). During the index procedure, interventions were performed with an intention to establish in-line arterial flow to the foot. At least one tibial artery was revascularized, and additional tibial vessels were treated based on the ease of the revascularization and operator preference. During repeat endovascular interventions, hemodynamically significant recurrent stenosis at the site of the initial lesion and any stenosis proximal or distal to this lesion were intervened upon to re-establish in-line flow to the foot. More than 30% residual stenosis was considered significant angiographically.[16] Tibial stenting was generally avoided and was used only as a bailout to treat flow-limiting dissections or persistent occlusions.

Concomitant femoropopliteal occlusions were recanalized and treated, primarily with angioplasty and selective stenting. Pedal angioplasty was performed to improve outflow in patients with tandem pedal lesions. All patients were treated with an antiplatelet agent, either clopidogrel or aspirin, unless there was a clear contraindication.

Follow-up protocol. All patients were followed clinically with serial noninvasive arterial studies. In addition, patients with tissue loss were followed in the outpatient clinic on a weekly basis for wound care. Noninvasive vascular laboratory surveillance was routinely performed on all patients at 1 month, 3 months, and 6 months postprocedure. Patients were then evaluated at 6-month intervals. The travel distance was used as a surrogate measure of the difficulty for patients to come back for frequent weekly wound care visits.

Tibial restenosis. Restenosis was detected by noninvasive imaging and angiography as needed. Restenosis was suspected based on noninvasive testing, which confirmed recurrent disease (ankle-brachial index decrease >0.15, dampened pulse volume recordings, or evidence of stenoses by duplex ultrasound scan), regardless of symptom status. Although there are no standard duplex criteria for classification of tibial stenoses, we have utilized PSV >300 cm/s and peak stenotic velocity to prestenotic velocity ratio of 3.5 as indicators of severe stenosis based on our local surveillance protocol.[17] Tibial restenosis was also suspected on clinical grounds if there was lack of improvement in wound healing 4 weeks after the TAEI, increased tissue compromise compared with initial presentation, or need for major amputation. This was confirmed on repeat angiography only in patients with recurrent symptoms or failure of wound healing. Wound healing was used as an additional surrogate clinical sign for restenosis. Patients with worsening wounds despite wound care and with absence of local confounding factors, such as infection or poor offloading, were reevaluated with angiography even if noninvasive testing was inconclusive for restenosis. Standard definitions of primary, primary-assisted, and secondary patency rates were used as previously described.[9]

Classification of disease distribution. The TransAtlantic Inter-Society Consensus document[18] (TASC I) tibial classification was used to describe the distribution and extent of occlusive disease, given that the TASC-II revision did not include a tibial classification. Popliteal and tibial runoff scores were calculated according to a modification of the Society for Vascular Surgery criteria as published by Davies et al.[19] The TASC-II classification was used to classify femoropopliteal disease into A, B, C and D.[20]

Statistical analysis. All statistical analyses were completed using SAS software (version 9.1; SAS Institute, Cary, NC). Univariate descriptive statistics were assessed for all patients' sex, age, and comorbid conditions as well as for key clinical measures described in the following section. Limb wound types prompting TAEI were compared for subsequent occurrence of restenosis using the Fisher exact test. A logistic regression model was built to identify patient characteristics explaining restenosis. Preoperative and postoperative popliteal and tibial runoff scores were compared in limbs that developed restenosis vs those that did not develop restenosis using the Student *t*-test. Limb loss in the restenosis and no restenosis groups was compared using the χ^2 test. Patency and limb loss were plotted using the Kaplan-Meier method.

RESULTS

A total of 235 limbs in 210 patients were treated with TAEI for CLI. Demographic data and comorbidities of patients undergoing TAEI are given in Table I. The indication for intervention included tissue loss in 165 limbs (70%) and rest pain in 70 limbs (30%; Table II). Tissue loss included gangrene (49%) and ulcers (51%), and involved the forefoot (80%), the heel (14%), or both (6%). Severe occlusive disease was present in the majority of limbs as reflected by the distribution of TASC-I lesions (Table III) and runoff scores (Table IV). Although the majority of patients who underwent an endovascular intervention were bypass candidates, several were not due to the lack of an adequate conduit or poor surgical risk. Most of the access was obtained in the femoral artery; in two patients (0.01%) a left brachial artery access was obtained.

Table I. Characteristics of patients undergoing TAEI

Characteristics	*All TAEI*	*TAEI with no restenosis*	*TAEI with restenosis*	P *value*
Male	126/210 (60.2%)	68/121 (56%)	58/89 (65%)	.48
Age, years	73.3	74.0	72.9	.76
Diabetes	137/210 (65.5%)	74/121 (61%)	63/89 (71%)	.32
Chronic renal failure	90/210 (43.1%)	45/121 (37%)	45/89 (50%)	.43
Ends-stage renal disease/dialysis	41/210 (19.5%)	20/121 (17%)	21/89 (24%)	.20
Hypertension	192/210 (92%)	109/121 (90%)	83/89 (94%)	.85
Statin therapy	113/210 (54%)	52/121 (43%)	61/89 (62%)	.33
Coronary artery bypass graft	50/210 (25%)	20/121 (17%)	30/89 (55%)	.12
Coronary artery disease	132/210 (63%)	74/121 (61%)	58/89 (66%)	.80
Chronic heart failure	63/210 (30%)	31/121 (26%)	32/89 (36%)	.50
Angina	16/210 (8%)	4/121 (3%)	12/89 (13%)	.77
Unstable angina	1/210 (0.4%)	0/121 (0%)	1/89 (1%)	.32
Myocardial infarction	62/210 (29%)	31/121 (26%)	31/89 (35%)	.35
Chronic obstructive pulmonary disease	40/210 (19%)	26/121 (21%)	14/89 (16%)	.42
History of cancer	32/210 (15%)	21/121 (17%)	11/89 (13%)	.66
History of tobacco	71/210 (34%)	30/121 (25%)	41/89 (46%)	.42

TAEI, Tibial artery endovascular intervention.

Table II. Indications for index TAEI in limbs

Indication	*All TAEI limbs*	*TAEI with no restenosis*	*TAEI with restenosis*	P *value*
Rest pain	70/235 (30%)	50/139 (36%)	20/96 (21%)	.78
Tissue loss	165/235 (70%)	89/139 (64%)	76/96 (79%)	
Nonhealing ulcer	84/165 (51%)	56/89 (63%)	28/76 (36.5%)	NS
Gangrene	81/165 (49%)	33/89 (37%)	48/76 (63.5%)	.0003
Tissue loss location				.12
Forefoot	132/165 (80%)	72/89 (80%)	61/76 (80%)	
Hindfoot	23/165 (14%)	14/89 (16%)	9/76 (11%)	
Both	10/165 (6%)	4/89 (4%)	6/76 (8%)	

NS, Not significant; *TAEI,* tibial artery endovascular intervention.

Table III. TASC I classification (extent of infrapopliteal disease)

	Limbs undergoing TAEI (N = 235)	*Limbs with no restenosis (N = 139)*	*Limbs with restenosis (N = 96)*	P *value*
TASC A	5/235 (2%)	5/139 (4%)	0/96 (0%)	.99
TASC B	47/235 (20%)	31/139 (22%)	16/96 (17%)	.99
TASC C	81/235 (34%)	46/139 (33%)	35/96 (36%)	.99
TASC D	102/235 (44%)	57/139 (41%)	45/96 (47%)	.99

TAEI, Tibial artery endovascular intervention; *TASC,* TransAtlantic Inter-Society Consensus.

In-line flow to the foot with at least one tibial vessel was achieved in 228 limbs (97%) during the index TAEI procedure; however, improvement in popliteal-tibial runoff score after the intervention was present in only 200 limbs (85%). Despite angiographic technical success with establishment of in-line flow to foot either directly or via peroneal artery collaterals, 35 limbs (15%) did not have significant improvement in runoff score due to compromised pedal runoff or persistent high-grade stenosis in the remaining tibial runoff vessels.

Isolated tibial interventions were performed in 106 limbs (45%), and concurrent multilevel interventions including tibial arteries were performed in 129 limbs (55%). Multilevel interventions included the femoropopliteal segment in 55 limbs (23.4%), the popliteal artery only in 41 limbs (17.6%), the superficial femoral artery only in 24 limbs (10.4%), and a bypass graft intervention in seven limbs (3.3%). Mean follow-up was 9 months (range, 1-36.9 months).

Tibial restenosis or reocclusion occurred in 96 limbs (41%) of 89 patients (42%) at 1 year. Mean time for detection of restenosis was 5.8 months ± 2.8 months (range, 0.5-27 months). Fifty-four percent of the patients needed to travel more than 35 miles for frequent wound care visits and were followed locally; these patients were temporarily lost to follow-up. The presentation of tibial restenosis included a persistent wound in 30 limbs (32%); recurrent, new, or worsened wound in 41 limbs (42%); rest pain in

Table IV. Modified Society for Vascular Surgery runoff scores

	All TAEI limbs	*Limbs with no restenosis*	*Limbs with restenosis*	P *value*
Preintervention runoff score	11.9 (5-19)	11.9 (6-19)	11.6 (5-19)	.52
Postintervention runoff score	6.6 (1-17.5)	6.4 (1-9)	6.7 (1-17.5)	.54
Runoff score improvement in index TAEI	5.3	5.5	4.9	.29

TAEI, Tibial artery endovascular intervention.

Table V. Logistic regression model to predict tibial restenosis

Variable	*OR*	*CI*	P *value*
Male	1.52	0.73-3.2	.27
Age	0.98	0.95-1.01	.19
Diabetes	0.89	0.40-1.97	.78
CRF/end-stage renal disease	5.57	0.01-1.25	.08
Hypertension	0.90	0.24-3.40	.88
Statins therapy	1.56	0.72-3.38	.26
Coronary artery bypass graft	1.12	0.45-2.83	.81
Coronary artery disease	0.99	0.38-2.62	.99
Chronic heart failure	1.34	0.56-3.19	.51
Angina	2.10	0.44-10.08	.35
Myocardial infarction	1.33	0.52-3.38	.55
Chronic obstructive pulmonary disease	0.33	0.11-0.95	.04
Tobacco use	0.56	0.22-1.41	.22
Smoking	1.28	0.68-2.40	.44
Gangrene	3.12	1.23-6.78	.03
Ulcer	1.86	0.56-3.48	.09
Improvement in runoff score	1.19	0.10-14.01	.89
Postprocedural runoff score	0.88	0.63-1.22	.44

CI, Confidence interval; *CRF,* chronic renal failure; *OR,* odds ratio.

15 limbs (16%); and asymptomatic in 10 limbs (10%) identified on noninvasive surveillance imaging. Restenosis was more common in patients undergoing TAEI for tissue loss, especially in patients presenting with gangrene (63.5% restenosis vs 37% no restenosis; $P = .0003$). The rate of restenosis in patients with ulcers only was not statistically significant (36.5% restenosis vs 62.5% no restenosis; $P = .157$).

Both groups were comparable in age, gender, and comorbidities (Tables I and V). There was a trend toward higher restenosis rates in patients with renal insufficiency[21] (odds ratio [OR], 5.57; $P = .08$), but this was unaffected by diabetes, statin therapy, or smoking ($P =$ NS). Similarly, the degree of improvement from preoperative runoff score to postoperative runoff score and the postoperative runoff score itself did not predict restenosis. However, gangrene as an indication for intervention was predictive of restenosis (OR, 3.12; $P = .03$). A similar trend was seen in ischemic ulcers but was not statistically significant (OR, 1.86; $P = .9$; Table V).

A secondary intervention was performed in 42 of 96 limbs (44%) with restenosis (Table VI). Balloon angioplasty was the most common modality used for reintervention (37/42 limbs [88%]). Adjunctive interventions included laser atherectomy (4/42 limbs [9.6%]) and thrombolysis (1/42 limbs [2.4%]). A major amputation was required in 26 of the 96 limbs (27%) that developed restenosis for a variety of reasons, which precluded limb salvage (Table VII), including poor surgical risk, lack of a target vessel, or nonsalvageable extremity with extensive tissue loss. Conversion to open surgical bypass was performed in 20 of the 96 limbs (21%) with restenosis, and clinical observation was performed in eight of 96 limbs (8%) in asymptomatic patients.

Table VI. Management of limbs with tibial restenosis

Interventions	*No. (%)*
Repeat TAEI	42/96 (44%)
Balloon angioplasty	37/42 (88%)
Laser atherectomy	4/42 (9.6%)
Thrombolysis	1/42 (2.4%)
Open surgical bypass	20/96 (21%)
Major amputation	26/96 (27%)
Clinical observation	8/96 (8%)

TAEI, Tibial artery endovascular intervention.

Additional episodes of restenosis were detected in 15 of 42 limbs (36%), which underwent a second reintervention. Of these 15 limbs that underwent re-reintervention, five (33%) required major amputation and three (20%) required a subsequent reintervention. Mean number of reinterventions was three (range, two to five interventions).

Patency rates at 1 year postintervention were estimated using Kaplan-Meier curves. The primary patency rate was 59% (136/235 limbs), the primary-assisted patency rate was 70% (165/235), and the secondary patency rate was 76% (179/235) at 1 year (Fig). The limb salvage rate at 1 year was 87% (204/235 limbs). The overall amputation rate was 13% (31/235 limbs), but limb loss was significantly higher in patients with recurrent stenosis (27% [26/97 limbs]) compared with patients who maintained primary patency (n = 5 [4%]; $P < .001$). Six patients (6/26 [23%]) who sustained limb loss were candidates for bypass but did not undergo close follow-up and progressed to an unsalvageable limb. Others were not candidates either because of lack of conduit or poor surgical risk.

Table VII lists the clinical characteristics of the patients with the 26 limbs (27%) that underwent major amputation after developing restenosis following TAEI. A mean of three TAEIs were performed prior to major amputation in these 26 limbs. The majority of amputations were performed in patients who were deemed to have

Table VII. Characteristics of patients undergoing major amputation after TAEI (N = 26) compared with all the patients (N = 210)

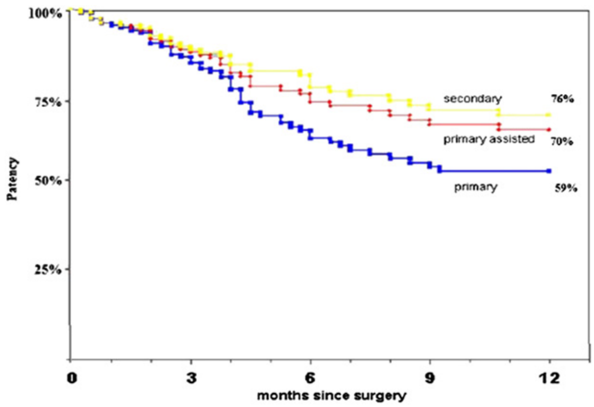
Characteristics	*No. (%) (N = 26)*	*No. (%) (N = 210)*
Age, years		
<59	2/26 (8%)	21/210 (10%)
60-69	8/26 (31%)	37/210 (18%)
70-79	11/26 (42%)	61/210 (29%)
>80	5/26 (19%)	83/210 (40%)
Mean	72.2 years	73.3 years
Cardiopulmonary risk		
Mild	3/26 (12%)	
Moderate	13/26 (50%)	
High	10/26 (38%)	
Renal status		
Normal	15/26 (58%)	169/210 (80%)
End-stage renal disease	11/26 (42%)	41/210 (20%)
Functional status		
Ambulatory	14/26 (54%)	
Limited ambulation	7/26 (27%)	
Nonambulatory	5/26 (19%)	
Adequate vein conduit		
Available	6/26 (23%)	
Not available	20/26 (77%)	
Extent of wound		
Salvageable	8/26 (31%)	
Nonsalvageable	18/26 (69%)	
Bypass target vessel		
No target	9/26 (35%)	
Target present	17/26 (65%)	
Previous coronary artery bypass graft	7/26 (27%)	50/210 (24%)
Previous open revascularization		
Ipsilateral limb	11/26 (42%)	
Contralateral limb	5/26 (19%)	
No. of TAEIs prior to major amputation		
Range	2-5	NA
Mean	3	
Time interval between TAEI and major amputation		
Range	7-332 days	NA
Distance traveled for follow-up clinic visit, miles		
Range	5-65	
Mean	22.5	
>35 miles of travel	14/26 (54%)	

NA, Not applicable; *TAEI,* tibial artery endovascular intervention.

nonsalvageable gangrene, severe soft tissue infection, or ischemic ulcers (18/26 [69%]). Although 17 of 26 limbs (65%) had a possible target vessel for bypass, the presence of severe infection of extensive gangrene led to major amputation. In 77% of limbs (20/26), the patient had no suitable vein for bypass conduit (including arm vein). The absence of vein conduits was secondary to a surgical harvest for multiple redo ipsilateral bypass before TAEI (11/26 patients) or for contralateral bypass (5/26 patients), arteriovenous fistula in patients with end-stage renal disease, presence of varicose veins, or sclerotic/atretic veins. Ten of the 26 patients (38%) undergoing major amputation had high or prohibitive cardiopulmonary operative risk. These major amputations were done under peripheral nerve block and required much less operative time. As such, they were believed to be better tolerated by patients with cardiac or pulmonary risk. The majority of patients (54%) were ambulatory at the time of amputation, 27% had limited ambulation, and 19% (n = 26) were nonambulatory. The amputation was performed between 7 and 332 days after TAEI. Patients had to travel between 5 and 65 miles (mean, 22.3 miles) for follow-up visits, and 14 of 26 patients (54%) had to travel more than 35 miles for follow-up visits. These patients mostly had frequent home visits by the wound care team and sparse clinic visits.

DISCUSSION

Restenosis after a tibial artery intervention has long been a criticism of this procedure. However, even with the high reported rates of restenosis approaching 50% to 60% at 1 year,[1] the clinical end points of limb salvage and patient survival continue to be comparable to those of open surgical revascularization.[1,22,23] Therefore, tibial vessel restenosis traditionally has been dismissed as clinically benign, especially because reinterventions may not be required after resolution of critical limb ischemia.



# of limbs at risk	0 months	3 months	6 months	9 months	12 months
Primary	235	180	154	143	138
Primary assisted	235	193	183	169	164
Secondary	235	197	186	171	179

Fig. Patency in limbs undergoing tibial artery endovascular interventions (TAEIs).

Although the literature is replete with studies comparing infrapopliteal angioplasty and open bypass showing acceptable limb salvage rates after intervention in patients with CLI,[1,4,13,16,24-26] no studies have focused on the repercussions of tibial restenosis, particularly in patients with extensive tissue loss or gangrene.

The current study demonstrates that TAEIs have a high rate of restenosis, which is in line with the published literature. However, our data suggest that these recurrent lesions do not seem to follow a benign clinical course. The present report demonstrates that patients with restenosis had a high rate of major amputation during follow-up despite initial technical success with tibial intervention. Several factors precluded limb salvage, including a prohibitive operative risk, absence of target vessel for surgical revascularization, nonfunctional status, or extensive wound progression that made further attempts at revascularization futile. It can be argued that these patients represent a selected group because aggressive endovascular interventions are offered to patients who traditionally may only be offered primary amputation. However, our study underlines the fact that patients who present with reversible tissue loss have no margin for error, and that tibial restenosis can result in progression of tissue loss beyond salvage The low limb salvage rates in this group of patients underline the need for close clinical and hemodynamic surveillance after TAEI. The presence of tissue loss, especially gangrene, was noted to be more common in patients who developed tibial artery restenosis and is a well-known risk factor for limb loss. Frequent, often weekly, wound care is crucial in patients with gangrene or extensive tissue loss treated with TAEI to detect early clinical signs of restenosis and initiate early revascularization as indicated, as previously reported by our group on the outcomes of wound healing after TAEI in patients with tissue loss.[9]

In our study, tibial restenosis was identified in 41% of the treated limbs despite adequate procedural technical success, hemodynamic improvement, and patency documented on the first postprocedure ultrasound surveillance. Most recurrences appeared early in the postprocedural period, with a mean time for detection of restenosis of 5 months. The early time frame to recurrence is critical in patients with tissue loss, as we previously reported a mean time to wound healing of 10.7 ± 7.4 months after TAEI for CLI.[9] Such patients are unlikely to have healed in such a short time frame and are at risk for early CLI progression to gangrene and subsequent limb loss. In a recent review of 13,258 Medicare patients across the United States (90% with tissue loss), an even higher major amputation rate (23.8%) was noted.[3] This is comparable to the amputation rate in our series of patients who developed restenosis (27% vs 4%). Also, several patients who eventually had limb loss were noted to have a significant travel time for follow-up, which might explain the less intensive surveillance. This finding suggests that patients with Rutherford classes 5 and 6 CLI may be better served with a more durable revascularization strategy with surgical bypass if they cannot adhere to a strict rigorous weekly clinical follow-up and structured surveillance. It is difficult to make comparative analysis between early open revascularization and TAEI based on this study because it was not designed to evaluate this question. However, it can be argued that a bypass with a vein or a prosthetic conduit may result in better limb salvage if performed early when the tissue loss is less extensive.[12,27,28]

The findings from the present study suggest that there is cohort of patients with tibial restenosis in which reinterventions may not be helpful and, in fact, may result in delay in open revascularization with resulting limb loss. As such, identifying such risk factors will be helpful in developing a patient-specific strategy for limb salvage.

It is interesting to note that gangrene as an indication for treatment was a predictor of restenosis following TAEI. It is thought that an increased proinflammatory state in patients with gangrene and foot sepsis might contribute to higher rates of early restenosis in the group of patients with extensive tissue necrosis or gangrene.[29] This again underscores the importance of a durable revascularization strategy in this patient population, which seems to be at increased risk for early failure with TAEI and possible progression of CLI. Patients with tissue loss and no surgical bypass options who undergo tibial reinterventions represent a particularly challenging subset because limb salvage is limited. Given the poor limb salvage rate, patients in that category with restenosis and extensive tissue loss perhaps should be offered an amputation as opposed to multiple reinterventions. The majority of patients in our series who presented with gangrene had a distal revascularization target, although most did not have an optimal conduit.

In this study, the burden of tibial and popliteal disease was calculated using the modified Society for Vascular Surgery runoff score system validated by Davies et al[19] given the lack of a tibial classification in the current TASC-II guidelines. We demonstrated a significant improvement in postprocedural runoff scores after intervention. However, the occurrence of tibial restenosis and the need for reintervention or eventual major amputation was not predictable based on the pre- or postintervention runoff score. It was also noted that although there was a similar TASC lesion distribution, the presentation was different with more gangrene in the restenosis group. The exact reason for the differences in presentation cannot be determined but can be postulated to be due to variations in the timing in seeking medical care and in the quality of runoff.

Forty-four percent of patients with restenosis underwent a repeat endovascular intervention, and 21% required an open surgical bypass. Among patients who underwent repeat endovascular intervention, the subsequent need for repeat intervention was high. The persistence with endovascular intervention was due to a combination of the patients' anatomic situation (target vessel or conduit limitations) and overall medical condition, and resulted in poor limb salvage rates. However, the reinterventions did appear to delay the time to limb loss, with a mean time to major amputation of 1 to 2 months from initial intervention. Despite an acceptable overall limb salvage rate of 87% at 1 year, which is similar to published data,[23] special consideration should be given to patients with gangrene or extensive tissue loss, who represented the majority of patients (70% [165/235]) in this series. Limb salvage in this subgroup is contingent on the understanding that the rates of restenosis and reinterventions are high with TAEI, and that the clinical course may not be benign and requires close rigorous follow-up.

The findings from the present study suggest that there is a cohort of patients with tibial restenosis for whom reinterventions may not be helpful and, in fact, may result in delay in open revascularization with resulting limb loss. Patients with gangrene had higher rates of restenosis and major amputation. Although such patients may be successfully treated with TAEI, early implementation of open surgical revascularization should be considered for those patients with tissue loss, in general, and gangrene, in particular, if they present with early restenosis or if they cannot adhere to a strict follow-up schedule. However, because this study is a nonrandomized retrospective study, whether an open revascularization would have outcomes better than the TAEI is unknown.

There are several limitations to this study. The retrospective design is likely to introduce a selection bias given the heterogeneous patient population treated by multiple surgeons who may be biased toward different revascularization techniques and devices. In addition, there are no consensus guidelines to classify tibial interventions, and different distributions of tissue loss and rest pain, which may lead to mixed results when comparing outcomes, may have resulted in misdiagnosis or delayed diagnosis of restenosis. Additionally, our study lacks comparative analysis among open revascularization, TAEI, and conservative therapy alone. Finally, the lack of validated duplex diagnostic criteria may have resulted in misdiagnosis or delayed diagnosis of restenosis.

Despite its limitations, the present study contributes to a patient-specific CLI treatment strategy. Until more durable results can be achieved with TAEI, perhaps with drug-eluting balloons and drug-eluting and/or bioabsorbable stents,[30] patients with extensive tissue loss or gangrene will need dedicated rigorous surveillance or alternative revascularization strategies when feasible. Stenting for tibial lesions has not been uniformly associated with favorable results, and drug-eluting balloons or stents are currently not available in the United States for this application but may provide a good option for patients with restenosis. In addition, when TAEIs are used for limb salvage in patients with no bypass options, a clear understanding of their limitation is crucial to setting realistic expectations for both the physician and the patient. Prior to embarking on an all-endovascular first policy, the results of this study should serve as an impetus for better treatment algorithms in patients with CLI and tissue loss in order to attain the best rates of limb salvage and wound healing.

CONCLUSIONS

TAEIs can be successfully used to treat patients with CLI, with acceptable limb salvage rates. Special attention should be given to patients with extensive tissue loss or gangrene because they are at risk for early restenosis and subsequent limb loss. Strict wound and hemodynamic surveillance, wound care, and timely reinterventions are crucial to achieve successful outcomes in this patient population. Amputation or alternative revascularization options, when feasible, should be considered in patients with restenosis and tissue loss given the high rate of limb loss with tibial reinterventions.

AUTHOR CONTRIBUTIONS

Conception and design: NS, RC
Analysis and interpretation: NS, RC
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Writing the article: NS, ND, LM, SL, MM, RC
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