Below-the-Ankle Interventions for Chronic Limb-Threatening Ischemia: Safety and Efficacy in an Office-Based Practice

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Abstract

Objective. To evaluate the safety and efficacy of below-the-ankle (BTA) intervention in the office-based setting for treatment of chronic limb-threatening ischemia (CLTI). **Methods.** A total of 599 sequential lower-extremity angiograms on 381 patients were retrospectively reviewed for BTA interventions over a 30-month period. BTA interventions were defined as angioplasty distal to the talar dome (dorsal) or below the mid calcaneus (plantar) on lateral digital subtraction angiography. **Results.** A total of 130 procedures met inclusion criteria for BTA interventions in 105 patients, all of which were performed for CLTI. Pedal-plantar loop revascularization was performed in 22/130 procedures (16.92%). A total of 109 different wounds were evaluated and followed. Average patient age was 71.5 years and 60.9% were men. Comorbidities included diabetes in 85.3%, smoking in 40.4%, hypertension in 90.2%, hyperlipidemia in 50.5%, diagnosed coronary artery disease in 38.8%, and chronic kidney disease in 35% (end-stage renal disease in 20%). There were no immediate procedure-related complications. The 30-day mortality rate was 0.95% (1/105 patients) and no major amputations occurred during that period. Two patients were lost to follow-up after the 30-day period. Twelve-month limb salvage rate was 98.1% (103/105 patients) and the amputation-free survival rate was 85.7% (90/105 patients). The wound-healing rate was 89.3% (75/84 patients) during the follow-up period (median, 363.5 days). **Conclusions.** CLTI is associated with a high rate of limb loss and mortality. For the most advanced distal arterial occlusive disease, intervening BTA has been associated with improved wound healing and decreased limb loss. The study results demonstrate that these procedures can be performed frequently in an office-based setting with low complication rates, even in patients with multiple comorbidities.

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Chronic limb-threatening ischemia (CLTI) is an advanced stage of lower-extremity peripheral arterial disease (PAD) characterized by ischemic rest pain and tissue loss, such as ulceration and gangrene. Arterial revascularization via endovascular treatment or surgical bypass has proven to be a valuable tool in dealing with CLTI, which accounts for a mean Medicare expenditure of $35,700 per patient-year.[1] Though data from a few recent international studies demonstrated a higher rate of wound healing and shorter time to wound healing in the inpatient hospital setting, safety and efficacy of below-the-ankle (BTA) interventions in the office-based setting is largely unreported.[2] Studies have consistently shown shortened time to wound healing, decreased amputation rates, and lower mortality rates with lower-extremity revascularization; exploring outcomes in an office-based setting addresses the perception that hospital-based procedures are safer and more effective than office-based revascularization of the lower extremity.[3] Only 50% of patients with CLTI will be alive with both limbs intact within 1 year of presentation.[4] Thus, elucidating the safety and efficacy of BTA angioplasty in an outpatient setting is important, as office-based practice may increase patient access to limb-preserving therapy, particularly in underserved and rural provinces.

Diabetes, smoking, and atherosclerotic disease are 3 of the most common risk factors that increase the likelihood for advanced

PAD.[5] At times, amputation is necessary to remove the dead and necrotic tissue from ischemia due to CLTI, accounting for an estimated 38%-82% of all lower-extremity amputations in the United States.[6,7] History of a prior amputation is associated with the need for subsequent proximal amputations, which are associated with an increased mortality of up to 18% in above-the-knee amputation (AKA) as opposed to 7% with transmetatarsal amputation (TMA).[8] This is especially true in patients with previous tissue loss, diabetes, and end-stage renal disease.[8-10]

BTA interventions remain relatively novel, and early data suggest improved wound healing and decrease in lower-extremity amputations, including above the ankle, BTA, ray, and toe amputations.[3] Studies showing the benefit of early intervention with below-the-knee angioplasty in regard to higher limb salvage and decreasing mortality could be theoretically extrapolated to BTA procedures.[3] The angiosome concept divides the foot into 6 "angiosomes" — 1 from the anterior tibial artery, 2 from the peroneal artery, and 3 from the posterior tibial artery.[5] This concept of direct revascularization has led to high rates of limb salvage and wound healing with bypass and endovascular therapy when compared with indirect revascularization of an ischemic area.[11,12] Targeting the angiosomes at a more distal level with BTA angioplasty may prove to be even more beneficial with regards to wound healing and limb salvage rates, while simultaneously decreasing morbidity and mortality from CLTI.[13]

Published data suggests that BTA angioplasty provides faster and higher rates of wound healing, in addition to decreased amputations, specifically in the moderate-risk population.[2,3] Further exploration of this topic is required to determine the feasibility and safety of these interventions in an office-based setting. The study aim is to examine the outcomes of BTA angioplasty in the office-based setting through a retrospective review of consecutive cases performed over a 30-month period. To our knowledge, there has been no study to date that has examined the outcomes in a large number of cases of BTA percutaneous transluminal angioplasty (PTA) in an office-based setting.

Methods

This study included patients with CLTI presenting with infrapopliteal arterial disease who underwent revascularization at a single-center office-based practice. All treated patients presented with rest pain, gangrene, and/or lower-extremity ulcerations for at least 2 weeks that were not amenable to routine medical therapy. A total of 599 consecutive lower-extremity angiograms on 381 patients were retrospectively reviewed for BTA interventions from July 2016 to December 2018. All 599 angiograms were independently reviewed by 2 interventional radiologists for BTA interventions. Exams lacking unanimous agreement were excluded from the cohort. BTA interventions were defined as angioplasty distal to the talar dome (dorsal) (**Figure 1**) or below the mid calcaneus (plantar) (**Figure 2**) on lateral digital subtraction angiography.

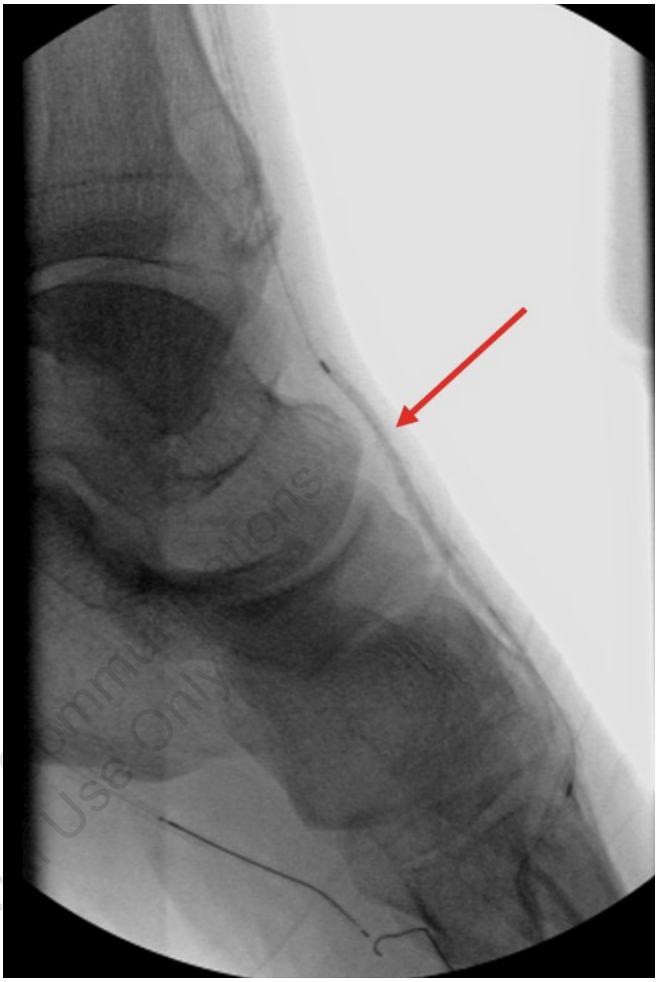

FIGURE 1. Below-the-ankle intervention definition: angioplasty distal to the talar dome (dorsal).

Rutherford classification of the study cohort was defined as the following: Rutherford 4 patients presented with ischemic rest pain; Rutherford 5 patients presented with minor tissue loss with ischemic nonhealing ulcer or with focal gangrene; and Rutherford 6 patients presented with major ischemic tissue loss extending above the transmetatarsal level.[14] BTA interventions consisted of dorsalis pedis, plantar, or pedal plantar loop angioplasty. All procedures were performed by a single board-certified and fellowship-trained interventional radiologist. All Rutherford 4 patients included in the cohort presented with foot pain at rest and non-invasive imaging findings of severe PAD in the ipsilateral lower extremity prior to undergoing angiography. The subsequent decision to treat with BTA-PTA was based on the absence of continuous in-line arterial flow to the foot, that was sufficient to cause rest pain.

Ultrasound was routinely used to interrogate and access the common femoral artery using the standard Seldinger technique.

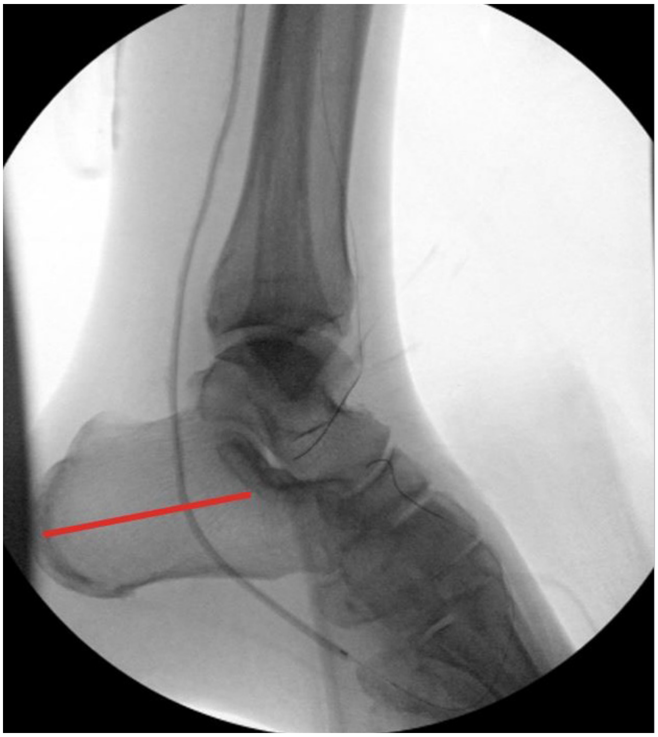

FIGURE 2. Below-the-ankle intervention definition: angioplasty below the mid calcaneus (plantar).

Antegrade puncture was the preferred method of access unless body habitus or characteristics of ipsilateral common femoral artery (large anterior wall calcified plaque, significant scar tissue, or narrow lumen diameter) were non-ideal. No radial artery access was performed, largely due to limitations of available device length. *Treatment of a tibioperoneal (TP) artery* was defined as atherectomy, PTA, or stent placement within the ipsilateral anterior tibial, posterior tibial, or peroneal artery. Commonly used devices for crossing BTA lesions in this study cohort included CXI (Cook) and Quick-Cross microcatheters (Philips) and an appropriate microwire. Treatment of BTA lesions in this study cohort predominantly consisted of a 2.0 mm balloon for pedal-plantar loop PTA and/or 2.5-mm diameter balloon for plantar artery and dorsalis pedis artery PTA. If a chronic total occlusion was not able to be crossed in the antegrade fashion due to plaque cap morphology, retrograde pedal artery access was obtained.[15] A StarClose SE closure device (Abbott Vascular) was routinely used to achieve arterial hemostasis. Images of representative procedures are included in **Figures 3-5**.

Chronic kidney disease was defined as a documented glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 for at least 3 months.[16] All wounds were categorized and followed by 2 interventional radiologists. Digital color photos were taken of all lower-extremity wounds at presentation and at each follow-up exam. Wound photos were stored within the patient's electronic medical record for documentation and reference purposes. Lower-extremity wounds

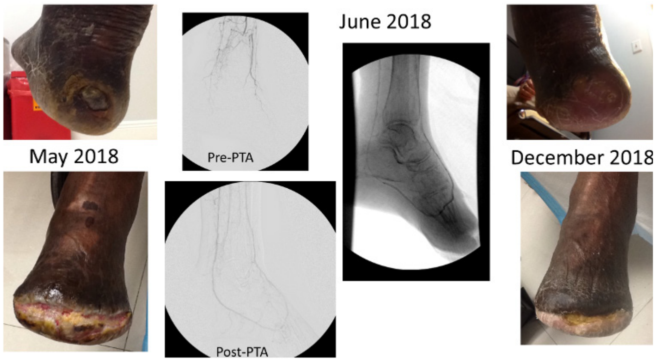

FIGURE 3. (From left to right panels) A 77-year-old man with hypertension and diabetes presented in May 2018 with a non-healing heel ulcer and transmetatarsal amputation wound. In June 2018, 2.0 mm balloon angioplasty of the plantar arch, as well as angioplasty of the anterior tibial, posterior tibial, and superficial femoral artery, was performed. Follow-up wound healing in December 2018.

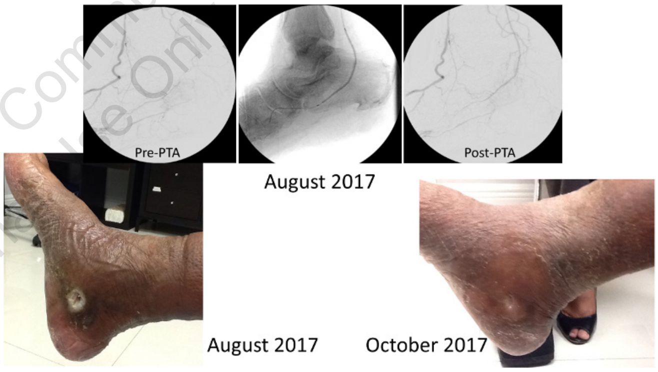

FIGURE 4. (From left to right panels) An 84-year-old woman with diabetes presented in August 2017 with a non-healing right medial heel ulcer. In August 2017, the medial plantar artery was balloon dilated using a 2 mm balloon. Follow-up wound healing is shown in October 2017.

FIGURE 5. (From left to right panels) A 69-year-old man with past medical history of diabetes, hypertension, and chronic kidney disease presented in August 2017 with non-healing transmetatarsal wound. In August 2017, angioplasty of the dorsalis pedis artery was performed using a 2.0 mm balloon. Follow-up wound healing is shown in April 2018.

TABLE 1. Procedural data.

Intervention Performed	Vessel Treated (n = 130)			
	SFA	Popliteal	TP	BTA
Atherectomy	28 (21.5%)	38 (29.2%)	121 (93.1%)	0 (0%)
PTA	33 (25.4%)	46 (35.4%)	125 (96.2%)	130 (100%)
Stent	19 (14.6%)	17 (13.1%)	15 (11.5%)	0 (0%)

Data presented as count (%).
BTA = below the ankle; PTA = percutaneous transluminal angioplasty; SFA = superficial femoral artery; TP = tibioperoneal artery.

were categorized according to the following locations: toes, heel, metatarsals, medial ankle, lateral ankle, or amputation site. The *follow-up period* was defined as the number of days between the initial BTA intervention and most recently documented clinical follow-up. *Major amputation* was defined as surgical removal of the lower limb proximal to the ankle. *Amputation-free survival* was defined as freedom from major amputation or mortality. *Limb salvage* was defined as absence of major amputation.

Results

Procedural data and patient characteristics are presented in **Table 1** and **Table 2**. A total of 130 procedures met inclusion criteria for BTA interventions in 105 patients, all of which were performed for CLTI. Rutherford classification was 4 in 6 patients, 5 in 69 patients, and 6 in 29 patients. Rest pain in the ipsilateral foot resolved in 5 of the 6 Rutherford 4 patients (83.3%). The 1 patient who did not experience relief of his foot pain also had significant neuropathy, which was likely the underlying cause. Pedal-plantar loop revascularization was performed in 22 of the 130 procedures (16.92%). Average patient age was 71.5 years and 60.9% were men. Noted comorbidities were hypertension in 90.2%, diabetes in 85.3%, hyperlipidemia in 50.5%, smoking in 40.4%, diagnosed coronary artery disease in 38.8%, and chronic kidney disease in 35.0% (end-stage renal disease in 20.0%). Details regarding other more proximal arteries treated concomitantly with BTA arteries are presented, which include laser atherectomy with Turbo-Elite (Philips), PTA, and stent placement. Neither atherectomy nor stent placement was performed BTA in the study cohort.

A total of 109 different BTA ischemic wounds in 99 patients were evaluated and followed. Of the 109 wounds, 97 (89.0%) occurred in diabetic patients and 51 (46.7%) occurred in patients with chronic kidney disease. There were no immediate procedure-related complications. The 30-day mortality rate was 0.95% (1/105 patients) and no major amputations occurred during that period. Two major amputations were required within 4 months of the first intervention. At 12 months, the limb-salvage rate was 98.1% (103/105 patients) and the amputation-free survival rate of 85.7% (90/105 patients). Two patients were lost to follow-up after the 30-day period. Of the 99 patients initially presenting with ischemic wounds (Rutherford class 5 or 6), 2 were lost to follow-up and 13 died prior to complete wound healing. Of the remaining 84 patients with wounds (Rutherford class 5 or 6) who remained alive and were not lost to follow-up, 75/84 patients (89.3%) were healed during the follow-up period (median follow-up, 363.5 days) (**Figures 3-5**).

TABLE 2. Patient characteristics.

Patient Characteristics	Reported Patients (n = 105)
Rutherford classification	
Class 4	6
Class 5	69
Class 6	29
Patient demographics	
Average patient age (years)	71.5
Male patients	64 (60.9%)
Female patients	41 (39.1%)
Comorbidities	
Diabetes mellitus	85.3%
Smoking	40.4%
Hypertension	90.2%
Hyperlipidemia	50.5%
Coronary artery disease	38.8%
Chronic kidney disease	35.0%
End-stage renal disease	20.0%
Patient outcomes	
Procedure-related complications	0
30-day mortality rate	0.95%
Major amputations	2
Lost to follow-up	2

Data presented as count, percentage, or count (percentage).

Discussion

This retrospective study highlights the clinical outcomes of BTA-PTA in patients with CLTI in a single-center, office-based setting. The study results demonstrate that BTA interventions in the office setting are both effective and safe, as the 12-month limb-salvage rate (98.1%), wound-healing rate (89.3%), and 30-day mortality rate (0.95%) illustrate. Despite a Rutherford index of 5 or 6 and multiple comorbidities in most patients, successful angioplasty was still performed with favorable outcomes. Thus, the authors propose that these data may help guide future management of CLTI patients who are at risk of limb loss, as the office-based setting may increase patient accessibility to limb-saving care.

A recent meta-analysis by Huizing et al has demonstrated promising yet incomplete evidence for the use of BTA-PTA in CLTI patients.[3] In this evidence review, BTA-PTA outcomes of 478 patients with 524 critically ischemic limbs were examined across 10 different studies. Limb-salvage and amputation-free survival rates at 12 months (0.92% and 0.78%, respectively) were used as overall outcome measures. Patient wound-healing rate was not used as an overall outcome in this analysis because some of the included studies did not use wound healing as a measure of outcome. The data gathered from the 109 wounds and 105 patients within our study provide supportive evidence to the aggregate pool of information on patient outcomes in BTA-PTA. Additionally, our reported rates of limb salvage, amputation-free survival, and wound healing are similar to previous studies demonstrating safety and effectiveness of BTA angioplasty.[2,3]

Furthermore, Huizing et al make note of several limitations shared among the analyzed BTA-PTA studies. Of these, the two most influential were a relatively small sample size (mean size of 48 patients) and lack of reporting loss to follow-up. The first limitation is addressed in the current study by reporting a sample size (n = 105) of over double the reported average in the Huizing et al meta-analysis. The use of a larger patient cohort provides a greater amount of data on outcomes for BTA-PTA procedures in symptomatic advanced PAD patients. The greater sample size also diminishes the loss of result quality that occurs when comparing multiple studies, wherein variance in inclusion criteria, outcome measurement, and data-gathering methods can obscure or alter the reported aggregate outcomes. The limitation of inadequate loss to follow-up reporting is rectified in the current study with a clear loss to follow-up rate of 1.9% (2 out of 105 patients). Adequate reporting of loss to follow-up provides an important context for interpreting rates of limb salvage, amputation-free survival, and wound healing. Overall, by addressing two of the primary limitations of prior reports, this study has added additional evidence on outcomes in BTA angioplasty for the treatment of CLTI.

The current study also adds to the current body of evidence linking chronic kidney disease as a risk factor for advanced PAD and non-healing ulcerations, particularly given that 35% of the patient cohort had chronic kidney disease.[17] Additionally, a higher percentage of patients (45.1%) presenting with ischemic wounds also had chronic kidney disease.

BTA-PTA is safe and efficacious in the office-based practice. Although this study was carried out in a single center, more than double the reported average number of patients was examined.[3] Our limb-salvage, amputation-free survival, and wound-healing rates in the office-based practice are on par with reported rates for studies conducted with hospitalized CLTI patients.[2,3] The ability to maintain accepted safety outcome measures in the office-based practice, even in patients with a higher baseline Rutherford index and multiple comorbidities, shows that patients can safely receive significant benefit from revascularization even in an outpatient office-based setting. This data may help to guide the safe future management of patients with CLTI and increase patient access to effective limb-saving care via the office-based setting, specifically in underserved communities and rural provinces with limited access to tertiary-care centers.

Study limitations. Study limitations include the retrospective design and the absence of a comparison group of patients treated contemporaneously with similar disease severity but without BTA intervention. An additional limitation is consistent collection of demographic data, as a private-practice office continually grows and learns to improve methods of collecting patient information. Standard patient questionnaires were developed to more accurately record demographics, such as comorbid conditions, pharmacological profile, and smoking status. It would also be prudent to collect an ankle-brachial index for each patient at follow-up visits. This would allow for more accurate examination of the ankle-brachial index in relation to wound-healing rates in patients with BTA-PTA for CLTI. As a retrospective analysis, the data pool for each patient has already been collected, so for future cases, complete standardization of the collection of demographics and variables to be measured could improve prospective studies and allow for the deeper examination of pharmacology, comorbidities, and ankle-brachial index in relation to the outcomes of BTA interventions.

Conclusion

CLTI is associated with a high rate of limb loss and mortality. This study adds to the existing body of evidence indicating that for the most advanced distal arterial occlusive disease, BTA intervention is associated with improved wound healing and decreased limb loss. Our results demonstrate that these procedures can be performed frequently in an office-based setting with low complication rates, even in patients with multiple comorbidities.

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