Clinical Investigation

JOURNAL OF ENDOVASCULAR THERAPY
A SAGE Publication
An official publication of the ISEVS

Journal of Endovascular Therapy
1–6

DOI: 10.1177/15266028251352772
www.jevt.org
Sage

Twelve-Month Outcomes of the Prospective, Multicenter, Single-Arm Study of the 355-nm Laser for Treatment of Below-the-Knee Arteries: Final Results of the Auryon BTK

Nicolas W. Shammas, MD, MS[1], Timothy Yates, MD[2], Ashwani Sastry, MD[3], Joseph Ricotta, MD[4], Robert Beasley, MD[2], Warren Swee, MD[2], Gail A. Shammas, BSN, RN[1], Sue Jones-Miller, MS[1], Venkat Shankarraman, PhD[5], and Steve Ratchford, PhD[5]

Abstract

Background: The Auryon laser atherectomy system has been shown to have high procedural success in the prospective, multicenter Auryon BTK study. We present the 12-month outcomes of the Auryon BTK in treating infrapopliteal arterial disease in patients with chronic limb-threatening ischemia (CLTI). **Methods:** Patients at 4 US centers with CLTI were prospectively enrolled in the Auryon BTK study after obtaining informed consent. The study was approved by a central ethics committee. The 30-day primary safety and procedural success were recently published. Secondary endpoints included target lesion revascularization (TLR), clinical patency (defined as peak systolic velocity ratio ≤2.4 and no TLR), major adverse limb events (amputation, target vessel revascularization, and/or all-cause mortality), Walking Impairment Questionnaire (WIQ), Rutherford Becker (RB) category, and EQ-5D quality of life questionnaire. Proportional and Kaplan–Meier (K-M) survival analysis were performed. **Results:** A total of 60 patients (61 lesions) were enrolled. At 12-month, 42 patients were still in the study (7 lost-to-follow-up, 5 withdrawals, 7 deceased). The mean age was 74.6 ± 10.3 years with 58.3% diabetics, 43.3% RB IV, and 56.7% RB V. Of the 61 lesions, 59% had severe calcification, 31.1% were chronic total occlusions, and 90.2% were de novo disease. Bailout stenting occurred in 1/61 lesions (1.6%). Proportional analysis for freedom from TLR at 1-year was 94.2%, and TVR was 89.4%. K-M analysis for freedom from TLR was 94.0% at 12-month. There was a significant difference in median WIQ score from to baseline to 3-month ($p = 0.0020$) and baseline to 6-month ($p = 0.0290$) but not from baseline to 12-month ($\Delta -0.073$, $p = 0.678$). Wounds healed in 33.3% (n = 4/12) of patients at 12-month. There was also a significant difference in median EQ-5D total score from baseline to 30-day ($p = 0.0030$), 3-month ($p = 0.0060$), 6-month ($p = 0.0500$), and 12-month ($p = 0.00005$). In addition, there was a significant median difference between 30-day ankle-brachial index (ABI) and baseline ABI ($p < 0.0005$) and the 12-month ABI and baseline ABI ($p = 0.2100$). Rutherford–Becker category improved by ≥1 category among 67.6% (n = 23/34) patients, stayed the same in 29.4% (n = 10/34) patients and worsened in 2.9% (n = 1/34) patients at 1-year. **Conclusion:** The 355-mm laser has a high rate of freedom from TLR at 12-month with a significant improvement in RB categories, WIQ and quality of life (EQ-5D).

Clinical Impact

The Auryon BTK demonstrates the safety and effectiveness of the 355-nm Auryon laser system in treating infrapopliteal arterial disease in patients with critical limb ischemia yielding high freedom from TLR and improvement in quality of life despite complex disease. The Auryon laser can treat all lesion morphologies below the knee including severe calcium and needs to be considered by operators for vessel prepping prior to adjunctive balloon angioplasty.

Keywords

Auryon laser, real world, prospective clinical trial, below the knee, critical limb-threatening ischemia

Introduction

The terminal manifestation of peripheral artery disease is chronic limb-threatening ischemia (CLTI) which has a grim, 20% to 25% 1-year mortality rate and 50% at 5-year morality rate.[1,2] Despite percutaneous transluminal angioplasty (PTA) being the mainstay for endovascular treatment of CLTI for 30 years,[3] patency rates remain 40% to 50% at

1 year with high amputation rates and frequent need for revascularization.[4,5] Catheter-based strategies are rapidly evolving to ameliorate this patient burden.

The Auryon laser atherectomy system (Angiodynamics, Inc, Latham, NY, USA) is one such treatment with excellent acute procedural and 30-day outcomes[6,7] due in part to its longer wavelength (355 nm)[8] and shorter pulse width (10–25 ns).[9] This unique technology leads to effective treatment of complex, severely calcified lesions,[10] while minimizing adventitial tears or need for bailout stenting.[11] Despite being a good choice for infrapopliteal arteries, data on the long-term outcome of the 355-nm laser remain limited,[12,13] especially among patients with CLTI. Therefore, the Auryon below the knee (Auryon BTK) study was an investigator-initiated, prospective, multicenter study designed to evaluate the 355-nm laser in treating infrapopliteal arteries in patients with CLTI. In this study, we present the 12-month outcomes of the Auryon laser in infrapopliteal arteries in patients with CLTI.

Methods

A total of 4 US centers enrolled patients in the Auryon BTK study. Primary safety endpoint as a composite of all-cause death, above-ankle amputation of the index limb, and reintervention of the index limb at 30-day along with primary performance as ≤30% residual stenosis for the treated segment of the vessel without serious angiographic complications (flow-limiting dissection [D-F], perforation, distal embolization, or acute vessel closure after the final treatment) were previously described.[7]

The following 12-month outcomes are presented:

1. Primary patency at 6- and 12-month defined as the absence of both total occlusion [100% diameter stenosis by duplex ultrasound (DUS)] or peak systolic velocity ratio (PSVR) > 2.4;
2. Target lesion revascularization (TLR) at 30-day, 6-month, and 12-month was defined as lesions that did undergo retreatment of the index lesion with an objective evidence of obstructive disease (occlusion or PSVR >2.4 by DUS). Freedom from TLR was determined based on index lesions that did not undergo TLR.
3. Ankle-brachial index (ABI) at baseline, 30-day, 6-month, and 12-month;
4. Number of healed wounds at 12-month;
5. Walking Impairment Questionnaire (WIQ)[14] and EQ-5D-5L[15] at baseline, 30-day, 6-month, and 12-month. The self-administered WIQ was obtained at baseline, 3-month, 6-month, and 12-month. The participant assessed the degree of difficulty in walking up to 5 blocks on a graded scale from 0 to 4. The higher the score, the less the difficulty in walking. The EQ-5D is a generic instrument to assess general quality of life (QOL). It is based on a descriptive system to assess mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The higher the number, the worse the QOL; and Rutherford–Becker category (RBC)[16] at baseline, 30-day, 6-month and 12-month.

The inclusion and exclusion criteria have been previously published.[7] All patients had CLTI, Rutherford category 4 to 5 in the target limb with both de novo or restenotic (no in-stent) lesions included. Only one target vessel was included in the study, and intraluminal crossing of the lesion was required. No other debulking devices were allowed.

Procedural details have also been previously published.[7] The laser was set to a fluence of 50 J/cm^2 first, followed by a fluence of 60 J/cm^2 if significant resistance was met in advancing the laser catheter. All lesions were treated with PTA with 1:1 balloon sizing. Core laboratory adjudication was performed for angiographic, intravascular ultrasound and DUS measurements.

Follow-up data were collected at discharge, 30 ± 7 days, 180 ± 30 days, and 360 ± 30 days.

Statistical Analysis

The published 30-day analysis accounted for 60 patients and 61 lesions. This follow-up analysis and comparisons were done with 60 vessels (1 vessel per patient) as the denominator. There were 3 TLRs. Clinically relevant TLR was not done because of the low number of TLRs; therefore, total TLR is reported.

During the follow-up analyses, the patency rate was calculated using PSVR ≤2.4 in patients with no prior TLR

[1]Midwest Cardiovascular Research Foundation, Davenport, IA, USA
[2]Palm Vascular Centers of Florida, Ft. Lauderdale, FL, USA
[3]Sunrise Vascular, Pembroke Pines, FL, USA
[4]Tenet Florida Cardiovascular Care, Delray, FL, USA
[5]Angiodynamics, Latham, NY, USA

Corresponding Author:
Nicolas W. Shammas, Midwest Cardiovascular Research Foundation, 630 East 4th Street, Davenport, IA 52801, USA.
Email: shammas@mchsi.com

and censoring patients who died, withdrawn, or lost to follow-up. Loss of patency included those with total occlusions and those with PSVR >2.4. The TLR and patency rates were cumulative and the reported TLR rates and patency rates are based on actual days from index occurrence. The RBC change from baseline was analyzed both as the number of category changes and whether the RBC was improved, stayed the same, or worsened by ≥1 category.

Descriptive analysis on all variables was performed. Continuous data were presented as mean ± standard deviation [median]; categorical data were provided as count/sample (percentage). Pearson's chi-square exact test, sign test, and Student t-test were used where appropriate. Normality and outlier tests were done with Anderson–Darling test and Grubbs test, respectively. Statistical significance was determined by a $p < 0.05$. Software used was Minitab 21 (State College, PA, USA) and Cytel Studio 12 (Cambridge, MA, USA). Survival analysis was performed to determine the probability (future chance) for patency and TLR at 1 year. Proportional analysis (actual occurrence) for patency and TLR at 1 year were also determined.

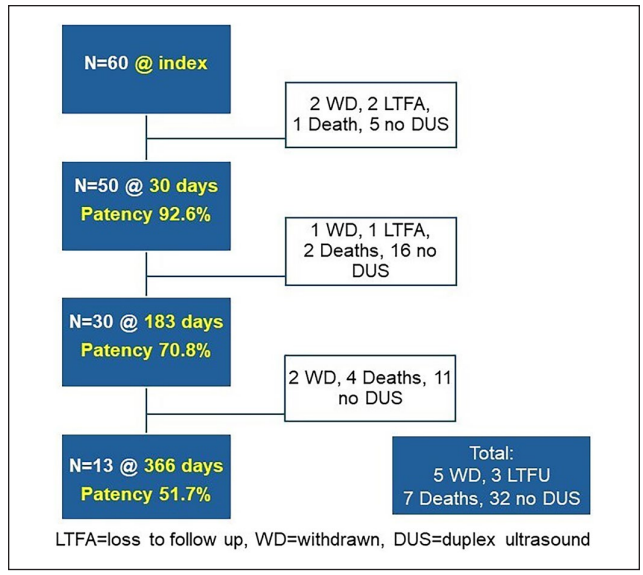

Figure 1. Flow diagram that shows patients' loss to follow-up, withdrawn from study, died, or did not have a duplex ultrasound at each time point when assessing patency.

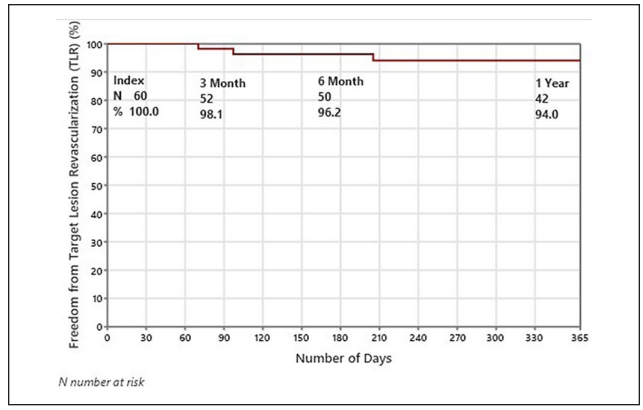

Figure 2. Freedom from target lesion revascularization at 1-year with the use of the 355-nm laser below the knee in chronic limb-threatening ischemia.

Results

A total of 60 patients were enrolled. At 1-year, 42 patients were still in the study (7 lost to follow-up, 5 withdrawals, and 7 died). The mean age was 74.6 ± 10.3 years with 58.3% diabetics, 43.3% Rutherford–Becker (RB) IV and 56.7% RB V.

Demographics, clinical, angiographic, and procedural outcomes were previously published.[7] Of the 61 lesions, 31.1% were total occlusions, 59% had severe calcification, and 90.2% of lesions were de novo. Thirty-four of 60 patients included had wounds. Baseline median diameter stenosis was 82.1%, post laser 56.5% and following angioplasty as adjunctive therapy 22.5%. Mean plaque burden was significantly reduced from 73.77% at baseline to 53.66% at end of procedure ($p = 0.001$). At 30 days, there was no TLR, TVR, or unplanned major amputation. One sudden cardiac death occurred likely secondary to access site major bleeding postprocedure. Bailout stenting occurred in 1 patient (1.6%) without any target vessel revascularization or amputations. At 1 year, anticoagulant and antiplatelet data were available on 35 patients. Of these, 34 patients were on 1 (n = 23) or 2 (n = 4) antiplatelet drugs and 7 were on oral anticoagulants with no antiplatelet. One patient was on no antiplatelet or anticoagulant but was on cilostazol.

Patency and TLR

The 12-month proportional patency rate was 62.5%, and Kaplan–Meier (K-M) probability patency rate was 51.7%. This is however, inconclusive given the small number of patients that underwent evaluation for patency at 1 year (n = 13). Patency rate was 88.9% (PSVR ≤2.4) at 30-day (n = 50 patients) and 70.8% at 6 months (n = 30 patients; Figure 1). Proportional analysis showed a freedom from TLR at 12-month was 94.0% and TVR 90.4%. K-M probability of freedom from TLR was 94% at 12-month (Figure 2). There were 7 deaths, 3 TLR, 5 withdrew consent, and 3 lost to follow-up.

Wound and ABI

At 12-month, 12 patients had their wounds evaluated, of which 4 had completely healed (33.3%). There was a significant median difference between 30-day ABI and

baseline ABI (0.23 ± 0.46, $p < 0.0005$) and the 12-month ABI and baseline ABI (0.28 ± 0.48, $p = 0.0210$). Only 1 minor amputation occurred at 1 year (metatarsal) in a target limb. There were no major amputations.

RBC, WIQ, EQ-5D

Of 43 patients, RBC improved by ≥1 category in 23 patients, stayed the same in 10 patients and worsened ≥1 in 1 patient. There was a significant increase in median WIQ score from baseline to 3-month (0.13 ± 0.29, $p = 0.0020$) and 6-month (0.14 ± 0.14, $p = 0.0290$), but not to 12-month ($\Delta -0.073 \pm 0.270$, $p = 0.678$). There was also a significant difference in the median EQ-5D total score from baseline to 30-day (-1.85 ± 4.50, $p = 0.0030$), 3-month (-2.00 ± 3.46, $p = 0.0060$), 6-month (-1.69 ± 4.16, $p = 0.0500$), and 12-month (-4.51 ± 6.30, $p = 0.0005$).

Discussion

The purpose of this investigator-initiated, prospective, multicenter study was to evaluate the 355-nm laser in treating infrapopliteal arteries in patients with CLTI. In this study, the 355-nm laser had excellent freedom from TLR and amputation, with only 1 patient requiring bailout stenting. The results are consistent with "leaving the least behind" strategy. These data are comparable to the bioresorbable stent placement in the LIFE-BTK trial,[17] which had a similar freedom from TLR and low amputation rate when treating patients with CLTI and infrapopliteal arteries. Proportional comparison of freedom from TLR in the Life BTK bioresorbable stent arm with freedom from TLR in the Auryon BTK showed no statistical difference (92.6% vs. 94.0%, respectively, $p = 1.000$) despite longer lesions (median 80 mm vs. 35 mm), more chronic total occlusions (31.1% vs. 15.1%), and more severe calcium (59.0% vs. 3%) in the Auryon BTK study. Although patency rate in the Auryon BTK appears comparable to historic, PTA controls,[4] patency data are inconclusive given the low number of patients who had a DUS at 1 year (13/60). The discrepancy between assessment techniques for patency and freedom from TLR has been well described.[18–20] Early patency may allow collaterals or wound healing to occur, leading to less need for additional revascularization on follow-up. Certainly, a randomized clinical trial is warranted between the 355-laser and PTA or bioresorbable stent to provide further comparison.

PTA remains the most commonly used procedure to treat infrapopliteal disease in patients with CLTI.[3] A high rate of amputation or TLR continues to be seen with PTA at 1 year,[4,5] warranting further technologic advancements to ameliorate recurrent treatments. Different endovascular modalities have been used to treat infrapopliteal vessels including atherectomy, drug coated balloons, specialty balloons, and stenting. Currently randomized data support the use of balloon expandable drug eluting stents (DES) (absorbable or not) as a superior modality to PTA to improve long-term patency[21] along with the combined endpoint of amputation, occlusion of the target vessel, clinically driven revascularization of the target lesion, and binary restenosis of the target lesion.[17] Yet, there are scarce data on the long-term outcomes of the 355-nm laser in treating infrapopliteal disease in CLTI patients.

Patency and TLR

Use of the 308 nm laser for popliteal and infrapopliteal patients with CLI had a primary patency of 42%,[22] 75%,[23] and 90%[24] at 12-months, highlighting the vast range of patency rates even among similar treatment modalities. In the current investigation, primary patency was comparable to previous laser atherectomy results at 12-months. Additionally, current 355 nm 12-month freedom from TLR rates of 94% appear similar to 308 nm TLR rates of ~90%[24] at 12-months, further highlighting long-term success rates of laser atherectomy in patients with CLTI. Yet, association between patency, TLR, and limb salvage is contentious,[25] warranting further review of wound healing.

Wound and ABI

Wound healing, wound healing rates, and ambulation time have all become important considerations for patients with CLTI.[26–29] Wound healing rates have remain relatively low, with only 26% of wounds healing within 3 months of SDF-1 plasmid treatment in the STOP-PAD trial.[30] Here, we present a 33% improvement in wound healing at 12-months, albeit among 12 evaluable patients. Additionally, there were not any major amputations noted. Given the association between wound severity and reintervention rates,[31] wound healing should be a critical endpoint when assessing long-term success from endovascular therapy. Future studies should more thoroughly investigate wound healing rates using the recommended wound, ischemia, and foot infection classification.[32,33] In the current study, wound healing coincided with sustained improvements in ABI as well. While ABI assessments do not always predict wound healing,[34] the need for improved perfusion pressures is often a pre-requisite for improvements in wound healing. Nonetheless, a more integrative approach may better determine long-term outcome success, leading to improvements in QOL.

RBC, WIQ, and EQ-5D

Most patients in the current investigation improved their RBC by at least 1 category, with only 1 patient having a worse RBC category at 12-months. Paradoxically,

significant improvements were seen at 6-months but not at 12-months for WIQ, yet improvements for EQ-5D were sustained out to 12-months. Together, these results represent significant improvements in QOL for these individuals 12-months after endovascular treatment with the 355 nm Auryon laser atherectomy system.

Conclusions

Overall, the 355 nm Auryon laser atherectomy system provides high procedural success while minimizing dissections or the need for bailout stenting. With a high rate of freedom from TLR at 12-month with a significant improvement in RB categories, WIQ and quality of life (EQ-5D), debulking with laser atherectomy prior to angioplasty continues to provide long-lasting improvements in patient-centered outcomes. These data warrant further examination in comparison to PTA alone among a larger population.

Limitation of the Study

Only 13 patients had DUS to evaluate patency at 12-months. The true patency of the 355-nm laser cannot therefore be accurately assessed from this study at 12-months. The 6-month patency was 70.8% with approximately half the patient evaluated. Additional data are needed to determine accurately the patency of the 355-nm laser at 12-months. It remains unclear what the mechanisms of restenosis are at 12-months, but it is likely to be a combination of recoil, smooth muscle proliferation, or thrombosis in small vessels with long, calcified, and occluded lesions. This is also a nonrandomized trial and was not powered to be compared to historic controls. Despite a relatively modest sample size, the study was prospective, and multicenter with balanced representation of patient's enrollment in all sites lending validity to the presented data.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Dr Shammas receives educational and research grants from Angiodynamics, Boston Scientific, Bard/BD, and Abbott. He is also on the speaker bureau of Janssen, Lilly, Boehringer Ingelheim, Merck and Bayer. Drs Shankaraman and Ratchford are employees of Angiodynamics. The 30-day findings of this study were presented at TCT-2023 in San Francisco on October 25, 2023 and published in the *Am J Cardiol*. 2024;219:1-8.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Unrestriced grant from Angiodynamics was provided to the Midwest Cardiovascular Research Foundation to conduct this study. Dr Shammas is the President of the Foundation.

ORCID iDs

Nicolas W. Shammas https://orcid.org/0000-0001-8279-0111
Robert Beasley https://orcid.org/0000-0002-4635-3392
Sue Jones-Miller https://orcid.org/0000-0001-9448-4701

References

1. Fereydooni A, Gorecka J, Dardik A. Using the epidemiology of critical limb ischemia to estimate the number of patients amenable to endovascular therapy. *Vasc Med Lond Engl*. 2020;25:78–87.
2. Kwong M, Rajasekar G, Utter GH, et al. Updated estimates for the burden of chronic limb-threatening ischemia in the Medicare population. *J Vasc Surg*. 2023;77:1760–1775.
3. Iyer SS, Dorros G, Zaitoun R, et al. Retrograde recanalization of an occluded posterior tibial artery by using a posterior tibial cutdown: two case reports. *Cathet Cardiovasc Diagn*. 1990;20:251–253.
4. Snyder DJ, Zilinyi RS, Pruthi S, et al. Percutaneous transluminal angioplasty for infrapopliteal chronic limb-threatening ischemia: a systematic review and meta-analysis of primary patency and binary restenosis rates. *J Endovasc Ther*. Published online November 26, 2023. doi:10.1177/15266028231212133
5. Mustapha JA, Finton SM, Diaz-Sandoval LJ, et al. Percutaneous transluminal angioplasty in patients with infrapopliteal arterial disease: systematic review and meta-analysis. *Circ Cardiovasc Interv*. 2016;9:e003468.
6. Shammas NW, Chandra P, Brodmannet M, et al. Acute and 30-day safety and effectiveness evaluation of Eximo Medical's B-Laser™, a novel atherectomy device, in subjects affected with infrainguinal peripheral arterial disease: results of the EX-PAD-03 trial. *Cardiovasc Revascularization Med Mol Interv*. 2020;21:86–92.
7. Shammas NW, Yates T, Sastry A, et al. Prospective, multicenter, single-arm study of the auryon laser system for treatment of below-the-knee arteries in patients with chronic limb-threatening ischemia: 30-day results of the Auryon BTK. *Am J Cardiol*. 2024;219:1–8.
8. Herzog A, Bogdan S, Glikson M, et al. Selective tissue ablation using laser radiation at 355 nm in lead extraction by a hybrid catheter; a preliminary report. *Lasers Surg Med*. 2016; 48:281–287.
9. Herzog A, Steinberg I, Ishaaya AA. Shaping photomechanical effects in tissue ablation using 355 nm laser pulses. *J Biophotonics*. 2017;10:1262–1270.
10. Rundback J, Kawai K, Sato Y, et al. Treatment effect of medial arterial calcification in below-knee after Auryon laser atherectomy using micro-CT and histologic evaluation. *Cardiovasc Revascularization Med Mol Interv*. 2023;57:18–24.
11. Shammas NW, Torey JT, Shammas WJ, et al. Intravascular ultrasound assessment and correlation with angiographic findings of arterial dissections following Auryon laser atherectomy and adjunctive balloon angioplasty: results of the iDissection Auryon Laser study. *J Endovasc Ther*. 2022;29:23–31.
12. Shammas NW, Shammas GA, Jones-Miller S, et al. Auryon laser in treating symptomatic infrainguinal arterial disease: 1-year outcome. *J Invasive Cardiol*. 2022;34:E496–E498.

13. Das TS, Shammas NW, Yoho JA, et al. Solid state, pulsed-wave 355 nm UV laser atherectomy debulking in the treatment of infrainguinal peripheral arterial disease: the Pathfinder Registry. *Catheter Cardiovasc Interv*. 2024;103:949–962.
14. Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011;20:1727–1736.
15. Regensteiner J, Steiner JF, Panzer RJ. Evaluation of walking impairment by questionnaire in patients with peripheral arterial disease. *J Vasc Med Biol*. 1990;2:142–152.
16. Rutherford RB, Baker JD, Ernst C, et al. Recommended standards for reports dealing with lower extremity ischemia: revised version. *J Vasc Surg*. 1997;26:517–538.
17. Varcoe RL, DeRubertis BG, Kolluri R, et al. Drug-eluting resorbable scaffold versus angioplasty for infrapopliteal artery disease. *N Engl J Med*. 2024;390:9–19.
18. Bosiers M, Peeters P, D'Archambeau O, et al. AMS INSIGHT—absorbable metal stent implantation for treatment of below-the-knee critical limb ischemia: 6-month analysis. *Cardiovasc Intervent Radiol*. 2009;32:424–435.
19. Favaretto E, Pili C, Amato A, et al. Analysis of agreement between Duplex ultrasound scanning and arteriography in patients with lower limb artery disease. *J Cardiovasc Med (Hagerstown)*. 2007;8:337–341.
20. Collins R, Burch J, Cranny G, et al. Duplex ultrasonography, magnetic resonance angiography, and computed tomography angiography for diagnosis and assessment of symptomatic, lower limb peripheral arterial disease: systematic review. *BMJ*. 2007;334:1257.
21. Trombert D, Caradu C, Brizzi V, et al. Evidence for the use of drug eluting stents in below-the-knee lesions. *J Cardiovasc Surg (Torino)*. 2015;56:67–71.
22. Steinkamp HJ, Rademaker J, Wissgott C, et al. Percutaneous transluminal laser angioplasty versus balloon dilation for treatment of popliteal artery occlusions. *J. Endovasc*. 2002;9:882–888.
23. Bosiers M, Peeters P, Elst FV, et al. Excimer laser assisted angioplasty for critical limb ischemia: results of the LACI Belgium study. *Eur J Vasc*. 2005;29:613–619.
24. Sultan S, Tawfick W, Hynes N. Cool excimer laser-assisted angioplasty (CELA) and tibial balloon angioplasty (TBA) in management of infragenicular arterial occlusion in critical lower limb ischemia (CLI). *Vasc Endovascular Surg*. 2013; 47:179–191.
25. Romiti M, Albers M, Brochado-Neto FC, et al. Meta-analysis of infrapopliteal angioplasty for chronic critical limb ischemia. *J Vasc Surg*. 2008;47:975–981.
26. Iida O, Nakamura M, Yamauchi Y, et al. 3-Year outcomes of the OLIVE Registry, a prospective multicenter study of patients with critical limb ischemia: a prospective, multi-center, three-year follow-up study on endovascular treatment for infra-inguinal vessel in patients with critical limb ischemia. *JACC Cardiovasc Interv*. 2015;8:1493–1502.
27. Reed GW, Salehi N, Giglou PR, et al. Time to wound healing and major adverse limb events in patients with critical limb ischemia treated with endovascular revascularization. *Ann Vasc Surg*. 2016;36:190–198.
28. Hata Y, Iida O, Mano T. Is angiosome-guided endovascular therapy worthwhile? *Ann Vasc Dis*. 2019;12:315–318.
29. Hata Y, Iida O, Okamoto S, et al. Additional risk stratification using local and systemic factors for patients with critical limb ischaemia undergoing endovascular therapy in the WIfI era. *Eur J Vasc Endovasc Surg*. 2019;58:548–555.
30. Shishehbor MH, Rundback J, Bunte M, et al. SDF-1 plasmid treatment for patients with peripheral artery disease (STOP-PAD): Randomized, double-blind, placebo-controlled clinical trial. *Vasc Med*. 2019;24:200–207.
31. Conte MS, Azene E, Doros G, et al. Secondary interventions following open vs endovascular revascularization for chronic limb threatening ischemia in the BEST-CLI trial. *J Vasc Surg*. 2024;79:1428–1437.e4.
32. Conte MS, Bradbury AW, Kolh P, et al. Global vascular guidelines on the management of chronic limb-threatening ischemia. *Eur J Vasc Endovasc Surg*. 2019;58: S1–S109.e33.
33. Mills JL, Conte MS, Armstrong DG, et al. The Society for Vascular Surgery Lower Extremity Threatened Limb Classification System: risk stratification based on wound, ischemia, and foot infection (WIfI). *J Vasc Surg*. 2014;59:220–234.e1–e2.
34. Argyriou C, Lazarides MK, Georgakarakos E, et al. Role of hemodynamic assessment and limitations in ankle-brachial pressure index, toe-brachial pressure index to predict wound healing after revascularization. *Int J Low Extrem Wounds*. 2024;23:7–11.