

Editorial

# The Challenges in Managing Peripheral Arterial Disease Complications

Federico Biscetti <sup>1,\*</sup>  and Andrea Flex <sup>1,2</sup>

<sup>1</sup> Cardiovascular Internal Medicine Unit, Department of Cardiovascular Sciences, Fondazione Policlinico Universitario A. Gemelli IRCCS, Largo Agostino Gemelli 8, 00168 Rome, Italy; andrea.flex@unicatt.it

<sup>2</sup> Department of Internal Medicine, Catholic University School of Medicine, Largo Agostino Gemelli 8, 00168 Rome, Italy

\* Correspondence: federico.biscetti@policlinicogemelli.it; Tel.: +39-06-3015-4293

Peripheral arterial disease (PAD) afflicts millions of people across the globe, with the severe form often culminating in chronic limb-threatening ischemia (CLTI) [1]. This serious condition may result in amputation and a heightened mortality risk [2]. PAD is poorly understood and often goes undiagnosed [3]. This lack of awareness contributes to the unfavorable progression of many patients, as the timely implementation of the appropriate therapeutic strategy is infrequent [4]. Addressing PAD early is crucial, and individuals with the vascular disease should promptly receive optimal medical intervention [1]. Beyond lifestyle modifications, like quitting smoking, engaging in regular physical activity, and achieving weight loss, a range of pharmaceutical treatments, including lipid-level-lowering drugs, antiplatelet agents, GLP-1 analogues, and rivaroxaban, can substantially enhance the overall clinical trajectory of the disease [5]. The efficacy of the currently utilized or investigated drugs for managing PAD hinges on their ability to counteract the pathological mechanisms associated with atherosclerosis factors, such as diabetes, dyslipidemia, and arterial hypertension, as well as the underlying mechanisms of the so-called “residual risk” [6]. Despite receiving optimal medical treatments, individuals with similar risk profiles may experience diverse outcomes, progressing toward CLTI in distinct ways [7]. Moreover, when PAD patients with CLTI undergo revascularization intervention, the results can vary significantly. While some patients experience no significant complications and derive substantial benefits from the procedure, others with a comparable baseline risk profile may encounter Major Adverse Limb Events (MALE) or Major Adverse Cardiovascular Events (MACE) shortly after intervention [8,9]. Numerous prior studies have established a connection between inflammation and the progression of atherosclerosis, as well as its detrimental impact on the CLTI patients undergoing revascularization [10,11]. Specifically, certain cytokines, such as interleukin (IL)-1, IL-6, tumor necrosis factor (TNF)-alpha, High mobility group box-1 (HMGB1), and Osteoprotegerin (OPG), are implicated in this and may serve as additional risk biomarkers [7]. Additionally, molecules like sortilin and omentin-1 influence low-density lipoprotein (LDL) cholesterol trafficking and adipose tissue metabolism and might play a predictive role in the occurrence of post-revascularization MALE and MACE [12,13]. Nevertheless, the current evidence cannot be used to advocate for the routine use of these biomarkers in risk stratification and guiding therapeutic decisions. Due to these considerations, individuals with CLTI frequently undergo multiple revascularization procedures [10]. Unfortunately, in cases where revascularization is not possible, lower limb amputation remains an all-too-common outcome [14]. In recent years, there has been a concerted effort to address the patients without therapeutic alternatives, with a dedicated focus on exploring novel approaches and strategies [15]. Revascularization is the primary recourse for CLTI; yet, for some “no-option” patients, the traditional methods are unviable. Deep vein arterialization (DVA) is a surgical intervention for no-option CLTI [16]. The



**Citation:** Biscetti, F.; Flex, A. The Challenges in Managing Peripheral Arterial Disease Complications. *Hearts* **2023**, *4*, 94–96. <https://doi.org/10.3390/hearts4040012>

Received: 15 November 2023

Accepted: 20 November 2023

Published: 1 December 2023



**Copyright:** © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

procedure involves establishing an arteriovenous fistula, connecting an artery to a vein. This connection facilitates blood flow redirection from the artery to the vein, circumventing the blocked arteries and enhancing the blood supply to the legs and feet. It is typically reserved for individuals with severe PAD and CLTI who are ineligible for alternative revascularization methods, like bypass surgery or angioplasty; DVA is considered when other options are not viable [16].

In this article [17], a 71-year-old man with CLTI initially underwent femoro-tibial bypass surgery, which was unsuccessful due to there being an unsatisfactory distal artery target. Consequently, the surgeon opted for DVA. The post-operative imaging revealed the success of the DVA, showcasing improved blood flow to the legs and feet. The patient experienced pain relief, retaining functionality in his toes.

This case underscores the efficacy of DVA as a viable treatment for severe PAD. However, it is crucial to emphasize that DVA is a complex procedure and should only be performed by skilled and experienced surgeons.

**Funding:** This research received no external funding.

**Conflicts of Interest:** The authors declare no conflict of interest.

## References

1. Aboyans, V.; Ricco, J.-B.; Bartelink, M.-L.E.L.; Björck, M.; Brodmann, M.; Cohnert, T.; Collet, J.-P.; Czerny, M.; De Carlo, M.; Debus, S.; et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in Collaboration with the European Society for Vascular Surgery (ESVS): Document Covering Atherosclerotic Disease of Extracranial Carotid and Vertebral, Mesenteric, Renal, Upper and Lower Extremity arteries Endorsed by: The European Stroke Organization (ESO) The Task Force for the Diagnosis and Treatment of Peripheral Arterial Diseases of the European Society of Cardiology (ESC) and of the European Society for Vascular Surgery (ESVS). *Eur. Heart J.* **2018**, *39*, 763–816. [[CrossRef](#)] [[PubMed](#)]
2. Voci, D.; Fedeli, U.; Valerio, L.; Schievano, E.; Righini, M.; Kucher, N.; Spirik, D.; Barco, S. Mortality Rate Related to Peripheral Arterial Disease: A Retrospective Analysis of Epidemiological Data (Years 2008–2019). *Nutr. Metab. Cardiovasc. Dis.* **2023**, *33*, 516–522. [[CrossRef](#)] [[PubMed](#)]
3. Aday, A.W.; Matsushita, K. Epidemiology of Peripheral Artery Disease and Polyvascular Disease. *Circ. Res.* **2021**, *128*, 1818–1832. [[CrossRef](#)] [[PubMed](#)]
4. Hirsch, A.T.; Hiatt, W.R. PAD Awareness, Risk, and Treatment: New Resources for Survival—The USA PARTNERS Program. *Vasc. Med.* **2001**, *6*, 9–12. [[CrossRef](#)] [[PubMed](#)]
5. Bonaca, M.P.; Hamburg, N.M.; Creager, M.A. Contemporary Medical Management of Peripheral Artery Disease. *Circ. Res.* **2021**, *128*, 1868–1884. [[CrossRef](#)] [[PubMed](#)]
6. Siniawski, D.; Masson, G.; Masson, W.; Barbagelata, L.; Destaville, J.; Lynch, S.; Vitagliano, L.; Parodi, J.B.; Berton, F.; Indavere, A.; et al. Residual Cardiovascular Risk, Use of Standard Care Treatments, and Achievement of Treatment Goals in Patients with Cardiovascular Disease. *Int. J. Cardiol. Cardiovasc. Risk Prev.* **2023**, *18*, 200198. [[CrossRef](#)] [[PubMed](#)]
7. Biscetti, F.; Ferraro, P.M.; Hiatt, W.R.; Angelini, F.; Nardella, E.; Cecchini, A.L.; Santoliquido, A.; Pitocco, D.; Landolfi, R.; Flex, A. Inflammatory Cytokines Associated with Failure of Lower-Extremity Endovascular Revascularization (LER): A Prospective Study of a Population with Diabetes. *Diabetes Care* **2019**, *42*, 1939–1945. [[CrossRef](#)] [[PubMed](#)]
8. Gutierrez, J.A.; Mulder, H.; Jones, W.S.; Rockhold, F.W.; Baumgartner, I.; Berger, J.S.; Blomster, J.I.; Fowkes, F.G.R.; Held, P.; Katona, B.G.; et al. Polyvascular Disease and Risk of Major Adverse Cardiovascular Events in Peripheral Artery Disease: A Secondary Analysis of the EUCLID Trial. *JAMA Netw. Open* **2018**, *1*, e185239. [[CrossRef](#)] [[PubMed](#)]
9. Fashandi, A.Z.; Mehaffey, J.H.; Hawkins, R.B.; Kron, I.L.; Upchurch, G.R.; Robinson, W.P. Major Adverse Limb Events and Major Adverse Cardiac Events after Contemporary Lower Extremity Bypass and Infrainguinal Endovascular Intervention in Patients with Claudication. *J. Vasc. Surg.* **2018**, *68*, 1817–1823. [[CrossRef](#)] [[PubMed](#)]
10. Beckman, J.A.; Schneider, P.A.; Conte, M.S. Advances in Revascularization for Peripheral Artery Disease: Revascularization in PAD. *Circ. Res.* **2021**, *128*, 1885–1912. [[CrossRef](#)] [[PubMed](#)]
11. Chan, N.C.; Xu, K.; de Vries, T.A.C.; Eikelboom, J.W.; Hirsh, J. Inflammation as a Mechanism and Therapeutic Target in Peripheral Artery Disease. *Can. J. Cardiol.* **2022**, *38*, 588–600. [[CrossRef](#)] [[PubMed](#)]
12. Biscetti, F.; Nardella, E.; Rando, M.M.; Cecchini, A.L.; Bonadia, N.; Bruno, P.; Angelini, F.; Di Stasi, C.; Contegiacomo, A.; Santoliquido, A.; et al. Sortilin Levels Correlate with Major Cardiovascular Events of Diabetic Patients with Peripheral Artery Disease Following Revascularization: A Prospective Study. *Cardiovasc. Diabetol.* **2020**, *19*, 147. [[CrossRef](#)] [[PubMed](#)]
13. Biscetti, F.; Nardella, E.; Rando, M.M.; Cecchini, A.L.; Angelini, F.; Cina, A.; Iezzi, R.; Filippini, M.; Santoliquido, A.; Pitocco, D.; et al. Association between Omentin-1 and Major Cardiovascular Events after Lower Extremity Endovascular Revascularization in Diabetic Patients: A Prospective Cohort Study. *Cardiovasc. Diabetol.* **2020**, *19*, 170. [[CrossRef](#)] [[PubMed](#)]

14. Swaminathan, A.; Vemulapalli, S.; Patel, M.R.; Jones, W.S. Lower Extremity Amputation in Peripheral Artery Disease: Improving Patient Outcomes. *Vasc. Health Risk Manag.* **2014**, *10*, 417–424. [[PubMed](#)]
15. Biscetti, F.; Gentileschi, S.; Bertucci, F.; Servillo, M.; Arena, V.; Angelini, F.; Stigliano, E.; Bonanno, G.; Scambia, G.; Sacchetti, B.; et al. The Angiogenic Properties of Human Adipose-Derived Stem Cells (HASCs) Are Modulated by the High Mobility Group Box Protein 1 (HMGB1). *Int. J. Cardiol.* **2017**, *249*, 349–356. [[CrossRef](#)] [[PubMed](#)]
16. Shishehbor, M.H.; Powell, R.J.; Montero-Baker, M.F.; Dua, A.; Martínez-Trabal, J.L.; Bunte, M.C.; Lee, A.C.; Mugglin, A.S.; Mills, J.L.; Farber, A.; et al. Transcatheter Arterialization of Deep Veins in Chronic Limb-Threatening Ischemia. *N. Engl. J. Med.* **2023**, *388*, 1171–1180. [[CrossRef](#)] [[PubMed](#)]
17. Parillo, M.; De Stefano, D.; Catanese, V.; Mallio, C.A.; Spinelli, F.; Stilo, F.; Quattrocchi, C.C. Conversion of Femoral-Tibial Bypass Surgery into Deep Vein Arterialization in a Patient with Severe Peripheral Artery Disease: Post-Operative Computed Tomography and Angiography Findings. *Hearts* **2023**, *4*, 12–19. [[CrossRef](#)]

**Disclaimer/Publisher’s Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.