Journal of the American Heart Association

EDITORIAL

From Purpose to Impact: Harnessing the Elements to Improve Peripheral Artery Disease Outcomes

Subhash Banerjee, MD; Lawrence Hoang, MD; Douglas E. Drachman, MD

It is increasingly well-appreciated that peripheral artery disease (PAD) confers significant risk for adverse cardiovascular and limb events. Our perspective on the morbidity of PAD has come into clearer focus in light of recent drug and device studies that have demonstrated significant improvements in PAD outcomes through administration of appropriate therapies.[1,2] At the same time, however, practice patterns continue to lag behind the evidence-base, where deep-rooted beliefs or dogma may thwart broader acceptance of clinical evidence into practice.

See Article by Weissler et al.

In this issue of the *Journal of the American Heart Association (JAHA)*, Weissler and colleagues examine the factors associated with adverse cardiovascular and limb events following endovascular revascularization in individuals over 65 years of age, using data linked from the American College of Cardiology PVI (Peripheral Vascular Intervention) registry to that of the Centers for Medicare and Medicaid Services of the United States between January 2015 and June 2017.[3] In this predominantly descriptive analysis, the authors dispel the notion that individuals with claudication undergoing lower extremity endovascular revascularization are at low risk of major adverse cardiovascular (MACE) and major adverse limb (MALE) events. Their analysis comprises a comparison of 30-day and 1-year outcomes for patients presenting with or without critical limb threatening ischemia (CLTI or non-CLTI, respectively). The associations between patient, PAD, and procedural characteristics and 1-year outcomes (MACE, MALE, readmission, and mortality) were also analyzed for patients undergoing CLTI-PVI using Cox proportional hazards regression. Through this analysis, Weissler et al. identify specific factors associated with adverse outcomes, thereby highlighting potential opportunities to change practice and improve outcomes of patients with PAD.

The investigators aimed to identify modifiable and non-modifiable factors that could be associated with MACE and MALE in patients undergoing PAD revascularization. Unfortunately, the association of patient, lesion, and intervention characteristics with outcomes were explored in patients with CLTI but not for those with claudication (ie, the cohort without CLTI) at 1 year. The authors indicate that there were few events in the group without CLTI, although this is contradictory to their observation in the Discussion that, "both CLTI-PVI and non-CLTI-PVI patients experienced similar rates of MI, stroke, and repeat revascularization." It may be instructive to examine the factors associated with 1-year MALE and MACE in the group without CLTI to understand similarities or differences with the outcomes in CLTI.

The findings summarized in table 3 are particularly instructive, highlighting a nearly 5% mortality at 1 year

Key Words: Editorials ■ critical limb threatening ischemia ■ intermittent claudication ■ peripheral artery disease

Correspondence to: Subhash Banerjee, MD, University of Texas Southwestern Medical Center, 4500 S Lancaster Road (111a), Dallas, TX 75230. Email: subhash.banerjee@utsouthwestern.edu
For Disclosures, see page 2.

JAHA is available at: www.ahajournals.org/journal/jaha

following PVI of patients without CLTI in the context of discharge prescriptions of antiplatelet agents in 96% and statins in 79% of patients. Although patients with CLTI may have even greater need for these guideline-directed therapies, they were paradoxically prescribed less frequently in the cohort with CLTI at discharge post-PVI (antiplatelet agents 88% and statins 66%). As highlighted by the authors, discharge guideline-directed medication prescriptions represent an important modifiable factor that could very likely improve outcomes in CLTI. One-year mortality in CLTI is expectedly very high at 26%. The high 1-year readmission rates following an index PVI in both the cohorts with CLTI (62%) and without CLTI (38%) are also noteworthy findings. Patients requiring readmission post-PVI have previously been shown to have inferior outcomes to those who do not require readmission.[4] Similarly, both groups had equally high rates of repeat revascularization (nearly 25%) at 1 year. The 7.5% repeat revascularization for patients without CLTI is unprecedented.[5] It is not possible to discern if a greater proportion of repeat procedures represent planned staged interventions, because the data sets used do not report that level of information. The high 1-year readmission rates in patients with CLTI discharged on antiplatelets, anticoagulants, or beta-blockers or the seemingly protective effects of higher body mass index, family history of coronary artery disease, or Rutherford 4 PAD symptoms are more likely related to unmeasurable confounders. The authors clearly identify the inherent limitations of the data sets examined for this analysis and highlight the particular challenges owing to the lack of ankle brachial or toe pressure indices, laterality, or index lesion reintervention, planned versus unplanned interventions, and laterality of amputations. That noted, the authors are to be commended for undertaking additional analyses to explore ipsilateral and contralateral contributions to amputation and assessing factors associated with 1-year MALE by excluding contralateral amputations to ratify consistency of their initial findings.

Finally, these data suggest that patients without CLTI-PVI cannot be assumed to have lower rates of adverse events based on their PAD severity alone. Additionally, many of the characteristics associated with higher MACE rates following a CLTI-PVI are not modifiable. These including end-stage renal disease requiring hemodialysis, age, severe lung disease, congestive heart failure, cerebrovascular disease, diabetes mellitus, and prior coronary artery bypass grafting. Factors associated with MALE were also primarily nonmodifiable factors, including end-stage renal disease, and other lesion and endovascular treatment features. There is clear need for including patients with end-stage renal disease or adverse lesion features into future clinical trials. Discharge medications, especially in patients with CLTI, represent an important, potentially modifiable factor that is associated with adverse 1-year outcomes following PVI.[6]

Despite inherent limitations in the data set, Weissler and colleagues should be congratulated for providing this real-world analysis of cardiovascular and limb outcomes following endovascular treatment of PAD in patients presenting with intermittent claudication and critical limb ischemia. By identifying modifiable and nonmodifiable factors and treatment gaps, the investigators have invigorated the sense of purpose for all practitioners engaged in the care of patients with PAD. The care continuum of PAD may not end with a successful intervention; improving patient-centered outcomes may require refining all the elements of PAD care, including aggressive secondary prevention medications, structured exercise programs for those with claudication or wound care, and surveillance strategies for CLTI. Through attention to all aspects of PAD care, we may continue to combat the morbidity associated with PAD and aim to save lives and limbs of patients undergoing endovascular treatment.

ARTICLE INFORMATION

Affiliations

University of Texas Southwestern Medical Center, Dallas, TX (S.B.); Methodist Hospital, Dallas, TX (L.H.); and Massachusetts General Hospital, Boston, MA (D.E.D.).

Disclosures

Subhash Banerjee reports honoraria from Medtronic, GE, and Cordis and has received institutional research grants from Boston Scientific Corporation and Chiesi. Douglas E. Drachman reports honoraria from Boston Scientific Corporation, Broadview Ventures, Cardiovascular Systems Inc., and Cordis. Lawrence Hoang has no disclosures to report.

REFERENCES

1. Jeger RV, Eccleshall S, Wan Ahmad WA, Ge J, Poerner TC, Shin E-S, Alfonso F, Latib A, Ong PJ, Rissanen TT, et al.; International DCB Consensus Group. Drug-coated balloons for coronary artery disease: third report of the International DCB Consensus Group. *JACC Cardiovasc Interv*. 2020;13:1391–1402. doi: 10.1016/j.jcin.2020.02.043
2. Bonaca MP, Bauersachs RM, Anand SS, Debus ES, Nehler MR, Patel MR, Fanelli F, Capell WH, Diao L, Jaeger N, et al. Rivaroxaban in peripheral artery disease after revascularization. *N Engl J Med*. 2020;382:1994–2004. doi: 10.1056/NEJMoa2000052
3. Weissler EH, Wang Y, Gales JM, Feldman DN, Arya S, Secemsky EA, Aronow HD, Hawkins BM, Gutierrez JA, Patel MR, et al. Cardiovascular and limb events following endovascular revascularization among patients ≥65 years old: an ACC PVI Registry Analysis. *J Am Heart Assoc*. 2022;11:e024279. doi: 10.1161/JAHA.121.024279
4. Anand SS, Caron F, Eikelboom JW, Bosch J, Dyal L, Aboyans V, Abola MT, Branch KRH, Keltai K, Bhatt DL, et al. Major adverse limb events and mortality in patients with peripheral artery disease: the COMPASS Trial. *J Am Coll Cardiol*. 2018;71:2306–2315. doi: 10.1016/j.jacc.2018.03.008
5. Patel K, Liu Y, Etaee F, Patel C, Monteleone P, Patel M, Amer Alaiti M, Metzger C, Banerjee A, Minniefield N, et al. Differences between patients with intermittent claudication and critical limb ischemia undergoing endovascular intervention: insights from the Excellence in Peripheral Artery Disease Registry. *Circ Cardiovasc Interv*. 2021;14:e010635. doi: 10.1161/CIRCINTERVENTIONS.121.010635
6. Bonaca MP, Hamburg NM, Creager MA. Contemporary medical management of peripheral artery disease. *Circ Res*. 2021;128:1868–1884. doi: 10.1161/CIRCRESAHA.121.318258