

We need more vascular research



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Peripheral arterial disease (PAD) remains a challenging disease for both the patient and the physician. In the majority of cases, PAD is asymptomatic or only mildly symptomatic, and is effectively managed with lifestyle modifications such as regular exercise and smoking cessation. However, a minority of patients have severe disease with approximately ~20% progressing to amputation or death within a year of diagnosis. It is crucial for these patients to receive timely and effective restoration of blood flow to their legs.

Medical interventions reduce disease progression but currently have a limited role in acutely improving perfusion to prevent local complications. Procedural interventions can quickly increase local or regional perfusion but are associated with a small but not insignificant rate of periprocedural and long-term complications, limited efficacy, such as ability to heal wounds or achieve meaningful activity, as well as limited durability. Some treatments lead to untoward consequences that are only discovered with clinical use, such as restenosis after angioplasty, stent fracture, and accelerated atherosclerosis after first generation drug-eluting stent placement.

The previous paradigms of treatments using large surgical procedures manipulating whole vessels via open incisions has been revolutionized, in some and many circumstances, by the ability to use minimally invasive

endovascular treatments via percutaneous needle access including wires, catheters, balloons, and stents. It is generally agreed that minimally invasive approaches can reduce morbidity and hospital length of stay costs, increasing satisfaction and the attractiveness of these approaches. However, the ability to treat vessels via minimally invasive approaches may also lead to overtreatment of areas with limited amounts of disease that would not be treated by open approaches, violating both traditional vascular surgical guidance, such as treatment of functional but not purely anatomic disease, as well as traditional surgical risk-benefit ratio guidance, such as avoiding tibial bypass for claudication.

The increasing variety of minimally invasive techniques to treat PAD has created a challenge; each therapeutic device has a specific mechanism of action that is suitable for specific types of lesions. Since PAD is heterogenous, with plaques composed of varying amounts of calcium, dense collagen, lipids, smooth muscle cells, and proteoglycan matrix, the response to various devices—such as atherectomy, lasers, and drills—depends on the composition of the treated plaque. Without the ability to easily differentiate patients and their plaques and thus select appropriate individualized treatments, clinicians frequently need to resort to a common approach to treat patients. In addition, currently used devices to treat PAD are typically based on designs to treat coronary arteries that have distinct pathophysiology from peripheral arteries, and thus efficacy of devices may vary. It is predictable that reported results are conflicting and not optimal. Further obscuring the appropriate use of these therapies are the robust financial incentives to practitioners and industry to provide these services that may rise to the level of abuse as highlighted in several recent articles in the press.¹⁻³

Improvement in outcomes for patients with PAD will require optimized utilization of our current technologies that are achieved via clinical trials such as BEST-CLI⁴ and regulatory oversight, with the goal of achieving durable and meaningful patient-centered outcomes. In addition, recent advances in disease classification, such as the WiFI and GLASS classifications,^{5,6} can lead to improved stratification of both disease and outcomes, reducing the heterogeneity of current studies to allow improved guidance and consensus as espoused by guidelines such as the Society for Vascular Surgery Clinical Practice Guidelines and appropriate use criteria.^{7,8}

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However, significant breakthroughs in patient care and outcomes require a more comprehensive approach to disease classification, understanding of mechanisms, as well as therapeutics both as currently applied as well as newly proposed. Our continual investment in translational research remains critical to understand all aspects of PAD and its treatment, including the development and progression of atherosclerosis leading to PAD, the effects of ischemia on tissue function that lead to reversible and irreversible symptoms, the development of new tools to diagnose and quantify the degree of ischemia locally and regionally with greater precision and accuracy, the discovery of novel treatments—both medical and procedural—for PAD, the need to increase durability of our treatments to achieve meaningful outcomes without increased rates of reintervention, as well as comparative efficacy analysis to promote optimal treatment paradigms in our health-care system. And, we must make the fundamental commitment to provide and optimize the equitable distribution of these treatments, matching treatment and effort to patients in need.

As such, it seems clear to us that additional translational research in vascular biology and technology is needed more than ever. The artist Laurie Anderson quoted her teacher: “If you think technology will solve your problems, you don’t understand technology—and you don’t understand your problems.”⁹ Translational vascular research brings us the necessary understanding of underlying diseases as well as our therapeutic technology, allowing us to apply technology appropriately and with specific functional outcomes in mind. This journal remains committed to publishing the

highest caliber basic and translational vascular research, allowing readers to access the best data to inform their decisions, ultimately to the practical benefit for our patients.

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