

Peripheral Arterial Disease in People With Diabetes: Consensus Statement Recommends Screening

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American Diabetes Association consensus statements, such as “Peripheral Arterial Disease in People with Diabetes” (reprinted in this issue starting on p. 181), are occasioned when clinicians need more specific guidance than is generally available and when evidence-based data remain insufficient for developing guidelines.

The consensus development panel for this statement was charged with addressing four issues around peripheral artery disease (PAD) and diabetes: 1) the epidemiology and impact, 2) the biology, 3) patient evaluation, and 4) best treatments. The consensus panel worked from an underlying assumption that PAD in people with diabetes is different from the vascular disease from other risk factors in its biology, in its clinical presentation, and in its management.

As far as the prevalence and impact, diabetes is the most powerful risk factor for PAD. Among those with diabetes, age, duration of diabetes, and the presence of neuropathy are particularly important as risk factors for the development of PAD.

With diabetes, there is usually a unique involvement of the tibial vessels below the knee. Because of the pattern of involvement distally, the majority of patients lack classic symptoms, such as claudication. In addition, there is an almost invariable association with neuropathy with blunted pain perception. Patients are therefore likely to experience more subtle symptoms than with classic claudication, for example, fatigue or poor functioning. A more devastating consequence of neuropathy is that PAD patients with diabetes present late, hav-

ing already developed limb-threatening ischemia with tissue loss, gangrene, or rest pain. This unfortunate progression lends urgency to the task of uncovering PAD in asymptomatic individuals in order to prevent amputation.

Beyond the threat to the limb, these patients face enormous cardiovascular and cerebrovascular risk. Over 5 years, 20% of PAD patients will sustain nonfatal myocardial infarction or stroke, and 30% will die, largely from cardiovascular disease.¹ For those with critical limb ischemia, the prognosis is worse: 30% will have amputations, and 20% will die within 6 months.² While the exact risk increment among diabetic patients with PAD is unknown, prospective cardiovascular clinical trial data assure us that patients with diabetes fare worse than their nondiabetic counterparts.

The true prevalence of PAD in individuals with diabetes has been difficult to determine because of the lack of symptoms and insensitive means of diagnosis. The ankle brachial index (ABI) has a high sensitivity and specificity for angiographically proven disease. Diagnosing PAD through ABI, the prevalence in individuals with diabetes > 40 years of age was 20%.³ That figure is higher than would be anticipated using only symptoms and absent pulses. In PAD patients > 50 years of age, the diabetes prevalence was 29%, again higher than anticipated.⁴ The unexpected high prevalence of PAD in the population with diabetes in a sense makes PAD a new public health issue.

The biology of PAD in diabetes is unique.⁵ The abnormal metabolic state in those with diabetes affects the vessel,

blood flow, and coagulability, and is, in a sense, a fulfillment of Virchow’s triad for thrombosis. While our knowledge is not yet specific to PAD, the atherogenic changes observed with diabetes in coronary and carotid artery disease may well occur in PAD. The growing association of elevated levels of C-reactive protein as both a marker and possible risk factor for atherothrombotic disease has been linked with PAD.⁶ The numerous factors that interplay in the atherogenic process in diabetes, including insulin resistance, abnormal free fatty acid metabolism, oxidative stress, and the accumulation of advanced glycation end products, result in endothelial dysfunction. Many other abnormalities of endothelial function have been identified, including impaired nitric oxide (NO) bioavailability (reducing NO-mediated vasodilatation and NO-mediated inhibition of inflammation and smooth muscle cell proliferation) and homeostasis.⁷

Ultimately, this translates into impaired vasoreactivity, stimulation of inflammatory pathways, and hypercoagulability. These effects, along with vascular smooth muscle cell abnormalities, not only promote atherosclerosis acceleration, but also lead to plaque destabilization and clinical events. In addition, the platelet is a strong link between impaired vascular function and thrombosis. In hyperglycemia, the platelet takes up more glucose, increasing oxidative stress and its tendency to aggregate. It is for these reasons that one can view diabetes as a unique risk factor for cardiovascular disease—not as an accelerator of disease, but as a cause that is distinct in its power, its mechanisms, and its expression.

It is important for clinicians to assess patients for PAD to identify those with high cardiovascular risk and those at risk for amputation. Because of the lack of symptoms in the premorbid period, it is important to screen those at risk. The consensus statement recommends screening for PAD in anyone with diabetes over 50 years of age. Those with other risk factors (e.g., smoking, advanced age, hypertension, and hyperlipidemia) or a duration of diabetes > 10 years should also be screened.

Measurement of ABI is more reliable and more specific than what can be learned from the history and physical exam. It is the ratio of the highest systolic blood pressure in the ankle divided by the highest systolic blood pressure at the arm. To perform ABI, a hand-held 5- to 10-MHz Doppler probe and a blood pressure cuff are required. Normal ABI results are 0.91–1.30, with significant obstruction indicated by an ABI < 0.90. Medial arterial calcification can make arteries at the ankle poorly compressible, giving a false elevation of the ABI, typically > 1.3. Such false negatives are not common enough, however, to detract from the value of the ABI as a screening tool. If one suspects noncompressible vessels, then more detailed evaluation with toe pressure or pulse volume recordings would be indicated.

For patients diagnosed with PAD, there are two goals of treatment: first, reducing the excessive cardiovascular risk and slowing the progression of disease, and second, addressing symptoms such as claudication and leg ischemia and preventing amputation. This means that patients should have aggressive risk factor interventions, especially blood pressure and lipid management and antiplatelet therapy. In addition, treatment and prevention of foot and lower extremity disease is also indicated.

Finally, it should be noted that ABI screening for PAD in patients with diabetes is enormously productive. As noted above, routine screening of individuals over 50 years of age can be expected to identify PAD in nearly one-third of individuals. Furthermore, identifying PAD before it has progressed to its more severe stages in this population allows us to offer effective treatments. These therapies may arrest PAD development and perhaps, as we have seen with regression of atherosclerosis through aggressive blood pressure and lipid control, reverse its advance. At the same time, we will undoubtedly be reducing cardiovascular risk.

The biggest “push back” since the release of this consensus statement in December, 2003, has been from clinicians who contend that an ABI measurement would not alter their clinical practice of identifying and treating all patients with diabetes as cardiovascular disease equivalents. Unfortunately, we do not always practice as our perception suggests, and < 50% of patients in the United States are receiving treatments according to accepted and published guidelines.⁸ This is truer for patients with diabetes, who achieve guideline targets even less frequently.⁹ In addition, measuring an ABI may unmask an asymptomatic patient with PAD who is at risk for amputation.

Other societies and health care organizations are recognizing the importance and impact of PAD. The American Heart Association and the American College of Cardiology are in the process of creating guidelines for PAD in the general population.

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