



Diabetes Group Warns Vascular Complication Is Underdiagnosed and Undertreated

Mike Mitka

PERIPHERAL ARTERIAL DISEASE (PAD) in individuals with diabetes is underdiagnosed and undertreated, leading to increased risk of mortality and morbidity, said researchers in a consensus statement issued by the American Diabetes Association (ADA).

The researchers warned that PAD can lead to amputations of the lower limbs and is associated with an increased risk of cardiovascular and cerebrovascular disease in all patients (*Diabetes Care*.2003;26:3333-3341). In patients with diabetes, the risks associated with PAD are even higher, said Peter Sheehan, MD, director of the Diabetes Foot and Ankle Center at the New York University School of Medicine.

"PAD in diabetes is different than PAD with other conditions," said Sheehan, who chaired the ADA panel that issued the consensus statement. "It's different for diabetes because of biology, clinical presentation, and treatment."

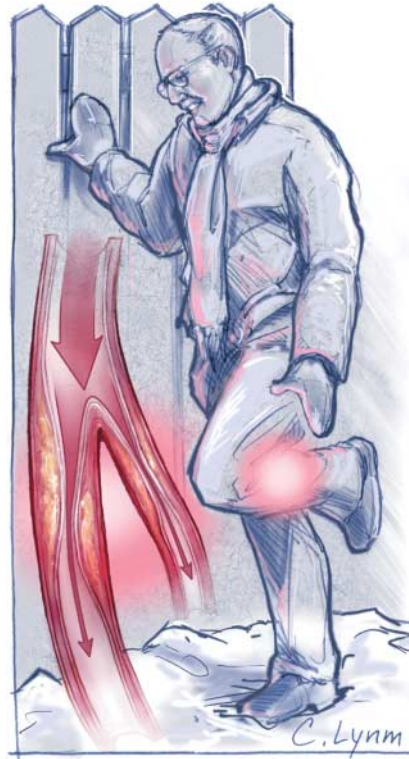
PAD is atherosclerotic occlusive disease in the legs and feet. While the most common symptom is intermittent claudication (calf pain during exercise with relief after stopping), the disease is also a marker for systemic vascular disease.

TWELVE MILLION AFFECTED

Scientists do not know exactly what percentage of patients with diabetes have PAD, a condition that affects an estimated 12 million individuals in the United States. Data from the Framingham Heart Study showed that 20% of symptomatic patients with PAD had diabetes; experts speculate that percentage is much higher, because many more individuals with PAD are asymptomatic.

The researchers estimated that among individuals with diabetes who are older than 50 years, one third have PAD.

According to the consensus statement, all diabetic patients who are older than 50 years should be screened for



Peripheral arterial disease (PAD), atherosclerotic occlusive disease in the legs and feet, can lead to amputation; it is also associated with an increased risk of cardiovascular and cerebrovascular disease, especially in patients with diabetes.

PAD. Screening was also advised for all patients with diabetes younger than 50 years who have other PAD-related risk factors, including diabetes duration for more than 10 years, hypertension, dyslipidemia, or a history of smoking.

The consensus panel said that while the majority of symptomatic patients remain stable, about 27% of patients with PAD have symptom progression over a 5-year period, with limb loss occurring in about 4%. Over the same time period, cardiovascular events in patients with PAD include nonfatal myocardial infarctions and stroke in 20% of patients; all-cause mortality is about 30%. Of patients with critical limb ischemia (more extreme presentations of PAD), 30% will have amputations and 20% will die within 6 months.

The consensus panel noted that progression and outcomes of PAD have not been specifically studied in patients with diabetes. But Sheehan noted that in prospective clinical trials of cardiovascular risk interventions, such as the Clopidogrel versus Aspirin in Patients at Risk of Ischemic Events (CAPRIE) trial, the event rates in patients with PAD and diabetes were higher than those with PAD only (*Lancet*. 1996; 348:1329-1339).

WORRISOME FACTORS

Two factors are worrisome to the consensus panel.

First, although PAD is more prevalent in individuals with diabetes, it may be harder to diagnose. Patients may not recognize the symptoms due to peripheral neuropathy, and physicians may not recognize the disease because the atherosclerotic lesions are more likely to be diffuse and distal compared with PAD lesions in nondiabetic patients. These factors create a higher risk for amputation, myocardial infarction, stroke, and death. Second, primary care physicians may lack appropriate lev-



els of awareness of PAD prevalence in general, and its association with diabetes in particular.

This disconnect between risk and physician awareness was highlighted in a multicenter, cross-sectional study conducted at 27 sites in 25 cities and at 350 primary care practices throughout the United States (*JAMA*. 2001;286:1317-1324). The study assessed the feasibility of detecting PAD in primary care clinics, patient and physician awareness of the disease, and intensity of risk factor treatment. **The researchers showed that while 83% of patients with a prior diagnosis of PAD (before trial enrollment) knew of their diagnosis, only 49% of their current physicians were aware of the diagnosis.**

In addition, although atherosclerosis risk factors were “very prevalent” in patients with PAD, these individuals received less intensive treatment for lipid abnormalities and hypertension and were prescribed antiplatelet therapy less often than were patients with cardiovascular disease.

“These results demonstrate that underdiagnosis of PAD in primary care practice may be a barrier to effective secondary prevention of the high ischemic cardiovascular risk associated with PAD,” the investigators concluded.

Those findings prompted the ADA to issue the consensus paper on PAD, Sheehan said. “Consensus statements are occasioned when there are clinical issues and insufficient evidence-based medicine to write treatment guidelines—that was the case with PAD and diabetes,” Sheehan said.

RECOMMENDATIONS

To best diagnose and evaluate PAD in patients with diabetes, the consensus panel recommended:

- Screening all patients older than 50 years and those younger than 50 years with other risk factors.
- Conducting a thorough medical history and physical examination to help identify those with PAD risk factors, symptoms of claudication, rest pain, and/or functional impairment.

- Visual inspection of the patient’s feet, as well as palpation of peripheral pulses.

- **Noninvasive evaluation for PAD using the ankle-brachial index.** This procedure involves using a Doppler device to measure the systolic blood pressures in the ankles and arms and calculate a ratio (using the systolic reading from the arm as the denominator). A ratio of 0.91 to 1.30 is considered normal, while severe obstruction is defined as less than 0.40. Such a test is usually performed at a noninvasive vascular laboratory, since most primary care offices do not have the equipment.

As for treatment, panel members said the approach should be two-fold: modifying primary and secondary cardiovascular disease risk factors and treat-

ing PAD symptoms—claudication and critical limb ischemia—thus limiting progression of disease.

Cardiovascular risk factor treatment includes smoking cessation, improved glycemic, lipid, and blood pressure control and antiplatelet therapy. Treatment of symptomatic PAD includes exercise rehabilitation and pharmacological therapies (such as cilostazol, an oral phosphodiesterase type III inhibitor which promotes blood flow to the legs) to treat claudication. For disabling claudication or critical limb ischemia, limb revascularization may be needed.

Sheehan said that he hoped the consensus paper, “helps clear up the misconception of the natural history of the disease.” □

New Anti-BSE Rules Imposed

Tracy Hampton, PhD

THE FOOD AND DRUG ADMINISTRATION (FDA) continues to implement more stringent regulations to thwart the potential spread of bovine spongiform encephalopathy (BSE, or “mad cow” disease) in the United States after the discovery of an infected Holstein in December. The agency has now imposed several bans that will affect human food, including dietary supplements, and cosmetics.

Material from “downer” cattle (animals too sick or injured to stand) or cattle that die before slaughter will be banned, along with other bovine-derived material, including risk materials from any cows 30 months or older (such as brain, skull, eyes, and spinal cord), as well as a portion of the small intestine and tonsils from all cattle.

Certain feeding practices have also been prohibited to help eliminate potential sources of BSE. Mammalian blood and blood products, “poultry litter” (bedding, spilled feed, feathers, and fecal matter from chicken coops), and “plate waste” (uneaten meat and scraps from restaurants) will be banned as feed

ingredients for ruminants. Spilled poultry feed may contain protein prohibited in ruminant feed, and plate waste could confound the FDA’s ability to analyze ruminant feed. Equipment, facilities, or production lines that use protein prohibited in ruminant feed must now be used exclusively for nonruminant animal feed.

The FDA also plans to intensify inspections of feed mills and renderers in 2004.

Guidelines issued by the World Organization for Animal Health (the international animal health standard-setting organization) state that animals born a year before or after detection of a BSE-positive animal are at highest risk. Twenty-five of the 81 animals in the positive cow’s birth herd fall into that category. As an added precaution, hundreds of additional cows that are either part of the birth herd or cannot be ruled out as not being part of the birth herd have been euthanized. Not all screening results are in, but so far, all tests for BSE are negative.

Updates from the US Department of Agriculture can be found at <http://www.usda.gov/BSE/>. □