

Essential Keys To Diagnosing And Treating PAD In Patients With Diabetes

Peripheral arterial disease (PAD) is an extremely prevalent, substantially underdiagnosed condition, which has a significant risk of morbidity and mortality. Recent data suggests that PAD affects nearly 18 million Americans and greater than 202 million globally.^{1,2} Patients with diabetes at highest risk include those age 50 or older, or those under age 50 with comorbid hypertension, hyperlipidemia or obesity. Individuals with a history of cardiovascular disease and those over age 65 are also at high risk.^{1,3}

Complicating the ability to diagnose PAD, approximately 50 percent of PAD patients are asymptomatic while another 33 percent have atypical symptomatology.⁴ Unfortunately, once diagnosed with PAD, 20 percent will experience a life-altering cardiovascular complication such as a myocardial infarction or cerebrovascular accident while 30 percent will experience a life-ending cardiovascular complication.⁵

Why Diabetes And PAD Are Frequent Comorbid Conditions

Diabetes mellitus is also a global health emergency.⁶ As of 2016, 422 million people had diabetes worldwide, up from an estimated 382 million people in 2013 and 108 million in 1980.^{7,8} The prevalence of diabetes varies worldwide. It is greater in middle-aged people in developing countries and people over 65 years of age in developed countries such as the United States.⁹

The U.S. has the unfortunate distinction of having the third largest number of adults suffering from diabetes.⁶ Currently, 14.3 percent of the U.S. population has diabetes with over 36 percent undiagnosed.¹⁰ Over the last 17 years, the U.S. prevalence of diabetes has approximately doubled in the two key age groups afflicted by PAD: those 45 to 64 years old



Here one can see the foot of a 55-year-old male with peripheral arterial disease (PAD) who had six prior bypass surgeries that failed. In patients with diabetes age 50 and older, 30 to 40 percent suffer from PAD.

and those 65 and older.¹⁰⁻¹⁵ By 2012, one-third of the elderly had diabetes while another 50 percent had pre-diabetes.¹⁰ In those between 45 to 64 years of age, 17.5 percent had diabetes and 45 percent had pre-diabetes.¹⁰

Diabetes mellitus and peripheral arterial disease do not just independently increase the risk for each other. Diabetes is synergistic with PAD. In the Framingham study, there was a 3.5 to 8.6 percent increase in developing PAD if the patient had diabetes.¹⁶ In the Hoorn study, the prevalence rate of an ankle brachial index (ABI) of <0.9 in individuals with normal glucose tolerance was 7 percent, which increased to 20.9 percent in patients with diabetes.¹⁷ Recent research demonstrates that these diseases share a common pathological pathway: insulin resistance.¹⁸

Simply put, PAD afflicts a greater per-

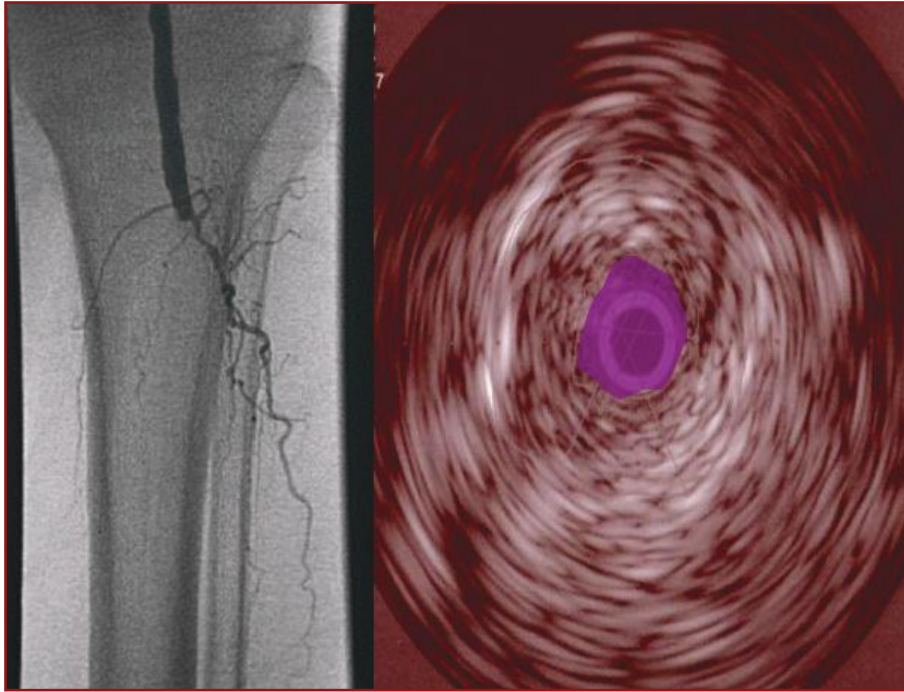
centage of people with diabetes than people without diabetes.¹⁹⁻²⁴ In patients with diabetes age 50 and older, 30 to 40 percent suffer from PAD.^{19,20,23,25,26} In contrast, the prevalence of PAD in those with normal glucose levels appears to be about 10 to 20 percent.^{19-22,24}

In patients with diabetes, the risk of PAD increases with age, duration of diabetes and the presence of peripheral neuropathy.²⁷ African-Americans and Hispanics with diabetes have a higher prevalence of PAD than non-Hispanic Caucasians.²⁷ Diabetes increases the risk of developing PAD by 1.5 to 4 times.²⁸ In addition, the likelihood of developing PAD increases with the severity of diabetes as measured by hemoglobin A1c (HbA1c).²⁹

In the past, the thinking was that the type of diabetes did not necessarily affect the prevalence of PAD with essentially identical prevalences found with type 1 and type 2 diabetes.³⁰ However, more recent studies have found a much higher prevalence of PAD (23.5 percent) in patients with type 1 diabetes than in those with type 2 diabetes.³¹ The vascular disease that arises from diabetes is primarily microangiopathy (abnormalities at the capillary level) and macroangiopathy (the result of arteriosclerosis).

Further complicating the diagnosis of PAD in patients with diabetes is the presence of peripheral neuropathy. Peripheral neuropathy and PAD are known risk factors for foot ulceration. Moulik and colleagues found that between 40 and 60 percent of patients with diabetic foot ulcers have PAD, which increased their risk of amputation and mortality.³² As the vascular disease progresses, tissue ulceration and ultimately gangrene develop if reperfusion does not occur.

Diabetes mellitus dramatically increases the morbidity and mortality associated with PAD, doubling the risk of cardiovas-



Angiogram (left) and computed tomography angiography (right) in the 55-year-old patient with PAD showed he had an occluded popliteal artery with no runoff vessels.

cular disease and leading to a profoundly increased incidence of stroke and coronary artery disease.³³ Nearly 75 percent of deaths in patients with diabetes are due to coronary artery disease.³⁴ Similarly, the majority of patients with PAD die from coronary artery disease (55 percent) or stroke (25 percent).³⁵ Less than 10 percent die from peripheral vascular events, most commonly from a ruptured aortic aneurysm.³⁵

A Closer Look At Adverse Outcomes With Diabetes And CLI

There is an even closer relationship between diabetes and critical limb ischemia (CLI), the most severe and deadly form of PAD. Although somewhat more than 14 percent of the U.S. population have diabetes, 60 to 80 percent of patients with CLI have diabetes.^{10,36,37}

Critical limb ischemia occurs when there is a sustained, severe decrease in leg blood flow, which, if untreated, leads to rest pain, ulcers and limb loss.³⁸ Unless patients with CLI have successful revascularization, the six-month mortality rate is 20 percent and the amputation rate is 40 percent.³⁷

Patients with diabetes present with advanced CLI because of the complex interplay of neuropathy, ischemia, microvascular dysfunction and infection.³⁹ In addition, patients with diabetes and PAD are more prone to developing sudden critical ischemia due to thrombosis or a pivotal event that rapidly leads to ulcers or infection.²⁷

Lower limb atherosclerotic disease is much more virulent in patients with diabetes. Patients with diabetes have more severe ischemia, a greater number of amputations, experience higher mortality and die at a younger age.⁴⁰ A higher percentage of patients with diabetes and PAD develop CLI and are at greater risk of progression to gangrene and amputation.^{37,41-43}

In the U.S., diabetes is the cause of 50 to 67 percent of all nontraumatic lower extremity amputations.^{44,45} Diabetes increases the risk of nontraumatic amputation by 28 times. The rate of amputation increases with age with the highest rates occurring in patients with diabetes age 75 and older.⁴⁵

Diabetes is an independent risk factor for amputation.³⁷ In patients with CLI,

the presence of diabetes increases the odds of undergoing amputation by more than twice.⁴⁶ Patients with diabetes also undergo major amputations at an earlier age, are more likely to require higher level initial amputations and frequently require contralateral amputations.^{37,47} In addition, the risk of amputation increases with the severity of diabetes as measured by HbA1c.⁴⁸

Diagnosing PAD In The Patient With Diabetes

Diagnosing PAD in the patient with diabetes begins with a comprehensive history identifying the risk factors, a family history of diabetes as well as noting any ulcerations, chronic wounds, prior vascular testing or prior diagnosis of PAD. Inquiring as to any lower extremity pain or cramping, especially with walking, may help to diagnose PAD.³²

Lower extremity clinical findings of PAD may include thin and trophic changes of the skin, increased distal cooling, diminished or absent digital hair, diminished or absent pulses, dependent rubor or pallor with limb elevation. Vascular assessment initially begins with non-invasive arterial studies of the lower extremities including an ABI, an exercise ABI, arterial Doppler with pulse volume recording (PVR) testing, and may necessitate more invasive vascular studies including computed tomography (CT) angiography, magnetic resonance angiography (MRA), and ultimately an angiogram.

A Quick Guide To PAD Treatment Options

Aggressive risk factor modification is needed to reduce cardiovascular mortality. Risk factor modification includes smoking cessation, weight reduction in those who are obese, blood glucose control in patients with diabetes and antihypertensive agents in those with abnormal blood pressure. Antiplatelets and antilipids are also part of standard medical management.^{5,49}

One can relieve intermittent claudication symptoms with supervised exercise therapy as well as cilostazol and statins.⁴⁹ Patients with severe progressive claudica-

tion and those suffering from CLI should have revascularization to reduce the risk of limb loss, relieve symptoms and improve quality of life.⁴⁹ Revascularization includes surgical bypass, endarterectomy and endovascular interventions.^{5,49} ■

Dr. Tursi is the Chief of Foot and Ankle Surgery at Our Lady of Lourdes Medical Center in Camden, N.J. He is a Fellow of the American College of Foot and Ankle Surgeons, and is the Foot and Ankle Specialist for the Philadelphia Flyers. Dr. Tursi is a Clinical Instructor with the University of Pennsylvania/Presbyterian Residency Program. He is the Podiatric and Wound Care Chairman for the New Cardiovascular Horizons annual conference, and the Chairman of the American Professional Wound Care Association.

Dr. Walker is the President of the Cardiovascular Institute of the South. He is a Clinical Professor of Medicine at the Louisiana State University School of Medicine in New Orleans and a Clinical Professor of Medicine at the Tulane University School of Medicine in New Orleans. Dr. Walker is the Chairman of the New Cardiovascular Horizons annual conference.

Ms. Yost is the President of the Sage Group, LLC in Beaufort, S.C. She is the Business of Peripheral Vascular Disease Chairman for the New Cardiovascular Horizons annual conference.

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