Peripheral Arterial Disease: Clinical Assessment and Indications for Revascularization in the Patient with Diabetes

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Peripheral arterial disease (PAD) is an under-recognized complication of diabetes. Recently, prevalence estimates in patients with diabetes over 50 years of age have been placed at 25% to 30%. The main reason for under-reporting is the largely asymptomatic nature of PAD in diabetes. Nonetheless, it is important to diagnose PAD because it is a marker of systemic atherosclerosis with excess cardiovascular risk, and it may identify a patient who may develop progressive disability and risk of limb loss. The most sensitive and specific diagnostic tool is an ankle-brachial index. Imaging studies are performed in patients who are candidates for revascularization. The most durable and effective revascularization procedure for PAD in diabetes is surgical bypass with saphenous vein as the conduit. Endovascular interventions are best used in patients with proximal disease with short-segment stenoses. The indications for revascularization have been immutable for decades, namely rest pain, ischemic ulceration, or gangrene. Presently, clinicians would include “selected” patients with intermittent claudication who have disabling symptoms and proximal disease above the inguinal ligament.

Introduction
Peripheral arterial disease (PAD) is a term that is defined as atherosclerotic occlusive disease of the lower extremities [1]. Diabetes is the most powerful risk factor for PAD, and the PAD prevalence among people with diabetes has recently been suggested to be much higher than previously anticipated.

The historic underestimation of PAD prevalence can be attributed to the largely silent nature of PAD in diabetes. When symptoms arise, however, they manifest as intermittent claudication—pain or cramping in the calf, thigh, or buttock with exercise that is reproducible and that is relieved by rest or critical limb ischemia (CLI), rest pain, ischemic ulceration, or gangrene in a patient with objective PAD.

The management of patients with diabetes and PAD is twofold: aggressive cardiovascular risk reduction and treatment of symptoms. Selected patients with claudication and most patients with CLI will benefit from revascularization, either open surgical procedures or endovascular interventions. New advances in surgical and endovascular techniques have resulted in improved outcomes and quality of life for patients with diabetes and PAD such that there may be emerging changes in the indications for revascularization, with less afflicted patients undergoing vascular intervention.

This review discusses the epidemiology of PAD in diabetes, its impact on the individual patient, and how PAD is best evaluated. Most importantly, newer surgical and endovascular techniques are assessed for the evidence-based recommendations for their indications, especially for selective patients with claudication.

PAD in Diabetes
The risk factors for PAD are similar to those for cardiovascular disease in general, and include smoking, hypertension, and hyperlipidemia [2]. Diabetes stands alone as a risk factor in its power and its unique pattern of vessel involvement. The PARTNERS (PAD Awareness, Risk, and Treatment: New Resources for Survival) study recently showed that the prevalence of PAD in patients with diabetes was much greater than anticipated, with an estimated 29% of patients with diabetes over age 50 being afflicted [3]. In another data set of type 1 and 2 diabetic patients over age 40, the prevalence was 20% [4].

The high prevalence of PAD in diabetes reflects the unique biology of diabetes and its acceleration of atherosclerosis that confers risk even before the onset of hyperglycemia. The metabolic state of “prediabetes” is characterized by insulin resistance, abnormal free fatty acid metabolism, and endothelial dysfunction resulting in abnormal vasoreactivity and deranged nitric oxide pathways [5]. With the onset of hyperglycemia, there is
additionally oxidative stress with free oxygen radicals adding to endothelial abnormalities. In concert with the formation of advanced glycation end products, oxidative stress contributes to activation of inflammatory pathways that are proatherogenic. Diabetes is also a hypercoagulable state with increased plasma fibrinogen, plasminogen activator inhibitor-1, and blood viscosity. Finally, the platelet is hyperactive with increased aggregation, contributing to increased atherothrombosis and progression of disease [6]. Thus, one can consider diabetes to be a unique form of atherosclerosis rather than simply an accelerator of it.

The pattern of vessel involvement underscores this uniqueness. Diabetes is solitary as a risk factor for PAD below the popliteal artery, commonly affecting the trifurcation vessels, namely the anterior and posterior tibial and the peroneal arteries. Usually there is reconstitution distally, with the pedal vessels generally spared [7]. This anatomic pattern is exploited when performing distal surgical bypass in patients with trifurcation disease.

The biology of PAD and its distal distribution also explains why patients with diabetes are generally asymptomatic. In addition, PAD in diabetes is almost invariably associated with distal sensory neuropathy, which may attenuate or eliminate any pain or discomfort of the legs [8]. The vascular involvement in the legs is akin to that in the coronaries in diabetes: diffuse, distal disease silently progressing under the veil of neuropathy.

Thus, most patients with diabetes and PAD will not complain of symptoms. Nonetheless, many will have significant functional impairments, such as slow walking speed and gait instability, that are commonly attributed to getting older [8]. Others may have atypical symptoms like fatigue and leg heaviness that may not be volunteered. A cycle of disability is sustained as a poorly functioning individual becomes less active, which results in progressive physical deconditioning.

Patients with PAD have a large systemic atherosclerotic burden and are at high risk for myocardial infarction, stroke, and cardiovascular death, with a 5-year event rate of 20% to 50% for fatal and nonfatal myocardial infarction and stroke. Thus, the diagnosis of PAD is considered a coronary artery disease equivalent and mandates aggressive risk factor intervention, especially for hypertension, hyperlipidemia, and antiplatelet therapy, preferably with clopidogrel [9].

The natural history of the limb in patients with PAD is not as striking as the life events: over 5 years most (~75%) remain stable—others progress, with 7% requiring revascularization and 4% requiring amputation [10]. It should be noted that the stability of the peripheral vasculature would have strong consideration in the evaluation of the patient for revascularization.

The importance of the diagnosis of PAD is twofold: it identifies a patient with high cardiovascular risk and it uncovers a patient who may have symptoms that can lead to disability and limb loss. A recent American Diabetes Association consensus statement recommends screening for PAD for all people with diabetes over 50 years of age or for those with other risk factors, even without symptoms [11].