PERIPHERAL VASCULAR DISORDERS IN DIABETIC FOOT PATIENTS

Essay

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INTRODUCTION

Foot complications are already a major cause of admissions for diabetes, and comprise a disproportionately high number of hospital days because of increased surgical procedures and prolonged length of stay**. *(Kenny; et al., 1995)***

Diabetes is an important risk factor for LEAD (lower extremity arterial disease). Hypertension, smoking, and hyperlipidemia, which are frequently present in patients with diabetes, contribute additional risk for vascular disease. The incidence and prevalence of LEAD increase with age in both diabetic and non diabetic subjects and, in those with diabetes, increase with duration of diabetes. Many elderly diabetic persons have LEAD at the time of diabetes diagnosis.

Diabetes accounts for about 50% of all non traumatic amputations in the United States. Mortality is increased in patients with LEAD, particularly: if foot ulcerations, infection, or gangrene occur**. *(Melton; et al., 1980)***

Numerous studies have successfully refuted the notion of "small vessel disease." in diabetic patients and histological studies demonstrate the presence of periodic acid Schiff-positive material occluding the small and medium-sized arterioles as the hallmark of microvascular disease in the patient with diabetes. ***(Strandness and Gibbons, 1964)***
Atherosclerotic peripheral vascular disease in patients with diabetes is a major factor in the progression of diabetic foot pathology. Patients with diabetes are noted to have a fourfold increase in the prevalence of atherosclerosis as well as a propensity for accelerated atherosclerosis. ***(Armstrong and Lavery, 1998)***

Recent technological advances over the past decade have enabled us to evaluate the functional microcirculation of the feet. Methods such as laser Doppler flowmetry, flow video microscopy, measurements of capillary pressure, and transcutaneous oxygen tension measurements have all been used. ***(Rendell; et al., 1989)***
Diabetic patients with signs or symptoms of vascular disease or absent pulses on screening foot examination should undergo ankle brachial pressure index (ABI).

If the diabetic foot ulcer does not heal with conservative measures or if bone, joint, or tendon is involved, digital subtraction arteriography should be performed.***(American Diabetes Association Consensus Statement, 2003)***
The approach to the diabetic patient with signs and symptoms of vascular occlusive disease is separate from that utilized in the non diabetic population.

The management of a patient that presents with an ischemic diabetic foot should be approached in a premeditated and stepwise fashion. The initial priority is the prompt and thorough drainage and/or debridement of any infected or necrotic tissue. Once the infection is controlled, the next step is determining the level of ischemia by urgent angiography then, planning for revascularization is undertaken. ***(American Diabetes Association Consensus Statement, 2003)***

New treatment modalities have emerged recently in the era of management of peripheral vascular disorders in diabetics, these include: Hyperbaric oxygen therapy , Stem cell therapy and Gene therapy.

AIM OF THE WORK

The aim of this study is to clarify the pathogenesis of vascular changes occurring in diabetic foot on macrovascular as well as microvascular levels , also we will discuss different diagnostic modalities to formulate the proper management of this major problem on evidence base medicine and according to international guidelines.

EPIDEMIOLOGY

Peripheral Arterial Disease (PAD) is defined as the group of disorders that affects any artery other than those which supply the heart ***(Mohler and Hirsch,2010).*** It has been found to be very common in different cultural settings ***(Cacoub; et al., 2009).***

PAD is a common disorder that affects up to 20% of the general population; the incidence of PAD rises with increased age ***(Pfeiffer; et al. ,2008) , (Ostchega; et al. ,2007).***

Diabetes is a common non-communicable disease worldwide. It has a significant impact on health because of its microvascular and macrovascular complications. Developing countries are facing the major impact of this disease ***(International Diabetes Federation ,2011).***

Diabetes is a well-known risk factor for PAD ***(Jensen; et al. ,2008).***

PAD is usually extensive and severe when associated with diabetes ***(Jude; et al.,2001).***

Diabetes is a risk factor for both PAD and PAD associated mortality ***(Leibson; et al. ,2004).*** and contributes to approximately half of all the amputations in individuals with diabetes ***(The Global Lower Extremity Amputation Study Group,2000).***

In people with diabetes, every 1% increase in glycated hemoglobin (A1C) corresponds to a 26% increased risk of PAD ***(Selvin; et al. ,2004).***

Clearly, diabetes increases the prevalence of PAD; it is estimated that the prevalence

of PAD in those with diabetes >40 years and >50 years of age is 20% and 29%, respectively ***(Hirsch; et al. ,2001).***

Screening for PAD is important for two main reasons. First, the majority of patients with PAD are asymptomatic, even

in symptomatic patients atypical symptoms are common ***(Makdisse; et al. , 2008) , (Bernstein; et al. ,2008).***

Moreover, asymptomatic disease can significantly increase the rate of progression to intermittent claudication, which could adversely affect the quality of life ***(Regensteiner; et al. ,2008).***

Second, PAD indicates generalized atherosclerosis and thus carries a very high risk for cardiovascular (CV) morbidity and mortality ***(Norman; et al. ,2006) , (Li; et al. , 2007).***

This is attributed to the fact that most of these patients have CV risk factors. Therefore, diagnosing PAD would be helpful to identify and modify the risk factors to decrease the burden of CV morbidity and mortality ***(Kröger; et al. , 2010).***

Frequency of PAD in our population assessed by the absence of peripheral pulses was 15.2%. However, pulse assessment has a high degree of interobserver variability. Ankle Brachial index (ABI) is more accurate and reproducible measurement for the detection of PDA ***(Hasimu; et al. ,2006).*** The prevalence of PDA in arab society was higher in males than females. This is in contrast to higher prevalence of PAD among females in China and India ***(Shen;et al. ,2006).***

Prevalence of PAD

PAD affects 8–12 million adults ≥ 40 years of age in the United States and affects similar proportions of men and women ***(Rosamond; et al. ,2008).***

About 20–30% of individuals with PAD have diabetes ***(Marso and Hiatt ,2006).***

Compared to whites, the likelihood of PAD is 50% greater among African Americans and 55% lower among Chinese ***(Allison; et al. ,2006).***

The National Health and Nutrition Examination Survey (NHANES) for 1999–2000 showed that the age-adjusted

prevalence of PAD was 11.7% in non-Hispanic whites, 19.5% in non-Hispanic blacks, and 15.6% in Hispanic men and women. The risk of PAD increases substantially with age.The prevalence of PAD is 4.8, 12.0, and 22.0% for men and women aged 60–69 years, 70–79 years, and ≥ 80 years, respectively ***(Ostchega; et al. , 2007).***

PAD is associated with significant morbidity and mortality. A low ABI (< 0.90) has been associated with an increased risk of all-cause mortality (relative risk [RR] 1.60; 95% confidence interval [CI] 1.32–1.95); cardiovascular mortality (RR 1.96; 95% CI 1.46–2.64); fatal and non-fatal coronary heart disease (RR 1.45; 95% CI 1.08–1.93); and fatal and non-fatal stroke (RR 1.35; 95% CI 1.10–1.65) ***(Heald; et al. ,2006).***

In a cross-sectional study that evaluated both walking impairment and quality of life among individuals with both PAD and other cardiovascular diseases, the impact of PAD on functional status was equal to or worse than that of individuals of comparable age with coronary and other cardiovascular diseases ***(Regensteiner; et al.,2008).***

Patients with diabetes are more likely to develop symptomatic PAD. In a cross-sectional study, lower-extremity function was assessed in 460 male and female patients with PAD, 147 of whom also had diabetes.Individuals with PAD and diabetes had worse lower-extremity function with shorter distances walked and at a slower pace than those with PAD alone, which may be explained by diabetes-related neuropathy ***(Dolan; et al. ,2002).***

Patients with both PAD and diabetes are at higher risk than PAD patients without diabetes for the progression of their PAD, as well as developing manifestations of coronary heart disease ***(Marso and Hiatt ,2006).***

The prevalence of amputation in PAD varies regionally, but overall risk is < 3–4% of the total PAD population. It is important to note that rates of leg amputation in individuals with PAD and diabetes are associated with great regional variation. These disparate rates are likely the result of differing care pathways offered to individuals at risk, further amplifying the national PAD outcomes health disparity ***(Wrobel; et al. ,2001).***

PATHOGENESIS

It has been nearly half a century since the concept of "small vessel disease" was introduced as a unique entity in the microvasculature of the patient with diabetes. This misconception was arrived at through a retrospective histological study demonstrating the presence of periodic acid Schiff-positive material occluding the arterioles in amputated limb specimens of patients with diabetes ***(Hussein, et al., 2011).***

From these observations, Goldenberg and his colleagues deduced that the deposits in the small and medium-sized arterioles were the hallmark of vascular disease in the patient with diabetes. Perpetuation of this erroneous idea led to the belief that preferential occlusion of the small vessels in the patient with diabetes produced a poorer prognosis with limited revascularization options.

Since then, numerous studies have successfully refuted the notion of "small vessel disease." In a blinded, prospective analysis of amputated limbs, periodic acid Schiff staining showed a similar meager pattern of occlusive disease in both diabetic and non diabetic limbs at the arteriole level ***(Chen, et al., 2012).***

Using a sophisticated casting technique, Conrad also demonstrated a lack of significant occlusive disease at the arteriole level in both the patients with and without diabetes. Furthermore, vascular reactivity in the vessels of patients with diabetes has been shown to be comparable to those of patients without diabetes based on physiological studies involving the administration of a papaverine (a vasodilator) into femoro-popliteal bypass grafts ***(Barner;et al.,1971).*** These data, coupled with a vast clinical experience of nearly three decades of successful arterial reconstruction in patients with diabetes, have

thoroughly dispelled the notion of diabetic "small vessel disease"***(Jurado, et al., 2008).***

However, recent work suggests that although an occlusive disease of the microcirculation does not exist, the microcirculation (predominantly capillaries and arterioles) is impaired in the patient with diabetes. In simplest terms, microvascular dysfunction in diabetes may be described by an increased vascular permeability and impaired autoregulation of blood flow and vascular tone. It is postulated that metabolic derangements as a result of hyperglycemia and insulin resistance work synergistically to cause microvascular dysfunction. Consequently, these metabolic alterations produce functional and structural changes at multiple levels within the arteriolar and capillary level.

Structural Changes In The Microcirculation

Basement Membrane Thickening

Structurally, the most notable changes in the microcirculation involve thickening of the basement membrane and an observed reduction in the capillary size ***(Jurado; et al. ,2008).***

However, the density of the skin capillaries does not differ from healthy subjects**.** These structural changes are more pronounced in the legs, likely the result of increased hydrostatic pressures in that part of the body**.** The extent of basement membrane thickening has also been observed to be related to the level of glycemic control, with increased basement thickening in poorly controlled patients with diabetes (***McDermott; et al. ,2008).***

Functional Changes In The Microcirculation

The observed failure of the microcirculation to vasodilate in response to injury has been described as a functional ischemia and has been demonstrated to be a result of a number of factors that play in the microcirculation of the patient with diabetes. Alteration in the microcirculation of the foot has been postulated to be an important factor in the poor wound healing associated with chronic diabetic foot ulcerations. Recent work has addressed these changes, with specific emphasis placed on the changes in the diabetic foot microcirculation, nerve function, and muscle metabolism ***(McDermott; et al. ,2008) .***

Diabetic Foot Microcirculation

The resting total skin microcirculation in the diabetic foot is comparable with that of the nondiabetic foot, when peripheral neuropathy is absent. However, when neuropathy is present, the capillary blood flow has been shown to be reduced ***(Veves; et al. ,1998).***