Treatment of Peripheral Arterial Disease of the Lower Extremities

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Risk factors that predispose to Peripheral Arterial Disease (PAD) include age, cigarette smoking, diabetes mellitus, hypertension, dyslipidemia, increased plasma homocysteine levels and hypothyroidism [1,2]. PAD coexists with other atherosclerotic disorders [3,4]. Persons with PAD are at increased risk for all-cause mortality, cardiovascular mortality and cardiovascular events [5-7].

Smoking cessation programs should be strongly encouraged in persons with PAD [1]. Hypertension should be adequately controlled to decrease cardiovascular mortality and morbidity in persons with PAD, with the blood pressure reduced to less than 140/90 mm Hg [1,8]. The hemoglobin A1c level should be reduced to less than 7.0% [1]. The serum low-density lipoprotein cholesterol level should be reduced to less than 70 mg/dl by treatment with statins, to reduce cardiovascular events and mortality [1,9-11], and to increase exercise time in patients with intermittent claudication [12,13].

The antiplatelet drugs aspirin or clopidogrel should be administered to patients with PAD, to reduce cardiovascular death, myocardial infarction and stroke [1,14]. At 1.9-year follow-up in the Clopidogrel versus Aspirin in Patients at Risk for Ischaemic Events (CAPRIE) trial, the annual incidence of vascular death, nonfatal myocardial infarction, and nonfatal stroke was 3.7% in persons randomized to clopidogrel versus 4.9% in persons randomized to aspirin, a 24% significant decrease with the use of clopidogrel [15].

Data from the Heart Outcomes Prevention Evaluation (HOPE) Study showed that ramipril 10 mg daily significantly decreased cardiovascular events in persons with symptomatic PAD, and in persons with asymptomatic PAD [16]. The American College of Cardiology (ACC)/American Heart Association (AHA) guidelines recommend treating persons with PAD with angiotensin-converting enzyme inhibitors, unless there are contraindications to the use of these drugs to reduce cardiovascular mortality and morbidity [1]. Beta blockers should also be used to treat coronary artery disease in patients with PAD, in the absence of contraindications to these drugs to reduce cardiovascular events and mortality [1,17].

Two drugs, pentoxifylline and cilostazol, have been approved by the United States Food and Drug Administration for symptomatic treatment of intermittent claudication. However, many studies have found no consistent improvement with pentoxifylline in patients with intermittent claudication, in comparison with placebo [18]. Cilostazol has been documented in numerous trials to improve exercise capacity in patients with intermittent claudication, and in a dose of 100 mg twice daily, was shown to be superior to both placebo and pentoxifylline [19]. Cilostazol should be administered to patients with PAD to increase walking distance, but should not be given to persons with PAD who also have heart failure. Other contraindications to the use of cilostazol include a creatinine clearance <25 ml/min, a known predisposition for bleeding, or coadministration of CYP3A4 or CYP2C19 inhibitors, such as cimetidine, diltiazem, erythromycin, ketoconazole, lansoprazole, omeprazole and HIV-1 protease inhibitors.

Exercise rehabilitation programs have been demonstrated to increase walking distance in persons with intermittent claudication through improvements in peripheral circulation, walking economy and cardiopulmonary function [20]. The optimal exercise program for improving claudication pain distance in persons with PAD uses intermittent walking to near-maximal pain during a program of at least 6 months [21]. The ACC/AHA guidelines recommend a supervised exercise program for patients with intermittent claudication [1].

The indications for lower extremity percutaneous transluminal angioplasty or bypass surgery are 1) incapacitating claudication in persons interfering with work or lifestyle; 2) limb salvage in persons with limb-threatening ischemia, as manifested by rest pain, nonhealing ulcers, and/or infection or gangrene; and 3) vasculogenic impotence [22].

Nonrandomized studies have demonstrated that both immediate and long-term survival is higher in patients having revascularization, rather than amputation for limb-threatening ischemia [23]. However, amputation of lower extremities should be performed if tissue loss has progressed beyond the point of salvage, if surgery is too risky, if life expectancy is very low, or if functional limitations diminish the benefit of limb salvage [24].

References


