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Editorial

Therapy of Peripheral Arterial Disease

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PAD is chronic arterial occlusive disease of the lower extremities caused by atherosclerosis. Significant independent risk factors for PAD in 467 men, mean age 80 years, and in 1,444 women, mean age 81 years, living in the community and seen in an academic geriatrics paractice were age (odds ratio = 1.05 for each 1-year increase in age in men and 1.03 for each 1-year increase in age in women); current cigarette smoking (odds ratio = 2.6 for men and 4.6 for women); systolic or diastolic hypertension (odds ratio = 2.2 for men and 2.8 for women); diabetes mellitus (odds ratio = 6.1 for men and 3.6 for women); serum high-density lipoprotein cholesterol (odds ratio = 0.95 for each 1 mg/dl increase in men and 0.97 for each 1 mg/dl increase in women); and serum low-density lipoprotein (LDL) cholesterol (odds ratio = 1.02 for each 1 mg/dl increase in men and in women) [1]. PAD coexists with other atherosclerotic disorders [2,3]. Patients with PAD are at increased risk for all-cause mortality, cardiovascular mortality, and cardiovascular events [4-6].

Smoking cessation programs should be strongly encouraged at each visit in patients with PAD [7]. Hypertension should be treated to reduce cardiovascular mortality and morbidity in patients with PAD with the blood pressure lowered to less than 140/90 mm Hg [7,8]. The hemoglobin A1c level should be lowered to less than 7.0% [7]. 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 [7,9-11] and to increase exercise time in patients with intermittent claudication [12-14].

The antiplatelet drugs aspirin or clopidogrel should be given to patients with PAD to lower the incidence of cardiovascular death, myocardial infarction and stroke [7,15]. 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 reduction with the use of clopidogrel [16].

Tthe Heart Outcomes Prevention Evaluation (HOPE) Study found that ramipril 10 mg daily lowered cardiovascular events in patients with symptomatic PAD and in patients with asymptomatic PAD [17]. The American College of Cardiology (ACC)/American Heart Association (AHA) guidelines recommend treating patients with PAD with angiotensin-converting enzyme inhibitors unless there are contraindications to these drugs to lower cardiovascular mortality and morbidity [7] Beta blockers should also be used to treat coronary artery disease in patients with PAD unless there are contraindications to these drugs to lower cardiovascular events and mortality [7,18].

Two drugs, pentoxifylline and cilostazol, have been approved by the United States Food and Drug Administration for symptomatic treatment of intermittent claudication. However, studies have found no consistent improvement with pentoxifylline in patients with intermittent claudication in comparison with placebo [19]. Cilostazol has been found in numerous studies 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 [20]. Cilostazol should be given to patients with PAD and intermittent claudication to increase walking distance but should not be given to patients who also have heart failure. Other contraindications to 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 found to increase walking distance in patients with intermittent claudication through improvements in peripheral circulation, walking economy, and cardiopulmonary function [21]. The optimal exercise program for improving claudication pain distance in patients with PAD uses intermittent walking to near-maximal pain during a program of at least 6 months [22]. The ACC/AHA guidelines recommend a supervised exercise program for patients who have intermittent claudication [7].

Iindications for lower extremity percutaneous transluminal angioplasty or bypass surgery are 1) incapacitating claudication in patients interfering with work or lifestyle; 2) limb salvage in patients with limb-threatening ischemia as manifested by rest pain, nonhealing ulcers, and/or infection or gangrene; and 3) vasculogenic impotence [23].

Nonrandomized studies have found that both immediate and long-term survival are higher in patients having revascularization rather than amputation for limb-threatening ischemia [24]. 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 reduce the benefit of limb salvage [25].

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