THE EFFECTIVE PHYSICIAN

Management of Peripheral Arterial Disease

BY WILLIAM E. GOLDEN, M.D., AND ROBERT H. HOPKINS, M.D.

Background

Diseases of arteries outside the coronary circulation contribute to significant morbidity and mortality in adults. The American College of Cardiology/American Heart Association recently released guidelines for the management of peripheral arterial disease (PAD) in the lower extremities, abdominal aorta, renovascular system, and mesenteric vascular beds. This review will focus on lower-extremity PAD.

Conclusions

The principal cause of lower extremity PAD is atherosclerosis. Risk factors, some of which are modifiable, include smoking, diabetes, hyperlipidemia, hypertension, and hyperhomocysteinemia. Patients with PAD are at high risk for future cardiovascular events.

The ankle-brachial index (ABI) is used in the assessment of PAD and is calculated by dividing the systolic pressure at the ankle by the systolic pressure in the brachial artery. The ABI is measured with a sphygmomanometer with an appropriately sized cuff and hand-held Doppler device. Normal values are 0.91-1.30.

Critical limb ischemia (CLI) is defined by the presence of ischemic rest pain, gangrene, or ischemic ulcers. Patients with these findings are likely to require amputation within 6 months if the disease is left untreated. But claudication does not usually progress to limb-threatening ischemia.

Implementation

Patients aged 50 years and older with atherosclerosis risk factors and all persons over 70 years should be assessed for history of walking impairment, claudication, nonhealing lower extremity wounds, and ischemic rest pain. The presence of any of these features suggests the presence of PAD.

The ABI should be measured in all patients suspected of having PAD. The toe-brachial index is a useful test for PAD in patients with noncompressible vessels, which render the ABI uninterpretable.

Exercise ABI is indicated in patients at risk of developing PAD who have a normal resting ABI; it can also provide objective evidence of the degree of functional limitation and response to therapy.

Patients with PAD should receive comprehensive treatment including tobacco cessation, lipid reduction, and hypertension control. The blood pressure goal should be less than 130/80 with diabetes or renal disease and less than 140/90 in other patients. In diabetics, PAD treatment should also include good glycemic control.

Aspirin (75-325 mg daily) or clopidogrel (75 mg daily) is indicated for antiplatelet therapy in patients with PAD. The available data do not support either aspirin/clopidogrel combination therapy or warfarin treatment to reduce the risk of future cardiovascular events.

Supervised exercise training is of benefit in many individuals with lower extremity PAD and is recommended as an initial treatment in patients with intermittent claudication.

Cilostazol (100 mg b.i.d.) is effective in many patients with claudication due to lower extremity PAD, and a therapeutic trial is indicated in such patients who do not have concomitant heart failure. Pentoxifylline (400 mg t.i.d.) may be tried as an alternative to cilostazol, but its clinical effectiveness is less well established.

None of the following medications/interventions have demonstrated efficacy in the treatment of vascular claudication: L-arginine, propionyl-L-carnitine, ginkgo biloba, oral vasodilator prostaglandins, vitamin E, and EDTA chelation. Some of these treatments may have harmful effects.

Duplex and continuous-wave ultrasonography, CT angiography, and MR angiography (with gadolinium contrast) all have utility in localizing vascular lesions in patients with PAD who are being evaluated for interventional management. Digital subtraction angiography is recommended for the evaluation of patients whose treatment plan includes revascularization.

Endovascular or surgical interventions are indicated for patients who have disability due to claudication, have failed to respond to medical interventions, have reasonable procedural risk, and are likely to benefit from the procedure. However, prophylactic endovascular or surgical intervention is not indicated in patients with asymptomatic lower extremity PAD. Patients who have undergone vascular interventions require regular surveillance for at least 2 years following the procedure.

Patients who have claudication symptoms before age 50 appear to have more aggressive atherosclerosis and have a worse prognosis for long-term response to vascular surgery; as such, surgery should be avoided in these patients if possible.

Patients with critical limb ischemia require urgent vascular evaluation to determine if the limb is salvageable, or whether amputation must be considered. Systemic antibiotics are indicated in patients with CLI and gangrene or skin ulceration, and intravenous prostaglandin E-1 for 7-28 days can reduce ischemic pain and facilitate ulcer healing in a subset of patients with CLI.

Catheter-based thrombolysis is effective and beneficial in patients with acute CLI (of less than 14 days), and mechanical thrombectomy can be a useful adjunct.

Reference

Hirsch, et al. ACC/AHA Guidelines for the Management of Patients with Peripheral Arterial Disease (Lower Extremity, Renal, Mesenteric and Abdominal Aortic): A Collaborative Report. American College of Cardiology Web Site: www.acc.org/clinical/guidelines/pad/index.pdf.

DR. GOLDEN (right) is professor of medicine and public health and DR. HOPKINS is associate director of the medicine/pediatrics residency program, University of Arkansas, Little Rock.

Fibrinogen and Coronary Disease Tied to PVD Risk

BY MARK S. LESNEY
Senior Editor

Coronary artery disease and elevated serum fibrinogen were stronger predictors of peripheral vascular disease in subjects younger than 60 years than in older subjects, according to a study based on data from the National Health and Nutrition Examination Survey 1999-2002.

Chronic renal insufficiency was more highly predictive of peripheral vascular disease (PVD) in subjects aged 60 years and over, according to Dr. Louis M. Messina and colleagues at the University of California, San Francisco. Their analysis was presented at the annual meeting of the Western Vascular Society, Deer Valley, Utah.

The researchers used the NHANES data to determine the prevalence of premature PVD in the U.S. population, and used presumptive risk factors as covariates to model the occurrence of PVD.

Premature PVD—occurring in patients under age 60 years—is associated with an extremely poor prognosis, including high rates of cardiovascular morbidity, limb loss, and premature death. Previous studies have been small, have dealt with a limited number of risk factors, and focused on coronary vascular disease as the outcome of interest, according to the researchers.

Based on the hypothesis that there was an interaction between risk factors and age, the investigators analyzed the data to compare the population aged less than 60 years (mean age approximately 49) with those 60 years and older (mean age approximately 70).

NHANES began to provide data in 1999 from detailed lower extremity examinations, including measurement of the ankle-brachial index (ABI). An ABI of less than 0.9 was considered indicative of lower peripheral vascular disease, according to the researchers, and was correlated with the other variables collected in the sampled population. Previous research has shown that a low ABI is one of the strongest predictors of cardiovascular morbidity and all-cause mortality.

The investigators compared data from 2,498 patients under age 60 with those from 2,585 patients aged 60 years and older. Peripheral vascular disease rates were approximately 2% in the younger group and 12% in the older group, a highly significant difference.

A history of coronary artery disease appeared to be highly predictive of PVD in persons who were under age 60 (premature PVD). The odds ratio was 2.9 for this younger group, compared with about 1.3 for the older population.

"It is not surprising that atherosclerotic disease in the peripheral vascular bed is found concomitantly with disease in the coronary vascular bed," the researchers wrote. "However, the strength of the interaction between younger and older patients deserves emphasis. PVD in the younger age group is much more strongly associated with other cardiovascular conditions than in the older population."

In an analysis of the other possible risk factors, they found that a 10-mg/dL increase in fibrinogen was associated with a 7% increase in odds in subjects under age 60, compared with a 3% increase in patients 60 years and older.

Although the authors did not believe this result was sufficient to indicate wide-scale screening of high fibrinogen levels to detect PVD, they did suggest that it may have clinical relevance for secondary intervention, since fibrates and niacin can lower fibrinogen levels.

In contrast, a decreased creatinine clearance was significantly associated with PVD in individuals aged 60 and older, with a 10-unit decrease in clearance affording a 16% increase in the odds ratio for PVD. There was no significant correlation in the younger age group, according to the researchers.

Strong risk factors that are independently associated with PVD regardless of age category include smoking and hypertension. Meta-analysis of plasma homocysteine levels showed only a weak association with the development of PVD.

Although there was no difference found in risk associated with gender between the age groups, being male was a significant overall predictor (odds ratio slightly greater than 2.0).

"This study is the first paper to address the question as to what risk factors for atherosclerosis might distinguish premature-onset atherosclerosis from that seen in the 60- and 70-year age groups," Dr. Messina said in an interview.

"That premature peripheral vascular disease is associated with elevated fibrinogen suggests what many had suspected but not proven, that premature PVD is associated with a 'hypercoagulable state.' The other important risk factor was the presence of coronary artery disease. That coronary artery disease correlated more closely with premature peripheral vascular disease in those less than 60 years of age is equally surprising," he added. ■

NHANES information and its data sets are at www.cdc.gov/nchs/nhanes.htm.

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