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Peripheral Arterial Disease in the Catheterization Laboratory: An Underdetected and Undertreated Risk Factor

Patients undergoing percutaneous coronary revascularization present an opportunity for physicians to focus on risk factor identification and treatment. Although strides have been made in the treatment of some risk factors such as hyperlipidemia, surprisingly, peripheral arterial disease (PAD) continues to be ignored as a risk factor in cardiology. It is embarrassing to think that patients may undergo canalization of their femoral arteries and angiography of their coronary arteries with no real thought given to the ascertainment of arterial disease in noncoronary segments. In the current issue of the *Mayo Clinic Proceedings*, Singh et al[1] call attention to the prevalence of manifest PAD in the percutaneous coronary intervention (PCI) population—18%—a number worthy of our notice. Furthermore, the in-hospital and long-term outcomes of patients with PAD are substantially worse than the outcomes of patients without PAD. This study, which included 1397 patients with PAD, is one of the largest of its kind.

Identification of PAD serves several useful purposes. Singh et al show that PAD identifies a patient population at particular risk of ischemic complications in both the short term and long term. In-hospital mortality rates were 3 times higher in patients with PAD compared with those without PAD—an important observation by Singh et al. Rates of in-hospital myocardial infarction, stroke, and transient ischemic attack were also higher, whereas rates of procedural success were lower. Other studies in contemporary PCI literature have corroborated this elevated risk for patients with PAD.[2,3]

Despite the fact that PAD poses a specific hazard to patients undergoing PCI, it is encouraging that Singh et al found that results of PCI have improved in recent years. This is due in large part to routine coronary stenting and superior generations of stents that are easier to deploy. Advances in pharmacotherapy such as intravenous glycoprotein IIb/IIIa inhibition and clopidogrel also have contributed to this improvement. Ongoing advances such as the incorporation of drug-eluting stents into routine practice will likely further improve the results obtained with PCI in patients with PAD, although this is unlikely to eliminate the gap between patients with and without PAD on end points such as death.

The rates of stroke as a complication of PCI were extremely low in this study; however, it is notable that the rate of stroke was twice as high in patients with PAD (0.6%), emphasizing again the need for special care during catheterization of patients with PAD. Use of smaller-diameter catheters and exchange length wires for all catheter exchanges may help minimize the embolic potential in patients with PAD. Also, patients with PAD who undergo PCI have a higher risk of bleeding complications. Singh et al report a risk of bleeding that is essentially doubled with PAD, with a transfusion rate of 11% vs 5.8%. Vascular access may be more complicated due to the presence of atherosclerosis and calcification in the artery being punctured. Potentially, improvements in adjunctive pharmacotherapy such as use of the direct thrombin inhibitor bivalirudin instead of heparin could minimize this bleeding hazard in patients with PAD.[4] More effective methods to provide hemostasis after arterial sheath removal also are being explored.

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Singh et al are to be commended for the comprehensive definition of PAD used in their study, which includes disease of the cranial and extracranial arteries, abdominal aortic aneurysm, and lower extremity arterial disease. It is appropriate that cerebrovascular disease be included in this definition. Indeed, the patient with involvement of 1 arterial bed has a high likelihood of either symptomatic or asymptomatic involvement of another arterial bed, and this global approach to atherothrombosis is the direction in which the field is heading.[5,6]

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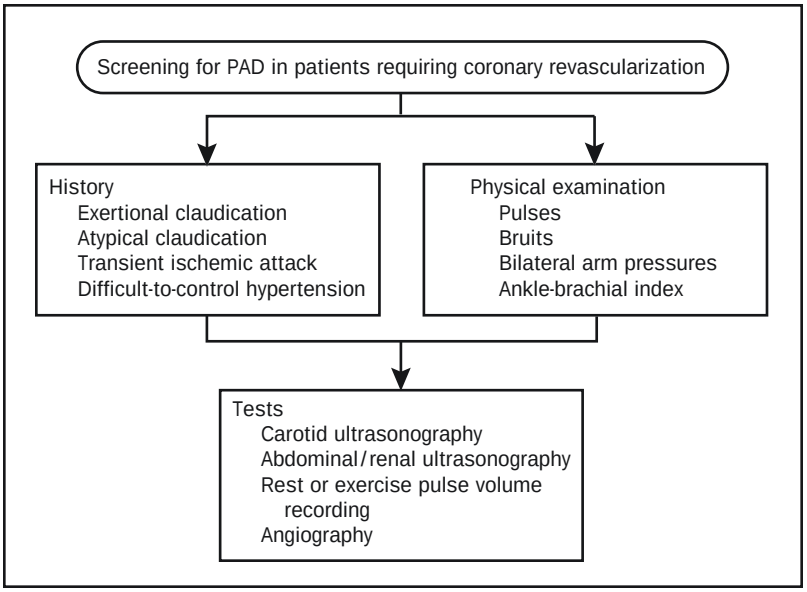

FIGURE 1. Algorithm for identifying peripheral arterial disease (PAD) in patients with coronary artery disease serious enough to warrant percutaneous (or surgical) revascularization. A history and physical examination geared toward identifying PAD should be performed. On the basis of this information and the level of overall patient risk factors, various noninvasive screening tests and, when appropriate, angiographic assessment should be considered.

Several simple measures could be instituted to detect PAD in patients requiring catheterization (Figure 1). Blood pressure levels should be measured in both arms to screen for subclavian artery stenosis, a particular concern in patients who have or may later receive internal mammary artery bypass grafts. All pulses should be examined carefully, including listening for carotid, subclavian, and femoral artery bruits. Ankle-brachial index (ABI) measurements also would be useful to screen for PAD.[7] Indeed, since blood pressure levels and pedal pulses are recorded routinely anyway, incorporation of ABI measurements would seem to be a natural step in the catheterization laboratory assessment as an extension of the physical examination.[8] Of course, a normal resting ABI would not rule out PAD; an exercise ABI should be obtained if claudication is clinically suspected. However, for PAD screening, a resting ABI would be a good start. In patients with hypertension and/or renal insufficiency, renal artery stenosis (RAS) should be considered a possible contributory factor, with perhaps noninvasive or invasive screening. In a catheterization laboratory setting, angiography may be an expedient screen for RAS. As suggested by prior work from the Mayo Clinic, RAS is highly prevalent among patients undergoing coronary angiography, particularly in those with hypertension, and screening abdominal angiography should be considered.[9] Other groups have confirmed these observations regarding the prevalence of previously undiagnosed RAS in the catheterization laboratory, with a potential benefit of percutaneous revascularization.[10-12]

Patients with PAD should be targeted for more aggressive medical therapy. As observed by Singh et al, patients with PAD were much more likely to have diabetes mellitus, hypertension, hypercholesterolemia, and renal dysfunction and to use tobacco. This multiplicity of risk factors likely contributes to some portion of the excess risk of patients with PAD. Of course, lifestyle modification, including tobacco cessation, an improved diet, and regular exercise with incorporation of a walking program, is critical. Antiplatelet therapy is particularly important for patients with PAD.[13,14] Likewise, statin therapy is of proven benefit in reducing cardiac events and may even have a role in improving claudication.[15-19] Angiotensin-converting enzyme inhibition is of great benefit, both in symptomatic and asymptomatic PAD.[20] In the future, therapy to increase high-density lipoprotein levels likely will play a prominent role in PAD. Although the argument could be made that all these forms of medical therapy would be indicated on the basis of coronary artery disease, the presence of concomitant PAD should lead to intensification of the medical regimen. Paradoxically, patients with PAD appear to receive less aggressive medical therapy; apparently, both patients and physicians underestimate the importance of PAD.[21-26]

Identification of PAD, beyond its role as a risk factor for cardiac disease, gives physicians an opportunity to deter-

mine whether a patient has claudication. Symptoms of claudication are not always typical.[27] Just as angina can be atypical or "silent," so too can PAD. Often, a functional impairment is present with PAD, even if classic claudication is not. When claudication seems to limit a patient's ability to walk (and exercise), percutaneous revascularization should be considered. Contemporary data show excellent outcomes with lower extremity angioplasty and stenting.[28] Outcomes will likely be better as peripheral interventional technology, such as drug-eluting stents for PAD, improves.[29]

Physicians in general and cardiologists in particular need to pay more attention to PAD. The catheterization laboratory often presents an opportunity to consider carotid stenosis, subclavian artery disease, RAS, iliofemoral disease, and abdominal aortic aneurysm as potential diagnoses and offers the option of immediate angiographic assessment. The article by Singh et al ought to serve as yet another call to action for more aggressive identification and treatment of PAD, especially in patients with established coronary artery disease.[30]

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1. Singh M, Lennon RJ, Darbar D, Gersh BJ, Holmes DR Jr, Rihal CS. Effect of peripheral arterial disease in patients undergoing percutaneous coronary intervention with intracoronary stents. *Mayo Clin Proc.* 2004;79:1113-1118.

2. Chiu JH, Topol EJ, Whitlow PL, et al. Peripheral vascular disease and one-year mortality following percutaneous coronary revascularization. *Am J Cardiol*. 2003;92:582-583.

3. Nikolsky E, Mehran R, Mintz GS, et al. Impact of symptomatic peripheral arterial disease on 1-year mortality in patients undergoing percutaneous coronary interventions. *J Endovasc Ther*. 2004;11:60-70.

4. Bhatt DL. Heparin in peripheral vascular intervention—time for a change? *J Invasive Cardiol*. 2003;15:249-250.

5. Chan AW. Expanding roles of the cardiovascular specialists in panvascular disease prevention and treatment. *Can J Cardiol*. 2004;20:535-544.

6. Jaff MR. Clinical evaluation and options for infrainguinal atherosclerosis therapy: when to intervene? *J Interv Cardiol*. 2001;14:529-532.

7. Resnick HE, Lindsay RS, McDermott MM, et al. Relationship of high and low ankle brachial index to all-cause and cardiovascular disease mortality: the Strong Heart Study. *Circulation*. 2004;109:733-739.

8. Dieter RS, Tomasson J, Gudjonsson T, et al. Lower extremity peripheral arterial disease in hospitalized patients with coronary artery disease. *Vasc Med*. 2003;8:233-236.

9. Rihal CS, Textor SC, Breen JF, et al. Incidental renal artery stenosis among a prospective cohort of hypertensive patients undergoing coronary angiography. *Mayo Clin Proc*. 2002;77:309-316.

10. White CJ. Screening renal artery angiography at the time of cardiac catheterization [editorial]. *Catheter Cardiovasc Interv*. 2003;60:295-296.

11. Khosla S, Kunjummen B, Manda R, et al. Prevalence of renal artery stenosis requiring revascularization in patients initially referred for coronary angiography. *Catheter Cardiovasc Interv*. 2003;58:400-403.

12. Bhatt DL. Embolization—a pathological mechanism in renal artery stenosis. *J Invasive Cardiol*. 2004;16:196-197.

13. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients [published correction appears in *BMJ*. 2002;324:141]. *BMJ*. 2002;324:71-86.

14. CAPRIE Steering Committee. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). *Lancet*. 1996;348:1329-1339.

15. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet*. 2002;360:7-22.

16. Mohler ER III, Hiatt WR, Creager MA. Cholesterol reduction with atorvastatin improves walking distance in patients with peripheral arterial disease. *Circulation*. 2003;108:1481-1486.

17. McDermott MM, Guralnik JM, Greenland P, et al. Statin use and leg functioning in patients with and without lower-extremity peripheral arterial disease. *Circulation*. 2003;107:757-761.

18. Aronow WS, Nayak D, Woodworth S, Ahn C. Effect of simvastatin versus placebo on treadmill exercise time until the onset of intermittent claudication in older patients with peripheral arterial disease at six months and at one year after treatment. *Am J Cardiol*. 2003;92:711-712.

19. Mondillo S, Ballo P, Barbati R, et al. Effects of simvastatin on walking performance and symptoms of intermittent claudication in hypercholesterolemic patients with peripheral vascular disease. *Am J Med*. 2003;114:359-364.

20. Ostergren J, Sleight P, Dagenais G, et al, HOPE Study Investigators. Impact of ramipril in patients with evidence of clinical or subclinical peripheral arterial disease. *Eur Heart J*. 2004;25:17-24.

21. McDermott MM, Mandapat AL, Moates A, et al. Knowledge and attitudes regarding cardiovascular disease risk and prevention in patients with coronary or peripheral arterial disease. *Arch Intern Med*. 2003;163:2157-2162.

22. Cotter G, Cannon CP, McCabe CH, et al, OPUS-TIMI 16 Investigators. Prior peripheral arterial disease and cerebrovascular disease are independent predictors of adverse outcome in patients with acute coronary syndromes: are we doing enough? results from the Orbofiban in Patients with Unstable Coronary Syndromes-Thrombolysis In Myocardial Infarction (OPUS-TIMI) 16 study. *Am Heart J*. 2003;145:622-627.

23. McDermott MM, Hahn EA, Greenland P, et al. Atherosclerotic risk factor reduction in peripheral arterial diseasea: results of a national physician survey. *J Gen Intern Med*. 2002;17:895-904.

24. Hirsch AT, Gotto AM Jr. Undertreatment of dyslipidemia in peripheral arterial disease and other high-risk populations: an opportunity for cardiovascular disease reduction. *Vasc Med*. 2002;7:323-331.

25. Mukherjee D, Lingam P, Chetcuti S, et al. Missed opportunities to treat atherosclerosis in patients undergoing peripheral vascular interventions: insights from the University of Michigan Peripheral Vascular Disease Quality Improvement Initiative (PVD-QI2). *Circulation*. 2002;106:1909-1912.

26. Hirsch AT, Criqui MH, Treat-Jacobson D, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA*. 2001;286:1317-1324.

27. McDermott MM, Greenland P, Liu K, et al. Leg symptoms in peripheral arterial disease: associated clinical characteristics and functional impairment. *JAMA*. 2001;286:1599-1606.

28. Cho L, Roffi M, Mukherjee D, Bhatt DL, Bajzer C, Yadav JS. Superficial femoral artery occlusion: nitinol stents achieve better flow and reduce the need for medications than balloon angioplasty alone. *J Invasive Cardiol*. 2003;15:198-200.

29. Duda SH, Pusich B, Richter G, et al. Sirolimus-eluting stents for the treatment of obstructive superficial femoral artery disease: six-month results. *Circulation*. 2002;106:1505-1509.

30. Belch JJ, Topol EJ, Agnelli G, et al, Prevention of Atherothrombotic Disease Network. Critical issues in peripheral arterial disease detection and management: a call to action. *Arch Intern Med*. 2003;163:884-892.