



Trends-in-Medicine

December 2005

by Lynne Peterson

Quick Pulse

Trends-in-Medicine has no financial connections with any pharmaceutical or medical device company. The information and opinions expressed have been compiled or arrived at from sources believed to be reliable and in good faith, but no liability is assumed for information contained in this newsletter. Copyright © 2005. This document may not be reproduced without written permission of the publisher.

Trends-in-Medicine

Stephen Snyder, Publisher
2731 N.E. Pinecrest Lakes Blvd.
Jensen Beach, FL 34957
772-334-7409 Fax 772-334-0856
www.trends-in-medicine.com

NEW GUIDELINES ISSUED FOR PERIPHERAL ARTERIAL DISEASE (PAD)

The American College of Cardiology (ACC) and the American Heart Association (AHA) recently announced new national guidelines designed to standardize the management, detection, and treatment of PAD. The guidelines were developed not just for specialists who perform the complex procedures used in the treatment of PAD, but also for primary care physicians, nurse practitioners, and physician assistants, all of whom make the initial diagnosis and initiate therapy. Carotid disease was not addressed because separate guidelines are being developed for that.

More than 12 million people in the United States are affected by PAD, a disease of the arteries that supply blood to the legs, feet, kidneys, and intestines. PAD occurs equally in men and women and affects nearly every American family in some way. It is usually caused by atherosclerosis and can occur silently without obvious symptoms for many years. PAD can lead to amputation of the extremities, as well as heart attacks, strokes, and impairment of kidney function.

Yet, experts believe diagnosis and treatment has been “suboptimal.” Guidelines chair Dr. Alan Hirsch of the University of Minnesota said, “Severe PAD is an overlooked medical emergency in the U.S.”

The new PAD guidelines strongly emphasize the fact that early detection and treatment of peripheral arterial disease can prevent disability and save lives. They urge doctors to perform – and patients to request – additional testing for PAD, including ultrasound, ankle brachial index tests, and manual palpation of the leg artery and abdomen, but the intent, experts insisted is not to change physician behavior as much as it is to standardize it. Dr. Hirsch said, “Doctors should routinely ask patients if they have symptoms and not wait for patients to volunteer... (Doctors should) ask specific questions to define high-risk groups, and initiate early therapy to maintain functional independence and decrease the risk of heart attack, stroke, and death.” Guidelines co-chair Dr. Norman Hertzner of the Cleveland Clinic said, “All physicians who treat these conditions need to be aware of the latest information on diagnosis and management. These guidelines present that information in an objective and dispassionate fashion... I hope these guidelines will lead to earlier identification of PAD and arterial aneurysms, before there is limb loss and other potentially avoidable complications occur.”

While the guidelines urge early diagnosis, they are not recommending treatment of asymptomatic patients. An interventional radiologist who helped write the guidelines said, “Asymptomatic patients are, to some extent, a time bomb for the future

...In treating specific blockages when a patient is asymptomatic, the guidelines state that there is no evidence that treating patients with lower extremity atherosclerotic disease is documented as being helpful. The justification for screening early is to adjust the risk factors and not necessarily to do an intervention. Dr. Hertz said, "We recommend avoiding certain practices that may be detrimental, such as lower extremity bypass grafting in asymptomatic patients." Dr. Michael Jaff of Harvard Medical School, who reviewed the guidelines, said, "This doesn't mean everyone will get metal inside an artery...but they will be given anticoagulants, the diabetes will be more aggressively controlled, lipids will be appropriately monitored, and patients will get more aggressive counseling on smoking cessation. I hope that is the message."

Treatment choices are still left to physicians. Dr. Hirsch noted, "There are a variety of effective treatments, including leg angioplasty, placement of stents, and vascular bypass...We believe there is an important concept of therapeutic choice. Each doctor and patient needs to be carefully offered a wide variety of strategies – interventions, medication, and catheter and surgical therapies."

However, atherectomy (e.g., FoxHollow's SilverHawk) was notably absent from this list, while stenting was included. Asked about the omission, Dr. Christopher White, editor-in-chief of *Catheterization and Cardiovascular Interventions*, said, "The data on atherectomy specifically have not been adequately tested in terms of efficacy. The safety of it has been demonstrated for >10 years, and it does appear to be reasonably safe. The real question that remains is the relative efficacy compared to other treatments available. The problem comes when you look at the cost of the devices. The guidelines did not specify the preference of one device over another, and I don't think we should...because the data are evolving. At the present time, atherectomy is not a preferred therapy."

Dr. Jaff agrees with the decision to leave atherectomy out. He said "The guidelines live by the letter of evidence-based medicine. There hasn't been, to my knowledge, a good head-to-head trial of an atherectomy device to either plain balloon angiography or stenting in lower extremity arteries...So, the (guidelines) authors made the decision because there was a lack of published data...With stenting, at least there is some prospective, independently-adjudicated data in lower extremity arteries, though the data are woefully inadequate compared to the coronary data, but at least there is something."

- **What does the lack of any recommendation about peripheral atherectomy mean for the clinical outlook?** Dr. Jaff said, "The safest thing is to choose to enroll patients in a clinical trial...so at least answers to questions can be generated. Other than that...doctors have to choose what they think is safest and most effective."
- **Is this the end of atherectomy?** Dr. Jaff said, "Absolutely not. There appear to be zealots in the atherectomy arena, and as long as they feel safe and are having

clinically beneficial results on their side, they will continue to use it, but I certainly hope we will start to see studies."

- **Will reimbursement for atherectomy be affected?** Dr. Jaff said, "Unless CMS now says it will only reimburse for devices used on-label or in a trial – and that has not been the approach in arteries – then probably they will continue to pay."

The guidelines were a collaborative effort of ACC, AHA, the Society for Vascular Medicine and Biology (SVMB), the Society of Interventional Radiology (SIR), the Society for Vascular Surgery (SVS), and the Society for Cardiovascular Angiography and Interventions (SCAI). They are likely to bring more patients in for treatment, especially since a national PAD public education campaign is planned. In addition, ACC and AHA are preparing easy-to-follow reference cards for residents and trainees.

A Johnson & Johnson official praised the guidelines, saying, "The guidelines underscore that there is a growing patient population that suffers from peripheral artery disease and an emergent demand for a wide range of technologies to treat the condition. Such a comprehensive, multidisciplinary look at this common condition is crucial to helping ensure the best possible treatment of the disease."

With respect to specific areas:

Critical limb ischemia. Dr. Ziv Haskal of New York-Presbyterian Hospital/Columbia University Medical Center who also served on the guidelines committee estimated that critical limb ischemia diagnosis is often delayed as long as four months, "That is time lost in the prevention of amputation. There are estimates that 70%-80% of American amputations may be related to critical limb ischemia, and 50%-60% of these may be preventable by early interventions – which means focusing physician attention on diagnosis, recognizing that the tools for diagnosis are non-invasive, well-established, and robust, and they should be used far more widely...followed by a rapid referral to specific vascular specialists."

Abdominal aortic aneurysms (AAAs). Some prominent people have died from ruptured aortic aneurysms, including Albert Einstein and George C. Scott. Sen. Robert Dole underwent an elective procedure for AAA. AAAs are particularly prevalent in smokers, and the guidelines make it a Class I recommendation that patients with a family history of AAA not smoke or discontinue smoking. The risk of rupture is directly related to diameter. The estimated rupture rate for a 6 cm AAA is 40%-50%.

The guidelines call for a single ultrasound screening of all men age 65-75 who ever smoked to see if they have an aneurysm. Dr. Enrico Ascher, President of the Society for Vascular Surgery, said, "Many of our patients have aneurysms

that are life threatening that we can not detect on physical exam. That is why there is a bill in Congress to approve a nationwide screening for patients ≥ 65 for this...We all should encourage Congress to approve screening using simple, quick, cheap ultrasound.” Dr. Jaff said, “I published a paper in January 2005 that said anyone over 65 who smoked or had a family history (of AAA) should have ultrasound...U.S. Preventive Services task force guidelines said they don’t agree, and only men age >65 who smoked should have screening, that not even a family history should prompt screening...I wholeheartedly disagree with that.”

For treatment, the new ACC/AHA guidelines discuss both surgery and endografts. Dr. Hertzner explained that there is a lower operative risk for endografts in patients with severe cardiac or pulmonary disease, but the difference in operative risk is less between open surgery and endografts in good-risk patients, “The trade-off for this lower early operative mortality in high-risk patients is that endografts have a higher late complication rate than open repair and require lifelong surveillance with CT to determine the stability of the endograft every six months or so. Survival differences on open vs. endograft equalize at about two years or less. There is no question endografting has undeniable appeal to patients... Late endograft complications may decline with improvements in the technology, and the technology is exploding, maturing at a rapid rate.”

Popliteal aneurysms. Vice President Dick Cheney underwent a procedure for a popliteal aneurysm earlier this year. Dr. Hertzner said, “A simple office palpation of the artery behind the leg can lead to at least a suspicion that can later be confirmed with ultrasound. Half the popliteal aneurysms occur bilaterally, and 40%-50% or more are associated with an abdominal aortic aneurysm of some size. So, the discovery of a popliteal aneurysm should lead to the investigation of the abdominal aorta.”

Popliteal aneurysms are traditionally treated by bypass, but endografts also can be used, and that is what Vice President Cheney had because of his previous cardiac history. Dr. Hertzner said, “Kinking of the grafts behind the knee have been the primary concern with endografts, but the technology is evolving so rapidly that this potential liability may be overcome in the near future.”

Renal stenting. An expert said, “In renal disease, where there is the least depth of solid evidence, we tried to highlight where evidence is lacking to identify areas of research...and to say where we know if something is good or if something is appropriate. These are areas where a lot of physicians are practicing without much awareness of the state of the literature, so we are trying to standardize knowledge and practice.” Dr. Jaff added, “The renal artery disease guidelines were appropriately conservative. Without the results of the CORAL or ASTRAL trials it is very hard to be dogmatic on

renal artery stenting. We certainly don’t have data on large prospect head-to-head trials that prove a patient who is stented will live longer, have fewer cardiovascular events, or have less risk of dialysis dependence. We just don’t have that, and until we do have those results, it will be very hard to tell. Practicing clinicians who are doing a lot of renal artery stenting are already saying, ‘The cat is out of the bag. How can you take a patient with significant hypertension and bilateral stenosis and offer only medication? How can you leave those arteries alone?’ That is the challenge of the CORAL trial, and we are having trouble enrolling patients because many doctors think the answer is already in.”

NOTE: The guidelines will be published in *Circulation: Journal of the American Heart Association* and the *Journal of the American College of Cardiology*. They also can be accessed on the ACC website: www.acc.org

Among the Class I recommendations in the guidelines are:

- Individuals at risk for lower extremity PAD should undergo a vascular review of symptoms to assess walking impairment, claudication, ischemic rest pain, and/or the presence of non-healing wounds. (*Level of Evidence: C*)
- Individuals at risk for lower extremity PAD should undergo comprehensive pulse examination and inspection of the feet. (*Level of Evidence: C*)
- Individuals over 50 years of age should be asked if they have a family history of a first-order relative with an abdominal aortic aneurysm. (*Level of Evidence: C*)
- Individuals with asymptomatic lower extremity PAD should be identified by examination and/or measurement of the ankle brachial index (ABI) so that therapeutic interventions known to diminish their increased risk of myocardial infarction (MI), stroke, and death may be offered. (*Level of Evidence: B*)
- Smoking cessation, lipid lowering, and diabetes and hypertension treatment according to current national treatment guidelines are recommended for individuals with asymptomatic lower extremity PAD. (*Level of Evidence: B*)
- Antiplatelet therapy is indicated for individuals with asymptomatic lower extremity PAD to reduce the risk of adverse cardiovascular ischemic events. (*Level of Evidence: C*)
- Patients with symptoms of intermittent claudication should undergo a vascular physical examination, including measurement of the ABI. (*Level of Evidence: B*)
- In patients with symptoms of intermittent claudication, the ABI should be measured after exercise if the resting index is normal. (*Level of Evidence: B*)

- Individuals with intermittent claudication who are offered the option of endovascular or surgical therapies should (a) be provided information regarding supervised claudication exercise therapy and pharmacotherapy; (b) receive comprehensive risk factor modification and antiplatelet therapy; (c) have a significant disability, either being unable to perform normal work or having serious impairment of other activities important to the patient; and (d) have lower extremity PAD lesion anatomy such that the revascularization procedure would have low risk and a high probability of initial and long-term success. *(Level of Evidence: C)*
- Patients with Critical Limb Ischemia should undergo expedited evaluation and treatment of factors that are known to increase the risk of amputation. *(Level of Evidence: C)*
- The resting ABI should be used to establish the lower extremity PAD diagnosis in patients with suspected lower extremity PAD, defined as individuals with exertional leg symptoms, with non-healing wounds, who are 70 years and older or who are 50 years and older with a history of smoking or diabetes. *(Level of Evidence: C)*
- The ABI should be measured in both legs in all new patients with PAD of any severity to confirm the diagnosis of lower extremity PAD and establish a baseline. *(Level of Evidence: B)*
- The toe brachial index should be used to establish the lower extremity PAD diagnosis in patients in whom lower extremity PAD is clinically suspected but in whom the ABI test is not reliable due to non-compressible vessels (usually patients with long-standing diabetes or advanced age). *(Level of Evidence: B)*
- Duplex ultrasound of the extremities is useful to diagnose anatomic location and degree of stenosis of PAD. *(Level of Evidence: A)*
- Duplex ultrasound is recommended for routine surveillance after femoral-popliteal or femorotibial-pedal bypass with a venous conduit. Minimum surveillance intervals are approximately 3, 6, and 12 months, and then yearly after graft placement. *(Level of Evidence: A)*
- Renal stent placement is indicated for ostial atherosclerotic RAS lesions that meet the clinical criteria for intervention. *(Level of Evidence: B)*
- Balloon angioplasty with bailout stent placement if necessary is recommended for fibromuscular dysplasia lesions. *(Level of Evidence: B)*

