New PAD Guidelines Highlight Endovascular Tx

BY BRUCE JANCIN
Denver Bureau

ROME — New international guidelines on the management of peripheral arterial disease recommend an expanded role for endovascular therapies at the expense of open surgical procedures, Dr. Lars Norgren reported at the annual meeting of the Cardiovascular and Interventional Radiological Society of Europe.

The first report of the TransAtlantic Inter-Society Consensus (TASC-I) on the management of peripheral arterial disease, published in 2000, recommended endovascular therapies as the procedures of choice in patients with morphologically focal type A lesions of the iliac or femoropopliteal arteries, and surgery for their opposite—type D lesions—which are diffuse, extensive, and multilevel.

This is a rapidly changing field, and the best form of interventional therapy remains in flux pending the outcome of trials.

DR. NORGREN

These recommendations remain unchanged in TASC-II, to be published late this year, although the length of stenosis that qualifies lesions as type A has been expanded. The big change in TASC-II involves the morphologically intermediate type B and type C lesions. TASC-I concluded that more evidence was needed before firm treatment recommendations for B and C lesions could be made, whereas TASC-II comes down in favor of endovascular therapy for type B and surgery for type C lesions, said Dr. Norgren, professor of surgery at Lund (Sweden) University.

"The patient's comorbidities, the informed patient's preferences, and local operators' success rates must be considered when making treatment recommendations for type B and C lesions," he added.

Dr. Norgren noted that this is a rapidly changing field, and the best form of interventional therapy for specific lesion types remains in flux pending the outcome of randomized trials. A feature of the TASC-II report that might be more important than the lesion-type treatment recommendations is TASC-II's conscious effort to address the new guidelines to primary care providers and other referring physicians, he said.

TASC-I was influential in the daily practice of vascular specialists, who tended to view the guidelines as an unbiased multidisciplinary expert consensus on how best to manage peripheral arterial disease (PAD). But TASC-I had little effect on patient referral patterns; indeed, the unwieldy 250-plus page report (J. Vasc. Surg. 2000;31:S1-296; Eur. J. Vasc. Endovasc. Surg. 2000; 19[Suppl. A]:S1-244; also available at www.tasc-pad.org) was largely ignored by primary care physicians and cardiologists.

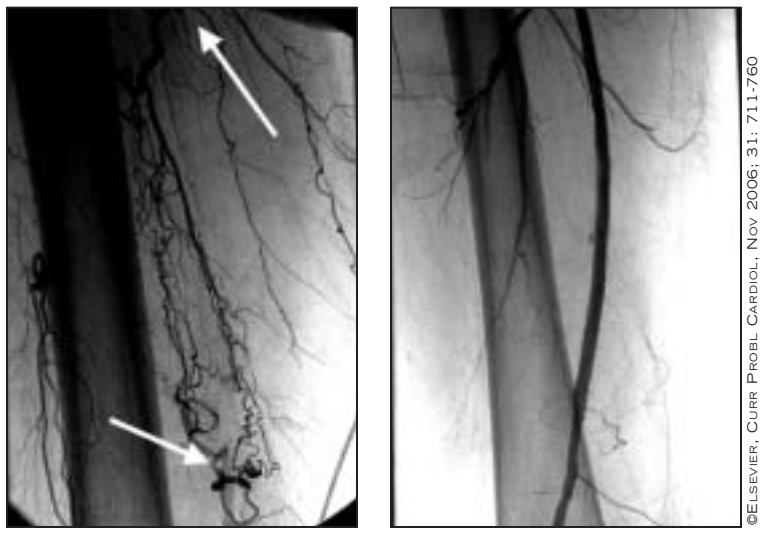
To overcome this shortcoming, TASC-II will be an abbreviated, more reader-friendly document. After its publication, members of the TASC-II working group will speak at meetings of the major primary care medical societies.

"We know that TASC-I had too much text, too much technical detail," Dr. Norgren said. "We've started again with the intention to keep more of the wording out."

In keeping with the new primary care focus, TASC-II emphasizes the high cardiovascular event rate in patients with intermittent claudication (IC), and the primacy of medical management in IC patients, including smoking cessation, diabetes control, hypertension management, and lipid-lowering therapy. The guidelines stress that all patients with symptomatic PAD should be on long-term antiplatelet therapy, with the best-quality evidence supporting aspirin.

A supervised exercise program should always be considered as part of the initial therapy of IC. "There is very little evidence that unsupervised exercise works," Dr. Norgren said.

TASC-II recommends a 3- to 6-month trial of pharmacotherapy with a vasoactive agent—cilostazol (Pletal) is the only one approved in the United States, and naftidrofuryl the sole European drug—as part of the initial therapy for IC. This is a stronger endorsement of pharmacotherapy than that made in TASC-I. In the interim, clinical trials have provided more persuasive evidence of efficacy by excluding patients with critical limb ischemia who, it's now clear, are unlikely to benefit from the drugs.



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Angiograms of a 68-year-old man show a 20-cm occlusion of the right superficial femoral artery (arrows, left) and the results of percutaneous revascularization with a stent (right).

Dr. Norgren's TASC-II presentation received a mixed reception. Some interventional radiologists declared that they already consider endovascular techniques the best procedures for many type C lesions and anticipate the day when type D femoropopliteal lesions will come within their purview as well.

But Dr. Cathal Kelly, a vascular surgeon at Beaumont Hospital, Dublin, said he is concerned that the guidelines rely on data reported from top-flight endovascular centers that achieve better results than those found in routine practice elsewhere.

He added that many endovascular therapists have perhaps too low a threshold for intervening in IC, given that it's largely a benign condition, with only about 5% of conservatively managed patients developing critical limb ischemia during a 5-year period. Dr. Kelly said "surgeons all over the world" are concerned that failed endovascular therapy for more complex lesions compromises the ability to perform successful bypass surgery and increases the risk of amputation. ■

Warfarin Plus Aspirin Flops for Peripheral Arterial Disease

BY BRUCE JANCIN
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BARCELONA — The combination of warfarin plus aspirin provided no benefit over aspirin alone in a major randomized trial involving more than 2,100 patients with peripheral arterial disease, Dr. Sonia Anand reported at the joint congress of the European Society of Cardiology and the World Heart Federation.

Moreover, the combination resulted in a 3.4-fold increase in life-threatening bleeding, compared with standard low-dose aspirin, added Dr. Anand of McMaster University, Hamilton, Ont.

She reported on 2,161 patients with peripheral arterial disease (PAD) at 80 centers in seven countries who participated in the Warfarin Antiplatelet Vascular Evaluation (WAVE) trial. Patients were randomized to low-dose aspirin at 81-325 mg/day or to aspirin plus warfarin with a target international normalized ratio of 1.8-3.5. The mean achieved INR was 2.2.

During 3 years of follow-up, the combined end point of cardiovascular death, MI, stroke, or severe coronary or peripheral arterial ischemia occurred in 15.9% of the combined therapy group and 17.4% on aspirin alone, a nonsignificant difference.

Life-threatening bleeding occurred in 4.0% of patients in the warfarin-aspirin arm and 1.2% with aspirin alone. Hemorrhagic stroke was 15 times more frequent in the combined therapy arm. Moderate bleeding occurred in 2.9% of patients on combination therapy, compared with 1.0% of those on aspirin alone.

The combination resulted in a 3.4-fold increase in life-threatening bleeding, compared with low-dose aspirin.

DR. ANAND

Discussant Dr. Freek W.A. Verheugt observed there is good evidence showing aspirin plus warfarin is superior to aspirin alone for the prevention of death, MI, and stroke in patients recovering from acute coronary syndromes. This was recently underscored in a metaanalysis by cardiologists at Catholic University, Rome, involving 14 randomized trials totaling more than 25,000 patients. The analysis concluded that combination therapy with a target INR of 2-3 conferred a 27% reduction in risk that dwarfed the doubled risk of major bleeding compared with aspirin alone (Eur. Heart J. 2006;27:519-26).

So why didn't aspirin plus warfarin show more benefit in the WAVE trial? Probably because the baseline risk in PAD patients was substantially lower than in the patients in the post-MI studies, meaning the potential for therapeutic benefit was less as well, said Dr. Verheugt, professor and head of cardiology at University Medical Center, Nijmegen, the Netherlands.

The negative WAVE findings leave PAD patients with a dearth of treatment options. Warfarin alone was of no benefit over aspirin in a large Dutch PAD trial. Clopidogrel plus aspirin provided no advantage over aspirin alone in the 15,603-patient Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance (CHARISMA) trial, in which one-third of participants had PAD.

And while clopidogrel alone resulted in a 24% reduction in vascular events compared with aspirin in patients with PAD in the nearly 20,000-patient Clopidogrel Versus Aspirin in Patients at Risk of Ischemic Events (CAPRIE) trial, the number needed to treat for 1 year to prevent one vascular event was 165. Moreover, CAPRIE is an old trial conducted in the prestatin, pre–ACE inhibitor era and is no longer relevant in contemporary practice, the cardiologist continued.

The best hope for patients with PAD, Dr. Verheugt added, probably lies in the improved antithrombotics now in the developmental pipeline. The investigational oral thrombin blockers and oral factor Xa inhibitors, either alone or with aspirin, are worthy of study in the PAD population. Unfortunately, the ongoing large clinical trials of these agents don't involve patients with PAD.

The WAVE trial was sponsored by the Canadian Institutes of Health Research and the Heart and Stroke Foundation of Canada. ■