LETTERS TO THE EDITOR

Regarding "Optimal therapy for advanced chronic venous insufficiency"

The article by Tawes et al (J Vasc Surg 2003;37:545-51) concerning subfascial endoscopic perforating vein surgery (SEPS) raised a number of questions. It is difficult to understand how the authors could conclude that "efficacy, safety, and durability of this operative protocol proved beneficial in our clinical experience with 832 patients during 9 years of follow-up," when mean follow-up was only 3½ years. How many patients completed 9 years of follow-up in this study?

What percentage of clinical improvement was due to SEPS versus saphenous vein stripping, which was performed in more than half of the patients? Concerning duplex scanning to detect venous insufficiency, should this be done with the patient sitting? Why were veins larger than 2.5 mm in diameter arbitrarily judged incompetent? It is not clear why it was stated that "duplex may be omitted by experienced surgeons." I am also concerned about the conclusion that "SEPS had significantly reduced [arteriovenous pressure]," when almost half the patients did not undergo the examination. Finally, have the authors recommended elastic stockings? If so, what role did this have in mean time to ulcer healing?

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doi:10.1016/S0741-5214(03)00479-8

Reply

As cited in our manuscript, controversy has existed for decades about the relative contribution of reflux in the deep, superficial, and perforator venous systems to chronic venous insufficiency (CVI). If it is accepted that major factors in the cause of CVI are pathologic hydrostatic (superficial) and hydrodynamic (perforator) forces, it does not require a quantum leap of faith to direct the operation to correct these sources of reflux and evaluate the outcome over a sufficient period of time. This was the bias and objective of our study.

Noninvasive technology (duplex scanning) is available that enables diagnosis and specifically targets these sources, and minimally invasive, video-assisted endoscopic surgery provides a reliable means for correction of perforator vessel reflux.

Until level I evidence is available, we offer our operative protocol, ie, subfascial endoscopic perforating vein surgery (SEPS) as an effective interim measure. Most ulcers healed in 7 weeks (mean). Almost 9 of 10 patients benefited over time; 416 patients were followed up for more than 3½ years, 60 patients for more than 5 years, and 22 patients for more than 9 years. Our approach was associated with a 3% complication rate (30 days). Inasmuch as most of the poor results (nonhealing or recurrence of CVI) occurred early, we consider SEPS not only efficacious, but also durable. Redo SEPS further improves long-term results (see Results).

With regard to duplex scanning, no cases had fewer than three positive reflux points; therefore "arbitrary" designations did not influence inclusion criteria or outcome (see Methods).

All patients were examined with their legs dependent (sitting or standing). All 832 patients underwent diagnostic duplex scanning. Additional preoperative mapping duplex scanning may be omitted by experienced surgeons with a sound knowledge of perforator topographic and operative anatomy, inasmuch as there was a disparity between perforator vessels mapped (mean, 4) versus those identified at surgery (mean, 7). However, mapping is a useful "targeting" method for the surgeon early in the learning curve.

The subset "Dusseldorf experience" demonstrated a significant decrease in AVP after SEPS, with significant improvement in VRT to normal (see Tables III and IV). This cohort was prospectively randomized, and provided objective statistical data to support our operative protocol. All cohort patients underwent greater saphenous vein ligation and stripping; therefore we did not introduce a variable for analysis (see data).

Elastic stockings are recommended, but their role was not evaluated in this study insofar as compliance and time to ulcer healing and disease recurrence.

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doi:10.1016/S0741-5214(03)00480-4

Regarding "The safety, efficacy, and pharmacoeconomics of low-dose alteplase compared with urokinase for catheter-directed thrombolysis of arterial and venous occlusions"

We read with interest the article by Sugimoto et al (J Vasc Surg 2003;37:512-7) reporting that continuous overnight infusion of low-dose tissue plasminogen activator (t-PA) combined with subtherapeutic dosage of heparin is equally efficacious and safe compared with urokinase for treatment of arterial occlusive disease and deep vein thrombosis. We would like to point out that both of these diseases and the effect of anticoagulant therapy demonstrate significant temporal variation, which should not be overlooked in planning studies and interpreting their results. Like many other acute cardiovascular events, acute arterial occlusion of the limbs[1] and pulmonary embolism[2] exhibit a circadian pattern of occurrence, with higher incidence in the morning. This morning excess appears to be related to increased platelet aggregability and reduced endogenous fibrinolysis during this time. Opposite circadian patterns, characterized by lower levels of tissue-type plasminogen-activator and higher values of t-PA and higher values of t-PA inhibitor-1, with variations up to 250%, have been reported.[3] On the other hand, circadian changes in anticoagulant effect of heparin, even when infused intravenously at a constant rate, have been reported.[4] Activated partial thromboplastin time (aPTT), thrombin time (TT), and coagulation factor Xa inhibition assay achieve maximal values at night, with differences between night and morning values of almost 50% for aPTT, 60% for TT, and 40% for factor Xa inhibition assay. As a consequence, a constant dose could have poor effects in the morning and enhance the risk for bleeding at night. A morning increase in resistance to thrombolysis performed to treat acute myocardial infarction has also been reported with both intracoronary urokinase[5] and intravenous t-PA.[6] In light of these data, it appears that, in comparing the efficacy and safety of various thrombolytic therapies, an imbalance in onset time of the event or time of administration of anticoagulant or fibrinolytic agent could justify possible differences in clinical outcome. Tailoring thrombolytic therapy and adjusting dosages according to

the high-risk time of onset of acute events could lead to better results in providing patency, reduced dosages during low-risk times, and less adverse hemorrhagic effects, and save drugs and money, as well.

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doi:10.1016/S0741-5214(03)00478-6