Surgical treatments are widely used in the management of patients with venous leg ulcers. Surgery is most effective in patients with pure superficial venous incompetence, a group which comprises up to 50% of all patients with venous leg ulcers. Surgical procedures are available for the repair of deep vein incompetence, but the use of these is restricted to younger, fitter patients since they require major surgical interventions. Compression stockings and bandages are highly effective at healing venous ulcers but require skilled use by medical and nursing practitioners as well as good compliance by the patient. Most leg ulcer healing studies show high levels of recurrence following healing achieved by compression. Currently a small number of drugs has been evaluated to assess efficacy in achieving leg ulcer healing. None is as effective as of high levels of compression and only one study has assessed the efficacy of a drug at preventing ulcer recurrence. No available drug will therefore replace the use of compression at present.

Examination of indices of venous function in many patients shows that patients with the more severe stages of venous disease have worse venous function. However, there is huge overlap between the venous function of patients with mild symptoms and those with severe ulceration. This implies considerable variation between patients in their susceptibility to skin damage and leg ulceration. The basis of this variability is far from understood and has its origin in the molecular mechanisms which underlie the development of leg ulceration. Much of my research has shown that a series of systemic inflammatory mechanisms are enabled in patients with venous disease, including those with skin damage. It has not been possible to identify markers which specifically identify patients at high risk of skin damage and ulceration, although some endothelial adhesion molecules are particularly raised in patients with skin changes. Assuming that the crucial factors which make some patients susceptible to the development of leg ulceration can be identified, it may be possible to influence these by receptor blockers or other pharmacological means.

The mechanisms by which compression achieves ulcer healing are not completely understood. There are some effects on the large veins in the leg, but these do not include restoration of valvular competence, however, venous reflux is reduced by high levels of compression. There is probably also an effect on the microcirculation. This appears to comprise acceleration in flow velocity in capillaries in response to low levels of compression. At very high levels of compression (>100 mmHg) capillary flow ceases. The acceleration in flow velocity at therapeutic levels of compression may cause a change in the way in which blood constituents interact with the capillary wall, modifying the inflammatory response. Understanding the biochemical basis of the effect of compression may allow us to identify mechanisms which could be influenced by pharmacological means.

It is highly likely that the factors resulting in susceptibility to leg ulceration will form a crucial part of many important disease processes. The incentive for the pharmaceutical industry to develop drugs which influence this area will be considerable. Using such drugs it may be possible to achieve venous ulcer healing without any modification to the amount of venous reflux in a limb.

DISCUSSION

DR. BERGAN: I enjoyed the presentation exceedingly, and I think the theme that comes out is that venous hypertension, as Philip said, is a triggering mechanism for leukocyte activation and leukocyte endothelial interactions. There’s no question that the intervention with this particular bioflavonoid, which is 90% Diosmin, affects leukocyte activation, and I think that Philip’s thesis of intervening at the stage of edema is probably a very good one. As you have shown, Dr. DePalma, the same patient can have equal hemodynamic venous insufficiency in both lower extremities, only one of which develops chronic venous insufficiency with all of the skin changes. Therefore, there is an additional factor with which venous hypertension is interacting. Pharmacologic intervention will stop that additional factor which is local leukocyte activation.

DR. EKLOF: That was a beautiful start to this session. Philip, you are using the C of the CEAP classification. We’ll listen to the French C later on today. Have you gone further into the classification of these ulcers that you were talking about? How many were post-thrombotic or secondary? How many were depending on primary venous disease?

DR. COLERIDGE SMITH: Yes, we did actually fully evaluate all aspects of the CEAP classification in our work, but for reasons you understand I presented the data in this way. In essence, a substantial proportion of our patients with venous ulceration and deep venous incompetence which accounted for more than half of our patients with the C4, 5, and 6 disease did have post-thrombotic deep vein changes.

DR. O’DONNELL: Philip that was a wonderfully illustrated talk, particularly a good advertisement for power pointers we were talking about in the LAX airport. I’m surprised that Professor Burnand is so quiet over there because, first of all, I quibble with your end points. You’re using ulcer healing, and most people feel I don’t care what you’ll use, you’ll get a relatively good rate of ulcer healing. I think really what we should be focusing on is ulcer recurrence and how we can prevent that. My second comment has to do with the flavonoid study. It reminds me of a comment by Hiram Polk when looking at prophylaxis treatment of wound infections. The incidence of healing in your control group was so low that any measurable improvement in the flavonoid group makes it look good. Would you comment?

DR. COLERIDGE SMITH: In the flavonoid study to which I referred, which is not my work but that of others and published in international scientific literature, the healing rate in the placebo group is low. The study was done by General Practitioners who used low compression. However, it was a randomized controlled study and it addressed ulcer healing. Your point about recurrence is, of course, very important, but ulcer healing is also very important. One needs to follow patients for around six months in order to establish the real complete ulcer healing rate, whereas if you’re following patients to assess their recurrence, then you have to follow


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them for years and probably need five times as many patients. So not surprisingly very few of those studies have actually been done.

DR. MYERS: Phillip, that’s all very interesting, but I guess you would be the first to agree that the results of drug treatment have been pretty lousy to date. If you had to guess, in what direction do you think the future research should go to find the magic drug that’s actually going to influence ulcer healing?

DR. COLERIDGE SMITH: I think that’s actually quite difficult. It depends on basic scientific research to establish the differences to which I was alluding. The differences that make patients susceptible to venous ulceration with the same abnormality of venous function, must depend upon endothelium and leukocytes, the way they interact, the reparative mechanisms, the vascular proliferation mechanisms.

DR. DEPALMA: How about doxycycline and tetracycline, metalloproteinase inhibitors?

DR. COLERIDGE SMITH: Yes, it’s possible.

DR. DEPALMA: They work pretty well, don’t they? I mean, the cytokine release that you’ve shown, these are drugs that work in that area.

DR. COLERIDGE SMITH: Yes. I mean, they address venous or ulcer healing mechanisms, but I’m not sure that they actually influence the rate of venous ulcer healing or ulcer recurrence.

DR. KRYLOV: A very short remark. The device to measure the toxicity of the skin should be nominated, because terminology is important, the elastometer. You measure elasticity of the skin, not the toxicity, and as such, this device called elastometer is very useful in another surgical specialty, in plastic surgery.

MECHANISM OF ACTION OF COMPRESSION THERAPY FOR VENOUS ULCERATION

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Until recently, the primary focus of research in chronic venous insufficiency has been the abnormal hemodynamics in the axial superficial and deep veins as well as the perforating veins. It is important to remember, however, that the target organ in chronic venous insufficiency is the skin and subcutaneous tissues. Abnormal venous hemodynamics somehow result in a myriad of changes in the skin and subcutaneous tissue that if unchecked eventually result in the formation of a venous ulcer. It is clear that over time, abnormal venous hemodynamics in the superficial, deep and perforating veins result in severe morphologic and functional changes in the cutaneous microcirculation. These changes included both destruction of dermal lymphatics as well as alterations in the morphology and probable function of the cutaneous capillary vessels.

The exact mechanism of action by which compressive therapy produces it’s obvious benefit in the treatment of chronic venous insufficiency is unknown. Compressive therapy may produce changes in axial venous hemodynamics and/or changes in cutaneous and subcutaneous physiology that result in improvement in chronic venous insufficiency.

The effect of compressive therapy on deep venous hemodynamics has been the topic of multiple studies. We and other investigators, using both invasive and noninvasive techniques, have been unable to demonstrate significant changes in ambulatory venous pressure or venous recovery times with the use of compressive therapy. Other researchers have described modest trends toward normal in measurements of venous hemodynamics with the use of compression stockings.

Improvements in skin and subcutaneous tissue microcirculatory hemodynamics may contribute to the benefit of compression therapy. Laser Doppler studies demonstrate a dependency induced resting cutaneous hyperemia in patients with chronic venous insufficiency, but not in normals. Using this technique, impairment of the so-called venoarteriolar reflex may improve with the application of 40mm compressive stocking. On the other hand, Xenon washout techniques used to measure dependent skin blood flow are unable to detect changes in chronic venous insufficiency patients compared to controls at rest or with exercise.

Another possible mechanism for the benefits of compression therapy is a direct effect on subcutaneous pressure. By increasing subcutaneous pressures compressive therapy may promote changes in Starling forces that promote reabsorption of the edema. Supine perimalleolar subcutaneous pressures rise with the application of elastic compression in limbs with chronic venous insufficiency. This rise in subcutaneous tissue pressure may act to counter transcapillary Starling forces favoring leaking of fluid out of the capillary. These observations parallel the fact that edema reduction is the rule in patients with chronic venous insufficiency who wear effective compressive therapy. Video microscopic techniques can also demonstrate increased sin capillary density with edema resolution. Cutaneous metabolism may improve following edema reabsorption due to enhanced diffusion of oxygen and other nutrients to the cellular elements of the skin and subcutaneous tissues.

DISCUSSION

DR. PARTSCH: Congratulations to this amount of data which you presented on compression. You have pointed out that you didn’t find any change of deep venous hemodynamics with your kind of compression. This is true for elastic stockings with a pressure of 30 millimeters of mercury as you have measured it. If you take stiff material, apply stiff bandages like Unna boots with a pressure of 50 millimeters of mercury to the distal lower leg, you would get very high peaks of working pressure, and you could show a clear influence on deep veins. You can even prove this by doing phlebography, that the deep veins are narrowed, and in this situation of stiff inelastic bandages, you could be able to show an improvement of venous hypertension. So at least we were able to show this in the study which I can send to you if you’re interested.

References
DR. MONETA: I think Dr. Partsch may be correct. The more pressure you can exert on the leg, the greater the chance you have of influencing what’s going on inside the leg. It’s always seemed to me a little strange that an elastic stocking on the surface of the leg could influence veins deep in the leg. After all, often you can hardly compress them, pushing hard with a duplex scanner.

UNIDENTIFIED SPEAKER: I enjoyed your talk very much and especially the part of the Starling mechanisms you pointed out. Do you have any clinical method to assess the lymphatic part of the equation? Is there any applicable method nowadays to assess the role of lymphatic flow disturbances in these patients?

DR. MONETA: We don’t have one and I don’t know of one. It would be interesting to know if there was. I can postulate that you could probably put a tracer in the skin and then subject the skin to compression and see how that tracer moves in normals versus noncompressed patients. The ability to do that exists. I haven’t tried it though.

DR. ABU-BAKER: Why is the varicose ulcer only found in human beings and not found in the animals?

DR. MONETA: I don’t think that’s the only example of human defects. I don’t know why. I suppose we weren’t designed to move on two feet originally.

DR. ABU-BAKER: Can the varicose ulcer have a genetic origin?

DR. BERGANT: The key feature is venous hypertension. So yes, primary varicose ulcers and postphlebitic skin changes are alike. The genetic factor is a predisposition to valve failure and wall failure.

DR. DEPALMA: Dr. Enrici, do you think there’s a genetic origin? Si or no?

DR. ENRICI: No.

DR. BURNAND: Yes, of course it has a genetic origin because patients who are Factor 5 Leiden deficient develop post-thrombotic ulcers, and that’s a genetic predisposition.

DR. MONETA: I don’t know of any data that venous ulceration is linked to any specific part on the genome. However, looking at various populations, it appears there are some groups more greatly affected than others. For example, it appears venous ulceration is more prevalent in Northern European than in Southern European people.

DR. LORD: The logic was unescapable. The previous studies have shown that you only need compression up to the knee. Now, passing on from that, does one need compression only in the area of the ulceration and immediately around it or should we maintain the compression all the way up to the knee? In other words, you’re showing that the compression has a local effect rather than effect on venous hemodynamics. So do we then logically progress and have smaller devices for local pressure rather than the general pressure all the way to the knee?

DR. MONETA: That sounds good to me. Many of us use various bolsters and other devices to try and add additional pressure at the site of the ulcer.

DR. BERNHARD: Excellent study, Greg. I just was wondering if you had or would correlate this with oxygen tension and does oxygen tension improve with various degrees of compression?

DR. MONETA: We haven’t done that, and as far as I know, the studies that have tried to look at oxygen tension in venous ulceration have been conflicting. Some people have found diminished oxygen levels in the skin and others have not.

CONTROVERSIES IN THE TREATMENT OF VENOUS ULCERS: SEPSING?

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A. Noel, MD, M. Kalra, MD

Subfascial endoscopic perforator vein surgery (SEPS), a minimally invasive operation for interruption of incompetent perforating veins has become increasingly popular and surgeons around the world have gained experience with the technique. SEPS is usually performed with ablation of the superficial reflux to treat patients with active or healed venous ulcers (Classes 6 and 5), although an increasing number of patients without ulcer history (Class 4) have also been treated with this technique. Although evidence on the effectiveness of SEPS has been accumulating, controversies on the usefulness of this operation still exist.

Is SEPS better than medical treatment?

Medical treatment of venous ulceration is time-intensive, requires strict patient compliance and has been associated with a high rate of ulcer recurrence. While claims about the superiority of medical treatment of venous ulcers have been made, the true endpoint, ulcer recurrence averaged 52% at 2 years in 8 studies, that included 488 limbs with Class 5 and Class 6 chronic venous disease (Table 1). Patients managed in an organized ulcer clinic, or inpatient unit do better than patients on minimally supervised home care. Clinical trials of strictly supervised medical management report success in healing of most ulcers over time (92-100%). However, the prolonged disability, prohibitive cost and high rates of ulcer recurrence (33-100%) despite highly skilled care remain a concern. Even in compliant patients, ulcer recurrence averaged 28%. In one small series of 11 patients, at 2 years after treatment, ulcers recurred in all (Table 1). In studies on conservative treatment more than 50% of the patients were noncompliant with compression. Ulcer recurrence rates following medical treatment range from 29 to 41% in compliant patients and from 71 to 100% in noncompliant patients.

These results compare unfavorably with those of SEPS with or without superficial reflux ablation. Individual series with SEPS have reported healing rates of 84-100% (average 90%) and recurrence rates of 0-22% at 2 years, with an average of 10% (Table 2). Mid-term (24 months) results in 146 patients followed up in the NASEPS registry demonstrated that cumulative ulcer healing at one year was 88%, with a median time to healing of 54 days. Cumulative ulcer recurrence at one year was 16% and at two years it was 28% (SE<10%). Post-thrombotic limbs had a higher two-year cumulative recurrence rate (46%) than those with primary valvular incompetence (20%) (p<0.05). Twenty-eight (23%) of the 122 patients who had active or healed ulcers (Class 5 or 6) before surgery, had active ulcer at last follow-up. Although no prospective, randomized comparison of these two modes of treatment exists, these data suggest, that SEPS, with ablation of superficial reflux, if indicated, is superior to medical management alone.

Is SEPS better than open perforator interruption?

Open ligation of incompetent perforating veins was described late
nearly 70 years ago by Linton.9 Ulcer recurrence rates following open perforator ligation range from 7-55%, averaging 22%. Although these are not significantly different from those following SEPS, wound complications following open perforator ligation have been frequent, ranging from 12% to 53%, and averaging 24%, resulting in prolonged hospitalization in most patients.

SEPS has the advantage of interrupting incompetent perforating veins in a bloodless field via small endoscopic ports placed remotely from the site of the ulceration. Lower morbidity and shorter hospital stay were reported with SEPS in a non-controlled trial that compared 37 SEPS procedures to 30 antedated open perforator ligations.10 In addition, the short-term effects on ulcer healing were comparable in the two groups. A single prospective randomized study has investigated the rate of wound complications following open perforator ligation and SEPS.11 Thirty-nine patients were randomized, and wound complications occurred in 53% in the open group versus in 0% in the SEPS group. During a mean follow-up of 21 months no ulcer recurrence was noted in either group of patients. The relative safety of SEPS was also confirmed in the North American (NASEPS) registry, where a 6% wound complication rate was reported, with one deep vein thrombosis at two months after surgery. The incidence of tibial nerve damage and deep vein thrombosis has been reported to be comparable to open surgery. Based on these data SEPS is at least equally effective and has the advantage of decreased morbidity and shorter hospital stay, when compared to open perforator ligation.

**Is SEPS indicated in addition to superficial reflux ablation?**

Superficial incompetence alone is found in about 10% of patients with venous ulcers. This subset of patients does well following saphenous vein ligation and stripping. The controversy arises in patients with concomitant perforator and/or deep vein incompetence. Experience with SEPS supports interruption of incompetent perforating veins and provides new data on the contribution of superficial and perforator vein incompetence in ambulatory venous hypertension indicating improved ulcer healing after elimination of both, superficial and perforator reflux.4,5 Patients with combined deep, perforator and superficial incompetence exhibited accelerated healing and improved venous hemodynamics after ablation of the incompetent superficial and perforator systems without intervention to the deep veins.12

However, clinical benefit attributed directly to interruption of incompetent perforating veins has been difficult to assess, since concomitant ablation of saphenous reflux is frequently performed. Also, ablation of superficial reflux alone has been reported to result in hemodynamic and clinical improvement in the presence of combined deep and superficial insufficiency.13,14 In addition, perforating veins are frequently interrupted during ablation of superficial reflux, even though this may be unintentional. Blind interruptions in the lipodermatosclerotic tissue, through small incisions or stab wounds, are frequently unsuccessful and incomplete.

A 55-80% recovery of competence in perforators previously demonstrated by duplex examination to be incompetent has been reported following sapheno-femoral and/or sapheno-popliteal ligation alone in patients with superficial and perforator incompetence, but no deep reflux.14,15 One series reported a relatively low ulcer recurrence rate of 9% at a 3.4 year median follow-up following sapheno-femoral ligation and stripping, without perforator surgery, in patients with superficial and perforator incompetence alone.16 However, patients with deep vein reflux or obstruction were excluded from this study. Since >50% of patients with venous ulceration have deep vein involvement, a recurrence rate of at least 20% could be predicted in all patients with venous ulcers undergoing superficial reflux ablation alone, without adding SEPS. Based on available data, the addition of SEPS could potentially decrease ulcer recurrence to as low as 10% at 2 years. Level 1 evidence to confirm these results is, however, not available.

**Solving the controversy – the NAVUS Trial**

Although it is confirmed that SEPS is an effective and safe treatment for interruption of incompetent perforator veins, the role for perforator interruption, with or without ablation of an incompetent superficial system, has not been confirmed. The superiority of surgical treatment over optimal medical treatment also remains to be established in a prospective randomized, multi-center trial. The North American Venous Ulcer Surgery (NAVUS) Trial has been designed to answer the role of surgery in the treatment of venous ulcers.

The NAVUS Trial is planned as a prospective, randomized, multi-center study, with the aim to compare clinical outcome following surgical treatment, consisting of (a) SEPS with concomitant ablation of superficial reflux, or (b) ablation of superficial reflux alone, to optimal medical management, in promoting ulcer healing, preventing ulcer recurrence or new ulceration in patients with chronic venous insufficiency. Patients with perforator incompetence alone, or those presenting with recurrence following ablation of superficial reflux, if randomized to the surgical arm, will be treated with SEPS alone. Patients in the surgical groups also will receive optimal medical therapy in addition to operative intervention. Both male and female patients, age 21 to age 80 years, with active venous ulceration (Class 6) or healed ulcers (Class 5) will be eligible for the trial. Five hundred and sixty patients will be randomized to medical treatment or one of the surgical treatment groups, over a two-year accrual period. The primary endpoint of the study is ulcer recurrence or appearance of new ulceration and the secondary endpoint is to assess the rate and time of ulcer healing. Patients will be followed at least 2 years after surgery to evaluate ulcer recurrence and assess hemodynamic improvement. Tertiary goals of the study are to: 1) identify factors associated with delayed ulcer healing and ulcer recurrence, 2) evaluate venous hemodynamic improvement following surgery, 3) assess quality of life, and 4) compare cost effectiveness of different treatment modalities. Subgroups in the surgical arm will be compared to assess the impact of addition of SEPS to superficial reflux ablation on ulcer healing, recurrence and improvement in venous function.

**References**


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**DISCUSSION**

**DR. BURNAND:** Peter, I don’t want to argue again about recurrence rates. I think you’re going to do this study and that’s going to give us the answer, and I think you should do the study. The question I’d like to come back to which is also from the first two speakers is the question—and this was from the Dutch group particularly that did it—is whether you believe that dealing with the perforating veins is going to actually heal the ulcer faster? I think that ulcers heal at a set rate and that nothing you do is going to improve on that. I agree with everything that Greg said. I think Philip is barking totally up the wrong tree because I don’t think we should be looking for drugs that encourage keratinocytes to migrate across ulcers faster. We should be looking at drugs that block the factors that inhibit keratinocytes from migrating and adhering. The real question is will SEPS actually speed the healing rate of ulcers that otherwise wouldn’t heal. Would you like to address that specific point?

**DR. GLOVICKI:** I think that’s a very important question, and I think only a multicenter randomized study like the NAVUS (North American Venous Ulcer Surgery) Trial will give us the answers. We frequently compare apples to oranges. I mean, there are patients with large ulcers and small ulcers, post-thrombotic ulcers and varicose ulcers, and there is such a variety of these in most studies that it is almost impossible to really tell whether there is indeed an effect on it. Of all the studies including our Mayo Clinic studies, and the North American SEPS study, where indeed the results were almost dismal because of the initial experience of the participating surgeons, the rate of ulcer healing was three times as fast as the healing that Greg Moneta reported from Portland.

**DR. COLERIDGE SMITH:** To respond to what Kevin was saying, the intention of my presentation was to say that if you find a drug or drugs which address the underlying mechanism causing the venous ulceration, that will modify the venous ulcer healing rate, and I think that things which actually interfere with the healing mechanism themselves are irrelevant. I have yet to see any evidence that healing is impaired in venous ulceration. Ulcers don’t heal in my view because the thing which caused the ulcer to appear in the first place is still there, whatever that may be.

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**Table 1.** Results of non-operative management for advanced chronic venous insufficiency

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Total Limbs*</th>
<th>Recurrence No. (%)</th>
<th>Followup (months)</th>
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<td>Negus, '85</td>
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<td>Erickson, '96</td>
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<td>Samson, '96</td>
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<td><strong>TOTAL</strong></td>
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<td><strong>252 (52)</strong></td>
<td><strong>27</strong></td>
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* Class 5 limbs + Class 6 limbs after ulcer healing. ** Class 5 limbs only

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**Table 2.** Results of SEPS in patients with advanced chronic venous insufficiency

<table>
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<tr>
<th>Author, Year</th>
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*Class 5 limbs + Class 6 limbs after ulcer healing.
DR. DEPALMA: It’s still there, but the SEPS gets rid of it perhaps?

DR. COLERIDGE SMITH: What we do with either superficial venous surgery, if that’s what’s required, or with SEPS is to remove the venous hypertension which causes the damage to the skin.

DR. BURNAND: That prevents recurrence, it doesn’t necessarily speed healing. The fact is that keratinocytes multiply at a certain rate, and they migrate at a certain rate, and there’s no evidence as yet, that I am aware of, that anything speeds this process. There’s quite a lot of evidence under some circumstances that some ulcers never heal, and it’s no good pretending that this doesn’t happen. Come on to our clinic. We do all the things that Greg has talked about and that you’ve talked about. The fact is that ten percent of venous ulcers don’t heal with compression treatment.

DR. COLERIDGE SMITH: And I would argue that is because the thing that caused them in the first place is still there along with the susceptibility of the patient to venous ulceration.

DR. GLOVICZKI: We know historically that when we put the patient in the hospital, elevate the leg, the ulcer heals faster. So if you have a technique which decreases ambulatory venous hypertension, I believe it helps healing the ulcer faster in ambulatory patients.

DR. EKLOF: Could you comment, Mr. Moderator, on the study? You should be neutral, but what do you think about the study that Peter is proposing?

DR. DEPALMA: What do I think about it? As I look at the number of combinations that are presented—and we make our living in my state based on odds—I see factorial 5 groups in that study. You know the study will be great if you can sort out the factorial 5 groups and get them compared; that is exactly my problem with prospective randomized studies. I think that Dr. Hull discussed it yesterday as well. So that ends my comment about it. I’d be willing to see, but with an open mind, if you can get appropriate CEAP classifications of the cohorts, that would be the number initial data required for exact comparisons.

CHRONIC VENOUS ULCER: HOW CORRECTION OF SUPERFICIAL REFUX ALTERS THE PATHOPHYSIOLOGY

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Chronic venous insufficiency manifests itself as hyperpigmentation, induration of the epidermis, dermis and subcutaneous tissue and venous ulceration. Histologically, capillary microscopy shows capillary proliferation which is best explained by elongation of capillary loops rather than increase in number of capillaries. The increased area of endothelium becomes a target for deposition of intercellular adhesion molecules and leukocytes. Leukocytes penetrate the endothelial intercellular barriers and are found in the subcutaneous interstitial tissues. The cells have been identified as macrophages and T lymphocytes.

The hemodynamic forces which act are those of gravitational reflux through axial veins and compartment pressure transmission through failed perforating vein valves. Correction of superficial reflux implies removal of the gravitational forces of venous hypertension and when this is combined with perforating vein interruption, the effects are to decrease venous hypertension in the skin and subcutaneous tissues. It is generally agreed that removing refluxing saphenous veins and their refluxing tributaries decreases distal venous hypertension. What is less well known is that deep venous reflux of primary origin rather than secondary to venous thrombosis is also improved by removing superficial reflux.

Increased dilation of the deep venous system accompanying superficial venous reflux was described by Fischer and Siebrecht in a phlebographic study as early as 1970. Fischer called attention to the fact that greater dilation of the deep veins was seen in the absence of post-thrombotic complications. In limbs with true post-thrombotic venous changes, these could be identified on phlebograms and the deep veins were found to be more constricted than in those limbs which exhibited superficial reflux and had no findings of venous thrombosis.

Our own observations in La Jolla have noted an increased diameter of deep veins that correlate with the presence of reflux. Some have suggested that correction of superficial reflux could be accomplished by narrowing of the valve annulus in incompetent saphenous veins.

Deep venous insufficiency has been found by others to exist in conjunction with saphenous venous insufficiency. This was considered to be a purely radiologic diagnosis before the advent of duplex ultrasound. The increased volume blood flow caused by saphenous reflux with reentry through perforating veins has been found to elongate and kink the femoral and popliteal veins as well as dilate the femoro-popliteal junction. Correction of superficial reflux has been found to restore perforating vein competency, and these findings together suggest that volume and perhaps velocity of blood flow in altering shear stress on the endothelium modifies the diameter and length of affected venous segments. Venous dilations and subsequent valvular insufficiency in response to such an increased volume flow may be dependent upon wall shear stress. This would be analogous to arterial elongation occurring proximal to chronic arteriovenous fistulas.

We have reported the extent of improvement in venous physiology which follows saphenous vein stripping. Total ablation of deep vein reflux in 27 of 29 limbs was the focus of our report. For the most part, the patients and the limbs reported at that time were early cases of venous insufficiency rather than classes 4, 5, and 6 of the CEAP classes. Four limbs were in what would now be classes 4, 5, and 6, five were in what would be in class 3, and the remainder of the 29 limbs were in class 2.

Labropoulos has reported on the same phenomenon. After excluding patients with previous deep venous thrombosis, Labropoulos studied 139 limbs. Eighty-four percent (84%) of these had reflux at the sapheno-femoral junction and 17% had reflux at the sapheno-popliteal junction. Femoral or deep popliteal reflux was present in 22% of these limbs and these were the focus of the study. Reflux was segmental in 28 of the 31 limbs and was limited to the area of the junction in 25 of these. The mean duration of deep venous reflux was 0.9 seconds and ranged from 0.6 to 3.7 seconds. An important feature of this was that this duration of reflux was significantly shorter than the reflux in the superficial veins which
averaged 2.6 seconds (p = 0.0001). Manual occlusion of the incompetent superficial veins reduced the duration of deep venous reflux but in this acute observation, the reflux was not totally abolished. It was found that the presence of deep venous reflux was associated with junctional reflux of high peak velocity and longer duration. Labropoulos concluded that the deep venous reflux characterized by being segmental and of short duration was associated with the presence of sapheno-femoral or sapheno-popliteal incompetence which had a high peak velocity and long duration of flow. He agreed that these findings explained why correction of superficial reflux alone abolishes deep venous insufficiency.

Assuming that superficial reflux and deep reflux produce distal venous hypertension, and that perforating vein incompetence transmits both static and dynamic exercise pressure to the skin, it is not surprising that in some limbs lipodermatosclerosis and ulceration occur and in others skin changes are absent. The differentiating factor between these extremes is, more likely than not, white blood cell trapping and activation. Limbs with normal skin would have an absence or decrease in trapping of leukocytes while those with the most profound changes would have maximum tissue destruction by the toxic factors liberated by activated leukocytes.

With that in mind, the combined operations of removal of axial venous hypertension and removal of compartmental venous hypertension by perforator vein interruption changes the pathophysiology of chronic venous insufficiency in two ways. The first is correction of the venous hypertensive effect and the second, correction of the activation of leukocytes in the dermato-elastic skin and areas of venous ulceration.

References

DISCUSSION

DR. BURNAND: I think there’s not much doubt that dealing with the saphenous vein will improve some patients with ulceration. It will prevent recurrence, and as you’ve shown, there are some very nice studies that support this hypothesis. We come back to the same question again, although it has two parts. One is: do you prevent recurrence? Two is: do you heal the ulcer faster? I don’t think there’s any evidence from any of the literature to date that stripping out the long saphenous vein makes the ulcer heal faster. That’s a study that needs to be done. In terms of preventing recurrence, as you say, you’ve got to be selective in the patients that you strip the long saphenous vein in. It’s not much good doing it in post-thrombotic legs with severe obstruction where the long saphenous is their only outflow.

DR. BERGAN: Clinically patients with some residual of the postphlebitic syndrome with some obstruction have been markedly benefited by stripping out the refluxing saphenous vein. I think we’ll hear more about that from Dr. Raju and Dr. Neglen.

DR. STRANDBYSS: I have a question of the panel. You know, a few years ago we did a study looking at levels of incompetence in patients who had a previous history of DVT with or without an ulcer, and one of the striking findings in our study was that they did’t have an ulcer, the greater saphenous vein was competent. But in the group that had developed a post-thrombotic ulcer, the greater saphenous vein was invariably incompetent, and I wonder if any members of the panel have any possible explanation for this. Why should the greater saphenous vein become incompetent from a previous history of DVT and not in some patients but in others?

DR. BURNAND: Well, I think the greater saphenous vein becomes incompetent in patients where there is obstruction. All the studies that we’ve ever done have shown that if you actually interrupt the saphenous under these circumstances, you can actually make the leg considerably worse. I can’t see that that’s necessarily opposed to yours. I think that the long saphenous vein can be a very important collateral. You have some patients where it may be the only collateral out of the leg, and anyone who strips that must be criminally insane in my view.

DR. BERGAN: However, there’s abundant clinical evidence that that statement is false.

DR. PERRIN: You have quoted the three studies in which superficial venous surgery has improved deep venous reflux, but when you look carefully at this study, the majority of the patient’s reflux were graded two or three according to Kistner classification and very few who had reflux graded 4 were improved.

DR. DEPALMA: In other words, your findings are negative.

DR. BERGAN: Well, that’s true, but I’m only addressing one of the variables in the equation. I’m certainly not against interrupting the perforating vein. I’m not against compression. I’m only taking the one characteristic assigned to me, that superficial reflux contributes to venous hypertension and should be part of the treatment.

DR. ABU-BAKER: So can stripping produce recurrent veins because of the main huntarian perforators were not ligated and then produce angiogenesis?

DR. BERGAN: Taking out the saphenous vein in the thigh will in most cases interrupt the Huntarian and the Dodd perforating veins. There are exceptions, of course, because veins don’t read anatomy books. Angiogenesis is an extremely interesting subject which could occupy the entire meeting. I’d rather not address that right now because I don’t think we know enough about it.

HOW MY METHOD OF TREATMENT CHANGES THE PATHOPHYSIOLOGY TO HEAL THE ULCER AND PREVENT RECURRENTNESS – REPAIRING PRIMARY REFUX

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The treatment has two aims: To heal the ulcer and prevent its recurrence.

Healing the ulcer: If the patient can walk with compression, an unmovable elastic bandage is applied and changed every 8-10 days.
Active reeducation of tibiotarsal joint is started when needed when the ulcer has become painless.

In case of non-healing after 2 months, the patient is hospitalized for bed rest. In very selected cases (large ulcer, extensive associated lipodermatosclerosis) “Shave therapy” is undertaken and followed by skin graft (8-12 days later), usually mesh graft.

Preventing recurrence: Non invasive investigations (Diagnosis level 2) are undertaken in order to precise hemodynamics. Primary deep vein reflux (superficial, deep, perforator) can be identified in almost all cases by Duplex scan. When primary deep vein reflux is identified, invasive investigations (ascending and descending Phlebography, AVP) are performed in absence of contraindication for Deep Venous Reflux surgery. We consider non-correctable coagulopathy (unusual in this etiology), stiff ankle after reeducation and nonactive patient as contraindications.

The question that emerges is what patients will benefit of Deep Venous Reconstructive Surgery (DVRS) when deep vein reflux is identified? Surgery may be considered:

- After failure of a correctly applied conservative treatment (compression).
- In patients who had been previously operated of their superficial insufficiency and/or perforator insufficiency when the ulcer recurs.
- When patients have a combination of venous superficial, and/or perforator insufficiency and deep venous reflux two therapeutic options are possible:

1st Option: Surgery of superficial venous insufficiency or/and perforator ligation (SEPS) followed by long-term compression are performed as first step and DVRS considered after failure of this treatment.

2nd Option: DVRS in combination with surgery of superficial venous insufficiency and/or perforator ligation are carried out at the same time.

Our policy is:

First option is chosen when Venous Refill Time (VRT) is significantly improved by tourniquet and above 12s., deep vein reflux (according to Kistner) grade 3 and feasibility of valve repair questionable on ascending and descending phlebography.

Second option is preferred when VRT is <12s. with tourniquet, deep vein reflux grade 4 and identification of a valve repairable at the femoral or popliteal level. When combined surgery is scheduled, surgery of superficial venous insufficiency and/or perforator liga-
tion is undertaken 2 or 3 days before valve repair.

We have not evaluated our personal data in option number one. Conversely we have results with the long-term follow-up (12-96 months -average 64) in 24 patients (C6) that have been treated according to option 2. One ulcer had not healed (4.1%) and three had recurred (12%). No or minor reflux had been identified in 18 and major reflux in 5 at the last duplex scan investigation. Related to the small number of patients included there is no significant correlation between clinical and hemodynamic (duplex scanning) results (P=0.1). VRT was normalized in 68% after valve repair. When there is a component of distal post thrombotic disease (9 patients) results provided by valve repair are less satisfactory (P=0.03) for clinical results and (P=0.05) for hemodynamics than in PVI. These personal results are in accordance with those published in the literature (Kistner, Raju, and Sottiurai).

DISCUSSION

DR. ENRICI: It’s very interesting data, Dr. Perrin. I think the best option to do is the valvuloplasty, and I want to ask you when you chose internal valvuloplasty versus external valvuloplasty.

DR. PERRIN: My reported results were from internal valvuloplasty.

HOW MY METHOD OF TREATMENT CHANGES THE PATHOPHYSIOLOGY TO HEAL THE ULCER AND PREVENT RECURRENCE-REPAIRING SECONDARY INCOMPETENCE

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The pathology of secondary incompetence is complex with associated obstructive and calf pump changes; collateral reflux is a major component as well. Post-thrombotic valve reflux has been traditionally attributed to the destruction of the valve structure by the organizing process. There is evidence that the process is more complex than this simplistic view. Approximately 25% of reconstructed valves in our experience had intact valve cusps despite clear evidence of trabeculae and other post-thrombotic changes around them. Direct repair of these valves was feasible. In some other cases, a sleeve of perivenous fibrosis appears to propagate from the area of thrombus spreading to envelope adjoining valve segments not directly involved in the thrombotic process. The resulting constriction and foreshortening of the valve housing appears to result in secondary incompetence of previously competent intact valve cusps. These are also amenable to direct valve repair techniques. Collateral reflux occurs through dilated axio-axial or tributary axial collaterals. The profunda femoris particularly plays a significant role in this regard. As a collateral pathway, the profunda femoris valve structures appear to become secondarily incompetent from dilatation even though they were not involved in the thrombotic process. On the other hand the collateral potential of superficial subcutaneous veins in post-thrombotic syndrome has been unduly exaggerated in the past. It appears that the outflow function of these “secondary” varicosities is very limited. They frequently function as major pathways of reflux significantly contributing to the pathology of post-thrombotic syndrome, over-shadowing any benefit derived from their outflow potential to the overall calf pump function.

We have taken an aggressive approach to the post-thrombotic limb, with the strategy of correcting, repairing or eliminating as many sources of reflux as practically feasible:

1. Saphenous reflux is eliminated by stripping, even though venograms may give the appearance of the saphenous functioning as
a collateral around the obstructed femoropopliteal segment. Resistance calculations and outflow measurements clearly indicate (n=51) that stripping did not compromise overall outflow but resulted in improvement of reflux parameters. No adverse clinical manifestations indicating outflow compromise was observed in any of these cases.

2. Multiple valve reconstructions: when the femoral area is explored, both the superficial femoral and profunda femoris are dissected out and the valve stations tested for reflux. Both valves are repaired when both are refluxive as is frequently the case. A combination of techniques including direct valve repairs, axillary valve transfers or even cryovalves are utilized as necessary to achieve this objective. Trans-commisural repairs are fast and are particularly utilitarian in this regard. The entire femoral confluence can be reconstructed if a suitable configuration of basilic, brachial and axillary confluence is available for use. Thirty to 40% of axillary valve are leaky in situ and should be repaired before transfer. The rapid trans-commisural technique was the most frequently used for this purpose. Poorly recanalized superficial femoral veins with little outflow function can be divided rather than repaired if there is axial transformation of the profunda femoris. The main repair in these cases will involve the enlarged profunda femoris vein. Actuarial ulcer healing in such profunda femoris repairs were 66% at 5 yrs. The adequacy and success of valve repairs is monitored by ambulatory pressure measurement, particularly venous refilling time (VFT) and venous filling index (VF90) with Air-plethysmography. A post-operative VFT that stayed below 5 seconds was associated with high recurrence and persistence of symptoms. It is our current policy to approach additional sites for valve reconstruction (IE Popliteal) as a second stage in such cases to improve the VFT beyond 5 seconds. In about 20% of cases the popliteal was the initial site of valve repair as this valve structure appeared to be relatively uninvolved in the thrombosis process compared to the femoral area on preoperative venograms.

3. “Blind” explorations: In several preoperative venograms the deep veins did not visualize and only the superficial veins appeared to fill with contrast. It is our premise that the limb cannot survive on a superficial venous network alone and adequate deep veins are bound to be present. We surmised that this venographic appearance is an artifact due to the complex flow patterns and regional pressure variations in the post-thrombotic extremity. “Blind” explorations of the femoral area in the groin has yielded patent repairable valve segments in the majority of such cases, despite venographic non-visualization. The saphenous was refluxive and was stripped in such cases without clinical or hemodynamic malsequaleae even though it appeared to be the only contrast visualized outflow tract.

4. Trabeculated post-thrombotic veins: Axillary valve transfers to trabeculated femoral veins have maintained an actuarial patency of >80% up to 10 yrs (n=83) with actuarial ulcer healing of 61%. Actuarial ulcer healing and repair patency in these cases has not been different from Venous reconstructions undertaken below open iliac venous segments.

5. Combined obstruction reflux: Obstructed or stenosed iliac venous segments are now stented first before valve reconstruction. Actuarial patency of >85% (2yrs) has been observed with impressive relief of the pain and swelling components of post-thrombotic syndrome. Thirty percent of open ulcers have been noted to heal as well following the stenting procedure alone allowing deferment of valve reconstruction. When disobliteration of the obstructed iliac segment has not been feasible, we have proceeded with valve reconstruction below the obstructed segment nevertheless (n=15). Actuarial ulcer healing and repair patency in these cases has not been different from valve reconstructions undertaken below open iliac venous segments.

References

CONTROVERSIES IN DIAGNOSIS – CLINICAL EVALUATION IN THE OFFICE

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A major function of the consultation is to determine why the patient has been referred. Many asymptomatic patients present to ask about the risk of future serious complications. Reassurance that the risk is small and that treatment can be instituted later in the few who do progress will frequently result in grateful relief that treatment can be deferred. Others demand treatment for cosmetic reasons and there must be frank discussion as to realistic expectations of results. Symptomatic patients should be carefully assessed from the history and examination to search for characteristic features of alternate ischaemic, arthritic or neuralgic causes for pain, perhaps leading to appropriate investigations. Symptoms from venous disease alone are usually not as characteristic. Further, marked venous aching or swelling can be associated with minimal or no varicose veins on examination. Complications of thrombophlebitis, lipodermatosclerosis, venous eczema or ulceration can usually be confidently diagnosed from the examination although these limbs will usually require further investigation, and mixed disease is common.

Much of the history revolves around enquiry from patients as to the cause of their varicose veins. They ask whether they are inherited, due to tight garments, aggravated by crossing their legs, or caused by prolonged standing or straining, at work or from sporting activities. They should be told that apart from pregnancy and a relation to body mass, there is no worthwhile evidence to incriminate any other cause. Enquiry about past deep vein thrombosis is often inconclusive. This must be one of the few diseases shown not to be caused by smoking.

Examination with the patient standing shows whether or not there are varicose veins, reticular veins or telangiectases. Unfortunately, many patients later shown by duplex scanning to have major venous reflux will have minimal or no apparent varicocities. Further, on a
clinical assessment as to whether varicocities affect the greater or lesser saphenous systems or perforators also relates poorly to objective studies by duplex scanning. A positive tourniquet test may support an obvious diagnosis of greater saphenous reflux but tourniquet tests are otherwise of little value. The continuous-wave pocket Doppler does not improve accuracy sufficient to avoid the need for duplex scanning in patients destined for intervention. Planning the best treatment for each patient requires more than office assessment alone. However, the office is the site for careful discussion of the findings from anatomical and physiological investigations to explain why the condition is best treated by conservative measures, sclerotherapy or surgery, and what the risks and reasonable outcome is likely to be.

DISCUSSION

DR. SUMNER: Contrary to what Ken says, I believe that the appearance of the venous ulcer on physical examination is pretty specific. You can often distinguish between an arterial and venous ulcer from across the room. I’m not talking about identifying the underlying venous pathology, which requires additional testing. Otherwise, I suspect that the initial clinical impression in most cases is reasonably accurate.

DR. RAJU: I think I would agree with that. Dr. Myers is going to respond.

DR. MYERS: Well, I omitted to mention that in my examination I take great care to feel the pulses, listen for bruits, assess for arterial disease, and of course, there is a group of patients, who present with arterial ulcers. I can tell that from the history of pain, and looking at the ulcer feeling the pulses. This is no longer a venous problem and it belongs to another meeting. The patient that I was talking about is the one who clearly has a venous ulcer with pigmentation around it, and where I suspect there may be an element of arterial disease. I want to be quite sure how large this element is. I want to know whether that’s something I should treat first or whether I can ignore it. It is this group of patients that I really have a lot of difficulty assessing and that’s where the vascular laboratory greatly helps me.

DR. PADBERG: One thing which I’ve noticed in my own experience, as the patients get older, which they seem to be throughout the world, identifying the arterial ulcer from the venous ulcer at the initial visit may be somewhat straightforward if indeed they have a fair amount of arterial disease, but after the patient has been in your clinics for many years with his third and fourth recurrence, he can sometimes slip up on you with a deterioration in his arterial circulation. You may not apply the same intensity of examination as your initial evaluation. You’ve already seen your ankle/brachial index. You did it four years ago. Well, ask, why do I need to redo it again? It’s those patients that we need to be particularly tuned to, because they’re the ones whose ulcers really get big, and then you ask yourself, well, why is all of a sudden this wound deteriorating? You check the simple things first and forget that it can change. Reassessment is appropriate when the wound or patient’s response changes. One other comment I might make to your examination, I have not thrown away my hand-held Doppler. I still use it routinely with my clinical examination in the standing position to evaluate the patients for simple incompetence. This helps to identify the presence of superficial venous disease, and helps to direct the workup and treatment to patients who have venous disease and away for those who don’t have venous disease but yet have recurrent ulceration of another form.

THE OFFICE - THE HAND-HELD DOPPLER

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Chronic venous insufficiency is ordinarily easily diagnosed in the clinic by inspecting the leg. Physical findings are characteristic and are among the most specific of any disease. But physical examination, other than identifying varicose veins, provides little information concerning the presence, location, and extent of venous obstruction or valvular incompetence.

Prior to the introduction of duplex scanning, examinations performed with continuous-wave (cw) Doppler devices were the only noninvasive way of obtaining objective anatomic information pertaining to the diagnosis of chronic venous insufficiency. This technique, while less precise than duplex scanning, still remains useful in the office or clinic, where duplex scanning may not be readily available, and may provide sufficient information in patients in whom compression therapy is selected as the initial therapeutic approach.

Methods

Any of a number of Doppler instruments are suitable, including those that are completely hand-held, but there are some advantages to using directional instruments with panel meters, especially when investigating venous incompetence. Studies are initially conducted in a warm room with the patient supine, tilted slightly foot down, and his or her legs in a relaxed position. At all levels of the leg, the first step is to identify the corresponding artery. The probe is then shifted slightly in the proper direction to optimize the venous signal. (In the absence of a B-mode image, this approach is critical to the identification of the proper vein.) Using signals from the corresponding artery as a guide, the examiner studies the common femoral, superficial femoral, popliteal, and posterior tibial veins as well as the above-knee and below knee greater saphenous veins. Normal venous signals are phasic with respiration and are easily augmented by gentle limb compression. Particular attention should be given to “spontaneous” (unaugmented) signals, which are always present in normal limbs at the popliteal and more proximal levels and are frequently present in the posterior tibial and saphenous veins at the ankle.

Absence of an augmented signal indicates that the insonated venous segment is totally occluded. Weak signals, however, may be obtained from adjacent collaterals or from partially recanalized veins. Although normal spontaneous signals imply patency, they can be obtained when veins are recanalized or when only one of a pair of duplicated veins is occluded. “Continuous” (non-phasic) signals are obtained from a patent vein when its axial continuation is occluded. (For example, a continuous signal in the common femoral vein implies obstruction of the iliac vein.) Increased flow in superficial veins is good but indirect evidence of deep venous obstruction.
Venous valvular incompetence can be detected by demonstrating flow reversal in a venous segment. At the common femoral level, a Valsalva maneuver will result in total cessation of phasic flow when there is at least one competent valve in the iliac or common femoral veins. Reflux at this level is indicative of valvular incompetence. Although a Valsalva maneuver may produce retrograde flow as far distally as the posterior tibial or saphenous vein at the ankle when all intervening valves are incompetent, the presence of a single competent valve at any level proximal to the site of the probe will prevent reflux.

To detect segmental incompetence below the groin, limb compression must be used. Compression above the probe closes all intervening competent valves, resulting in temporary cessation of flow (Figure). If, however, the intervening valves are incompetent, flow reversal is detected at the probe site during limb compression followed by an antrage surge of blood when compression is released. This produces an easily recognized “to-and-fro” signal. When the leg is compressed below the site of the probe, an antegrade flow signal is first heard. Upon release of compression, flow ceases temporarily when the intervening valves are competent but reverses when the valves are incompetent, again producing a “to-and-fro” sound.

While these studies can be performed with the patient supine, the standing position more closely approximates the physiologic conditions in which reflux is important. Manual or tourniquet compression of the greater saphenous vein at the upper thigh or the lesser saphenous vein at the upper calf may clarify whether reflux in the common femoral vein or popliteal vein is due to incompetence of the superficial or deep systems.

Limitations and Accuracy

A major drawback of hand-held Doppler examinations is the inability to be certain which veins are being studied. Errors occur when veins are duplicated or when collateral veins or tributary veins are inadvertently sonicated. With the possible exception of the posterior tibial veins, deep calf veins and intramuscular veins cannot be selectively identified. Moreover, the extent of obstruction or the precise location of incompetent valves cannot be determined, and the severity of reflux cannot be estimated. Because of the complicated anatomy, attempts to detect and accurately locate incompetent perforating veins with the cw-Doppler have been disappointing.

There is little objective information validating the accuracy of cw-Doppler for diagnosing valvular incompetence. According to Nicolaides et al., popliteal reflux can be detected with a sensitivity of 100% and a specificity of 92%. Evers and Wuppermann reported a sensitivity of 71% and a specificity of 92% for identifying the post-thrombotic syndrome. Greater saphenous vein incompetence was diagnosed with a sensitivity of 73% and a specificity of 85% in a study reported by McMullin and Coleridge Smith, but the sensitivity for lesser saphenous vein incompetence was only 33%.

Applications

The hand-held Doppler provides a quick and readily available method for verifying the diagnosis of chronic venous insufficiency in outpatients. Concomitant arterial obstruction can be detected and, if present, its severity evaluated by measuring the ankle/brachial pressure index. If nonoperative measures (elastic stockings, Unna boots, or non-elastic support) are chosen as the initial therapeutic approach, no other testing is required. When valvuloplasty, valve transplantation, venous bypass, or perforator ligation is contemplated in patients with recalcitrant disease, further studies with duplex scanning are necessary to define more precisely the location and extent of valvular incompetence or chronic venous obstruction.

In patients with uncomplicated primary varicose veins, hand-held Doppler surveys usually suffice to identify incompetent superficial venous segments and to locate major communications with the deep system that feed the varicosities - information vital to the effective treatment of this disease.

References

AN EVALUATION IN EUROPE OF THE C OF CEAP
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Background
Everyone knows the CEAP classification, as it is the most recent, complete and precise and the best structured. It classifies the four main aspects of CVI: Clinical signs, Etiology, Anatomical sites and Pathophysiological problems. A group of three severity scores is added allowing numerical evaluation of the course of the disease. Therefore this classification is ideal.¹

Objective
To evaluate, in a routine clinical setting, the information associated with each Clinical class of CEAP, and the consistency of their hierarchy.

Material
Patients residing in Europe and presenting with venous disease. Data were immediately checked into a computer program, called the European Phlebology File (EPF). This program created by a European group of 30 angiologists in 1997, has been set up in order to make Venous Epidemiological Investigations. It includes elements of the CEAP classification, but also a number of items not included in the C of CEAP. It automatically calculates C, E, A, P and the three scores for each patient. It also uses a data entry system, which can be transferred by e-mail. With this EPF the CEAP classification can be used in everyday practice.

Method
The preliminary multicentric validation of this new software dedicated to the management of venous diseases made this work possible. Sixty-one angiologists from 10 different European countries entered a total of 872 patients' exhaustive records. The data were analyzed in order to evaluate the information value of each of the 7 Clinical classes (C0 to C6) and to test the consistency of their hierarchical graduation, using both monovariate and multivariate statistical techniques performed through SPSS/PC Software on the database of 1,744 lower limbs.

Result
The population consisted of 872 patients coming from France, Italy, Belgium, Holland, Austria, Germany, Switzerland, UK, Greece and Spain. Seven hundred women (80.3%) and 172 men (19.7%), average 53.1 years old (maximum 100 years minimum 18 years). Their average weight is 68 kg and average height 166 cm. Seventy percent of the female patients had been pregnant. Compression therapy has been used in 30%, sclerotherapy in 23% and previous venous surgery performed in 16% of the patients.

The distribution of the lower extremities according to the 7 Clinical classes of CEAP was relatively homogeneous.

The etiology of CVI consist of primary 82.6% and secondary (post-thrombotic syndrome) 17.4%.

Post-thrombotic syndrome, age greater than median 52 years (p=50%) and history of pregnancy (p=70.4%) were significantly associated with classes of higher order.

Regarding between classes consistency, classes 3rd to 6th classes showed a good hierarchical agreement, although it should be noted that 13.6% of patients with open or cicatricial venous ulcers did not show associated skin changes validating classes 4-5-6.

Excepting the corona phlebectatica, the presence of telangiectasia did not seem to correlate with the other venous signs.

Association pattern of skin changes in class 4 showed that lipodermatosclerosis and atrophic blanche are of more severe significance than pigmentation.

Conclusion
The information summarized by the CEAP clinical classes are of good practical relevance, but is of a composite constitution. Further discussions and works are needed.

References

DISCUSSION
DR. PADBERG: You mentioned venous eczema as it was missing from CEAP. That also disturbed some of us statewide. Did you include that in the new European classification, and if so, did you differentiate between dry and wet eczema?

DR. CORNU-THENARD: We of course took the item “Eczema” but we didn’t mention if it was dry or wet. On the other hand we asked for the size, as for pigmentation, lipodermatosclerosis like it is done for ulcers.

DR. STRANDNESS: Andre, do you have a laptop computer in your examining room so that when you’re taking the history and you’re doing the examination this is all entered at the time?

DR. CORNU-THENARD: Yes, since the beginning of this year.

DR. RUTHERFORD: This was a very nice presentation. As Andre already knows, there’s an ad hoc committee of the American Venous Forum that is working on a similar approach but has gone beyond the clinical score that was included in CEAP. We will be making recommendations for severity scoring along similar lines, and I will present that on Friday. However, I would like to point out that one of the important characteristics you need in such a scoring system is that each of the elements can be graded in levels that can actually reflect change that comes with treatment, and it has to reflect it fairly promptly. In some elements, for example, the induration and subcutaneous fibrosis associated with dermatofibrosis are not going to change very quickly with treatment and unless you can come up with attributes that you can score that will show change, it remains primarily a static classification system. So we need to score elements that will show the effect of treatment and produce a difference in score with treatment, and that’s what our committee is aiming for. Therefore, I would like to ask you, have you
compared your scores before and after treatment?

DR. CORNU-THENARD: We didn't do this yet -- The actual idea is to evaluate our computerized phlebological file to see if everything is in. Later on we will try to implement this idea, to compare the score between the first and following examinations.

DR. RAJU: Thank you. I think the point that Bob raised is quite appropriate. -- There's clear evidence that the larger the ulcer it takes much, much longer to heal. I don't know whether that's true of dermatitis. I've seen extensive dermatitis heal pretty rapidly after treatment. There's no time element difference.

SENSORY IMPAIRMENT: A FEATURE OF CHRONIC VENOUS INSUFFICIENCY

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Although not widely recognized clinically, impaired peripheral sensation may feature in the morbidity of chronic venous insufficiency (CVI). Evidence of neuropathy in the foot of limbs with CVI was reported by several investigators. Minor trauma, such as scratching from pruritis, will often initiate venous ulceration. Accordingly, we conducted a clinical evaluation of 23 limbs in 14 male patients to determine whether a sensory neuropathy is present, and if so, to determine its extent and distribution.

Sensory thresholds in CEAP Class 2 limbs (n=11) were compared with CEAP class 5 limbs (n=12) at nine different sites on the foot, ankle, calf, thigh, and palm: thenar and hypothenar thresholds were measured as internal controls (Figure). These sites included both those areas usually associated with venous insufficiency and those areas usually not affected by venous insufficiency. Exclusions included diabetes, prior ipsilateral extremity surgery, absence of objective findings of venous insufficiency or other diseases associated with neuropathy.

Sensory thresholds were measured with a pressure aesthesiometer consisting of 20 nylon filaments calibrated to buckle on application of a graduated longitudinal force (F) ranging from 4.5mg to 447Grams. Pressure applied by the Semmes-Weinstein filaments is expressed as the log\(^{10}\) (F in mg)/(10). This logarithmic scale expresses the threshold as a linear relationship with corresponding values ranging from 1.65-6.65.4

A complete, sensory-motor assessment of the limb consisting of deep tendon reflexes (DTR), vibration, proprioception, motor strength, and light touch, was performed by an experienced neurosurgeon. Venous reflux was determined by duplex ultrasound and air plethysmography.

Results

Sensory thresholds at the most common site of venous ulceration—just proximal to the medial malleolus—were significantly (p<0.05) different between CEAP 2 (median 3.61) and CEAP 5 (median 4.65) limbs (Table 1). A significantly different median threshold was also observed at four other sites: just proximal to the lateral malleolus, the proximal medial and lateral calf, and the thigh. The remainder of the tested sites were not different between CEAP 2 and CEAP 5 limbs (Table 1). Profoundly abnormal examinations were recorded in 3 individuals from class 5 who were unable to appreciate the presence of even the thickest, most rigid (6.65) filament. Morphologic studies from our institution identified destruction of cutaneous nerve fibers in areas subjected to chronic venous hypertension.

Sensory abnormalities coincided with the extent of trophic changes and did not reflect specific dermatomal or cutaneous nerve distributions. In addition to light touch or pinprick, vibration sense and DTR’s were also significantly worse in those with severe CVI. The magnitude of the sensory impairment observed in the CEAP, 5 limbs (5.31 and 5.07, Table 2) was similar to that reported as a significant sensory threshold in diabetes or leprosy (5.07).3,5 In prospective studies, the inability of the diabetic subject to appreciate the application of a 5.07 filament was associated with subsequent ulceration of the plantar surface skin of the foot.5 Previously determined normal sensory thresholds for the foot and hand are noted in Table 1.5,3 Prospective identification of limbs at risk would provide a logical opportunity for follow-up evaluation of this potential risk factor for ulcer recurrence in CVI. Although the appropriate level of sensory impairment which would be associated with such increased risk is undetermined at this time, the ease and convenience of this examination lends itself to screening at an initial examination for planning treatment of CVI.

Sensory neuropathy is a feature of severe CVI, and its distribution is coincident with trophic changes. As this is often unappreciated by the patient, it may contribute to the propensity for deterioration from minor trauma.

References


See Table 1 and 2 on next page

DISCUSSION

DR. COLERIDGE SMITH: That’s certainly good interesting data, and that follows on from our own investigations. I always regarded the neurological damage as collateral damage, if you like, from all the other inflammatory processes that go on in the skin of patients with venous disease, but clearly with such severe sensory neuropathy, there is a very strong chance that this will contribute to failure of healing and perhaps the likelihood of additional ulcers. In our own work we deliberately looked remote from the site of the ulcer to avoid any local effect which we thought was quite probable and only looked at the nerves which had passed the site of the ulcer going deep to the deep fascia to reach the foot. Even there we found peripheral neuropathy. This was in the smallest nerve fibers which might be those that regulate the microcirculation. So I’m glad to see that our original work has been confirmed by your careful studies.

DR. PADBERG: We have concentrated on demonstrating the
TABLE 1.—Sensory thresholds were measured at nine different anatomic sites innervated by different nerve roots and cutaneous nerves. CEAP class 2 (mild CVI) and CEAP class 5 (severe CVI) limbs.

<table>
<thead>
<tr>
<th>Site</th>
<th>Dermatome</th>
<th>Peripheral Nerve</th>
<th>Trunk</th>
<th>CEAP, 2 (N=11)</th>
<th>P’ values</th>
<th>CEAP, 5 (N=12)</th>
<th>Published Normals**</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. 1st web space</td>
<td>L5-S1</td>
<td>Deep Peroneal N</td>
<td></td>
<td>3.22 (2.44-4.08)</td>
<td>NS</td>
<td>4.08 (2.83-5.07)</td>
<td>3.87±0.07</td>
</tr>
<tr>
<td>2. Dorsal foot</td>
<td>L5</td>
<td>Superficial Peroneal N</td>
<td></td>
<td>3.22 (2.44-4.17)</td>
<td>NS</td>
<td>4.24 (2.83-5.07)</td>
<td>3.81±0.07</td>
</tr>
<tr>
<td>3. Supramalleolar Medial + 5 cm</td>
<td>L4</td>
<td>Saphenous N</td>
<td></td>
<td>3.61 (2.44-4.17)</td>
<td>.0001</td>
<td>4.65 (4.08-6.65)</td>
<td></td>
</tr>
<tr>
<td>4. Supramalleolar Lateral + 5 cm</td>
<td>S1</td>
<td>Sural N</td>
<td></td>
<td>3.84 (2.44-4.17)</td>
<td>.0039</td>
<td>4.45 (3.84-6.45)</td>
<td></td>
</tr>
<tr>
<td>5. Proximal Calf, Medial +25 cm</td>
<td>L4</td>
<td>Saphenous N</td>
<td></td>
<td>3.22 (2.36-4.08)</td>
<td>.00021</td>
<td>4.24 (3.22-4.94)</td>
<td></td>
</tr>
<tr>
<td>6. Proximal Calf, Lateral + 25 cm</td>
<td>L5</td>
<td>Lateral Sural Cutaneous N</td>
<td></td>
<td>3.22 (2.36-4.17)</td>
<td>.007</td>
<td>4.17 (3.22-5.18)</td>
<td></td>
</tr>
<tr>
<td>7. Anterior Thigh, Knee +10 cm</td>
<td>L2-L4 vs L3-4</td>
<td>Ant Femoral Cutaneous N</td>
<td></td>
<td>2.83 (2.44-4.17)</td>
<td>.007</td>
<td>3.96 (3.36-6.10)</td>
<td></td>
</tr>
<tr>
<td>8. Palm, Thenar</td>
<td>C7</td>
<td>Median N</td>
<td></td>
<td>3.22 (2.44-3.23)</td>
<td>NS</td>
<td>3.03 (1.65-4.08)</td>
<td>2.44-2.83</td>
</tr>
<tr>
<td>9. Palm, Hypothenar</td>
<td>T1</td>
<td>Ulnar N</td>
<td></td>
<td>3.22 (2.44-3.84)</td>
<td>NS</td>
<td>3.22 (1.65-4.17)</td>
<td>2.44-2.83</td>
</tr>
</tbody>
</table>

Values for sensory thresholds are expressed as log(10) [F in mg/(10); Median (Low value–High value), *P values derived from Wilcoxon rank sum test and specified if significant (if p>.05, NS). L, lumbar; S, sacral; C, cervical; T, thoracic; N, nerve. ** Holewski reported as mean±SEM.

TABLE 2.—Least sensitive filament thresholds as determined by different examiners in comparison of CEAP,2 and CEAP,5 limbs.

<table>
<thead>
<tr>
<th>SITES OF SENSORY THRESHOLD DETERMINATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Dorsal Web Space</td>
</tr>
<tr>
<td>2. Dorsal Foot</td>
</tr>
<tr>
<td>3. Medial Ankle</td>
</tr>
<tr>
<td>4. Lateral Ankle</td>
</tr>
<tr>
<td>5. Medial Calf</td>
</tr>
<tr>
<td>6. Lateral Calf</td>
</tr>
<tr>
<td>7. Suprapatellar</td>
</tr>
<tr>
<td>8,9. Palm—Thenar and Hypothenar</td>
</tr>
</tbody>
</table>

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DR. VILLAVICENCIO: Yes. I want to congratulate Frank Padberg for his astute observations that really document what we have seen. We have observed, while operating on people with severe venous hypertension, especially working on the lesser saphenous area of the ankle, that the sural nerve, both in people with chronic venous insufficiency as well as a congenital malformation with severe venous insufficiency, and complex varicose veins, that the nerves which surround the nerves are very dilated. Often one might confuse the saphenous vein with the lesser saphenous vein at the ankle level. This reflects basically that the nervous venous system drains into the general system and is also hypertensive. This might reflect on the findings that Dr. Padberg just has presented to us.

DR. THORPE: I also found your study very interesting. I’d like to offer that we see a lot of the chronic post-thrombotic people which are years out and very severe, but not necessarily C5 or 6 but mostly C4 with bad edema and very hard calves. After we treat them they spontaneously offer that they can feel their leg again. They didn’t realize how numb their leg was, and that it feels more like their normal leg or opposite leg. So there’s apparently an element of reversible nerve loss that is associated with this chronic severe edema. I’m wondering if you can apply your testing to patients who are C5 and C4 and correlate that to the amount of circumferential edema.

DR. PADBERG: Thank you. That’s a good question. Just as
Philip indicated, we avoided the C6 links because of the questions 1) how do you measure the nerve endings in an open ulcer and 2) would that color the result? We are measuring C4 links at this point in time. I would present that data. We only don't have an adequate patient sample with all of the appropriate exclusions to give you the data that you’re looking for. The advantage of this test, I think, is that it’s very, very simple. It’s very straightforward to do. You all need is a set of filaments. You don’t even have to buy the big set. I think to get an estimate of what the level of impairment in an individual patient may be. In the absence of the filaments, simple testing of sharp objects will identify severe impairment. I do think this, there is probably an element of reversibility. As Bob Rutherford suggested earlier, the question of lipodermatosclerosis or fibrosis being reversible is probably less likely. The edema, of course, you’ve seen respond, and now you’re telling us that the nerve complaints, the subjective nerve complaints that you’ve seen, have also responded. So I think that this is an element which we will need to evaluate as we go on.

DR. ABU-BAKER: So I thank all of you for your good works, but I’d like to ask only one question. Why is the venous ulcer predominantly in the third internal inferior part of the leg, and not on the external side?

DR. MYERS: I think the question is why do we usually have ulcers on the medial side of the ankle, not on the lateral side of the ankle. That’s an excellent Israeli study that shows that ulcers on the lateral aspect of the ankle are usually associated with short saphenous reflux whereas ulcers on the medial aspect may be associated either with short or long saphenous reflux. This ignores the deep venous component. We found the same, though not quite as strongly as the Israeli group.

DR. PADBERG: I’ll just comment that the neurologic abnormality also points to the lateral ankle as being subject to the insult of the venous hypertension. We too see lateral ulceration. I can’t agree that Arie Bass’ study was as tight as our own experience, but I believe the concept is valid.

DR. TRIPATHI: This is a question for Frank. Do you think that just peripheral sensory neuropathy is occurring in chronic venous insufficiency, or is there any autonomic neuropathy and have you studied that?

DR. PADBERG: I specifically have not. You actually may want to have Philip answer that question. He was looking at an autonomic neuropathy using the vasodilatory flare response on the sole of the foot.

DR. TRIPATHI: I want to ask whether in chronic venous insufficiency, the deeper venous compartments have autonomic neuropathy? After correction of superficial vein incompetence, we often see some correction of deep vein incompetence and perforator incompetence. I wonder if there is an autonomic neurohumoral role in the reversal of the deep vein incompetence and perforator incompetence?

DR. PADBERG: Like John Bergan and Cliff Sales, we have observed reflux in the deep venous system which corrected as a result of surgical intervention on the superficial system. I would expect that if the reflux is severe enough to create this type of neurologic abnormality, that we would be able to measure an improvement there as well. It will probably take some time to get enough patients that fit the category necessary to make that conclusion.

DR. COLERIDGE SMITH: Exactly the same point occurred to me, and we never got around to investigating the autonomic parts of the system, but the same class of nerve fibers where we found neuropathy would be responsible for autonomic control of the microcirculation in the leg including, the deep compartments. There is a paper which suggests that this actually is the case, that there is an autonomic nerve problem in people with chronic venous disease distal to the level of the venous disease.

RELIABILITY OF CLINICAL DIAGNOSIS IN VARICOSE VEINS: A PROSPECTIVE COMPARISON BETWEEN CLINICAL EXAMINATION AND DOPPLER ULTRASOUND

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R. Volkmann, MD

PURPOSE
The accuracy of examining lower extremity varicosity has only been clinically questioned. Therefore, we initiated a prospective study to compare the outcome of the clinical investigation with 2-D Color Doppler ultrasound, which is a more objective method of examining venous anatomy and function.

METHODS
Ten experienced surgeons agreed to participate in this prospective study of patients with varicose veins, free of leg ulcers. The use of a hand-held Doppler was optional. At the patients’ first visit, a study protocol was filled out with the clinical diagnosis and sent to the coordinator of the study. After that, the patient was referred to a vascular ultrasound unit. The result of the Duplex study was documented on another protocol and sent to the coordinator for comparison with the first protocol.

PATIENT MATERIAL
In 214 legs of 183 patients complete first and second protocols were obtained for comparison and statistical analysis.

RESULTS
In more than 20%, the function of the greater as well as lesser saphenous veins was misdiagnosed by the clinical examination. A slight improvement was observed when the lesser saphenous vein was evaluated with a hand-held Doppler, which, however, was not true for the hand-held Doppler investigation of the greater saphenous vein. Thigh perforator (Hunter) insufficiency was overestimated. In more than 50% of the patients, substantial errors in the clinical evaluation was found as compared to the color Doppler. The clinical detection of insufficient perforating veins was unreliable. According to color doppler, no predilection site for insufficient lower leg perforating veins could be defined.

CONCLUSION
Preoperative clinical evaluation of varicose veins is unreliable as compared with diagnostic Duplex ultrasound. Surgical therapies,
which are planned on the clinical diagnosis only, may lead to mistreatment of a substantial number of patients.

DISCUSSION

DR. PADBERG: It appears that you’ve succinctly summarized many of the issues that led to the development of the CEAP classification. In Sweden you are talking about clinical examination and you are talking about duplex examination and you’re still trying to figure out what we’re talking about in terms of identifying the disease and the pathophysiology in our group of patients that we can generalize to a specific individual and offer a treatment plan that would then lead us to a conclusion. My question from that leads to our gold standard for diagnosis. Thus one of the things that we might like to know a little bit more about your study is, was there a standardization for the clinical or the duplex examination? And if so, how did you do that amongst these disparate and geographically separate sites?

DR. HOLM: No. There was no standardization. This study reflects reality around the country. That’s how our surgeons judge their patients. That’s how the laboratories determine if this is an insufficient vein or not and that varies in different laboratories. So about half of the surgeons used hand-held Doppler and about half of the laboratories used a time definition of what is an insufficiency or not. In reality the problem of defining an insufficiency as reflux of half a second or one second or two seconds was a very rare problem. I think it was clear in most cases if it was a competent vein or a vein with clear insufficiency.

DR. DEPALMA: I really enjoyed this study because it’s precisely what we found in a paper published four or five years ago, and someone accused us of not being able to use a hand-held Doppler. However, the question I would like to ask is did you have a look at how obese the patients were? It seems that the results with the hand held and the physical examination are worse when the tissue overlying the venous structures two and a half centimeters. Did you have any idea of that?

DR. HOLM: I’m sorry. It was not part of the protocol, and it would be very difficult to reconstruct. I don’t know.

DR. DEPALMA: I’d be interested in the panel’s opinions about the penetration of the conventional hand-held Doppler perhaps as a limiting factor here.

DR. STRANDNESS: It’s not a limiting factor, Ralph. It’s dependent on the transmitting frequency.

DR. O’DONNELL: Just a comment, first of all, about your gold standard. Unfortunately, I think using duplex ultrasound as your gold standard to judge where perforating veins are is fool’s gold. You really need to operatively identify it, No. 1, particularly in the light of Puric’s study which showed a very poor correlation between duplex assessment of where perforators were and whether they’re incompetent and evaluation at surgery. The second thing is about 25 years ago we showed similar results as far as identifying the perforator veins with continuous wave Doppler, but in assessing whether there was greater saphenous incompetence, the CW Doppler seemed to be little bit better.

THE VASCULAR LAB-DUPLEX IN REFLUX

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It appears to be well established that the changes in the deep venous system that can follow an episode of acute deep vein thrombosis (DVT) vary both in terms of location and extent. The primary changes that occur are the development of chronic occlusion and the appearance of valvular reflux.1,2 The factors that have a great effect on outcome are based on the extent of the abnormality and its effects on the hemodynamics of venous flow. While there is still some uncertainty and disagreement on the etiology of the post-thrombotic changes that occur in the lower leg, most investigators cannot escape the key role of altered pressure-flow relationships that develop particularly below the knee.3

With regard to the issue of obstruction, this can be documented both by venography and more recently by duplex scanning. This would not appear to be a problem given our advances in technology. The issue with regard to valvular function is less clear and open to more discussion both with regard to the distribution of the valves and their potential for causing problems when they become incompetent. The valves themselves have a distribution which obviously must play a role in their importance from a clinical standpoint. This factor must be considered as follows:4

1) there are no valves in the IVC;
2) in the common iliac vein approximately 1-7% will have a valve(s);
3) in the external iliac 24% will have a valve(s);
4) 67% of the common femoral veins will have one or more valves;
5) the superficial femoral vein will have one or more valves in 90% of individuals;
6) there is usually one or two valves in the popliteal area;
7) there are hundreds of valves in the deep veins below the knee;
8) there is commonly a valve at the point of entrance of the greater and lesser saphenous veins into the deep system. Valves are a constant finding in the major superficial veins but their numbers are variable.

It should be obvious that detection of valvular reflux can be of a global or segmental nature.5 Global reflux has been studied by plethysmographic methods by many investigators. This information will be presented by other speakers in this meeting.

Our interest extends back to when continuous wave Doppler was first used and demonstrated the capability of documenting the direction of venous flow as influenced by a variety of maneuvers. While this method could be used for segmental studies, it was hampered by the lack of an imaging component. To overcome these problems, we first began examining this problem in 1988.6,7

Our approach was based on the observation that reflux should be studied with the patient in the upright position where the effect of gravity can be taken into account. The procedure involved the use of segmental cuffs placed at several levels of the limb. The cuffs were as follows:
(1) upper thigh-24 cm;
(2) 12 cm for the calf;
(3) 7 cm for the foot.

With the patient standing and the transducer of the duplex scanner placed just proximal (toward the heart) of the upper end of the cuff, the cuff would be rapidly inflated for a period of 3 seconds after which the cuff was deflated very rapidly (within 0.3 second). The inflation/deflation sequences are repeated for each level of the limb with the time of valve closure vs. reflux are documented on a strip chart recording. In our study of normal subjects (N=32), 95% of the valves achieved closure in <0.5 seconds.

Since many labs might not be able to use the cuff method, we studied the effects of using the Valsalva maneuver and limb compression with the patient in a -10 degrees of Trendelenburg. When this form of study was done the time to valve closure in normal subjects was 1.77±0.96 sec compared to 0.69±0.83 sec (means and SD). In clinical practice we suggest that a valve closure time of <0.5 sec be used for the upright cuff method and <2.0 sec for the -10 degree position.8

A major advantage of this method is that it can be used to document segmental reflux in the position which leads to the major pressure and flow relationships on the venous system.9,10 A disadvantage is that we have not yet been able to document the extent to which the duration of reflux influences the outcome after an episode of DVT.

References

DISCUSSION

DR. SUMNER: Gene, how important are the below knee valves to the exam and do you look at the peroneal, posterior tibial, anterior tibial, and the whole gamut on each study or what?

DR. STRANDNESS: Well, let's go back to the patient with varicose veins. I want to know two things. Number one, is the deep system competent or incompetent and that would also involve looking at the veins below the knee. The second thing I want to know is exactly what elements of the superficial system are incompetent. In our research studies we look at all these views. We look at the posterior tibial, the peroneal. We don't look at the anterior tibial. I think Tony Comerota made a point about that. Why this vein doesn't get involved, we don't know. We look at the greater saphenous and also the lesser saphenous. So we can map out at each visit exactly which segments are incompetent and which are not.

DR. RAJU: Dr. Strandness, is there any way to quantify all of this?

DR. STRANDNESS: No. One of the disadvantages, of course, is we can't relate necessarily the reflux time, to the long-term outcome. We can't do that yet. I don't know of any way at the present time to document that. Perhaps you know a better way to do this, but from the standpoint of ultrasound, all you can say is the valves in the segment which you're looking at have a valve closure time which is abnormal. That's all you can say.

DR. RAJU: Can you calculate the volume from the diameter?

DR. STRANDNESS: I think whenever you start trying to calculate volume flow in the arterial or the venous system using ultrasound or actually any method, it becomes very difficult. I would caution trying this since any changes in the diameter of that vein invalidate the measurement. There are also considerations with regard to ultrasound per se that also make it difficult.

DR. GOREN: I have a very simple question concerning both duplex and Doppler examination: Can the presence of a competent valve in the common femoral vein cover up - during VALSALVA maneuver - an incompetence of the saphenous femoral junction?

DR. STRANDNESS: That's a good question, Dr. Goren. That's something I've thought about. When I put these slides together and was looking at the anatomic distribution of the valves, I asked myself the same question, would a competent valve in the common femoral vein, invalidate what you want to look at in the thigh, in practice this does not appear to be the case, but I think it's a consideration that we have to take into account.

DR. RAJU: Ken Myers published a paper saying just the opposite. Ken, do you have anything to say about that? Your publication in the Journal of Vascular Surgery basically said the deep venous reflux of the common femoral and popliteal veins were almost always associated with short and long saphenous reflux.

DR. MYERS: Yes. I don't see how you can get reflux down into the long saphenous vein unless there is reflux through the common femoral into that vein. So we defined common femoral reflux as reflux to the vein below the saphenofemoral junction. Three years ago I asked the question here and I ask it again. I don't understand how short saphenous reflux occurs given that virtually all of our patients have competent valves in the superficial femoral vein. Where does the blood come from?

DR. COLERIDGE SMITH: Well, the answer is quite simple, Ken. It comes through orthograde flow, up the popliteal vein, below the saphenopopliteal junction.

DR. MYERS: No, that's not right because I've got short saphenous reflux, and if I elevate my leg to empty it of blood and then hang it down, it immediately fills, but my deep valves are normal. So where does the blood come from?

DR. VOLKMANN: There might be small muscular and perforator veins one wouldn't see with the Doppler which may be the source of distal leakage you are addressing.

DR. MYERS: Within two seconds? It seems too quick for me.

DR. VOLKMANN: I have another question to Dr. Strandness. Do you agree that there might be a possibility to state falsely competent valves in cases of widened axial collaterals or doubled pathways where the blood is going through these pathways and not through the vein you are focusing the Doppler on.
The air plethysmograph, or APG, (ACI Medical, Inc., Sun Valley, CA) is a powerful research tool which has contributed substantially to our better understanding of lower extremity venous disease. The APG quantifies several hemodynamic factors associated with varicose veins and skin changes of the leg such as: obstruction (OF), venous filling index (VFI; a measurement of reflux), ejection fraction (EF; a measure of calf muscle pump efficiency), and residual volume fraction (RVF; an estimate of ambulatory venous pressure). With this ability to quantify various hemodynamic parameters, however, arose further questions regarding the interpretation of APG test results. Several such questions included: 1) Are APG test results reproducible?; 2) Is APG a good test for venous obstruction?; 3) Can APG distinguish between sites of reflux?; and 4) Is APG important for daily practice?

Are APG test results reproducible?
Katz, et al.1 studied 50 legs in 25 healthy volunteers and found good test-retest reliability for venous volume (VV), VFI, EF, and RVF. The correlation coefficient for RVF was lowest (0.63), perhaps influenced by the vigor with which a patient performs the 10 tiptoe exercises. The volunteers also showed a statistically significant decrease in VFT90 (time to achieve 90% of venous volume) and an increase in VFI from 1.9 to 2.3 ml/sec (p=0.039), when comparing morning to late afternoon measurements. The authors detected no daily variation in EF or RVF. Seven of 50 extremities (14%) in 5 volunteers (20%) had a normal VFI in the morning which became abnormal in the afternoon, although the differences were very small in 5 of 7 limbs and could be explained by increases in resting arterial inflow. This study points out that valvular incompetence may develop as a consequence of daily activity. Yang, et al.2 examined the variation and reliability of APG parameters in 17 patients (18 limbs). They found that the coefficients of variation for repeated measurements ranged from 7.5 to 27% for most APG parameters. VFI and EF showed moderate degrees of variation when measured on different days (coefficient of variation/method error of 13.4% and 10.7%, respectively). In addition, the difference between the mean of 3 tests and mean of 10 tests for most APG parameters varied from -8.6% to 5.0%. These variations were deemed acceptable in daily practice and argued that performing more than 3 tests was unnecessary. They concluded that APG is very unlikely to detect small changes in VFI and EF, an important fact to consider when assessing treatments designed to improve calf pump function or reduce reflux.

Is APG a good test for venous obstruction?
The relationship between OF by APG and arm/foot venous pressure differential is illustrated in Figure 46, page 61 in Reference 3. The figure compares OF in 15 limbs with deep venous reflux but no obstruction (arm/foot pressure differential < 5 mmHg) to 8 limbs with venographic deep venous obstruction (arm/foot pressure differential > 5 mmHg). The median value and 90% range for each group are clearly discriminated, lending support for OF by APG as an accurate and non-invasive method of determining the severity of outflow obstruction. Belcaro, et al.4 provide a superb summary of data relevant to variability of APG parameters and obstruction.

Can APG distinguish between sites of reflux?
APG primarily measures thigh to calf reflux. APG may not detect isolated thigh or isolated calf vein reflux. It may be useful in determining the relative contribution of deep versus superficial vein reflux in those patients who have combined deep and superficial venous incompetence. One must also consider the effect of increased arterial inflow due to hyperemic skin or exercise (eg. 10 tiptoe movements needed to determine RVF) when interpreting the VFI.

Is APG important for daily practice?
For most patients with primary varicose veins and/or spider veins, the parameters measured by APG have little or no impact on their surgical or medical management. The separation and quantification of each parameter is most important in more complex patients with combined obstruction and reflux which may involve superficial, deep and perforating veins. Nicolaides, et al.5 discuss in detail how APG impacts on patient management in an excellent summary monograph. Further, Bays, et al.6 compare APG to PPG for measurement of clinically significant venous reflux and note the high sensitivity of PPG refill times to identify reflux (100%), but low specificity (60%). They conclude that the combination of APG and duplex scan currently provide the best means to assess venous reflux. Some vascular labs now use APG as a screening tool to identify the presence of obstruction or reflux and allow a more focused and comprehensive venous duplex examination.

The above questions are but a few of those which arise during interpretation of the APG test. We hope this topic will stimulate further discussion on the role of APG (and other methods) in the study of chronic venous disease.

References

DISCUSSION

DR. PADBERG: That was a very nice review, Paul. I would like to bring one point into focus, and that is the variability that we’re talking about in VFI which has raised a lot of concern amongst the faculty and other members that are dealing with venous disease. It’s really the same level of tests/retests reproducibility which we have all accepted many years ago as part of the ankle/brachial index. You recall, I’m sure, the discussions in the journal several years ago about whether it should be 10, 15, 20 percent, and by and large most of us accepted a 10 to 15 percent variance. So this is clearly within that ballpark. As regards the time of day issue, we’ve been wrestling with that too as part of a research study that we’re doing that it does involve APG measurements. And recognizing that it’s only 10 percent, I wonder if we ought to just take Tony’s number of two and make it 2.5, in which case even your afternoon study is within the normal limit. It doesn’t matter when you do the test if you’re willing to accept that. One other final comment. You mentioned APG and its variability in terms of looking at the time and usefulness in practice. Although we haven’t used it for that, we have noted, as has Andrew Bradbury in the Edinburgh group that an abnormality in the VFI, meaning it’s gone from normal to abnormal. They used foot volume plethysmography, a similar test of reflux and its volume, which presaged the identification by duplex exam of surgically correctable venous insufficiency, in their case a missed popliteal and – lesser saphenous and saphenofemoral recurrence.

DR. CORDTS: Although we’re five miles away from Straub, we do very little deep venous reconstruction, and I would say that we infrequently use the test. I use the test on occasion to confirm the findings of the duplex scan prior to surgery in patients with primary varicose veins, but for the most part, it’s confined to patients in whom I’m contemplating deep venous reconstruction. So I think what it’s helped me do is more in understanding the pathophysiology of the disease than helping in the management of a patient on a day-to-day basis.

DR. RAJU: We also found that VFI-90 is useful. VV sometimes is useful. The RVF and other parameters are generally not useful.

DR. THORPE: Dr. Rutherford and others encouraged me to do hemodynamic testing on a lot of patients we’ve treated, and what I’ve found in the before and after APG, and I wondered if you’ve seen this, although you say you don’t do a lot of deep venous reconstruction, it is that if the outflow fraction is decreased, then that leads you to think that there is obstruction. But in many of our patients we see total obstruction of the iliac system and there is such good collateral flow that the outflow fraction is absolutely normal. And, in fact, you don’t see any reflux until you open that up and get enough flow. So you get a normal reflux index and a normal outflow fraction when they have significant obstruction and significant reflux. How often do you think that’s happening?

DR. CORDTS: I don’t know, but I worry about it. The outflow fraction portion of the APG: my understanding of it is woeful at this point. I don’t understand how a single bolus of blood from the thigh (the OF test by APG) can adequately test, for example, a common iliac vein obstruction. Perhaps the arm foot venous pressure differential is better, but I’m sure that the outflow fraction by APG is not adequate.

DR. STRANDNESS: I just have one question. Can you distinguish the level of reflux in terms of segments and its effect on VFI? In other words, common femoral, superficial femoral, below the knee popliteal. Have you tried to break it down and segment the VFI.

DR. CORDTS: I’m not sure we have. Dr. Strandness. If you have a competent popliteal valve, you may have a normal venous filling index. So you may find incompetence by duplex scan, but you have a normal venous filling index.

EVALUATION OF OBSTRUCTION

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Ascending and antegrade transfemoral phlebography is the time-honored way to describe venous obstruction. Injection of contrast dye into the venous system may delineate the distribution and nature of the morphologic changes, including occlusion, stenosis and presence of collateral circulation, but does not provide any information whether there is a significant functional hemodynamic obstruction to the venous outflow or not. The development of collaterals can either be seen as an indicator of obstruction with an attempt to compensate a significant obstruction, or a compensatory mechanism neutralizing the outflow obstruction by bypassing it. The mechanism and induction of collateral formation are unclear.

The degree of hemodynamic obstruction depends on multiple factors, e.g., the number, location, degree of narrowing, and length of the lesions, development of collaterals, and the volume flow varying at rest and during exercise. To achieve proper sensitivity of any laboratory test, outflow must be augmented to a reproducible and physiologic level to be able to detect a significant obstruction and assess result after reconstruction.

Obstruction in the post-thrombotic lower extremity is especially difficult to evaluate. It would be easy to accept the lesion as causative in a patient with a unilateral lower limb swelling and pain, and radiologic finding of an isolated single obstruction in the iliac vein. Such a lesion could be caused by tumor, enlarged lymph nodes, retroperitoneal fibrosis, trauma, vein compression by the transversing artery etc. Additional information is necessary to direct treatment in a lower extremity with post-thrombotic disease with a combination of multi-level reflux and obstruction involving the whole limb and the iliac segment.

There is to date no dependable non-invasive method to assess outflow obstruction in chronic venous insufficiency. Calf vein outflow fraction determination using plethysmographic methods is reliable in acute axial vein thrombosis, but it may be falsely negative in the later chronic course of the disease. Alternative non-invasive methods are under evaluation. Instead of using the simple outflow fraction, the outflow curve can be analyzed by plotting the volume
The invasive test combination of the arm-foot vein pressure differential and the foot vein pressure elevation after reactive hyperemia seems to be the most reliable investigation currently available for detection and grading of global obstruction. However, the hyperemia flow induced by the tourniquet ischemia may not be reproducible in repeat tests or the flow high enough to detect a significant stenosis in all conditions. An additional disadvantage is the inability to define the location of the most significant obstruction in multi-level disease. No correlation has been found between this method and the number and sites of obstruction or development of collaterals.

Invasive pull-through pressure gradient over a lesion or pressure increase peripherally to the lesion with augmentation of venous inflow may be indicative of a significant stenosis. For this purpose transducer-tip catheters can be used with high accuracy. Augmentation of flow can be induced by twenty forceful calf muscle contractions by an awake patient, by injection of papaverine (30-60mg) into the ipsilateral femoral artery and by ischemia induced by a tourniquet (300mmHg pressure for 3 min). It appears that a pre-stenotic pressure rise of >2-4 mmHg on provocation and a slow return to base level (>30s) indicate a hemodynamically significant obstruction. The critical value for venous pressure gradient in borderline obstruction needs to be further elucidated. The main difficulty is the lack of a "gold standard". The result may have to be related to clinical outcome after treatment. Certainly a much smaller gradient than encountered in arterial disease will be significant.

Intravenous ultrasound (IVUS) has been shown to be superior to phlebography in detecting the morphology of the obstruction. This device accurately outlines the configuration (circular structure or slit like), length of obstruction, and vein wall density. It is probable that the flow through a compressed vein is inhibited as compared to a circular vessel, even if the transverse surface area is the same. Software built into the IVUS apparatus allows accurate calculations of cross-areas and diameters.

The interest in obstruction is on the increase as percutaneous endovascular procedures are refined to facilitate the treatment of venous obstruction. Therefore, it is important to find reliable tests to identify critical lesions and for post-operative objective assessment. Although obstruction is considered less important than reflux in the pathophysiology post-thrombotic disease, as many as 20-30% of patients have significant contribution by out-flow obstruction. When tests become more refined, this figure may be shown to underestimate the importance of venous obstruction.

**DISCUSSION**

**DR. SUMNER:** I didn’t quite catch whether you measured the popliteal venous pressure at the same time you measured the pressure at the ankle?

**DR. NEGLEN:** Yes. We’re inserting two Millar™ probes, transducer tipped catheters, and place them at the same level in the popliteal, and long saphenous veins, and simultaneously you measure the dorsal foot vein pressure with the transducer at catheter tip level.

**DR. SUMNER:** What’s interesting is that Ludbrook did this same sort of study many years ago (1963). He found that there was only a modest decrease in popliteal venous pressure after exercise - the decrease being roughly the same in normal limbs and in limbs with varying degrees of venous reflux. While venous pressure at the ankle decreased markedly after exercise in the normal limbs, ambulatory venous pressure in limbs with incompetent valves was abnormally high. So it seems that, in contrast to the venous pressure at the ankle, popliteal venous pressure is relatively unaffected by the presence or absence of venous reflux.

**DR. NEGLEN:** No, this is true. This is our observation too, that in many patients with normal venous hemodynamics in all tested aspects, that pressure fluctuations are limited. However, usually we find a slight 20 to 30 percent decrease in popliteal vein although it might be 50 or 60 percent in the dorsal vein. But in 10 to 15 patients we have actually seen an increase of the pressure in the popliteal vein which has not been described before. This must be due to some sort of outflow obstruction at the knee level or above, which does not reveal itself in other hemodynamic tests, e.g. the dorsal vein pressure. I agree with you that there is very little fluctuation in normal patients with exercise in the popliteal vein.

**DR. STRANDNESS:** If you have an outflow obstruction and you exercise the pressure in the vein below the occlusion has to go up. John Hobbs, for example, many years ago showed that if you look at people with venous claudication, a key factor is the great increase in venous pressure that you get with exercise.

**DR. NEGLEN:** I agree. The point is that these patients have normal outflow fraction, normal dorsal foot vein pressure, no reflux, and will not be found to have any venous problem unless you do the popliteal vein pressure measurement.

**DR. PADBERG:** I’d like to congratulate the both of you for tackling one of the issues that I think really leaves all of us many questions, and that is how do we define obstruction? It’s something we do very poorly. Although it’s a part of all of our scales, there’s very little of it that we really don’t have a precise definition for obstruction. As you pointed out, it really takes a lot of obstruction to get to the point where the collateral capacity is overwhelmed. My question has to do with IVUS. I presume that you do this as an intraoperative event since most of the valves are competent -- unless you’re studying only incompetent veins, you would have to pass it from below up; is that correct? Tell us a little bit about that.

**DR. NEGLEN:** We are performing the IVUS investigation during surgery, and we have only used IVUS in obstruction detection in the iliac segment from the common femoral proximally. It is used in situations with presence of pelvic collaterals, but no obvious obstruction detected on the venogram. In that situation it can be performed in the radiology suite or in the OR. We have used IVUS in the OR since we have an interventional suite. It is helpful evaluating obstruction in post-thrombotic disease but more so in other types presence of collaterals, due to non-thrombotic obstruction e.g. iliac vein compression syndrome. We have found significant difference between degree of obstruction seen on the venogram compared with the IVUS. Very short obstructions have been drowned in x-ray contrast, but revealed with IVUS.

**DR. PERRIN:** I have two questions. The first one is can you give us more details on how you measure the pressure at the popliteal level and at the femoral level? And second, sometimes femoral
obstruction is very difficult to assess. Have you tried to compare the pressure gradient between femoral and popliteal veins?

DR. NEGLEN: After the insertion the level of transducer tips are directed by fluoroscopy. So we know the exact anatomical level. Then we stand the patient up and she/he does 10 toe stands similar to the ambulatory venous pressure. So that’s the exercise inducing the hyperemia. The second question was?

DR. NEGLEN: No, we haven’t done that. That is what is in the pipeline, and we would like to do it in awake patients that are erect. So that’s why you need to push the catheter, if you can, all the way up to the femoral vein and then do a pull-through pressure measurement with that catheter. We haven’t done that.

DR. VOLKMAN: We in Sweden have a long tradition of using plethysmography for detecting outflow obstruction in the lower leg, and I would like to comment on your statement about the usefulness of this method in patients with venous outflow obstruction. In the acute state of venous obstruction when there haven’t been developed any collaterals, you will find a delay of the venous outflow using one of the available plethysmographic methods. In the chronic state, of course, I agree that one might find totally negative findings. That’s why we have not done that, but I would like to comment on your statement about the usefulness of this method in patients with venous outflow obstruction. In the acute state of venous obstruction, when there haven’t been developed any collaterals, you will find a delay of the venous outflow using one of the available plethysmographic methods. In the chronic state, of course, I agree that one might find totally negative findings, i.e. normal outflow rates through collaterals, and that this might occur in cases of thrombosis of the proximal abdominal veins.

DR. NEGLEN: Yes, I agree with you. I failed to tell you that this is a study in chronic venous obstruction. We know this from IPG and other plethysmographic studies done in the United States through the years when before we got the duplex Doppler to diagnose DVT with an acute obstruction. Of course it is of no value today to be used in diagnosis of acute DVT since we’re using duplex. It has been shown that when the condition also shows exactly what the fact is, that when it turns chronic, the IPG is of no use and neither is the APG.

DR. VOLKMAN: I have another comment on the different time constants within the venous outflow curve such as addressed in your speech. As more centrally the obstruction is situated, as faster outflow rates will be observed initially, due to the filling up of patent vein segments in the nearby of the gauge. Then, in the later stage, you might observe a slowing down of the venous outflow rates, since the patent vein compartment is filled up, and venous outflow now is limited by the obstruction itself.

DR. NEGLEN: Oh, I totally agree with that. That is our hypothesis. You can have these resistances and capacitances either in line with each other, being the proximal and distal, or maybe beside each other too. You have exactly described our hypothesis.

DR. ABU-BAKER: So I would like to thank you for your very excellent presentation. My question is how can you use intravascular ultrasound in segmentary superficial thrombophlebitis.

DR. NEGLEN: Well, you seem to have an interest in superficial phlebitis. I don’t think that we should use the intravascular ultrasound at all with superficial thrombophlebitis. I think we should, use duplex scanning for diagnosis, if necessary. IVUS doesn’t have any role in superficial thrombophlebitis.

DR. TRIPATHI: I have an idea. I want to propose a new way to measure pressure differential other than the arm-foot vein differential -- this question is to Dr. Raju. I wanted to ask you if it would be better, if one femoro-popliteal venous system is involved with deep vein obstruction and the other leg is not, then if you put a transducer or a cannula into the opposite side femoral vein and then do a proximal foot to distal femoral venous differential because you’re measuring pressure & flow in contralateral unaffected femoral vein which is good control to the vein which is affected, that would give you a more accurate idea of the differential than the arm to foot.

DR. RAJU: We haven’t tried that really.

DR. TRIPATHI: That’s why I said it’s an idea.

INVASIVE PROCEDURES: DESCENDING VENOGRAm

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It has been known for some time that there is very poor correlation between descending venography and global physiological measures of reflux such as ambulatory venous pressure measurement and Valsalva foot venous pressure measurement. In an analysis of 56 lower limbs presenting with chronic venous insufficiency, the positive predictive value and negative predictive value of Duplex examination in the erect position to diagnose class 4 or higher skin changes were 86% and 78% respectively. The corresponding figures for descending venography using the Kistner classification was 44% and 63% respectively. As a result duplex examination in the erect position has superseded descending venography to identify clinically relevant refluxive venous valve segments. The technique of descending venography does remain indispensable to the operating surgeon to provide the anatomical detail necessary for surgical exploration. In this context, a hard copy record of valve station locations, anatomical position of the axial vein and tributaries as well refluxive collaterals are very helpful to the surgeon in the operating room. Descending venography is not always reliable in predicting the absence or presence of repairable valve leaflets at the valve stations; both false positive and false negatives occur. Repairable valve leaflets during surgical exploration were actually found in 25% of cases (n=24) predicted to have no repairable leaflets based on preoperative descending venography. Presumably massive reflux of contrast through the valve station had obscured the presence of leaflets. Conversely, among 118 cases thought to have repairable valve cusps based on preoperative descending venography, none were found at surgery in 11%; trabecular strands and intimal thickening had mimicked the appearance of valve leaflets on descending venography and had been falsely interpreted to represent such. In view of this, an axilla is always prepared and kept ready for an axillary transfer procedure, even when a direct valvuloplasty appears feasible on preoperative descending venography.

Since the role of descending venography has changed from diagnostic to one of preoperative roadmap in recent years, earlier arguments regarding the best technique to perform the procedure have now become moot. For example it was argued that the supine technique of descending venography was more specific than the 70% erect technique. Considering the changed role of descending venography, the best technique at the present time is clearly one that
produces the best and most extensive reflux contrast opacification of the venous tree. A 60% head elevation with standardized Valsalva yielded 84% reflux opacification of the distal venous tree compared to only 42% opacification with the patient in the supine position performing a standardized Valsalva technique. The former technique is therefore in current use in our institution.

**References**


**DISCUSSION**

UNIDENTIFIED SPEAKER: Just looking at your presentation, it reminds me that we’ve been trying to assess obstruction also in another area which is the ovarian veins, and we always used an angiography which gives us a very precise delineation of where the flow goes and where collateral go and that gives you a very good idea what to do surgically or nonsurgically. Have you used that video angiography in your cases in which you are going to do surgery any or do you use static images like you showed?

DR. RAU: Until about two years ago we were using static images in our institution, but they have new equipment and they use cine and these are representative cut films. I think that’s the way to go.

DR. KRYLOV: Can you tell us because your presentation is very persuasive, over 400 venograms carefully evaluated, what will be your personal decision if you were to have a patient to be operated on with a reconstruction of the valves which you will do? Would you operate on him without the venogram only on the basis of the duplex examination? I can tell you that my question is based on my personal negative experience because I was persuaded by the radiologist. He showed me that the valve is present and when I opened the vein, I didn’t find the valve. What will be your policy in that case?

DR. RAU: Well, as I said, we always keep one axilla prepared. If you don’t find a valve, you go on to an axillary vein transfer. We do an axillary vein transfer if we don’t find a valve.

DR. KRYLOV: So your answer is positive? You will operate on the patient without performing a venogram?

DR. RAU: We never operate on a patient without a venogram.

DR. KRYLOV: Always to make the venogram?

DR. RAU: Yes.

**DIAGNOSIS OF VENOUS ULCER – THE ST. THOMAS’ WAY**

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The diagnosis of a venous ulcer at St. Thomas’ is initially based on clinical assessment. A history of venous thrombosis or varicose vein surgery is indicative of a venous ulcer, but the classic appearances of a medial or lateral sloping edged ulcer in the gaiter region of the leg surrounded by lipodermatosclerosis is strongly suggestive, providing there are normal pedal pulses and a normal doppler pressure index. We measure the hemoglobin, auto antibodies and blood sugar routinely and then apply compression therapy.

Definitive diagnosis is only made when healing has occurred. All patients then undergo duplex scanning of the deep, superficial and perforating veins and have a foot volumetry study performed. All patients also have bipedal ascending venograms to assess the presence of post thrombotic damage, which at present, influences our management and also affects the subsequent prognosis of the ulcer.

We have shown that the duplex scan cannot detect all cases of post-thrombotic damage, and although we have abandoned descending venography, we still carry out standard bipedal ascending venography in all patients. An abnormal half refilling time on foot volumetry is used as the index investigation for diagnosing or undiagnosing venous ulceration. This cannot be measured accurately until the ulcer has healed. Atypical ulcers are excluded from trials and are usually biopsied ab initio.

**DISCUSSION**

DR. MYERS: The first thing, I would have to say Kevin, is that I’m delighted that we agree on so many points. I’m also delighted that you have plenty of time in your consultations to go through all of these things that I also go through. Of course, I limited my talk by being required to limit my presentation to ten minutes only whereas I noticed that you spoke for several minutes beyond your allocated ten minutes so that you had much more to say, including many points that I would have liked to have made. Now I’ll limit my response to a couple of points because we have so many people who want to ask some serious questions. If you wish to come and show us how to do a tourniquet test, that’s fine. However, don’t show me your colleagues. Show my ultrasonographer. I’ll back him every time. He’ll show you reflux better than you can with your tourniquet. So I think you’re wasting your time, even if you are better than me, which is quite probably true.

DR. VOLKMAN: We are also using foot volumetry, and we believe also that it is a valid method for assessment of venous function. However, we have a problem with venous ulcers which are usually located at the place where the foot is exposed for the water level of the plethysmograph. So how are you doing?

DR. BURNAND: I’m sorry. You didn’t get the message of the talk which was essentially we do a clinical diagnosis providing that we’re happy that they’ve got a venous ulcer, and that diagnosis is always confirmed once the ulcer has healed. In other words, we do not do the foot volumetry at the time that they have an open ulcer. It’s obtained once the ulcer has healed and I think that’s important because I think if you’ve got a patient with a big open ulcer on the medial malleolus they cannot adequately exercise their calf pump. We’ve got some evidence to show this. We have done the test in patients with open ulcers and shown that they get a considerable improvement in their half refilling time once the ulcer has healed.

DR. STRANDNESS: Kevin, I wanted to ask you a question. If you had a patient who comes in with an ulcer in the gaiter area with pigmented skin, he has incompetence in the deep venous system, and a history of deep venous thrombosis in the past, are you going to do foot volumetry, ascending venography, descending venography, APG? I think this gets to be a bit ridiculous in terms of the workup. What are you doing all these tests for when you’ve got a simple...
straightforward problem like the one I mentioned?

DR. BURNAND: Well, I’m doing the test because if I don’t do the tests, I won’t have enough information to give you on the CEAP classification in order that I can actually put the patients into a study, that you will accept. So all the patients that we’re doing that are part of clinical studies. If we weren’t doing the studies, if you’re asking me to what I’d limit the investigations to. I would do an anatomical test on all patients, an ascending venogram. I think Peter Neglen made the argument very cogently. I actually would go along with Raju too on this that I think there’s not much doubt an anatomical test is helpful, and I would do a foot volumetry as my one other test. I’d be really interested to hear what your thoughts are about the nature of the ulcer if you discover saphenous reflux on duplex scan. Gene. I’m not talking about popliteal reflux this time. I’m talking about just long saphenous vein reflux. Does that prove the patient has got a venous ulcer?

DR. STRANDNESS: Well, of course not. The great majority of patients with greater saphenous incompetence never develop venous ulcers. That’s why you scan the deep venous system in patients who present with a venous ulcer.

DR. BURNAND: So we can all agree that 80-90% of the ulcers are venous. The problem comes with the other 10-20% where there’s a great deal of doubt. What are you going to take as your gold standard test for diagnosis in these cases.

DR. STRANDNESS: If you want to talk about anatomic verification of the site of disease, then I don’t think venography is any better than duplex. And, in fact, the best studies that have been done in the United States looking at the problems associated with venography were done at the Massachusetts General Hospital by Dr. Athanasouls. He noted that with an injection on the dorsum of the foot, you see the profunda femoris vein half the time and you see the iliac veins only 20 percent of the time. In the United States of America right now, at present, we can’t do ascending venography on a routine basis to evaluate people with venous disease. This is not going to sell. It’s too expensive, it’s painful, and it causes complications.

DR. BURNAND: Well, can I just answer that very briefly? In terms of the profunda femoris vein I agree. It’s sometimes extremely difficult to see that. In terms of the iliac veins, that’s simply not our experience, and we can show you the venograms. We get good views of these vessels. It depends on how you do the venograms. In terms of the pain and the other problems, a lot of these have been eliminated by the use of nonionic contrast media. Most of the problems are that people have done really very poor quality venographic studies, some of which we’ve seen today. The picture that I showed you of the IVC and the iliac veins was done from a peripheral leg injection, not from proximal leg injection.

DR. STRANDNESS: Kevin, there’s no doubt that some people - I said that 20 percent of the time with an ascending venogram you can’t see the iliac veins. I know in England that what you often do is you stick a needle in the common femoral vein to get the rest of the examination done. I’m just saying that in the United States, we cannot do venography on every patient who comes in with venous disease.

DR. BURNAND: But it seems in Jackson you can; is that right?

DR. RAJU: Those patients go to surgery. So it becomes justifiable, I think.

DR. PADBERG: What a wealth of things to discuss. Like you, we’ve had several problems identifying what the other components of ulceration may be. In my experience I find that the majority of patients who fall into that “I won’t heal” category are very often nonvenous and nonarterial. We get to the answer and we fix that. Your laundry list I guess leaves us all a little bit overwhelmed. I’m sure some of those are English diseases alone, but sickle cell of course should be checked, as you have, for those of the appropriate genetic background but psoriasis is a real tough problem for me. How do I distinguish the psoriatic who has evidence of venous disease from someone who has a venous origin ulcer, whether we call it varicose or post-thrombotic? Along the same lines, the question of your testing to identify venous or nonvenous demands that you do a physiologic hemodynamic test. So I assume from your discussion with Gene, that a duplex is totally insufficient to do that.

DR. BURNAND: We’ve looked at duplex, and we’ve done it purely on the basis of duplex. That will under-read the abnormalities you get from a calf volume, refit test. Some of the time I think that the duplex scan demonstrates superficial reflux in limbs that have another cause for their ulceration. Then in other limbs you’ll find a normal duplex, and yet the calf pump is inadequate. Whether this is because the patient has osteoarthritis of the knees, whether it’s because they’ve got a fixed ankle, I don’t know, but I don’t think there is a one perfect test that says that the patient has a venous ulcer.

DR. PADBERG: Is that why you still have that chapter in your book on calf pump dysfunction as opposed to the others?

DR. BURNAND: Well, yes. Norman is very keen on that, and I think he’s probably right. It isn’t just an overall thing. I get upset when I hear people just talking about reflux and obstruction as the only problems because there’s probably more to it than that. And actually, Peter Neglen said something good again today that we could agree on. That there’s a sort of physiological obstruction from the peri-fibrotic changes around the vein. If you operate on a post-thrombotic valve, you find that you have to actually dig out of the surrounding fibrous tissue, and this must in some way be helping to cause the post-thrombotic physiological obstruction that Peter was talking about.

DR. MYERS: To try and be a little bit serious, could I make a comment about that list? I couldn’t see the list from here but it looked to be pretty comprehensive to me. However, let’s be real. I’ve never diagnosed any of those conditions at the first visit. I don’t make a great effort to distinguish them early on and I’m interested that you required a biopsy to take and confirm that carcinoma - even I would have picked that one. I’m talking about most of the patients who come into my rooms, most of whom have either venous, arterial or mixed disease. Now, the way that I sort out the rest of those patients is not to spend half an hour with them totally befuddling them with a whole variety of peculiar questions about peculiar diseases at the first visit. These will emerge within the first few weeks of my treating them. If that ulcer conforms and does all the right things that I expect with my regime of treatment, then I will continue to treat that ulcer until it heals. If it shows any unusual features whatsoever either in the history or the examination as it unfolds, or failure to heal as I would expect, then I have a very low threshold for taking biopsies and even taking a history and examining the patient. We’re not in disagreement. I think that your comments are a little bit excessive.
REcurrent Varices After Surgery (REVAS)

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REcurrent Varices After Surgery (REVAS) are a common, complex, and costly problem. Frequency of REVAS is stated between 20 to 80% depending on the duration of the follow-up assessment and the definition given to this status. The consensus meeting (Paris 1998, July) decided to adopt a clinical definition: presence of varicose veins in a lower limb previously operated on for varices, that includes: true recurrences, residual veins and varicose veins due to progress of the disease. There are no socio-economic data relating to REVAS at present. Its pathology has been poorly correlated with clinical examination and operative findings.

Clinical diagnosis including continuous wave Doppler examination (diagnosis level 1) remains essential but does not allow a precise assessment of REVAS. Consequently, the use of imaging investigations is mandatory. Duplex scan is considered as the method of choice (diagnosis level 2) but venography (diagnosis level 3) remains a valuable tool. Both clinical diagnosis and imaging investigations allow proposing a classification for every day usage and forthcoming studies. This new classification is using the CEAP that has to be expanded to define Topographic sites (T), Nature (N), and Sources (S) of recurrence, magnitude of reflux (R), and possible contributory factors (F): general or/and specific.

Methods for REVAS treatment include compression, drugs, and operational procedures: sclerotherapy and redo-surgery. Operational procedures share the same goals: to eliminate reflux from deep to superficial systems and to suppress varices. Sclerotherapy and ultrasound-guided sclerotherapy have been used with different protocols but according to the working group this technique is worth further evaluation. Surgery techniques can be divided in 2 groups: Procedures intending to suppress reflux from the deep to superficial venous systems (sapheno-femoral or sapheno-popliteal junctions, pelvic veins, thigh and leg perforators) and procedures for eradicating varicose veins.

There was no general consensus at this time for using sclerotherapy, surgery or both to treat REVAS. Nevertheless it has been stated that indications for treating REVAS are dependent on patient’s complaint, clinical and instrumental findings. Very few data were available to estimate the REVAS treatment results.

Factors of recurrence and recommendations for primary prevention have been debated:

Factors of recurrence:
1. Recurrence due to residual veins in an incomplete primary planned treatment: tactical error, technical error, and incomplete treatment.
2. Recurrence due to evolution/progression of varicosed disease: there are no scientific data concerning the mechanisms responsible but clinical observation suggest a list of factors: sex, heredity, hormonal status (especially pregnancy), occupation, sports, nutritional habits, and deep venous reflux.

Recommendations for primary prevention:
1. Preoperative duplex mapping is strongly recommended.
2. Surgical technique: flush ligation of sapheno-femoral and sapheno-popliteal junctions, trunk removal is also recommended.
3. Perioperative treatment: Low-molecular weight heparin routine prescription is not mandatory and should follow general rules for DVT prophylaxis. Long term compression might prevent REVAS but no current data exist.
4. Follow-up: Patient should be assessed clinically and by Duplex early in order to identify persistent reflux and presence of residual veins. Long-term follow-up should be carried out in all patients a minimum time of 5 years. Post-operative sclerotherapy is thought to enhance the quality of surgical treatment results.

In conclusion, guidelines for well-planned prospective studies are strongly recommended.

Specific recommendations for future studies:

1. Epidemiology & socioeconomics:
Prospective epidemiological studies with adequate duration of follow-up are required in which risk factors, investigations, treatment procedures and socioeconomic aspects are documented in detail from the outset.

2. Pathology:
Better understanding is required concerning the correlation between pre- and postoperative patterns of anatomy and physiology, the interventions, whether surgical or sclerotherapy and the pathological processes of recurrence;

3. Patient Assessment:
Further studies on the relationship between symptomatology and objective assessments would be valuable.

The indications for intervention in venous disease should be fully documented e.g., by the CEAP classification and disability scores. However since the symptoms customarily attributed to varicose veins are in the main non-specific, they should be supported, in studies of recurrent varicose veins, by objective assessments with duplex scanning and/or tests of venous function before and after intervention. In order to evaluate and compare outcome therapies it is essential that patient populations be fully defined both in terms of their clinical status and the patterns of valvular insufficiency in the superficial and deep systems before and after the intervention.
4. Therapy:
Many prospective studies and clinical trials are required. A few examples follow.
• Risk factors for varicose recurrence.
• The relationship between varicose recurrence, pre- and post-operative patterns of venous insufficiency and the nature of their interventions.
• The value of routine preoperative duplex scanning prior to first time surgery for varicose veins.
• The value of routine post-operative scanning in the early detection and management of persisting reflux.
• The relationship between hemodynamic and clinical recurrence.
• The role of compression therapy in preventing recurrence.
• Measures to prevent neovascularization.
• Role of follow-up sclerotherapy after surgery in preventing recurrence.
• Ultrasound guided sclerotherapy versus conventional sclerotherapy in junctional recurrence and perforator incompetence.

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DISCUSSION

DR. VILLAVICENCIO: Michel, I enjoyed your review of the different causes of recurrence in varicose veins and we obviously have identified many of the ones you have mentioned. The reason for arising here is to warn our audience that aside from the prospective study, randomized or not randomized you will embark on to detect the causes, we will be seeing more recurrences in the future because there is an epidemic of ambulatory phlebectomies in which the saphenofemoral junction is not properly dissected and ligated. Also, the saphenopopliteal junction is just ligated with a vein hook. This has been done by some of our colleagues, I am very aware of that and it's been published too. So, I'm afraid that we will be seeing this problem more and more. I think the presentation/publication or your work should be of an urgent nature to bring to the attention of everybody doing surgery, which is the problem, and how to correct it. In our review of over 1,000 cases at the Military Central Hospital in Mexico City during the 20 years that I worked there, we identified, just like you did, the most important causes of recurrence to be the groin. This means an improper operation of the groin. That was number one. The other cause was missed perforators. We didn't classify exactly where they were, but we described them. The third cause was a combination of the two. Those are the two most important causes. Incomplete surgery at the junctions and also missing duplications. You may have a double saphenous vein and you missed one. So we must educate our people on anatomy and how to do a proper operation. I congratulate you on bringing this very important subject to us.

DR. PERRIN: I would say that happily in France the great majority of venous survey for varicose veins is performed by a vascular surgeon but, in fact, I would say phlebologists or angiologists who are not trained in surgery practice some treatment of the superficial venous vein, and probably we will find a lot of technical failure rate in REVAS. Neovascularization, it's very important. We have assessed our patients and it's common. We've identified now what are the factors that can lessen the number of neovascularizations. They have no answer. You know, a lot of papers have been published to put a patch to close the fascia, but we have no real significant data for that.

DR. RUTHERFORD: Michel, you said that your randomized trial was about ready, and I wonder if you can give us some details about the trial. Basically what are you going to be comparing, which two treatments? You have a lot of variables there that you obtained for us and I'm not sure how you're going to be able to stratify your groups in a way that will make them comparable when you compare treatments. So could you give us a little more detail on that?

DR. PERRIN: Okay. I think the most important thing was classification. We will establish a forum based on the classification, and as you have seen, we have a lot of information on that probably that could help in order to -- because a lot of different situations to find out what is the best way to treat them, to investigate them, but we don't have the answer. It's just the starting of the study, but the forum, I think, will be in a few months because it's submitted for publication to a very good international journal. I am awaiting their answer. That is my answer.

DR. EKLOF: It was a pleasure to be part of this consensus conference. As it happened, on the 12th of July the French won the World Cup in soccer. On the 13th they had the big parade with the French champions on Champs Elysee, and on the 14th it was the National Day. I don't think France had been on such a nationalistic top since the French revolution as it was during these three days and then the meeting started. So all our French friends, they were really geared up, and Michel and Jean Jerome particularly had done a great job to prepare this conference through the French group. We had the CEAP and now we have the REVAS and we have the French C in CEAP. There is so much going on which is absolutely necessary to be able to progress in this field of venous surgery. Why I rose was basically to ask you about publication. Where do we stand right now? I think it's important that we get this out. Like CEAP, which is published now in 24 international journals all over the world. So at least the base is out and the same should be true for your REVAS.

DR. MARCUSON: I am a little concerned about the suggestion that with the increase in the frequency of ambulatory surgery that we might get worse results. Certainly the thrust of training and the performance of surgery on an ambulatory basis in the United Kingdom has been towards the most senior people doing it, and to have juniors learning on ambulatory cases is wrong. I don't think the profession should stand idly by. It's really a plea to make sure that when we do ambulatory surgery, which is obviously excellent for many cases of varicose veins, that we should still reach the highest standards.

DR. BURNAND: As far as the publication of your paper is concerned, that is, of course, sub judice and I couldn't possibly comment on that. What I was going to say to you is rather what Bob Rutherford had to say, which is it seems to me that you should concentrate on one area rather than throwing your net too wide. Why not just tell us about groin recurrences or popliteal fossa recurrences and concentrate on one or both of those rather than try and put everything in? I would guess this would cover 75 percent of the major recurrences from the surgical point of view. The other brief comment was that in both those two areas the operations are not without their problems and have a risk of complications, particu
we’ve seen major problems with lymphoceles occurring and all sorts of mayhem from recurrent exploration of the popliteal fossa which often has to be done through a very unsightly scar.

DR. CORNU-THENARD: Michel, the CEAP classification is already not easy to use daily because there is a lot of items to answer. As you know, our European team with Hugo Partsch, Philip Coleridge Smith, you, and others has set up a computerized file. With it it’s not necessary to know each chapter of this CEAP classification. Here with your REVAS there are more items. So it’s more difficult to use it daily. Do you imagine setting up a computerized file for this REVAS or do you think it’s not necessary?

DR. PERRIN: No. I think you can fill the form out in five minutes. If the patient is well prepared before surgery, you can fill out the form in five minutes, and if you want to start a study, you must have a lot of data in my opinion. Probably for daily use it’s not convenient, but for prospective study I think we need it.

**VENOUS OUTCOMES ASSESSMENT IN CHRONIC VENOUS DISEASE**

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Clinical papers from earlier times often characterized treatment groups with chronic venous insufficiency (CVI) simply in terms of the percent with “stasis dermatitis” or “stasis ulcers”, the latter sometimes separated into healed or active groups. Pain and swelling were also mentioned, and even graded sometimes, in an attempt to show symptomatic relief from treatment. The individual components of stasis dermatitis (cutaneous pigmentation, inflammation/induration, subcutaneous fibrosis) were graded in various ways in the more detailed reports, but none of the above were ever standardized in a universally accepted way. Furthermore, the background of conservative therapy, e.g. the impact of differences in compliance with the recommended use of elastic stockings and leg elevation, particularly in the period following the procedure being evaluated, was rarely taken into consideration. After a variable period of follow-up after treatment, the percent of ulcers healed, or staying healed after treatment, or, if patients with stasis dermatitis were included, the percentage without a new ulcer were commonly reported as evidence of improvement. As the use of life table methods became popular among vascular surgeons, primarily as a way of reporting patency rates, it was occasionally applied to such reports, in characterizing the “ulcer free interval”. Such was the state of the art before reporting standards were developed.

The first version of the SVS/ISCVS reporting standards in venous disease, published in 1988,1 did much to improve this. In addition to proposing a risk factor grading system for assessing the risk of deep venous thrombosis (DVT), and making recommendations for reports on pulmonary embolism, it proposed a 3 level classification for CVI, suggested that the anatomy and etiology of the venous disease be described, and recommended using functional means of objective assessment before and after treatment, specifically ambulatory venous pressures (AVP) or one of the then current non-invasive tests (NIT’s) for assessing obstruction or reflux. It also recommended a +3 to -3 scale for gauging change in status after treatment, much like that proposed for lower extremity arterial disease,2 in which change in clinical class plus a significant change in a physiologic test value were required in order to claim significant improvement (or worsening).

Subsequently, a consensus meeting of an ad hoc international committee of the American Venous Forum (AVF) was held in Hawaii in 1994 at which the CEAP system of classification of venous disease was conceived and developed.3 The CEAP system categorizes the basic elements of the venous condition at a given point in time. It separately categorizes the clinical condition of the extremity (“C”), the etiology (“E”), the anatomic location of the problem (“A”) and the underlying pathophysiology (“P”). The major value of this classification is to standardize the key elements in a way that patients or groups of patients with venous disease can either be distinguished from each other, or grouped in common classes and compared in a standard manner in reports from different practice groups or institutions. This system was recommended and outlined as the main feature of a revision in the venous reporting standards published in 1995.4 It has also been promulgated in the Venous Handbook.5

Methods of outcomes assessment need to be able to gauge change in status following treatment in a meaningful and objective way, and for purposes of analysis and comparison, are usually quantitative rather than qualitative. When applied to venous disease, outcomes assessment requires a method, or methods of placing the result of treatment in context with the clinical setting and the individual patient’s reaction to a particular state of venous abnormality. It should result in a practical analysis of the success of a given treatment over time, whether applied to a group of patients of varying levels of severity or patients grouped into similar levels of severity. Both, but particularly the former, require a quantitative method of gauging the severity of disease. Properly comparing the outcomes of two or more treatments in the same institution, or the reported results of the same treatment from different institutions, or using different adjective measures, is not possible if the relative severity of the underlying disease in the treatment groups is unknown or not known to be equivalent. A scheme to gauge the relative severity of disease must not be static but also be able reflect changes in severity with time and with superimposed treatment. The universal use of a system properly designed along these lines, will allow groups of similar degrees of severity to be entered into clinical trials and compared in regard to outcome following different therapies and the reported outcomes following a given treatment by different practices, groups, or institutions knowing the relative severity of disease of the patients in each report. Thus a venous severity scoring system is an essential component of proper venous outcomes assessment.

However a venous severity scoring system will be of limited value if it, or some adjunctive method, does not allow for changes or differences in the background of conservative therapy. Furthermore, in addition to such methods, patient based assessment of the impact of treatment on quality of life (QOL) is needed, and, as these may be too complex for routine clinical practice, a simple venous disability scale is also needed.

The change in venous status scale featured in the current venous reporting standards is conceptually sound, i.e. a categorical change
in clinical status combined with a significant change in an objective functional test in a -3 to -3 scale, but it depends on the reliability of such tests. What constitutes “abnormal” and what constitutes “significant change” in these tests, and which tests and values are appropriate and equivalent for use as objective gauges of reflux, obstruction or global venous function, deserves clarification and standardization.

Currently an ad hoc committee of the American Venous Forum, chaired by the speaker, is developing additional methods of assessment for the standardized reporting of chronic venous disease and its management. They are addressing the needs outlined above and the draft proposal will ultimately include a venous severity scoring system with clinical and anatomic-pathophysiologic scores (the latter based on duplex findings), recommendations for dealing with a background of conservative therapy in evaluating an interventional treatment or procedure, the identification and grading of factors affecting the long-term outcome of deep venous thrombosis, an updated comparison of venous diagnostic tests and their ability to assess venous dysfunction, a comparison of patient based assessments of the impact of venous disease and its treatment on their quality of life, with a recommended QOL instrument, and a simplified venous disability score. Not all these elements are fully developed or agreed upon, but submission of the final draft for approval is expected in early 2000. The various proposals are too extensive to cover in this brief presentation but some of the preliminary recommendations, such as the different options in the venous severity scoring system, will be presented in order to obtain input from other experts at this symposium.

Caveat: In developing new methods for venous outcomes assessment, especially venous severity scores, it is important to avoid confusion with, or under-mining the existing venous reporting standards and particularly the CEAP classification system. The importance of the uniform classification framework provided by CEAP is acknowledged. The executive committee of the AVF, who own its copyright, while not wishing to change the basic system, recognizes it as a dynamic document which will need to be augmented or changed with time. It is a well developed classification system, but does not fulfill the additional needs outlined above. Thus, the goal of the current ad hoc committee is not to replace or change any aspect of CEAP, but to augment it with additional compatible methods to further improve our ability to assess venous outcomes.

* Excerpts from an early draft of the American Venous Forum’s ad hoc committee on venous outcomes assessment have been used in preparing this abstract.

References
VALVULOPLASTY AND PRIMARY VENOUS INSUFFICIENCY

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Objective
The study was designed to evaluate the effect of superficial femoral vein (SFV) valvuloplasty on the progression of primary chronic vein insufficiency in patients with SFV and greater saphenous vein (GSV) reflux.

Design
A prospective, randomized, controlled, two-phase study.

Material
168 patients (169 extremities) with primary chronic venous insufficiency (CVI) were enrolled in phase 1. All patients were treated with elastic compression for 5 years. 128 patients who remained in the study at the end of the 5th year were randomized to have either GSV stripping (control group, n=64) or combination of GSV stripping and SFV valvuloplasty (study group, n=64).

Methods
Clinical assessment and duplex ultrasound examination were the main methods of the investigation.

Main Outcome Measurements
Change in clinical class (CEAP), reflux duration time, reflux volume index.

Results
During phase 1 of the study, two types of clinical dynamics were identified. Stable dynamics in patients with no change in clinical class (n=43), and progressive dynamics in patients with at least one class increase during 5 years of observation (n=82). Increase of reflux was registered in 74% of extremities with progressive dynamics and in 47% of extremities with stable dynamics (p<0.01). After surgical treatment, improvement was found in 90% of the extremities with stable dynamics in the control group and in 95% of the extremities with stable dynamics in the study group (p>0.05). In extremities with progressive dynamics, 51% of the control group and 80% of the study group demonstrated improvement (p<0.01). In 45 extremities after valvuloplasty, the corrected valve remained competent. In 12 extremities, reflux reappeared and in 10 extremities reflux increased starting from 12 months after valvuloplasty. Clinical aggravation was observed in 8% of the extremities with corrected valve and in 50% of the extremities with increased reflux (p<0.01).

Conclusion
Correction of a single incompetent valve of the SFV makes a significant difference in the results of treatment and changes the course of primary CVI.

QUO VADIS SESSION

INTRODUCTION
The final session of the meeting is devoted to a consideration of where the field of chronic venous disease should be directed, i.e. where do we go from here?, or Quo Vadis. Each panelist has been asked to summarize his thoughts in a two to three minute presentation to be followed by free interchange between the panelists and the audience.

DR. KISTNER: As an introduction to the Quo Vadis session (where do we go from here?) I'd like to ask Mike Dalsing to tell us about his communication with NIH, and some of the activities in the American Venous Forum.

DR. DALSING: Bob asked me to give a little introduction to this part of the symposium devoted to the question: “Where are we going in venous surgery?” because I was privileged back in June of this year to be involved with an NIH study group dealing with clinical research of thromboembolic diseases. The physician group was basically 12 representatives from private practice, academia, and industry. Dr. Gangulu from the NIH called the meeting to order and Dr. Barbara Alving welcomed all of the attendants on behalf of the NIH. Basically there were three major areas of presentation from which recommendations were supposed to be made of high priority for future research emphasis. The presentations were generally of a hematologic or medical slant. I was the only surgeon involved in this group. The first major topic involved hormonal modulation and the risk of thrombosis. Throughout a woman’s life basic hormonal changes occur such as during pregnancy, menopause, while taking oral contraceptives, or during the treatment of breast cancer or its prevention. An example of that would be the new Serm’s drugs. These events usually place the patient at increased risk for venous thrombosis. Fetal loss may also be associated with hypercoagulability, but anticoagulation also has its down side. So it was thought by the presenters of this topic that the pathophysiologic issues risk benefit stratification for different treatments and for different disease states, and optimal therapy were all potential areas of future investigation. The second topic of discussion involved the epidemiology and genetics of venous thromboembolism. Genetics, as a factor in venous thrombosis, is becoming increasingly evident. We know that ourselves. Just about every year we have more and more possible genetic reasons for thrombosis. In fact, the clinical manifestation of venous thrombosis is probably due to a genetic predisposition triggered by various environmental factors. The presenters thought that the human gene project may actually suggest an ever-increasing number of potential genetic avenues for potential clotting problems and may even provide materials for direct study. The presenters thought that to study each potential genetic deviant path of thrombosis would be impractical. However, a specimen data base of approximately five to 10,000 patients afflicted with DVT in addition to unaffected control, (e.g. relatives) managed appropriately to ensure long-term storage of these specimens for analysis as new information became available might be feasible. The clinical data from these patients might provide a clue to the environmental factors, and even provide long-term results of what happens to these patients with acute disease which later becomes a chronic problem. The final discussion topic was the
optimal management of venous thromboembolism. Optimal medical therapy for the acute event was discussed, as was the topic of length of chronic anticoagulation treatment after the initial event to prevent recurrence. Special emphasis was placed on thrombolytic therapy for patients with pulmonary emboli who were hemodynamically stable but had right ventricular dysfunction. The use of thrombolytic therapy for acute DVT was my assigned topic. Its use for ameliorating the acute symptoms as well as preventing long-term sequelae could be championed based on trends noted in the literature. In addition, I reported on the surgical therapy of chronic venous disease emphasizing the importance of superficial, perforator, and deep disease. Repair of venous insufficiency by valvuloplasty, transposition, and transplantation operations were all discussed. A quick survey of the experts gathered at this conference basically showed that over 50 percent of my colleague participants did not realize that there was any surgical option for these patients at all. They didn’t realize that you could impact the deep system in any constructive manner. Obviously the word has not spread from us to our general colleagues in medicine. The high priority recommendations emphasized epidemiology, pathophysiology, and possibly the implementation by the NIH of a program to encourage young investigators to become active in the field of venous thromboembolic research. Many of the topics would be further discussed within the NIH itself to generate a more focused approach. So my general impression is that there appears to be a renewed NIH interest in venous disease. It has probably resulted from the efforts of national organizations such as the American Venous Forum. It’s research and executive committee engaged in an active dialog with representatives of the NIH at least two years prior to this working group meeting. Furthermore, national symposia such as the one we are currently attending have drawn attention to this disease as one that people are actually interested in. I believe that my participation as a surgeon in the recent working group was at least partially due to these efforts. My interpretation of the interactions I have had with the NIH representatives suggest an active desire to obtain and consider high quality research submissions, especially with a clinical slant. And, in fact, this whole conference was basically based on the clinical agenda of this disease. My impression is that the NIH has not had recent activity on this front of any significant degree, certainly nothing to the degree to which they obtain arterial research requests. Now exists a window of opportunity to seek funding for venous research projects. It was a pleasure to be involved in this working group. It was eye opening to me to see how things are accomplished. Certainly, I think surgeons, in particular, have very little input into this process in general. But, I think that being involved with this process and understanding the way the NIH seems to be going is critical to any success for future funding.

DR. BELCARO: One of the major problems with venous disease is that anywhere you go the reimbursement for venous procedure is not very high in comparison with arterial surgery. So I think that some stage people working in the field should make known that this is an important factor because many doctors, many physicians, many people working in the field prefer to do an aneurysm, prefer to do an arterial procedure than a venous problem. From our point of view, to do an amputation, which takes really very little surgical skill. You get three times more compensation than doing a valvuloplasty. This is a serious problem which impairs the possibility of improving this kind of surgery. Now, is this problem considered important (the fact that reimbursement is not really very high for venous procedures)? For instance, considering sclerotherapy, you can treat effectively patients with sclerotherapy, but you don’t get too much money. Very often in one hour with surgery you can get ten times more money than doing a nonsurgical procedure (sclerotherapy). So I think that the lack of improvement of all this field and the lack of evolution in the last few years is due mainly to the presence of several regulatory problems including the limited amount of money and reimbursement policy.

DR. DALSING: I think, in general, our ability to educate both our medical colleagues as well as the general population who are involved in reimbursement issues has been a major problem. To change reimbursement, at least in the United States, you have to go through a very lengthy process. You have to modify CPT codes and then, go through a change in billing. It’s a major event. In reality, what occurs is that those concerned with this process set a certain number of procedures that they’re going to try to change that year. You can not change everything at once. We haven’t been aggressive enough in suggesting that venous surgery is one area that has been ignored in this process and is a major problem for our patients.

DR. O’DONNELL: Let me respond wearing my Hospital Administrator’s hat. I agree with you, Michael. I think the economic pressure is to reimburse not only surgeons less for procedures such as aneurysms, but also hospitals less. The entire pay scale, if you will, for vascular surgery has been derived from and influenced by the Medicare/HICFA base that our colleague, Dr. Norm Hertzer, and subsequent colleagues labored on our behalf. This scale is based on, if you will, the degree of difficulty of the procedure. Thus a base was developed and then a family of increasing technical difficult procedures was scaled by consensus of vascular surgeons. I don’t think valvuloplasty or venous reconstructive surgery has been given the appropriate scale of difficulty. A lot of surgeons have been discussing this situation with Medicare, but I don’t think we’re going to get any place.

DR. DALSING: I can tell you that NIH’s emphasis, at least at the conclusion of this meeting, was more in the epidemiologic and the pathophysiologic fields, especially the problem with hormonal modulation in women. That was a major topic, and I’m sure that’s going to be part of the way that the funding is going to go. However, I think that all the things that were presented actually will filter through the NIH hierarchy. Then they’ll come up with some kind of focus. One of the other major areas that all of us at the meeting felt was important, all 12 of the physicians present, was that young investigators have to be promoted in this field and maybe actually have a special program for that purpose because otherwise no major change can be expected.

DR. STRANDNESS: Maybe a lot of you don’t understand how the NIH works in terms of research, but basically there are two ways you can get money out of the NIH. One is to apply with a specific research proposal. When that is sent to NIH, it goes to the division of research grants. They assign the grant to the study sections. At the division of research grants, the proposal is examined to determine which group should carry out the review. Sometimes your grant will go to a study section that bears very little relationship to the research being proposed. You do not have a say as to which study section your grant will go. We tried very hard to get a study section
devoted to issues related to peripheral vascular disease. The NIH has never approved this even up to the present time. The other way you can apply for money is to apply for directed research proposed by the NIH. The director of the NHLBI has about ten percent of his budget which can be used for targeted research. I served on the cardiology advisory committee for the National Heart and Lung Institute for four years, and during that time I found out how the mechanism works. It’s very slow. It’s extremely painful. You may spend months arguing over whether one should pursue the research only at the end then you may find the leadership does not approve.

DR. BELCARO: I think that both for grant application, and for the Medicare reimbursement system, the real point in venous disease, and peripheral vascular disease, is that we don’t have a hard end point. The most successful field for grants and for reimbursement is at the moment, strokes. In stroke you change or decrease the number of strokes. You may change mortality. So you have a very specific hard point. The point was that after two years of treating these patients with PGE1 you have a decreased number of patients with stroke and decreased cardiovascular mortality. I give you an example. We conducted a European study on claudication, and did a comparison between short and long-term PGE1 treatment and we changed the distance of claudication (i.e. from 200 meters to one kilometer). They said to us “what is your hard-point?” So in venous disease and peripheral vascular disease, if we don’t find a hard point which may be really relevant to both regulatory authorities and grant authorities, we’re not going to have credibility to get a large grant. We perform all these demanding treatments like valvuloplasty, but what is going to change? The hard point in venous disease is not mortality. It’s not morbidity. It’s really the cost. So anytime we apply for a grant we have the same problem in Europe. If you apply for a study on stroke, which has been considered the most successful field of grant application, it is relatively more possible to get a grant. It doesn’t matter what kind of project you want to do. If you apply for venous disease or peripheral vascular disease, nobody seems to care very much. So in venous disease we need to find a hard point, and I think the hard point in venous disease in this specific topic if you want to study valvuloplasty is the fact that you reduce costs because the patient doesn’t come back to the hospital or require treatments anymore.

DR. STRANDNESS: I wish I could look in the future. I always get a little bit despondent when I think about this problem because it seems that from our vantage point and from a research standpoint, there is very little interest in the diseases of the peripheral vascular system. So when you listen to all the work that’s being discussed in this meeting, nearly every topic that’s been brought up here is crying for good research. This takes money. Randomized trials are extremely difficult to do, they are very costly, and on the other hand I don’t see how we’re going to settle some of the problems that we talked about today without these trials. If you’re going to go through the NIH channels, the review process is very tough. The other issue, which is very important today, relates to the gender and racial mix of your study population. Every three months I have to certify to the NIH that my patients fit the racial mix of our population. If we do not meet 80 percent of the goals, they can withdraw funding. There are only two sources of money, one is private industry with the second being the NIH. Millions of dollars has been spent by private industry to fund research looking at low molecular heparin. I think this is a tough issue. Our field is crying for good research.

DR. KISTNER: Gene, do you have specific areas that you would stratify or prioritize?

DR. STRANDNESS: Well, I think the epidemiology of chronic venous disease is an important issue. I think Dr. Dalising pointed that out. The NIH appears to agree with that. We need to get epidemiologic data on the impact of the disease on our population. Outcome research is becoming more important because it involves how our health care dollar is spent. If we can show that one form of therapy is beneficial from an economic standpoint, then we have a winner. For example, sclerotherapy versus maybe saphenous vein stripping is an area that could be examined. However, they would have to excite the interest of the study section that is looking at the grant. Industry looks at this from a different standpoint. The most difficult problem is to get funding from the NIH. It may be easier to get funding from industry. Some companies now that are beginning to look at that, particularly with regard to compression therapy. For example, we have received a grant examining the role of support stockings after an episode of DVT. Companies are looking for objective data supporting the use of their product. With regard to valvuloplasty, there will be a problem with numbers to obtain suitable groups for study and comparison. It’s a numbers game.

DR. KISTNER: The study of epidemiology, and the collection of more basic data may be along the lines of what Gianni is talking about concerning the cost implications of chronic venous disease.

DR. STRANDNESS: See, Dr. Wakefield is lucky because he’s working in an area that has some hard science. I think you are more likely to get funding for that kind of research. I would be interested in Dr. O’Donnell’s thoughts on this subject since he is in the forefront of health care delivery.

DR. O’DONNELL: I would like to expand on the research aspect and through it address Gene’s questions. It was through the foresight of the executive committee of the American Venous Forum that rekindled relations with NIH. Like Gene, I agree that there will be much interest from NIH when there is some socio-political value to people at NIH to study venous disease, therefore until we define our “constituents” by epidemiologic studies, we will be unable to convince NIH that venous disease is important. Certainly today in vascular disease, it’s the age of the woman. A great deal of the funding currently is directed at hormonal influences on vascular disease. In our institution, Mike Mendelson has received several grants centered around the role of estrogen in the vessel wall, and that ties into something that’s currently socio-politically important. Thus I agree that until we get the epidemiologic data, we won’t be able to influence NIH. Epidemiology is the subject that Bob Kistner has talked about for five to ten years. At every executive committee meeting of the AVF Bob emphasized the need for epidemiologic studies. Where do I think venous research and treatment are going to go? I think we need to look at the target organ of chronic venous insufficiency - the dermis, and understand it better. Under influence of hypertension the skin develops the venous ulcer thus I believe medical therapy will be designed around a better understanding of dermal pathophysiology that will help heal the ulcer or prevent skin from progressing from lipodermatosclerosis and pigmentation stage to frank ulceration. Industry will be very supportive of this research direction because it can be translated rapidly into potential drug therapy. We will see more and more activity in this area. Which is
again, industry targeted. With the loss of urokinase as a lytic agent and physician’s uncertainty about the correct dosage of TPA, will see heightened interest in safer and more effective lytic therapy for deep venous thrombosis. In addition something that hasn’t been discussed much here at this conference is upper extremity venous disease, and in particular its chronic sequela. As we employ more intravenous catheters for chemotherapy, we need better ways of treating the chronic forms. Finally, the age-old question that is hotly debated is whether elastic stockings are more effective than surgery. And by “surgery” I mean surgery to the superficial venous system for someone with Stage V VI disease, the NAVUS study will address that question and I hope that there will be NIH funding for that study.

Dr. Raju was very eloquent this morning citing the problems with the studies supporting elastic stocking - no pun intended. I feel, I’m sure as he does, that in venous disease we are in a position similar to where the carotid surgery was when carotid endarterectomy for patients with asymptomatic lesions was questioned. We knew it worked, but we couldn’t prove it to our medical colleagues until we had the ACAS trial. I think we need a similar type of trial to prove that surgery is effective for advanced chronic venous insufficiency. The first two areas that I have mentioned are definitely outcome and industry related, and I think industry will support such things as that. I hope NIH will support the clinical outcome trial.

Dr. KISTNER: Are we talking about acute disease enough or are we focusing on chronic here?

Dr. O’DONNELL: I’m focusing on chronic because I feel that our medical colleagues are focusing on acute disease. Perhaps as Gene has suggested, vascular surgeons need to become more involved in the acute disease process in order to develop funding in this area.

Dr. WAKEFIELD: The person that was the head of the meeting that Mike was at, Pan Ganguly, who is the leader of Thrombosis and Hemostasis at NIH has told us on a number of occasions that NIH has renewed interest in venous disease. He has actually offered to look at one or two-page abstracts of ideas that individuals have and then help guide those ideas into the correct study section and into the right area of the NIH. So at least there are contacts at NIH who know about venous disease and the American Venous Forum. I believe there is a window of opportunity at NIH that we can and should explore. I think right now NIH is more interested in clinically oriented research than basic science research from us, but I think they would be willing to look at both clinical and basic research. So I believe that if you have an idea that you want to see whether or not NIH would be interested in having you pursue, what you should do is send a one or two-page abstract to the national office of the American Venous Forum, and that will be forwarded on to NIH for feedback. I think that it is remarkable and very good that NIH has made this offer to us.

Dr. BELCARO: The European community medicine Control Agency has issued a regulatory observation form for people assessing grants. As soon as you present a grant the most important thing is the hard end point you have. Chronic venous disease is very similar to asthma, for instance, or chronic lung problems, and in these cases the cost (not only the open cost of treatment, but the hidden costs like the number of days lost at work and the quality of life) are the target points. So chronic venous disease is not a disease you can measure with hard points like pulmonary embolism. Why do companies focus on pulmonary embolism? Why do they spend all these millions? Because they have something very easy to show. You treat patients with low molecular weight Heparin and you decrease the number of deaths from PE from 20 to 10. So you have a hard point and it’s very easy to show. It’s very easy for the companies to produce a new drug because then they convince the authorities that it’s very effective as they have a visible hard point.

The philosophy of the management of venous diseases is just to follow an example like asthma or something similar and focus on what is the entity of venous disease according to costs and considering all costs together. Until we find a way of selling venous disease to grant authorities and to the Medicare or the equivalent of Medicare, (National Health systems) the quantity of money for venous diseases will be extremely low. There is no progress if there is no money. The industrial support is fragmented in many products, but no company is actually selling anything so important in chronic venous disease so much that the interests can push the research.

So the problem we have is what we’re doing in venous disease is relatively cheap. And there’s no way we can get big grants.

Dr. MYERS: With just three minutes to talk, I thought that I would not attempt to give any broad overview of the topic. In particular, I anticipate that other panelists will address some of the important issues of comparing treatments in a scientifically rigorous way. I thought that I would just refer to two areas that have captured my attention recently, even though they are not necessarily the most important areas in this field. First in Australia and I would suspect in many other countries, there has been a phenomenon over the last few years which I find very disturbing. This is the introduction of a whole variety of topical dressings for ulcers made of seaweed and other gloopy materials that are hydrophilic and very costly, which companies recommend be applied in a variety of ways that are very clever according to the nature of the ulcer. The companies have I think been deliberately clever in training many of our nursing staff to learn these new and important techniques. Indeed, if doctors nowadays argue with the use of these preparations, nursing eyebrows will be raised behind their back. At our recent Australian Phlebotomy meeting, one of our colleagues, Gabriel McMullen who is well known to many of you, delivered a paper in which she stated her review of the entire literature on these agents forced her to come to the conclusion, that none had been shown scientifically to be of any better than a simple gauze dressing. You may well refute this but, I think the danger has been the development in our country of a shift of emphasis of treatment to the nursing staff, away from the doctor, and away from the fundamental treatment of the ulcer, I believe, which is compression bandaging. I think that this has been to the detriment of good care of an ulcer. This is a fairly mundane issue in the context of trials and so forth, but at the workplace I think it is very important. Although it may tell me that Gabriel was wrong, I think that further rigorous trials are required to show whether the dressings are of value. The second point that I thought I would make is totally different. At the first of these meetings six years ago we were asked at the end to state what we thought would be new when we met again in three years time. I was somewhat desperate for ideas but came up with the statement that I felt that percutaneous endovascular treatment would be a rapidly expanding field. Well, this meeting has shown us a good deal of that, but I think it’s just the beginning. Three weeks ago I was extremely fortunate to be at a
meeting in Buenos Aires where at least two groups are doing very interesting work which, just like endoluminal grafting for aneurysms, will create as much controversy as it solves problems, but which the patients, I believe, will want us to embrace. This involves percutaneous occlusion of saphenous veins by capped covered stents, and by occlusion of perforating veins which frankly is a lot more simple than SEPS or anything else we've been doing (by percutaneous coil embolization). With clinical reports of these now appearing in the French journal, Phlebology in particular, I think we'll hear a lot more of them in the future, and I think this will be one of the technical areas that will create its next set of controversies when we meet in three years time. I think that's all I would like to say. The only thing I would like to reiterate is Tom O'Donnell's point that the most interesting trial in Australia, if it could be mounted, would be to answer the very simple question as to whether best surgical treatment is really any better than best conservative treatment for patients with ulcers, particularly in older patients.

DR. GLOVICZKI: My interest certainly at this point is chronic venous disease and in that area, C5/C6 patients with advanced disease and venous ulcerations. The two North American SEPS Registries, that we reported, kind of convinced me that there is much more to do in this area, and the question is not SEPS, and whether SEPS is effective or not. The question is compression treatment cost effective? Does it provide better quality of life or does it prevent recurrence or heal ulcerations and how does that compare to the best surgical management? So the new NIH grant that we plan to submit, really deals with current best management of venous ulceration. If it gets funded, we'll bring more evidence on the effectiveness of surgical treatment versus best medical management. SEPS is the secondary issue of this grant, and not the primary issue. The primary issue is what's the best treatment to prevent ulcer recurrence? The secondary aim is ulcer healing and rapidity of ulcer healing, and then tertiary aims are if SEPS is effective in addition to superficial reflux ablation, what is the hemodynamic benefit, and what is the quality of life and what is a cost effective treatment? The American Venous Forum is an ideal organization to support, organize, and conduct this study because we need 30 centers with ten patients per year into the study, C5 and C6 patients. The design is obviously a multi-center prospective, controlled and randomized study. One arm is the best medical treatment and a second arm is surgical treatment. We are going to plan to enter 560 patients into the study, and on Page 64 of your handout I described the design of the study which will be called the NAVUS trial which is the abbreviation of North American Venous Ulcer Surgery Trial. The surgical arm will be randomized to two groups: one with stripping and ablation of superficial reflux with avulsion of varicose veins, and the second will be stripping, ablation, and SEPS. It is a long study. It's five years. We will need your support if ever gets funded.

DR. KISTNER: And the funding will come from NIH, federal funding? You don't have any other source?

DR. GLOVICZKI: The funding has to come from the NIH because of the magnitude of the budget. I have fortunately fantastic support at this point from multiple departments of the Mayo Clinic which includes two biostatisticians, the chairman of the health science department, two economists, and a department which is called the MPAC, which is the Mayo Physician Alliance Center which is specialized to multi-center studies. They will set it up, instruct the centers, put the questionnaire on the Internet, collect the data through the Internet. So the support service appears ideal, and that's why I have decided to submit this proposal.

DR. DALSING: The only question I have is how are you going to accomplish the quality of life assessment or the cost containment issues because I think those are two important end points that the federal funding agencies will consider. I think healing the ulcer is important clinically but really doesn't make an impact on the people who must fund many important projects. They want to know if it's going to cost less and what's going to happen to the quality of life of a large group of American citizens.

DR. GLOVICZKI: That's right. Well, again, that deadline is February 1st, and I obviously need a generic quality of life assessment just like the short form 36, but we also need an English language disease specific quality of life questionnaire. The best that I got at this point was from Dr. Comerota. I think that is currently probably the best that's available for us.

DR. RUTHERFORD: In regard to the quality of life questionnaire, I commented in my talk earlier today that there are three of them, and if Tony Comerota is here he might comment on this, but the one that he used has 80 questions on top of an SF-36. That's a lot to handle. One of the things that our subcommittee is trying to do is come up with a better quality of life questionnaire. Now for my own comments -- there are three major points I want to touch on. We've had a reality check from Gene Strandness about research funding. Gene usually gives us a reality check, and it's usually pretty depressing, but it is what the situation really is and it's important that we understand it. Then Mike Dalsing told us he was the only vascular surgeon on this 12-man committee on venous research and nobody else on the committee had even heard of venous surgery being an option. So I think recognition is a problem and maybe we have to somehow readdress our product a little bit. Consider how well Orange Roughy has done in restaurants after they've changed to that from its original name, the New Zealand Slimehead. But I think maybe we have to readdress our product in relation to what's best for the patient. We tend to think of what's best for ourselves, but if we can put things in terms of what's best for the patient, it will be more accepted, and patient based assessments are an important point of this thrust. I'm glad that point came out. Now we all would like to see progress in the diagnosis and treatment of venous disease in the new millennium. The question is how do you best achieve these broad goals. One, of course, has already been mentioned before, namely basic research but the focus has been on obtaining NIH funding, and in turn on achieving recognition by the NIH. But I agree with Bob Kistner, I think we need to educate the NIH, in terms of what the patient needs and not what NIH currently perceives it wants. I think we should approach it in that way. In terms of basic research, we tend to think in terms of the basic methodology and molecular biology, you know, oxygen radical, cytokines, leukocyte adhesion, and so forth, but we really haven't studied the basic pathophysiology yet. For example, we've been lysing clots with lytic agents for years yet we don't have good studies to show what these lytic agents do to endothelium. We're using them all the time and increasing high dose UK, all that, but nobody has really studied their effects. We've been talking here all this week about how soon do you have to remove venous clot to get an effective return of venous endothelial function and preserve the valves and so forth, but

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nobody has done the basic research of serial removing of clot X number of days after thrombosis and studying the underlying changes and when they become fixed and irreversible. I could go on and on. There’s a lot of basic research to be done, but it doesn’t have to be complex. There’s a lot of basic pathophysiology studies that deserve to be done. The second point I want to make is while I continue to be impressed with how much experienced, technical skill and careful, detailed observation my colleagues put in their clinical studies, I am also impressed with how little our colleagues in other fields pay attention to what we do. I’m getting back to the matter of recognition again. We are routinely dismissed by Russell Hull and his colleagues as not having Level 1 evidence, and we’re looked down at by people who are career trialists. But it’s easy to do prospective randomized trials for new antithrombotic drugs, for example, low molecular weight heparin. These are easy to do, but it’s very hard to develop that kind of data for chronic venous disease. You can’t solve everything with randomized trials. It’s hard to apply to emerging technology, particularly if the procedures are applied sparingly, as they probably should be. The numbers are small and the patients don’t want to be randomized. They want the new treatment. Nevertheless we have to change the way we do clinical research. We’ve got to get away from these uncontrolled observational studies that we keep reporting to each other. Even though there may be a lot of important observations in them, uncontrolled clinical trials or studies must be eschewed. If we can’t do prospective randomized trials, then we need to at least do controlled comparisons, with comparable cases based on disease severity scoring, but also using improved methods of outcome assessment. We’ve talked about some of them, particularly quality of life instruments and other patient-based assessments. In addition we need cost effectiveness studies. If we can address the cost of different options in treating venous disease we’re going to get attention. Obviously things like uniform reporting standards go without saying. I think we can upgrade our clinical studies to a level of evidence which is quite acceptable without necessarily trying to solve everything with prospective randomized trials. The third area involves communication and education. I’m really concerned that the physicians who first see patients with acute and chronic venous disease, the primary care physicians, internists, and other specialists don’t know nearly as much about these problems as we do, and yet they are on the front line in terms of decision making. I think somehow we need to change this, and I thought of how we might do it. One solution would be to band together and develop management decision algorithms that are society approved on the management of acute and chronic venous disease. I think they could have some impact. They should impress HFCA and other third party health care decision-makers. The problem I see with that approach relates to something we have observed with the expert panels at this meeting, namely no one seems to be able to agree on how to manage a particular case. So how can we tell other physicians, and come up with management algorithms until we can agree among ourselves. Those are some of the thoughts I had, but my final thought is that we should take a page out of our hosts’ book. They have developed this wonderful venue where venous experts from many different countries come together and exchange ideas, and I think we need to do that more. I think we should give our hosts a show of appreciation for showing us the way, the way we can make more of an impact on the progress of the management of venous disease. Let’s make this an international effort. Thank you.

DR. STRANDNESS: I strongly believe that we must publish some of our best work in non-surgical journals. We must get our message to the general medical community. The best studies we have done from my laboratory in Seattle have gone to non-surgical journals. For example, “The Shrinking Kidney” was published in the American Journal of Hypertension, the next follow-up was published in Kidney International, and the last one on “Natural History of Renal Atherosclerosis” was published in Circulation. You don’t get the attention you need from putting it in the Journal of Vascular Surgery. If I want to talk to surgeons, okay, I’ll go to the Journal of Vascular Surgery. If you publish in non-surgical journals, it has a big impact. An example of how this can work and get national attention was the issue of “The Shrinking Kidney” and its relationships to the problem of ischemic renal failure. When that issue became known to the nephrologists and the internists, the interest in duplex ultrasound to detect renal artery stenosis increased. Duplex has been accepted by the FDA as a method of not only selecting patients with the problem and for follow-up as well. There are two national studies being done looking at the role of stents in renal artery stenosis. This all came about because the nonsurgical community became aware of the problem. The other problem is it’s tough. The review process for the best medical journal is very difficult. However, if you make it through the review process, a lot of people are going to read it. The medical journals such as the Archives of Internal Medicine have a wide distribution. I think that one must pick a good journal and go with it.

DR. PERRIN: As I started the job, my first concern was how to prevent recurrent veins after surgery. Two hundred fifty thousand patients are operated on every year in France for varicose veins. That is a lot of money, and the rate of recurrence is between 10 to 30 percent. So we really need prospective studies to identify all of the possible factors that contribute to recurrence including general factors, techniques, classification of disease, and so on, because that is very important in terms of cost. I think that in the future venous surgery will change very quickly. Invasive endovascular surgery, as previously mentioned by Dr. Myers, will replace ancillary procedure. That is not only true for deep venous surgery but also for superficial venous surgery, but in order to know our efficiency the new treatments will have to be very careful to include an estimate of cost effectiveness of the new treatments. To achieve outcome of treatment we have to evaluate patients precisely clinically for treatment. CEAP is a clinical classification that can be perhaps extended or completed as proposed this afternoon by Dr. Rutherford. State of art of instrumental investigation have been established by Dr. Geux in a meeting in France, and probably the next step will be to try to establish a correlation between clinical findings and hemodynamics. We need that.

DR. RAJU: Bob and Bo, thank you for allowing me to participate in this wonderful meeting, and the free-for-all this morning especially. If we look at valve reconstruction data, if you look at survival curves for axillary vein transfer, for example, you would find that there is a 30 percent loss in the first year. The bulk of the loss comes within a couple of months actually. This is not due to thrombosis because the axillary vein conduits remain open. I was talking to Roger Lane who had done a lot of animal work. He told me that if
you put PTFE around these axillary vein valves, there is an encroaching fibrinization invading the valve. Maybe that's why we are losing 20, 30 percent of these valves in the first few months. In previous conversation with Dr. Peter Gloviczki, he told me that I should be using silicone rather than PTFE wraps because, with silicone, there is no connective tissue reactivity at all. So that's what we are doing. We are beginning to put silicone wraps around our axillary vein grafts rather than PTFE. In the same context, if you look at direct vein reconstruction, not axillary vein valves, the same type of phenomenon happens. You lose about 20, 30 percent rather quickly after valvuloplasty. Roger Lane told me that he has done angioscopy of these valves that were repaired with sutures. He saw that after a few months the valve station dilates and the sutures tear out. Dr. Kistner had re-explored an external valve repair and seen the sutures tear out. So it seems logical to me to wrap these valves after valvuloplasty with some type of support so that they don't tear out. Now, the results should be available pretty soon because you can follow this with duplex and calculate the rate of duplex deterioration for valves that are wrapped and those that are not wrapped. As you know, in chronic venous disease no matter what you do, stripping or valve reconstruction or whatever, swelling may improve, but it's a very gradual process over a period of time. In many patients it may get better, but it does not completely disappear. But with iliac vein lesions you can often see dramatic and complete resolution of swelling with stenting. It's quite exciting to me. We do not have objective measures of either swelling or pain. I came across a publication recently where there's some work being done with functional MRI scan looking at pain in the cortical areas. The traditional view is that pain is centered in the sub cortical areas, but with functional MRI some evidence is building up that this is actually a frontal lobe activity in chronic pain syndromes. So we may be on the threshold of having some type of objective test to measure pain as linked to chronic venous disease. I think this is terribly important in patients who want to claim disability because they still have pain. Objective evaluation of swelling, I think, is a little bit more difficult. Together with Dr. Neglen, we have in our own practice instituted questionnaires to assess swelling. One is to ask the patient if the swelling is better or worse. We all know that's terribly subjective. Somewhat less subjective is to ask the patient if the swelling goes down at night, how soon does it maximize on the next day. That gives you, I think, a somewhat less subjective measure of what the swelling is doing. And finally we plan to do plethysmography at the end of the day, put the patients to bed, and do plethysmography again first thing next morning before they get out of bed. Finally, what about venous physiology? I think most of the circulation research is focused on arterial disease, and our concepts are extrapolated from our experience with arteriograms and arterial disease to venous disease. For example, in the last two days we have debated the saphenous vein being the sole outflow from the leg, which I think is a hangover from our interpretation of arteriograms. In the venous system, if you have as little as one or two millimeter gradient difference, the flow pattern is going to change. Some of our ignorance in the area, I think, is because there has not been an analysis of the venous system on the basis of what is already known in hydraulic engineering. There are books on networks, and the veins are the ultimate network in the body. Of course, you throw in a wrinkle by putting in collapsible tubes, but all of that knowledge is available in fluid mechanics. It just has not been applied to venous system.

DR. RUTHERFORD: Gene and I were just talking, and we had talked earlier about the web master for the American Venous forum web site, and it reminded me that one of the things we have not mentioned today and should not overlook is the potential for what can be done on the Internet in terms of recognition of venous disease and its proper management. I think we really need to think about how to use the Internet in gaining proper recognition.

DR. MYERS: In Australia we have two societies, the Australian and New Zealand Society of Phlebology, which is primarily surgical, and the Sclerotherapy Association of Australia which is predominantly nonsurgical phlebology. The Sclerotherapy Society itself has a 15, 20-page web site, and all of its members would have their own web site. It would be bad business not to be on it. The hit rate for those and the work generated are apparently phenomenal. This may be a purely commercial activity, but it can also be a good educational activity. I recently accidentally got onto another web site because of a new procedure I had done, and my secretary was overwhelmed for the next month by the response. You're absolutely right that people are obsessed by this now, and many will simply not go out and seek treatment until they've checked it out on the Internet.

DR. GLOVICZKI: I just have one sentence to say. I tried to reserve SEPS.com and was disappointed that it's taken. It's a hot web site, Gene. Sony took SEPS. It's actually the web site of Sony Electronic Printing Services.

DR. DEPALMA: I feel most humble in commenting because there have been many wise things said. The basis of science has got to be quantification. I think Drs. Tom O'Donnell and Gene Strandness and Robert Rutherford all hit on that. The thing to look at is the effect of venous hypertension on the dermis which can be impacted in a variety of ways which can be quantified, and in my opinion, this has been done in a preliminary way. There is no question that effective surgery will yield much less time with an open ulcer, much quicker healing, and many fewer recurrences. In fact, we ourselves did this study with cohorts in a cross over study. I believe that what Dr. Rutherford said is very right. I worry greatly about the tendency for people to just cite prospective randomized control, as the answer to all issues. The best approach would be surgical versus but medical therapy for venous disease. Actually, in surgical matters, perhaps only 40 percent of surgical interventions can be gauged. Yes, you can do prospective studies with Heparin and low molecular weight Heparin or these can be done with antibiotics dealing with a single or a few variables. When you deal with comparisons of particular surgical interventions there is a need to do a cohort precisely matched study. I would not restrict interventions in the venous system to one or two interventions. As we learned today, enormous disparity amongst effective approaches to the venous system exist. The case that Dr. Kistner showed us with the effective anastomosis of the Giaconini vein and the lateral femoral vein is something that none of us thought of. And, in fact, this worked. So in terms of the basic science of the venous system, I think the problem is that the venous system is a chaotic and fractal system in the true sense of that word. There are mathematics to deal with fractal systems. The mathematics of chaos is still a little beyond us and our linear thinking. If we could focus our efforts on understanding how a small change like one competent valve at the origin of the superficial...
femoral vein might change the dynamics at the ankle, we will be on our way to a better understanding. I feel quite humble in closing this symposium with another comment. I do not believe that we completely understand the anatomy of the venous system and its variations. I think that there are misconceptions about how many perforators there are, where they are and which ones should be interrupted. Jan Holm's study shows that most of these are halfway up the leg, but also the intra malleolar ones can be important. I thank you for the opportunity of commenting.

DR. GOREN: I have always looked up to the academic surgical establishment for knowledge, guidance and education, public education included. While I am not part of this establishment anymore, this attitude of mine has not and will not change. I am concerned, however, that your voices as educators of the lay public in the field of vein disorders is not heard at all or only very little. You are too isolated in your institutions and the public does not hear you loud and clear. The written and electronic media is using false "gurus" who are misleading the naive reader or the listener for their own selfish interests. The tabloid National Enquirer of June 1, 1993, published an article on guided injection treatment for varicose veins. Moreover, just recently, the November 1999 issue of Allure magazine already reported about a new and "revolutionary" method for treating varicose veins. We all know the fate of the guided injection method as well as the still questionable results of the radio frequency approach remain unubstantiated as presented in this meeting. I would like to see the academic surgical establishment and/or the American Venous Forum more involved in public education.

DR. KISTNER: I think we have to make our case in America for the importance of venous disease because there's a lack of general realization of how frequent it is, how much time lost from work there is, or how much pain, suffering and disability comes from it. I think we have to look toward demographics and epidemiologic studies performed here in the U.S., and that they be based on objective testing. I think we have to gather data about the cost of chronic venous disease, and probably of acute venous disease, in order to make known what a huge impact this is. Given that sort of data, I think we can command attention. Prior to that I don't know if we can. And, of course, going along with all of this is the need for education, which is enormous. It's not just the public that needs education, it is also our own profession. All of the comments that were made about where we publish our data and get the word out are very germane.