limbs as compared with 104 of 240 limbs (43%) and 54 of 240 limbs (23%) in groups AbL and NL; $P = .0000$ and $P = .003$, respectively. In 4 of 23 (17%) limbs in group AbL, lymphangiography normalized after stenting. Quality of life scores in group AbL showed significant improvement in the work-related leg swelling category, but the other four categories were unimproved. Quality of life scores in group NL showed significant improvement in the work-related leg swelling, pain, and sleep categories and in the cumulative score. These outcome scores were significantly greater in group NL as compared with group AbL.

Conclusions: Clinical features and abnormal lymphangiography in swollen limbs with chronic venous disease cannot reliably differentiate primary from venous lymphedema. Intravascular ultrasound-guided iliac venous stenting in limbs with abnormal lymphangiograms provides substantial relief of leg swelling in almost half of the cases, but the outcome is superior in patients with normal lymphangiograms. Despite abnormal lymphangiogram, it appears to be beneficial to diagnose and stent underlying iliac vein obstruction.

Reduced Expression of Soluble Urokinase Receptor Fragment DII-III Predicts Venous Ulcers that Fail to Heal

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Background: The plasminogen activator system may be critical for venous ulcer healing. Urokinase plasminogen activator receptor, which is composed of 3 domains (DI, DII, and DIII), is expressed in the epidermal layers of the ulcer edge. This receptor may be cleaved in the linker region between DI and DII, yielding two separate fragments (DI and DII-III) and exposing a highly chemotactic area on the DII-III domain that is a potent inducer of cell migration. This study compares levels of soluble urokinase plasminogen activator receptor (suPAR; DI-III) and its fragments in exudates from healing and nonhealing venous ulcers.

Methods: Patients with venous ulcers (CEAP C6 disease) were recruited from a dedicated leg ulcer clinic. Venous etiology was confirmed on venous duplex. Ulcer exudates were aspirated from Opsite-covered ulcers at recruitment. Acute wound exudates were collected from split skin graft donor sites to act as controls. All exudates were centrifuged at 16,000 g for 10 minutes at 4°C and supernatants aliquoted, snap-frozen, and stored at −80°C until assayed. All patients were treated with standard compression dressings and prospectively followed for ulcer healing, defined as complete re-epithelialization of the ulcer within 6 months. Time-resolved fluorescence immunoassays were validated and used to measure levels of suPAR and its fragments, DI and DII-III in wound exudates. Levels were normalized against soluble protein concentration (mg/mL). Statistical analysis was carried out using unpaired *t* test.

Results: Exudates were collected from 25 patients with venous ulcers (13 females, 12 males; median age, 68 years; range, 34-92 years). Nine patients were defined as healers. Control (acute) wound exudates were obtained from seven patients (four females, three males; median age, 78 years; range, 47-88 years). Healers had significantly higher levels of DII-III (138 ± 19 fmol/mg) compared with non-healers (47 ± 7 fmol/mg; $P < .0001$) and controls (41 ± 19 fmol/mg; $P < .005$). suPAR levels were higher in both healers (19 ± 5 fmol/mg) and controls (32 ± 3 fmol/mg) compared with non-healers (8 ± 1 fmol/mg; $P < .05$ for both). There was no significant difference in the levels of DI fragment between any of the groups.

Conclusions: This is the first study to show that suPAR and its fragments are present in venous ulcer exudates. Levels of suPAR and its DII-III fragment were significantly lower in poorly healing ulcers, with the latter providing a better discrimination between the groups. Low levels of the nonproteolytic DII-III fragment, known to stimulate cell migration, could be a useful predictor of ulcers that would benefit from early skin grafting. This fragment may also represent a novel target for treatment to promote venous ulcer healing.

Failure of Microvenous Valves in Small Superficial Veins: A Key to the Development of Venous Ulcers

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Background: While some patients who develop gross varicose veins with marked reflux fail to go on to develop the skin changes of venous insufficiency and ulceration, other patients with similarly severe varicose veins do develop these complications. Why this is so is not understood. Differences in compliance in the varicose veins have been suggested. This study using retrograde resin caste venography explores another possible factor.

Methods: Resin castes were made of the superficial venous system in amputated lower limbs using retrograde filling from the great saphenous vein (GSV; similar in concept to retrograde venography to show valve incompetence in the deep venous system). Resin was injected into the GSV at the level of the medial malleolus. Outflow vessels were ligated, directing resin into the small superficial veins. This could only occur if valves guarding these regions were either absent or incompetent. Following hardening of the resin and chemical maceration of the tissues, the remaining caste was examined with a dissecting microscope for the presence of valves as identified by their unique imprint in the resin. Valves were mapped to display their (1) competence, (2) diameter, and (3) position in the branching network extending to the GSV.

Two groups of limbs were examined: a) those where duplex ultrasound prior to amputation had shown no reflux in the great saphenous vein; and b) where reflux was present along with skin changes of venous insufficiency.

Results: Variable levels of reflux were demonstrated, from the seven limbs with normal GSV, through several generations of small veins, even out to the small venular networks in the skin. Most of the 247 microvalves identified were in the third generation of small veins from the GSV, and these appeared to be most critical, as their failure most often lead to reflux directly into the skin network. There was no such reflux seen in the leg of the youngest subject.

In the four limbs with venous insufficiency with venous ulcer formation, there was dramatic extensive incompetence of the microvenous valves and appearance of resin into tortuous varicose networks in the area and into the distended capillaries.

Conclusions: Reflux and valvular incompetence occurs in the small superficial veins of the normal lower leg in the absence of reflux in the GSV. This may increase with age and with loss of tissue support around these small veins. We suggest that varicose veins only go on to damage the skin when they are associated with areas of failure of microvenous valves.

A Comparison of the Villalta and Venous Clinical Severity Scoring Instruments in the Assessment of Post-thrombotic Syndrome

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Background: Post-thrombotic syndrome (PTS) is a common chronic complication of acute deep venous thrombosis (DVT), with as many as two-thirds of patients developing symptoms of pain, edema, hyperpigmentation, or ulceration. There exist multiple instruments to assess PTS, including the commonly used scoring systems put forth by Villalta et al and the American Venous Forum's Venous Clinical Severity Score (VCSS). At present, studies comparing the two in their ability to identify and grade the severity of PTS do not exist. This is important to enable comparison of studies that have used different instruments to assess PTS. The purpose of this study is to compare the two instruments as part of a larger randomized controlled study that assessed the impact of graduated compressive stockings in the prevention of PTS.

Methods: One hundred thirty-eight extremities in 69 consecutive patients with an acute DVT documented by duplex ultrasonography were randomized to treatment with graduated compressive stockings that provided compression of 30 to 40 mm Hg or no stockings to assess impact of graduated compressive stockings on the prevention of PTS. As part of this study, these patients were sequentially followed at months 1, 3, 6, 12, 18, and 24 following diagnosis of DVT. PTS scores as defined by Villalta et al (PTSV) and the VCSS were assessed at these follow up visits. The PTSV was scored as absent (score <3 or $=3$ without objective criteria), mild to moderate (score ≥ 3 with one objective criteria), or severe (score ≥ 4), while the VCSS was assessed as absent (score ≤ 3), mild to moderate (score 4-7), and severe (score ≥ 8), based on performance characteristics of the VCSS. Each extremity was considered separately for analysis. The two instruments were compared using Pearson X^2 analysis at various time points mentioned above. Additionally, correlational statistics including Spearman correlation and gamma statistic were computed.

Results: A significant difference was not detected in the ability of PTSV and VCSS instruments to detect mild to moderate disease (Spearman correlation, 0.41-0.73; gamma statistic, 0.71-0.98; $P < .05$). For severe disease, the X^2 test suggests a difference in the ability of the two instruments to detect disease, although there exists good correlation (Spearman correlation, 0.20-0.59; gamma statistic, 0.71-1.0; $P < .05$) between the two instruments.

Conclusions: Both PTSV and the VCSS scoring systems are important tools in the identification and follow up of PTS. There exists agreement between the two instruments for detecting both mild to moderate and severe disease.

The Need for an Intersociety Consensus Guideline for Venous Ulcer

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Background: Due to their recurrence and prolonged healing time, venous ulcers (VU) consume considerable resources in healthcare systems–up to 1% of healthcare budgets in some industrialized countries. Best practice guidelines (GLs) incorporate evidence-based diagnostic and therapeutic recommendations in a cost-effective manner and have been associated