with improved and effective outcomes for many diseases (eg, deep vein thrombosis/pulmonary embolism).

Objectives: In order to develop a more universal GL we determined whether there are common elements in GLs for venous ulcers and their evidentiary strength.

Methods: A systematic analysis of GLs for venous ulcers that were identified through http://clinicaltrials.gov, a government-sponsored Web site, and from experts outside the US.

Results: Ten of 12 GL on venous ulcers (seven from North America and five from Europe) were evidence-based, with the majority using the GRADE method. Only two had been developed or updated within the last 3 years. Venous duplex and ankle-brachial index were recommended in all. Debridement was suggested in two, while simple nonadherent wound dressings were favored in nine, and hydrocolloid in two. Only one GL discussed a range of dressing options, dependent on the condition of the venous ulcers. High-pressure multi-layer compression bandages were favored in 10. Only two focused on the importance of improving ankle joint mobility.

Conclusions: While there are numerous evidence-based GLs for venous ulcers, the majority may lag recent developments in the field. There is agreement on two elements–dressings and compression, among the various GLs, which should facilitate the development of a consensus GL, similar to that for deep vein thrombosis/pulmonary embolism. To improve patient care and reduce wasted resources, it is imperative for specialty societies to join together and develop this consensus document.

Axial Transformation of the Profunda Vein Sustains Ilio-Caval Stenting in Postthrombotic Limbs

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Background: The profunda femoris vein provides an important collateral pathway when the femoral vein is obstructed by thrombosis. There is a special subset of limbs with severe obstructive postthrombotic disease in which the profunda femoris vein enlarges to a variable extent (axial transformation) to compensate for severe chronic post-thrombotic obstruction of the femoral vein. In extreme cases, the profunda femoris vein completely replaces the femoral vein as the main outflow source for the limb. This study aims to assess patency and clinical outcome after stenting of the femoro-iliocaval venous outflow in presence of femoral vein obstruction with axial transformation of the profunda vein.

Methods: Limbs with ilio-caval obstruction combined with varying degrees of axial transformation and obstruction of the femoral vein were identified. The patent proximal profunda vein was usually image by duplex ultrasound scanning, but the complete transformation and the popliteal vein connection frequently required visualization by ascending venography. The profunda vein was accessed by direct puncture in the proximal thigh or selective catherization of the profunda-popliteal connection following popliteal vein cannulation. Stents were also placed through the obstructed femoral vein after puncture in the thigh area, ensuring that the stent extended caudally to just above the profunda vein. Stent patency was followed by venogram or ultrasound imaging. Symptoms of pain (Visual Analogue Scale, 0-10), swelling (grade, 0-3), and ulcer healing were recorded prospectively.

Results: Thirty-two limbs in 31 patients (median age, 50 years; range, 22-77 years; female/male ratio, 3/1; left/right limb ratio, 2.6/1; C5-6 = 37%; obstruction combined with reflux in 68%) were included in this study. Stents could be placed in all but two patients (failed recanalization). No major complications occurred. Twenty-eight limbs were followed for 17 months (median; range, 1-133 months). The cumulative primary, assisted primary, and secondary patency rates at 4 years were 38%, 88%, and 88%. Leg ulcer was found in four patients; three ulcerated limbs healed. Cumulative complete relief and improvement of pain (Visual Analogue Scale drop ≥ 3) and swelling (≥ 1) at 4 years were 62% and 70%, and 39% and 84%, respectively.

Conclusions: It may appear to be impossible to stent patients with extensive post-thrombotic obstructive disease because of perceived poor inflow. It is worthwhile to identify the presence of an axial profunda vein transformation in these limbs. Caudad extension of stenting of the femoro-ilio-caval venous outflow to just above or into a patent profunda vein transformation in the presence of an obstructed femoral vein results in satisfactorily high patency rates and substantial symptomatic relief. Additional nonvisualized axial collateralization may also contribute to these results.

Role of Vein Tissue Nitric Oxide and Hyperpolarization in Venous Relaxation: Implications in Venous Insufficiency Disease

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Background: Vein wall dilation may play a role in varicose veins. However, the cellular mechanisms involved in vein tissue relaxation are not clearly understood. We have previously demonstrated that matrix metalloproteinase-2 induces venous relaxation and hyperpolarization. The purpose of this study was to further characterize the venous relaxation pathways and the K^+-channels involved in hyperpolarization.

Methods: Circular segments of inferior vena cava were isolated from male rats, and suspended between two wires in a tissue bath for measurement of isometric contraction/relaxation. Following contraction to 96 mM KCl and phenylephrine (PHE; 10^{-5} M), veins were treated with acetylcholine (ach; 10^{-9} to 10^{-5} M), and venous relaxation was measured. To measure the nitric oxide- and prostacyclin (PGI_2)-dependent relaxation, veins were treated with L-NAME (3×10^{-4} M) and indomethacin (10^{-5} M), respectively. To measure the hyperpolarization pathway, the tissues were treated with tetraethylammonium (TEA; 10^{-3} M), a nonselective blocker of K^+ channels. To test for the contribution of a specific K^+-channel, the effects of K^+-channel blockers on ach-induced inferior vena cava relaxation were tested: apamine (small conductance Ca^{2+}-dependent, 10^{-7} M), iberiotoxin (IbTx; large conductance Ca^{2+}-dependent, 10^{-8} M), 4-aminopyridine (4-AP; voltage-dependent, 10^{-3} M), and glibenclamide (GLB; ATP-dependent, 10^{-5} M). Relaxation data are presented as % means ± SEM.

Results: ach caused concentration-dependent relaxation of PHE contraction (max, 48.3 ± 5.4). In the presence of L-NAME, ach-induced relaxation was reduced (max, 28.8 ± 5.7; $P = .009$). Addition of sodium nitroprusside (10^{-5} M) caused further relaxation to 87.7 ± 2.5, indicating that the VSM relaxation mechanisms are intact. ODQ (inhibitor of guanylate cyclase and cGMP production, 10^{-5} M) inhibited ach-induced relaxation (34.9 ± 12.2), supporting a role of nitric oxide-cGMP relaxation pathway. In the presence of L-NAME and indomethacin, ach still produced significant relaxation (45.3 ± 5.4) that was abolished in the presence of TEA (0.7 ± 0.5). Cromakalim, activator of K^+ channels, caused dose-dependent relaxation (max, 94.2 ± 0.8) that was inhibited in inferior vena cava precontracted with 96 mM KCl (1.6 ± 0.1), indicating that the inferior vena cava has functional K^+-channels involved in relaxation. In veins precontracted with PHE, specific K^+-channel blockers caused significant inhibition of ach relaxation: apamine, 4.8 ± 0.3; IbTx, 7.5 ± 2.5; 4-AP, 0.0 ± 0.0; GLB, 9.2 ± 0.8.

Conclusions: A significant component of venous relaxation involves the nitric oxide-cGMP pathway. An additional component of venous relaxation involves hyperpolarization and activation of various types of K^+ channels. Increased vein tissue nitric oxide-cGMP activity and membrane hyperpolarization could promote venous dilation and varicose vein formation, and localized vein delivery of specific blockers of the nitric oxide-cGMP pathway and K^+-channels may be useful in the management of venous insufficiency disease.

Change in Venous Outflow Patterns of the Leg after High Ligation and Stripping of Great Saphenous Vein and Phlebectomies

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Background: High ligation and stripping of great saphenous vein (GSV) is still the method of choice for treatment of varicose veins in most parts of the world. Recurrence rate is high, and new endovenous modalities are developed where one of the advantages is to avoid the incision in the groin. This study was undertaken to clarify the change of venous outflow after high ligation and stripping of GSV and phlebectomies.

Methods: Forty-five patients (50 legs) with primary varicose veins with reflux of GSV (C2-C4b) participated in this study. They were examined before and 1-3 months after surgery using multi-detector computed tomography (CT) venography (venous outflow evaluated after dye injection in the medial marginal vein of the foot until appearance of dye in the inferior vena cava) and air-plethysmography (venous filling index and outflow fraction [OF]). All participants underwent stripping of GSV from sapheno-femoral junction to knee level with the complete interruption of saphenous confluence and stab avulsion of varicose veins.

Results: CT venography visualized new superficial venous networks at calf and thigh in 40 of 50 legs, where the main distribution was 20 legs at calf, 16 legs at thigh, and four legs at both calf and thigh. Average venous filling index was significantly reduced from 4.62 mL/s to 1.85 mL/s after surgery, OF from 58.8% to 43.8%. Comparing OF in the 40 patients where CT venography showed new superficial venous network after surgery with the ten patients without this finding, there was a significant decrease in the first group (50.4% to 44.6%) but no change in the second group (47.7% to 48.5%).

Conclusions: After high ligation and stripping of the incompetent GSV above the knee with phlebectomies, 80% of the legs showed new superficial venous networks draining the venous outflow from the distal GSV using CT venography. This may reflect the decreased venous hypertension or a compensatory development of superficial veins after removal of the GSV outflow.