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Late Complications of Deep Venous Thrombosis: Painful Swollen Extremities and Non Healing Ulcers

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1. Introduction

Patients with complications of deep vein thrombosis (DVT) experience a “life changing event” stemming from their DVT. Constant swelling, pain and discoloration of the involved lower extremity are common. These symptoms result from “venous hypertension secondary to reflux, obstruction, or insufficiency of muscle pumps” (Kearon 2003; Labropoulos 2004). Although the symptoms are well described, patients often have no plan for long term follow up after the acute DVT event. The venous system adjusts to impaired valvular function and obstructed outflow venous channels in the first year following the DVT. A life long commitment to compression hose therapy (Franks, Moffatt et al. 1995) with ambulation and extremity elevation at rest will minimize swelling and pain. Unfortunately, in the acute phase patients often cannot tolerate compression hose but they should be “coached” into compression hose as soon as possible. “60% of patients post DVT develop post thrombotic syndrome (Ashrani, Silverstein et al. 2009); fitted, graded compression hose reduce the rate in half” (Kahn ; Brandjes, Buller et al. 1997; Pirard, Bellens et al. 2008). Following a course of anticoagulation and advice for compression hose therapy, DVT patients usually are followed by their primary care provider. Recently there has been increasing interest in more closely following DVT patients. A duplex supervised by a vascular/vein specialist should be performed to assess the “pumping” capacity, available venous channels and valvular competence a few weeks to months after a DVT event (van Ramshorst, van Bemmelen et al. 1994; Caps, Manzo et al. 1995; Salcuni, Fiorentino et al. 1996; Nicolaidis 2000). This is especially indicated if patients experience persistent pain and swelling, or if a change occurs in the status of the limb swelling and pain after a long stable period, or if there is continued increase in pigmentation in the pressurized area. Chronic complications, post thrombotic syndrome (PTS), can present clinically depending on the initial severity of the deep venous abnormality, but may also develop abnormalities in the years following a DVT (Bradbury 2010). The overwhelming goal of the treatment of complicated post DVT patients is to preserve skin integrity and to prevent or heal ulceration (Kearon 2004; Bradbury 2010). Pain, infection, and loss of function result in a significant cost to the patient and the community as a whole.

2. Anatomy

Veins are substantially different from arteries and exist as a network of thin channels with little intrinsic muscular wall. Large intramuscular veins like the gastrocnemius vein can

dilate with the muscle relaxed and empty with calf muscular contraction. The veins in the calf muscles (May 1975) and the plantar venous plexus (Corley, Broderick et al. 2010) are major components of the muscular pump but all muscular veins contribute as do the superficial systems to the return of extremity venous blood. Obstruction leads to dilation of these deep muscular veins and perforating vein connections to the subdermal veins.

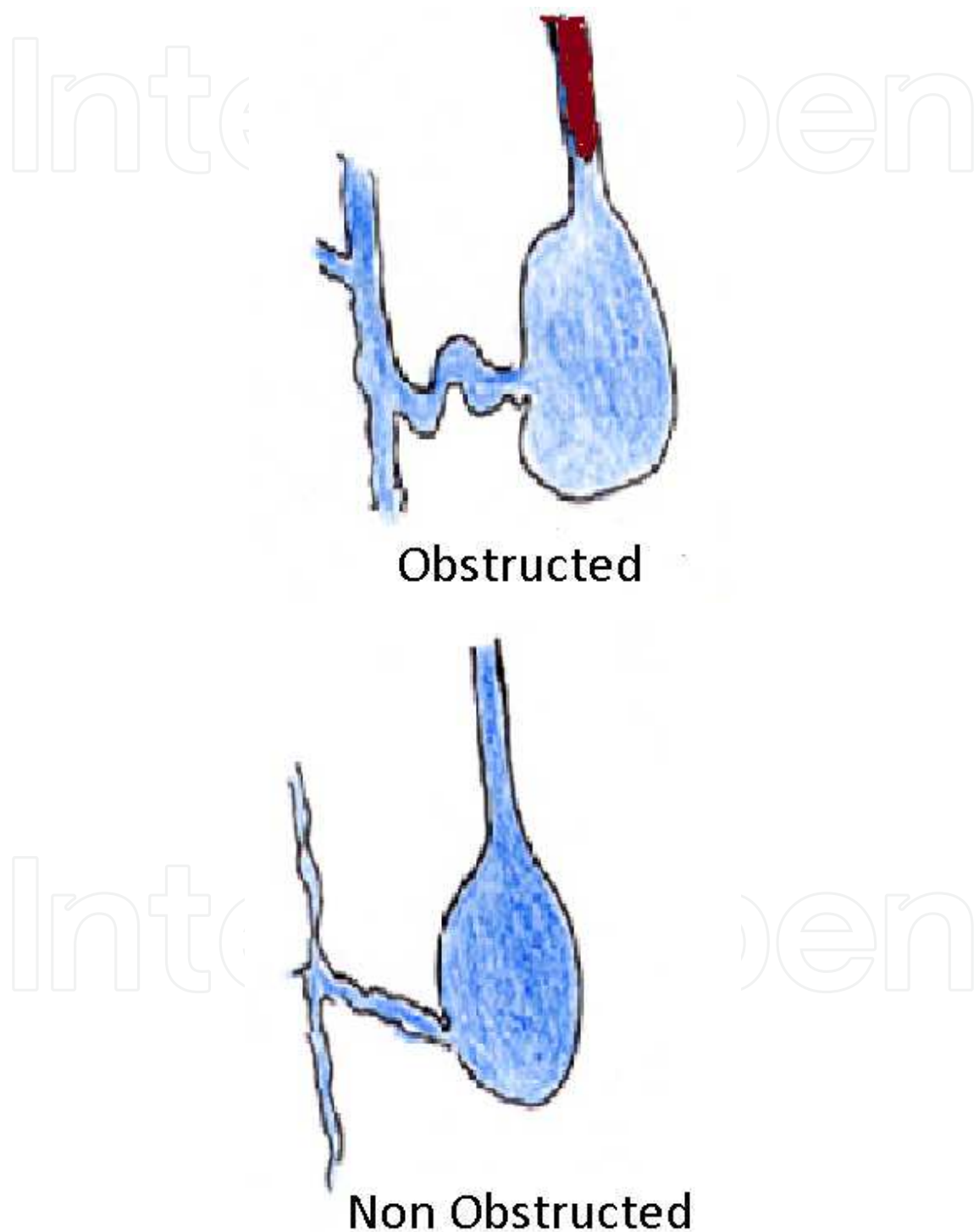


Fig. 1. Diagram of muscular pump with and without obstructing venous thrombosis. Note, bulging sub dermal veins.

Veins that connect the subdermal veins and saphenous veins to the deep vein are called perforating veins. The muscular vascular pedicle usually enters the proximal portion of the muscle with the distal muscle and tendons are relatively less vascular. The perforating veins usually follow the cutaneous nerves in a neurovascular bundle. The increased volume and eventually pressure to the subdermal (reticular) veins leads to expansion of the subcutaneous vascular space. The actual distribution of venous blood and pressure is distributed through this system and related to the configuration of each pressurized subdermal vein complex. Three different complexities have been described as the perforating vein (P) exits the deep fascia to enter a sub dermal vein (Hern and Mortimer 1999; Schaverien, Saint-Cyr et al. 2008).

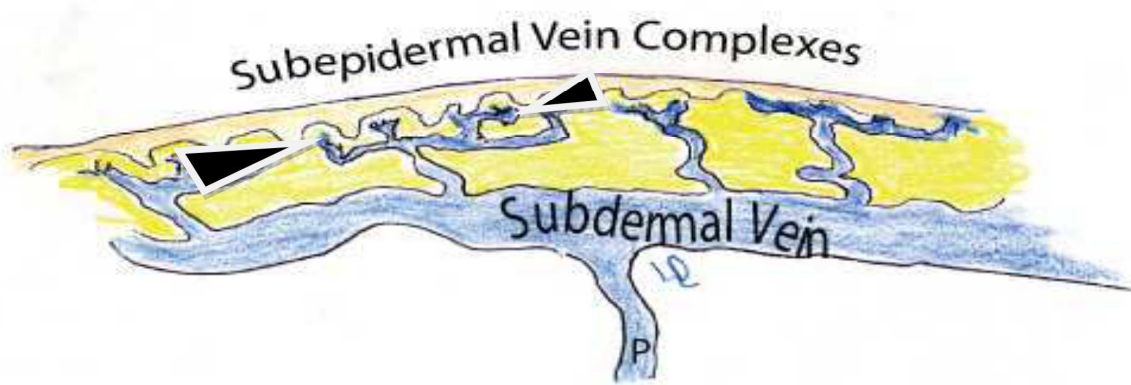


Fig. 2. Diagram of perforating vein, subdermal vein and subepidermal vein complexes.

Terminal Branches distribute the pressurized blood over this distribution. This increased pressure leads to dilation and increased tortuosity of the distal arterioles and capillaries. That associated edema of the epidermal papillae, impaired skin nutrition and eventual ulceration (Hern and Mortimer 1999). The figures below show a normal venogram demonstrating venous filling and pumping for an injection of a vein in the foot. Varicose veins and abnormal perforating veins are also visualized on venography (figure 4). The resultant dilation of the subdermal veins also can be documented in the clinic with duplex imaging (Hanrahan, Araki et al. 1991; Stuart, Lee et al. 2001). This anatomy is complex and pressurization can affect the viability of the overlying dermis. Plastic surgeons have recognized and studied this venous anatomy (Schaverien, Saint-Cyr et al. 2008). In this work there are excellent figures with the anatomy of the epidermal and subdermal venous anatomy and emphasizes the role of the perforating vein and the complex of subdermal veins in the outcome of "anterolateral thigh perforator flap".

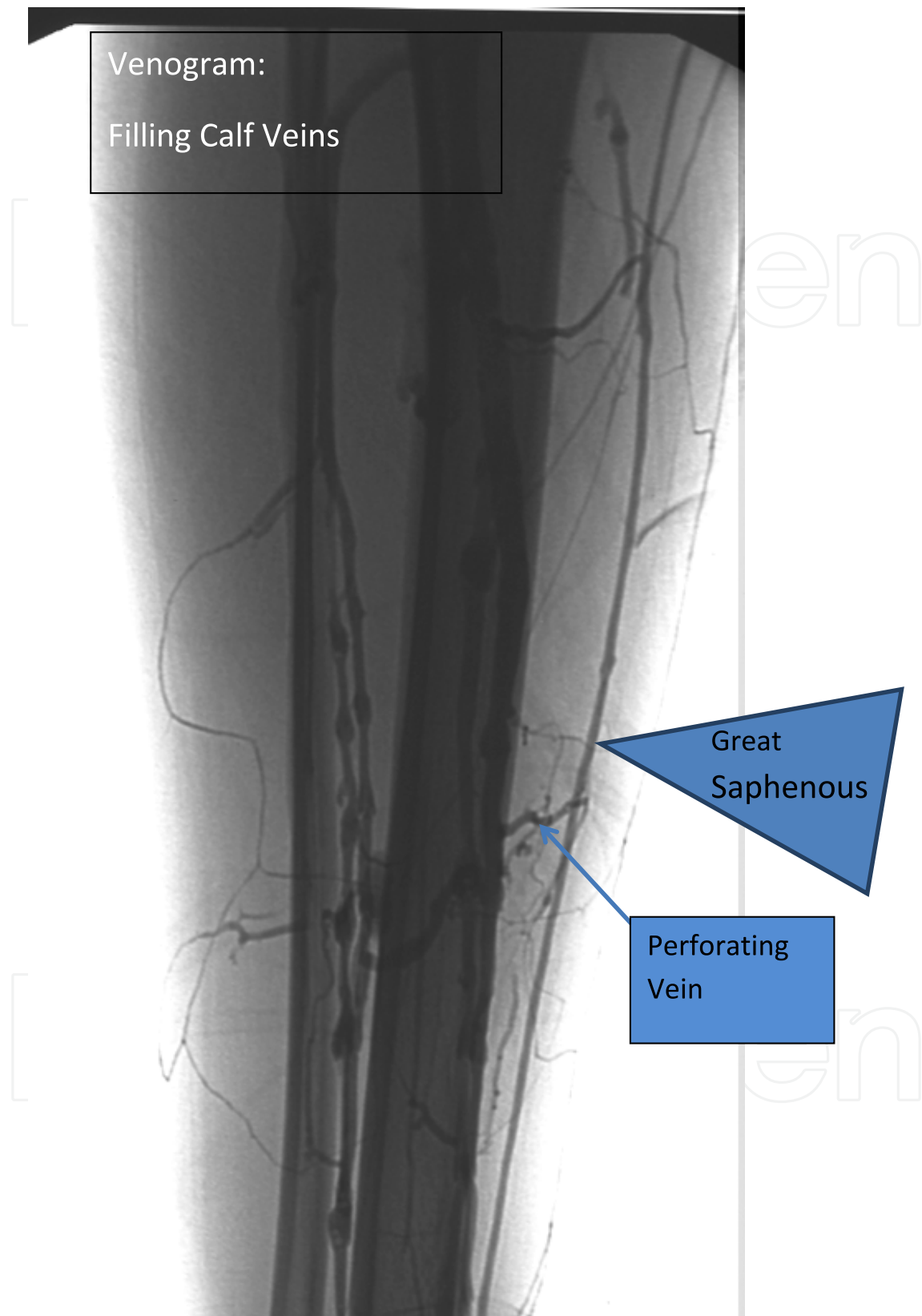


Fig. 3A. A foot veins has been injected with the patient at rest and the standing at 60 degree tilt. The extremity is non-weight bearing. The deep system fills preferentially. The great saphenous vein is small and perforating veins are demonstrated.

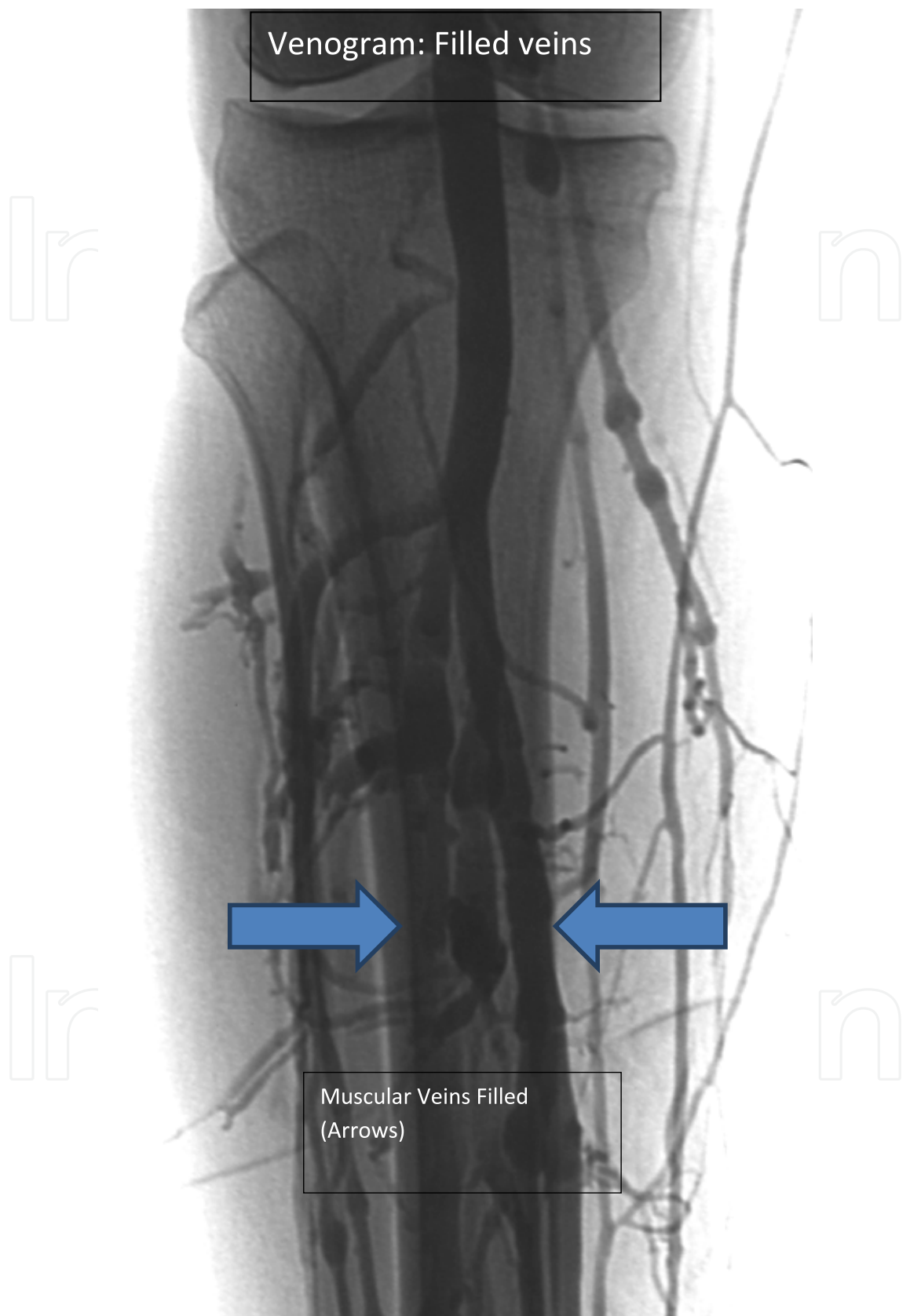


Fig. 3B. The deep veins of the calf fill and enlarge with the great saphenous vein remaining small. Normal perforating vein function.

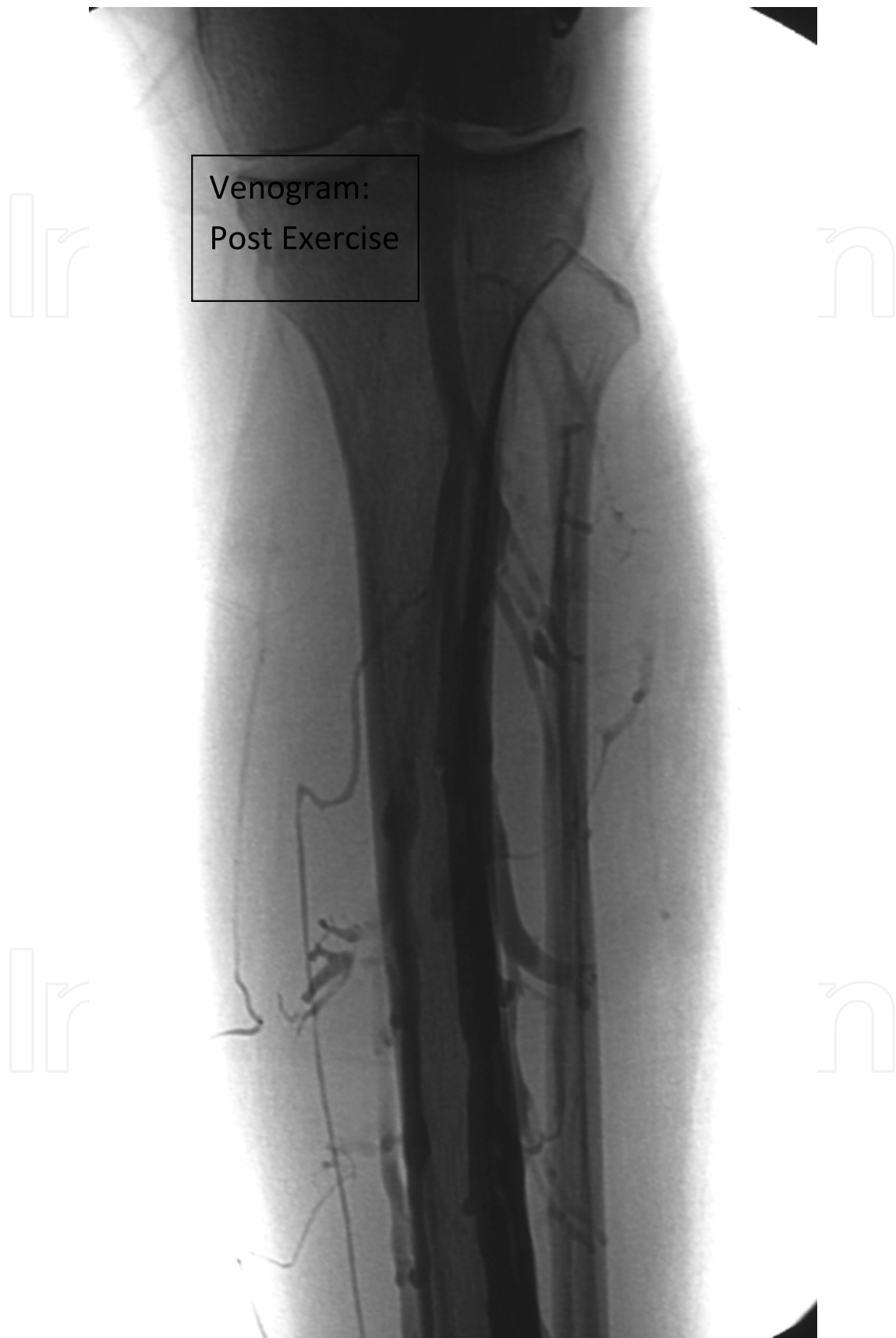


Fig. 3C. Following muscular contraction, the deep and superficial calf veins empty

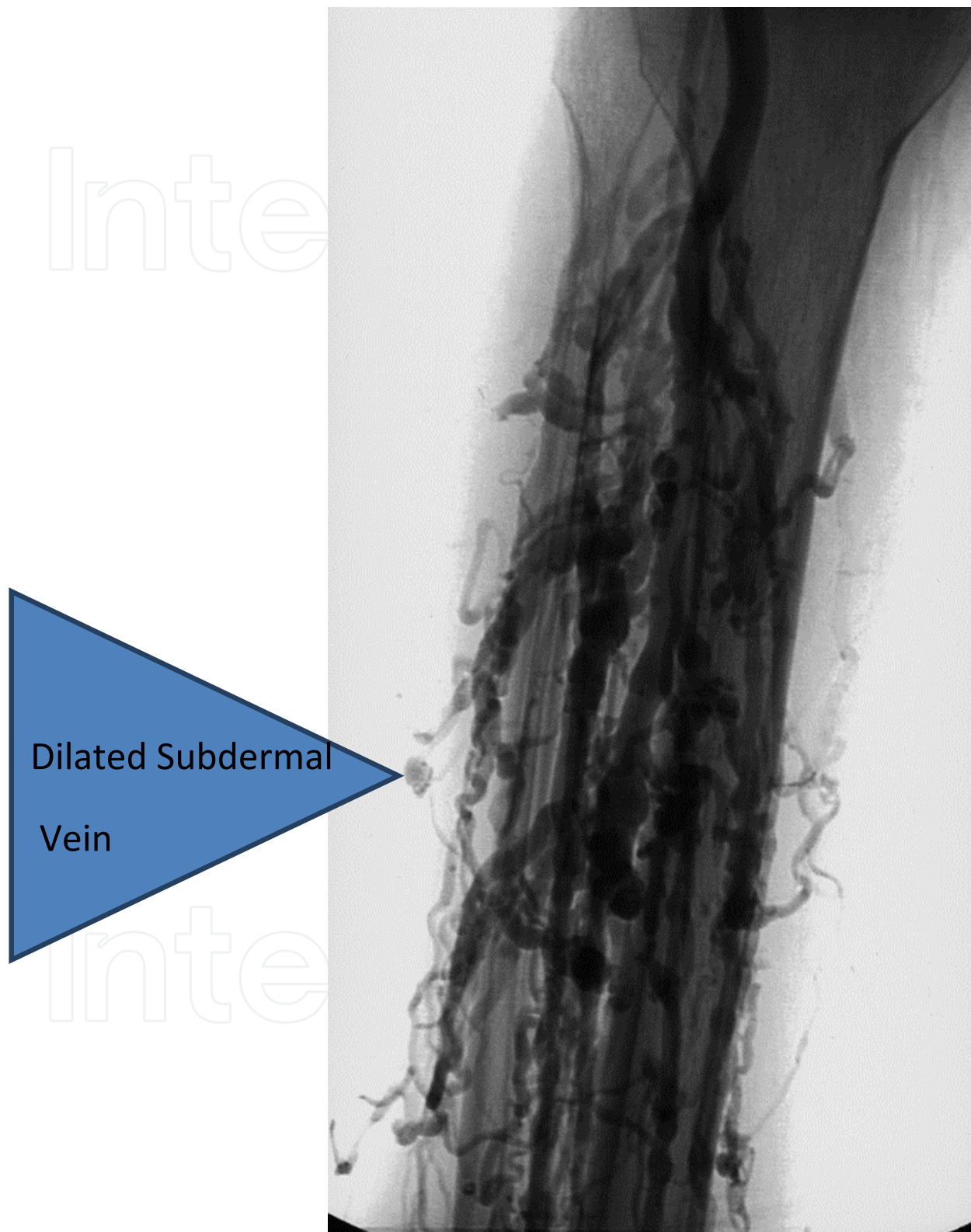


Fig. 4. Patient with proximal venous obstruction. Demonstrating dilation of subdermal vein complexes.

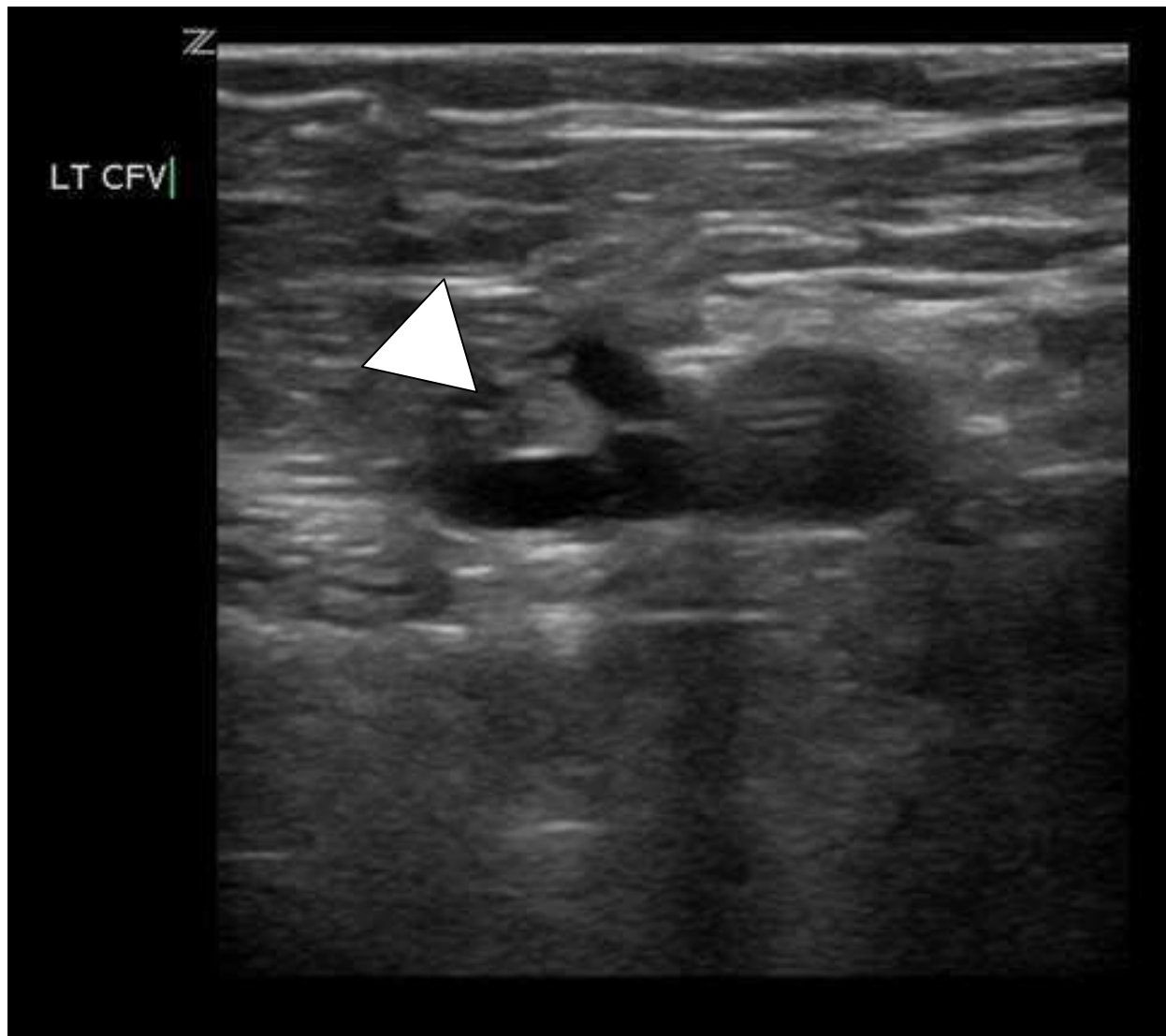


Fig. 5. Venous thrombosis left common femoral vein after 6 months, arrowhead.

After a DVT, the clinician should be aware of the early signs of a post thrombotic syndrome. At every stage following DVT there is a role for follow up in a center for vascular care and DVT patients should be alerted to the symptoms of venous hypertension, so that progression of the disease can be minimized early. The progression from increased skin pigmentation to non-healing ulceration can be prevented. Most patients cannot wear graded compression hose acutely, but as the swelling and tenderness subside the patients should be encouraged to wear compression before skin changes develop. Local venous hypertension from distal reflux leads to the skin changes and are usually associated with pain and swelling. The venous hypertension can persist and develop increasing pain and skin abnormalities including ulceration despite optimum compression hose therapy (Feltz and Rooke 2005). In addition to pressurization of the subdermal veins patient develop tense swelling of the affected lower extremity, lymph edema (Shrubb and Mason 2006). Figure 5 shows thrombus in the femoral vein that is chronic and non-occluding. The patient, though



Fig. 6. Lymph edema 6 months following DVT in left femoral vein (figure 5).

wearing compression dressings as much as possible showed tense swelling of the leg to the ankle. 4 months following her initial visit and 7 months following the DVT the femoral vein thrombus had resolved by duplex, the only residual thrombus was a partially occluding thrombus in the popliteal vein. The gastrocnemius veins cleared with exercise and no reflux could be demonstrated in the femoral or common femoral veins by duplex. Lymph edema can persist following DVT despite resolution of deep venous reflux and obstruction. This patient had skin thickening and pitting edema, which is classified as Stage II lymph edema. Evaluating these patients require a clinical examination and duplex. Occasionally, unusual conditions may arise compressing the venous return (Bekou, Galis et al. 2011). The value of an evaluation of patients with suspected DVT is emphasized by a group studied where DVT (the thrombosis in the outflow veins) was found in “213 (28.6%) of 745 suspected cases”. The clinical examination including sonography revealed, chronic vein thrombosis and superficial vein thrombosis, 122 patients (28%, and 76 patients with lymph edema (13.3%)(Taute, Melnyk et al. 2010). In acute venous hypertension may obstruct the lymphatic in the acute phase leading to the lymph edema seen as a result of gynecologic surgery where rich protein fluid absorption from the interstitium results (Bollinger, Isenring et al. 1982; Shrubbs and Mason 2006; Ohba, Todo et al. 2011). “In severe CVI leading to tropical changes of the skin lymphatic microangiopathy was detected. Obliterations of parts of the superficial capillary network, phenomena of cutaneous reflux and increased permeability of capillary fragments occurred. These findings contrast to primary lymph edema where the rete remains intact..”(Bollinger, Isenring et al. 1982). Imbalances between extracellular matrix synthesis and degradation has been found associated with chronic non healing ulcers(Moor, Vachon et al. 2009). Compression therapy is often painful. Physical therapy with massage and mechanical lymph edema pumps may be helpful but remain controversial; level one efficacy studies are not available. The patient in the example responded to the lymph edema pump, Flexitouch, Tactile Systems Technology, Inc Minneapolis, MN, USA).

Symptom severity and CEAP grade increase can be correlated to Perforating vein reflux. Perforating vein reflux is found in less than 10% of patients with CEAP grade 0 but there is an increase from 46% with Grade 2/3, 82% at with grade 4 and 90% with grade 5/6 (healed/open ulcers) (Stuart, Lee et al. 2001; Raju and Neglen 2009)

2.1 Ulcers with pain not responding to compression dressings

Evaluation of such patients by duplex can reveal large venous complexes deep the ulcers that impede healing and contribute to the pain. Sclerotherapy and Ablation (Radiofrequency Ablation(Marsh, Price et al. 2010) and Endovascular Laser(Proebstle and Herdemann 2007)) procedure can enhance healing.

Sclerotherapy has been used for many years, but targeting the subepidermal veins by ultrasound imaging can improve outcomes. Sodium Tetracyl sulfate (Sotradecol, 1 & 3 %, Angiodynamics, NJ) has been used. Other sclerosants included Pilodocanol, Asclera, and Aethoxysklerol approved only for small varicose veins, and hypertonic saline. Recently, steam has been used in a few patients with non healing ulcer. Steam would have the advantage of “percolating” into the target subepidermal vein complexes. Steam scalds the veins and coagulates the luminal contents. Further development studies are ongoing (Milleret 2011).



Fig. 7A. Patient with non healing ulcers years after DVT despite compression therapy.

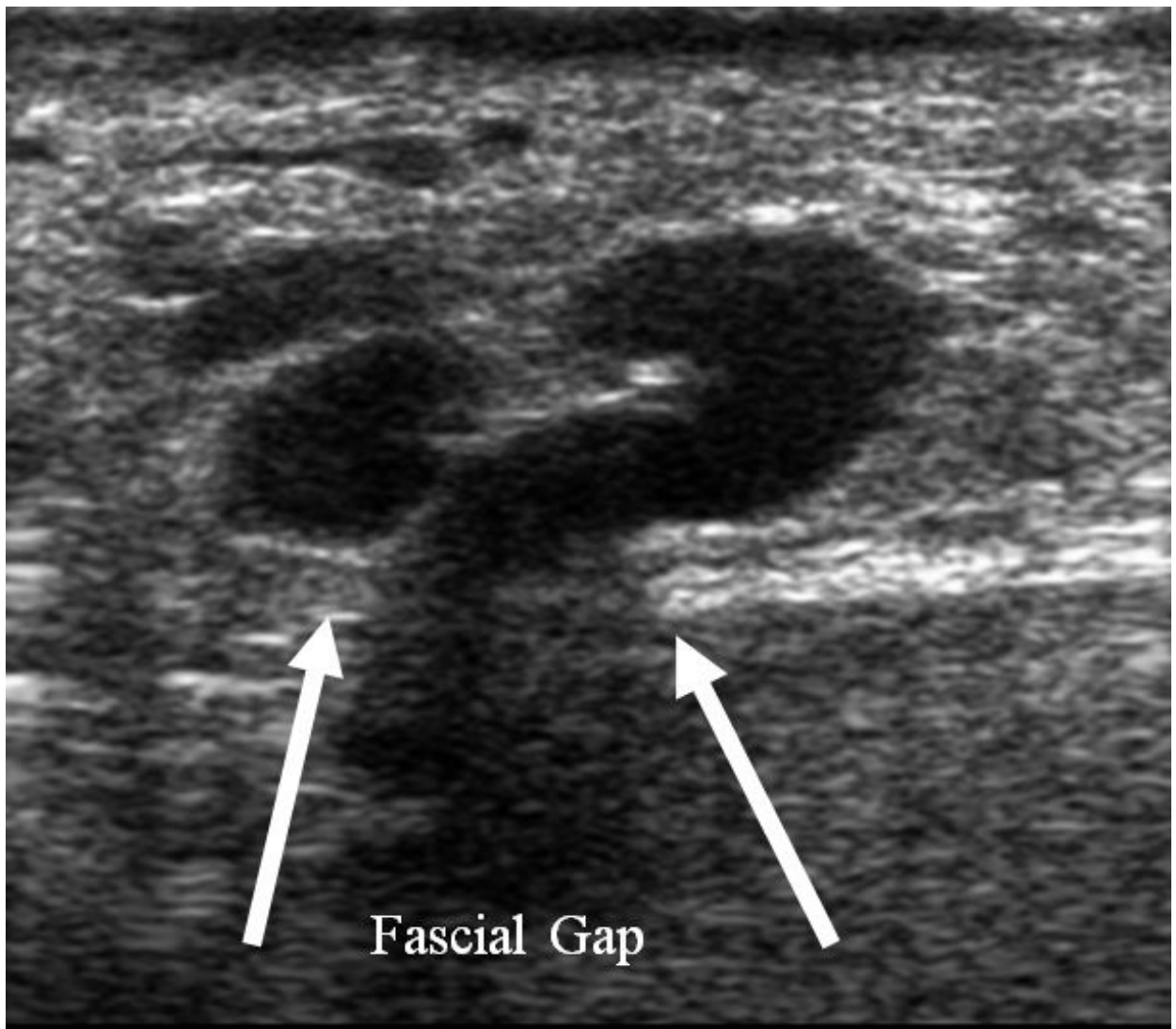


Fig. 7B. Pressuring perforating vein with incompetence by duplex.

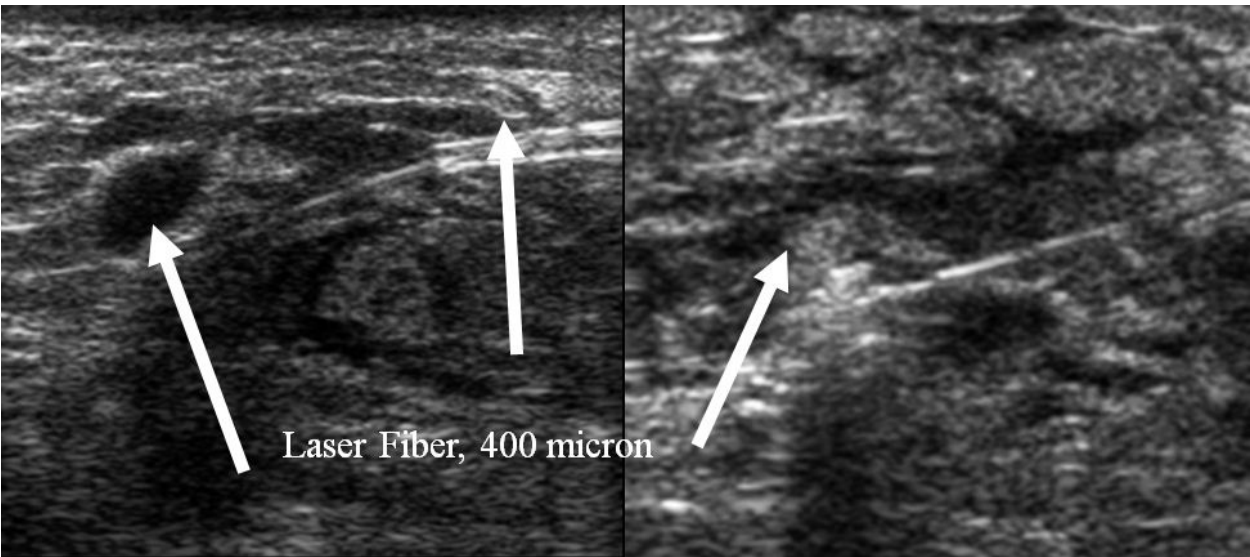


Fig. 7C. Intra procedural imaging of laser closure.

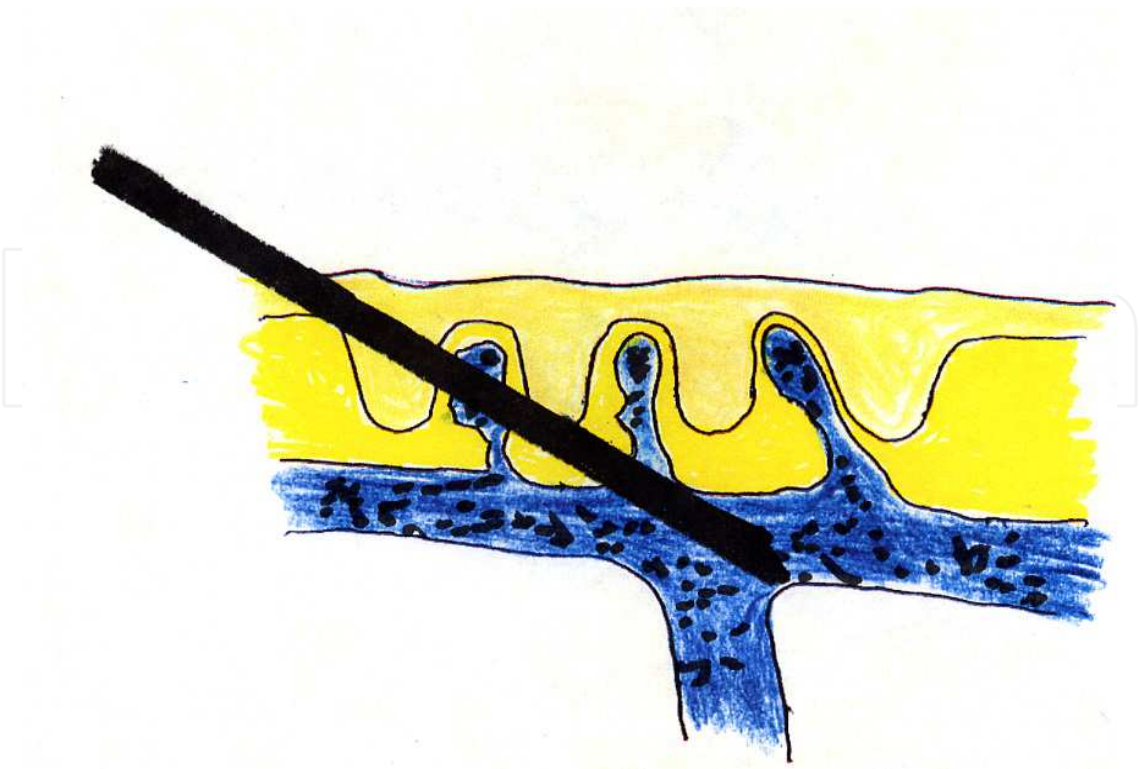


Fig. 8A. Diagram of foam sclerotherapy.



Fig. 8B. Intra procedural imaging of foam sclerotherapy.



Fig. 9. Photograph of above patient after few weeks of foam and laser therapy.

Figures 7, 8 and 9 demonstrates an obese patient that has been in compression dressings, una boot or dynaflex for the last several years. Large non healing ulcers Figure 7A, Pressurizing perforating vein demonstrated, not seen incompetent by duplex, Figure 7B, Closure of perforating vein with laser fiber, Figure 7C. Diagram of foam sclerotherapy, Figure 8A Foam seen in veins deep to ulcer Figure 8B.

2.2 Arteriovenous malformations post venous thrombosis

Patients who start to develop lower extremity pain post DVT that is not controlled by compression therapy should be evaluated. Some patients will show arterial signals on duplex distal to venous occlusions. The high flow inflow from the AVM can be found with duplex. The natural history of the neovascularity in the thrombus is unknown but has been described in the cerebral sinus post thrombosis and in the peripheral veins (Link, Garza et al. ; Chikamatsu, Nagashima et al. 2001; Aboian, Daniels et al. 2009). Many of these patients have been found to be factor V Leiden positive (Link, Garza et al.). There is evidence that the veins are not passive and may play a significant and dynamic role in revascularization through angiogenesis (Aboian, Daniels et al. 2009). It is unclear whether the AVF/AVM in thrombus is transitory or may remain permanent. Figure 10A shows a chronic occlusion of the left internal iliac vein (presumably May-Thurner Syndrome (May R 1957; Fazel, Froehlich et al. 2007) in a patient followed by her primary care physician for many years without a specific, etiologic diagnosis. She developed large open and painful ulcers. The large collateral veins on her abdomen were unsightly but was not her concern, Figure 10. (Link 2011)



Fig. 10A. Patient with chronic left iliac vein occlusion after more than 20 years.



Fig. 10B. Non healing ulcers, extremely painful, patient's main complaint.

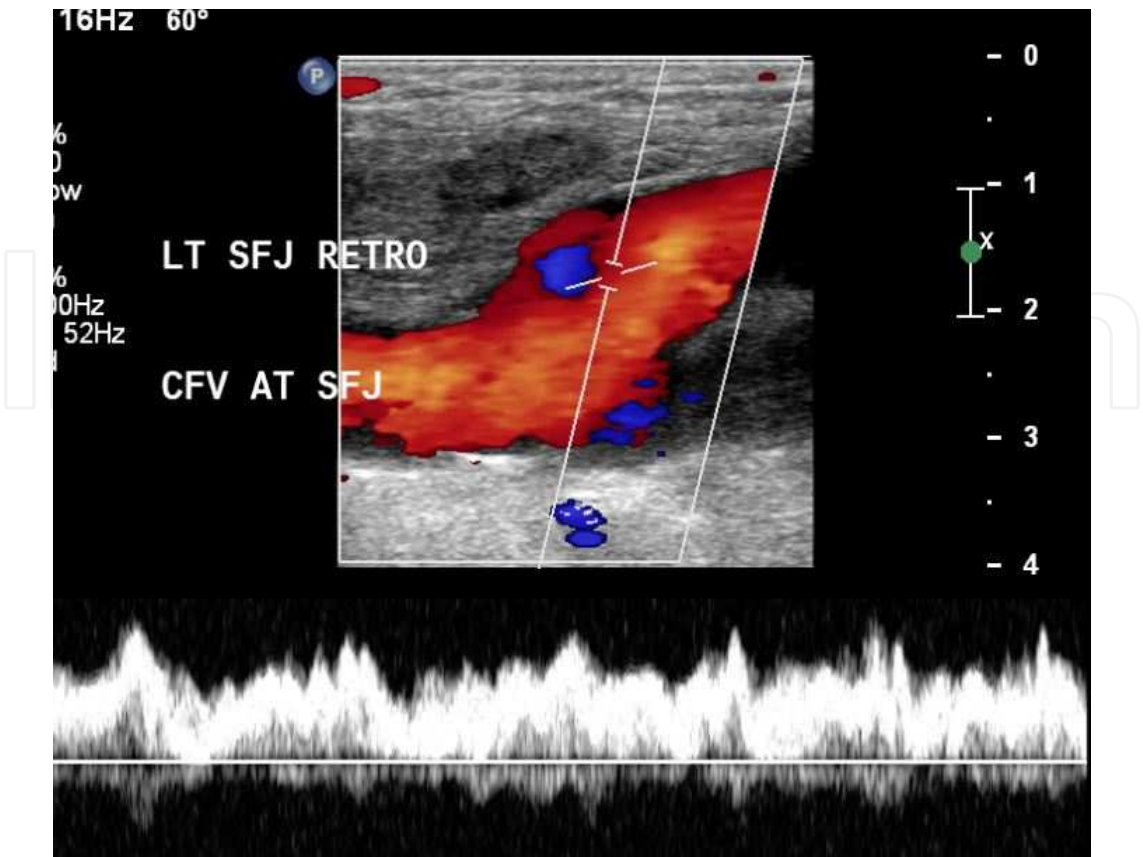


Fig. 10C. Duplex of left common femoral vein showing high flow with arterial pulses.



Fig. 11. Foam Sclerotherapy procedure in above patient (Figure 10).



Fig. 11B. Photograph showing complete healing of ulcers; patient now pain free.

Duplex examination Figure 10C showed high velocity flow in the patient's femoral vein distal to the occluded external iliac vein. An arteriogram showed a large pelvic AVM with outflow to the deep pelvic veins and to the distal veins in the left lower extremity. Occlusion of the AVM was performed with injectable ethyl vinyl alcohol polymer dissolved in DMSO (Onyx, EV3 Neurovascular, Irvine, CA) (Link 2011). The pain in the ulcerated areas improved but persisted despite compression dressings being applied weekly. Endovenous Laser Ablation (EVLT) of the veins deep to the ulcers and foam sclerotherapy (0.5% Sodium tetradecyl *Sotradecol*, angiodynamics, Queensbury, NY) was then performed on this patient). Following the procedures the ulcers healed and the patient was pain free. Interventions for this condition have included an outflow procedure to reduce the venous

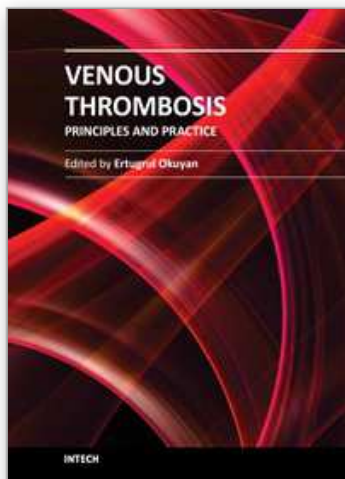
hypertension with transcatheter embolization of the arteriovenous channels from the feeding arteries (Chikamatsu, Nagashima et al. 2001). Successful treatment of the pain has been achieved in localized femoral vein AVM lesions by transcatheter injection of the feeding arteries with anhydrous alcohol combined with tissue adhesive (n-Butyl Cyanoacrylate, nbca, Trufill, Cordis neurovascular, Miami Lakes, Florida)(Link, Garza et al.). Non healing painful ulcers can be seen in end stage renal disease patients as a result of venous hypertension from their arteriovenous access,(George, Jhawar et al. 2008).

Patients who develop DVT should be followed for complications during and after the period of anticoagulation. Emphasis on compression and lymph edema treatment should lead to improved outcomes. Severe post thrombotic syndrome patients should be managed in a vascular group and some will respond to ablative and injection therapies.

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According to Virchow's triad, venous thrombosis can occur as a result of one or more of three factors: changes in the dynamics of the blood flow, endothelial injury/dysfunction of the blood vessel and hypercoagulability. The blood in the veins is constantly forming microscopic thrombi that are routinely broken down by the body, and significant clotting can occur only when the balance of thrombus formation and resolution is altered. This book is a fresh synthesis of venous thromboembolism care and considers the opinions and studies from different fields of medicine. As venous thrombosis spectrum is wide and can affect many organ systems, from deep veins of the leg to the cerebral venous system, our intent is for this to be a comprehensive, up-to-date and readable book. We tried to present a synthesis of existing material infused with new ideas and perspectives and authors own clinical studies and even case-reports.

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