SCIENTIFIC ARTICLE

Laser, "Closure", Stents and Other New Technology in the Treatment of Venous Disease

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Fast changing technology has introduced new treatment options in both acute and chronic venous insufficiency. While the experience is still relatively new, these approaches hold the promise of less invasiveness, shorter hospital stay, better symptom relief and superior or equal short-term outcome. Evaluation of long-term results will necessarily take many more years of experience in the context of the slow evolution of venous disease. A brief overview of emerging technologies punctuated with our own available experience is provided below.

Radiofrequency and Laser Ablation of Long Saphenous Vein

The percutaneous ablation techniques aim to replace traditional stripping of the long saphenous vein. Patients with varicose veins, particularly those on the medial side of the limb, usually have underlying main trunk (saphenous) reflux that feeds into the non-truncal varicosities. Removal of the varices alone without correcting the long saphenous reflux increases recurrence.[1] On the other hand, removal of only the saphenous reflux will result in early "recurrence" of the residual varicose veins. Therefore, any type of saphenous ablation should be combined with removal of non-truncal varices. The latter is now cosmetically accomplished through micro incisions (stab avulsion technique, "hook phlebectomy"). The minute scars usually fade into invisibility in a few months.

Radiofrequency (RF, VNUS® Medical Technologies, Inc., Sunnyvale, CA) and endovenous laser (EVLT®, Diomed, Inc., Andover, MA) aim to accomplish saphenous ablation through different forms of heat and eliminate the need for the groin incision (Fig. 1 and 2). The proposed advantage is less pain and discomfort in the thigh area and, therefore, an earlier return to work. Claims have been made that RF results in non-thrombotic involution of the saphenous vein[2] ("closure"), though in practice we have found thrombotic destruction to be a common pathway after either technique. We have until now an experience of 301 treatments (RF 170, EVLT® 131). In out experience, follow-up with ultrasound show a higher rate of residual reflux following RF than after EVLT® (Table I). If the main trunk of the long saphenous vein has recanalized, surgical stripping is required.

Table I. Postoperative complications (<30 days) and outcome: Laser (EVLT®, n=131) and radiofrequency (RF, n=170) techniques at 3-6 months follow-up with Duplex ultrasound scanning (follow-up of 51/131 in the EVLT® group, and 125/170 in the RF group).

	EVLT® (n=131)	RF (n=170)
Thrombophlebitis	8 (6%)	11 (6%)
Ecchymosis	9 (7%)	3 (2%)
Pain	2 (2%)	0 (0%)
Swelling	1 (1%)	1 (1%)
Residual reflux§	8/51 (16%)	44/125 (35%)

§ = remaining truncal and tributary incompetence

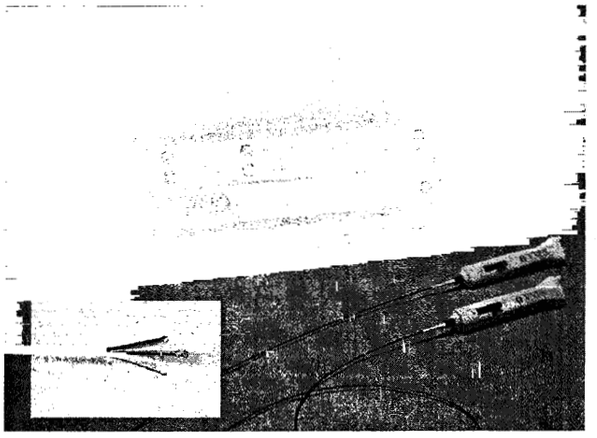

Figure 1. The generator and catheters used for obliteration by radiofrequency. The expanded tip of the Closure® catheter with typical electrodes (inset).

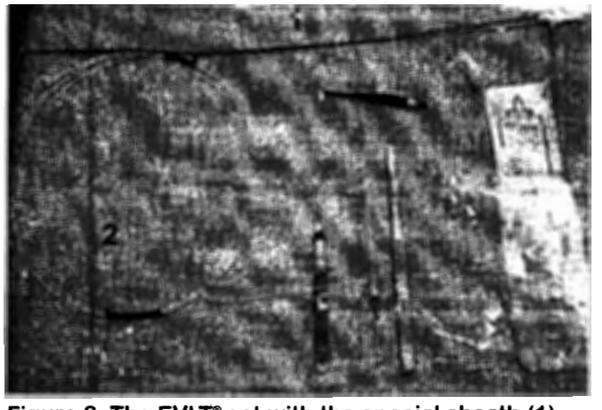

Figure 2. The EVLT® set with the special sheath (1) through which the thin laser fiber (2) is inserted. By retracting the protective sheath the tip of the fiber is released and the laser beam activated during pullback.

However, it has to be recognized that the technique of surgical stripping has also evolved significantly through the decades. Yesterday's scar prone saphenous vein stripping from groin to foot with large incisions and painful recovery has now been refined to a minimally invasive intervention with immediate ambulation. The groin and distal incisions can be very small with ultrasound localization of the saphenous vein. The primary tributaries at the saphenofemoral junction are individually divided and the saphenous trunk is removed by inversion in retrograde direction. Stripping below the knee is not necessary, and this minimizes any neuropathy caused by trauma to the saphenous nerve.[3] Non-truncal varices are removed at the same sitting.

The complications with the newer percutaneous techniques are somewhat different from surgical stripping, but the percentage incidence is very similar. In addition to less postoperative pain, the main attraction is that the newer techniques can be performed percutaneously as office procedures under local anesthesia. Device manufacturers have heavily promoted them by direct advertisement to the public as "revolutionary". While the glint of modern technology has a certain appeal, the cost of generator equipment and supplies are several times higher than traditional stripping. When carried out as stand alone office procedures, a later separate procedure for removal of non-truncal varices under general or regional anesthesia is required. If sclerotherapy is employed for treating the varices, multiple sessions over several months are usually necessary – a tedious process with uncertain outcome compared to surgery. Local complications of stab avulsions such as pain, hematoma and wound infection, though low in overall incidence, often overshadow any morbidity savings achieved with the newer technologies. Thus from the viewpoint of treating the entire varicose limb, not just the saphenous component, RF and EVLT® seem to offer the patient limited objective benefit.

The attractiveness of a "simple" percutaneous procedure with lesser pain and discomfort afterwards and prospects of returning to work earlier may, however, be decisive for many patients in today's busy world. This would be especially true, when venous

Table II. Characteristics of limbs with non-thrombotic and thrombotic iliac vein obstruction.

	Non-thrombotic Obstruction (n=438 limbs)	Thrombotic Obstruction (n=396 limbs)
Female/male ratio	3.9/1	1.7/1
Left/right limb ratio	3.1/1	1.8/1
Median (range), years	54 (14-90)	52 (18-87)

stripping is perceived as major surgery. We find the percutaneous approach to saphenous ablation an attractive feature when other procedures such as venous stenting (also percutaneous) have to be carried out in the same session to treat chronic venous insufficiency. The necessity for anticoagulation during stenting may result in bleeding in the stripping channel after open surgery, which may prolong the procedure or even result in postponement of the planned concurrent intervention.

A controversial argument has been advanced by proponents of RF saphenous ablation. They maintain that RF ablation may retard neovascularization at the sapheno-femoral junction, which is recognized as a cause of recurrence.[2] Traditionally, the complete division of all primary tributaries at the upper end of the saphenous vein has been emphasized to prevent recurrence of varicose veins. They may later enlarge providing a source of recurrent reflux to secondary varices below. These tributaries are, however, left untreated by the newer heat based techniques by necessity. Placement of the probes too close to the sapheno-femoral junction may result in thermal injury to the femoral vein and cause subsequent deep vein thrombosis. Based on short-term duplex observations, proponents argue that preservation of the primary tributaries (veins draining the abdominal wall and groin area) with prograde flow at the sapheno-femoral junction actually may be an advantage. It may forestall local venous congestion thereby decreasing chances of neovascularization and recurrent reflux. The systemic nature of varicose vein disease with inherent vein wall weakness is the major cause of recurrence and will be unaffected regardless of the technique used. In our own experience, we have already seen early recurrence of reflux fed by the preserved tributaries in approximately 5% of cases at two years following RF ablation. Our expectation is that the long-term clinical recurrence rates will likely be unaffected, if not increased, by the newer technologies. Only time will tell.

Venous Stents

In the last few years, the crucial role of the obstructed iliac venous segment in the genesis of chronic venous insufficiency syndromes (CVI) has become apparent.[4-6] Etiology of the obstruction is post-thrombotic in approximately half of the limbs stented in our practice and in the remaining half non-thrombotic (total number of 843 limbs; female/male ratio 2.5/1; left/right limb ratio 2.4/1; median age 53 years [range 14-90], non-thrombotic/thrombotic obstruction ratio 1.1/1). The non-thrombotic variety was popularized by May and Thurner[7] in Europe and later by Cockett and colleagues[8] in UK during the middle of the last century. They are variously known as May-Thurner or Cockett syndrome according to geographical affinity. The initiating lesion was thought to be compression of the left iliac vein by the right iliac artery at the vessel crossing. Cockett[8-10] advanced the notion that the syndrome afflicted predominantly young women and mostly involved the left lower extremity. Most phlebologists have considered the syndrome to be a relatively rare form of CVI, accounting for no more than 5% of cases.

The observed low prevalence of the non-thrombotic obstruction was based on venography. We now know, however, that single-plane venography has poor sensitivity in diagnosis of the syndrome. The detection of the obstructive lesion is all too frequently compromised by its discrete nature (many are membranous), oblique orientation and by too little or too much contrast for proper delineation. Single-plane transfemoral venography, which is seldom routinely performed in most centers, is only about 50% sensitive and traditional ascending venography much less. The advent of intravascular ultrasound (IVUS) has altered the epidemiologic perspective dramatically.[6,11] Using this new diagnostic modality, non-thrombotic iliac vein obstructions are now seen as occurring quite frequently in the CVI population affecting all ages, both sexes and either the right or the left lower limb (Table II, Fig. 3).

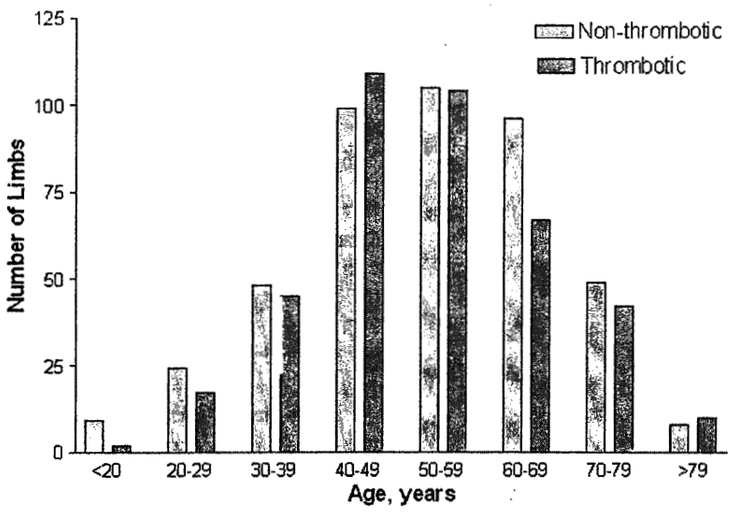

Figure 3. Age distribution in the groups of limbs with non-thrombotic (n=438) and thrombotic (n=396) limbs.

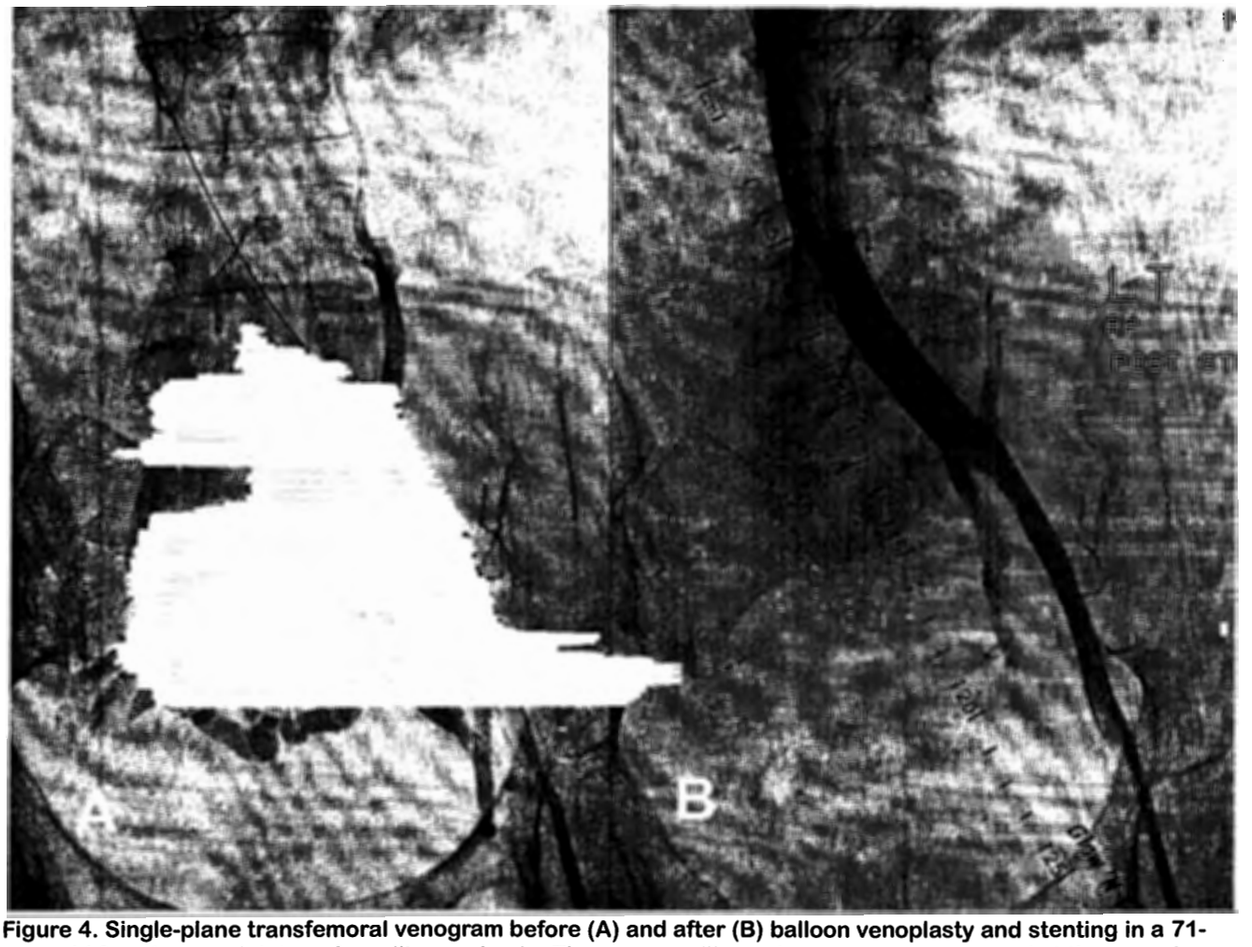

Figure 4. Single-plane transfemoral venogram before (A) and after (B) balloon venoplasty and stenting in a 71-year-old female complaining of swelling and pain. The common iliac vein appears compressed at the vessel crossing. The marked collateral veins all but disappear following stent insertion as a sign of decreased venous pressure.

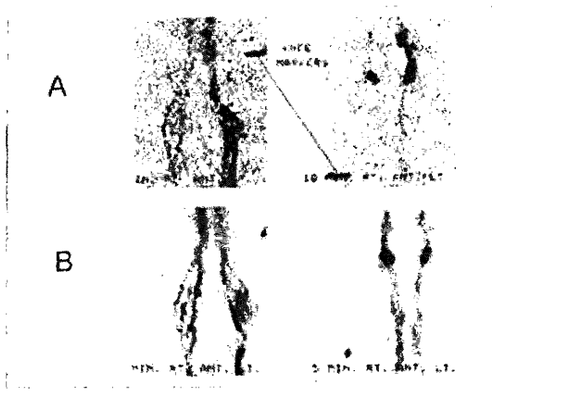

Figure 5. Lymphoscintigraphy of the lower extremities before (A) and after (B) stenting of the right iliac. The markedly reduced activity of the right leg is normalized after the stenting.

One interesting group of patients is the geriatric population, particularly women. Limb swelling in patients aged sixty or higher is often dismissed as due to fluid overload, hormonal imbalance, renal dysfunction or a "touch" of congestive failure. Limb swelling often combined with pain is poorly tolerated in this age group, with the diminished social and personal resources to pursue chronic conservative therapy. Such patients are frequently placed on diuretics with no apparent benefit to decreasing the limb swelling. It usually only increase their fluid intake to compensate for the forced diuresis. If properly investigated, either a May-Thurner type or post-thrombotic lesion is often discovered. Arteriosclerosis of the compressing artery and senile venous sclerosis may have etiologic roles. Recurrent cellulitis in the swollen extremity is often an indicator of the underlying obstructive lesion. Iliac vein stenting can stop the recurrent infections and frequently results in dramatic relief of pain and swelling in these individuals improving mobility and quality of life (Fig. 4).[12]

While the importance of iliac vein outflow obstruction is increasingly recognized the pathophysiology is poorly understood. Venous stasis ulcerations are traditionally attributed to reflux and not obstruction. Despite this observation, more than 50% of ulcerated limbs heal their ulcers after a venous stenting alone, even when the reflux component remains uncorrected.[12,13] Patients with swollen limbs mistakenly labeled as lymphedema based on clinical grounds or lymphoscintigraphy have also benefited from venous stenting.[14] Apparently a relative lymphatic dysfunction may frequently recover after stent placement to correct outflow obstruction (Fig. 5). Therefore, a thorough venous investigation is indicated in patients presenting with limb swelling regardless of the clinical impression.

Iliac vein stents enjoy impressive intermediate term secondary patency (92% at 3.5 years), and symptom relief. Prevalence of swelling decreased by 33% and almost 50% of the patients became completely free of pain (Table III). The majority of limbs with venous stasis ulcer healed (21/36, 58%), despite presence of untreated reflux in most of these limbs. The procedure has negligible morbidity (< 1%) and zero mortality in our own total experience of 834 treated limbs, including 110 patients (13%) over the age of 70 years. Thus, stent placement is a low risk, percutaneous outpatient procedure (23h hospital admission) with excellent results and it is applicable in many patients with CVI.

		Pre-stenting	Post-stenting
Swelling	Number of limbs	436	352
	Prevalence	377 (86%)	185 (53%)
	Grade (median [range])	2 [0-3]	0 [0-3]***
Pain	Number of limbs	421	348
	Prevalence	321 (76%)	99 (28%)
	Score (median [range])	4 [0-9]	0 [0-9]***

*** $p<0.001$

Table III. Clinical result of degree of pain (visual analogue scale, 0-10), swelling (grade 0-3) pre-stenting as compared to post-stenting in patients with and without concomitant reflux. The reflux remained uncorrected during the observation period of 13±12 (SD) months (range: 1-66 months).

Even totally occluded iliac veins can be successfully recannalized.[15] It does not preclude later open surgery to correct obstruction or reflux, if the stent procedure was to fail. Not surprisingly, venous stenting has become the first line of treatment in many symptomatic patients with CVI. A small number of patients who do not respond adequately to saphenous ablation or venous stenting will require valve reconstruction. Fears of inducing DVT by open or closed venous interventions have been allayed by accumulated experience. The incidence is even lower than most other surgical procedures.[16] Surprisingly, aspirin (81mg) alone has been adequate negating the need for warfarin treatment in the majority of cases.

Thrombolysis and Mechanical Thrombectomy

In chronic venous disease, such as the postthrombotic syndrome, symptoms evolve over many years. Venous decompensation may not become evident until years or even decades after the initial episode of thrombosis, sometimes due to another thrombotic insult. Postthrombotic syndrome is, therefore, rarely on the radar screen of many primary care physicians when treating patients with acute DVT. The main concern is pulmonary embolism, which may be dramatic in its presentation and sometimes, though rarely, lethal (about 3%). From a public health perspective, the incidence (approximately 60%), long term morbidity, associated disability, and costs of treatment (direct and indirect) of postthrombotic syndrome, far outweighs the impact of pulmonary embolism.

The pathophysiology of postthrombotic syndrome is a combination of outflow obstruction and reflux in the majority of patients.[17] The obstruction results from unresolved thrombus organizing into intraluminal fibrous tissue. Following thrombosis, only 20-30% of iliac veins completely resolve spontaneously on conservative treatment, while the remaining veins only recanalize partly. Most authors agree that elimination of the initial thrombus load will likely reduce or eliminate any long-term obstructive component. It is especially important that the iliac vein, which is the common outflow tract of the lower extremity, remains patent. Chronic obstruction of this segment appears to result in more severe symptoms than lower segmental blockage,[18,19] since collateralization compensates distal better than proximal obstructions.[20,21] As indicated above, obstruction appears to be at least as important, if not more, as reflux for development of symptoms. The mechanism of onset of postthrombotic reflux is not well understood, but it is believed that the valve leaflets are destroyed or in some cases rendered incompetent though preserved in the inflammatory response to the presence of clot. [22-23]

The standard treatment of DVT is initial heparinization followed by oral anticoagulation. It is well known that heparin, including the newer low molecular weight analogues, only stabilizes the thrombus in lower extremity veins. Complete resolution with anticoagulation alone is rare.[24] Because of the potential benefits of elimination of the acute thrombus load, treatment of DVT has lately focused on pharmacological thrombolysis or mechanical removal. Many lytic agents are currently available and are widely used in cardiac, stroke and dialysis access related applications. To be effective in the treatment of lower extremity DVT, the agent has to be delivered by a catheter inserted directly into the venous clot. Catheter-directed venous thrombolysis of the iliofemoral segment clearly achieves its primary goal of clearing clot.[18] An underlying organic obstructive lesion (often May-Thurner type), presumably the initiator of the thrombosis, is revealed in approximately 30% of the patients and will require stenting. Patency appears to be maintained in the intermediate term. The major disadvantage with thrombolysis is the increased risk of bleeding. In a nationwide registry of 473 cases, 54 of the patients (11%) had major bleeding complications, mostly from the venous insertion site (21/54, 39%) and into the retroperitoneal space (7/54, 7%).[25] No deaths were reported as result of these complications. The overall mortality was low (0.4%). Only two patients (0.4%) suffered intracerebral hemorrhage as a complication of lytic therapy. Onset was unpredictable and no predisposing risk factors could be identified. Despite the low frequency, the risk of this serious complication has somewhat dampened enthusiasm for pharmacolysis, although the frequency of bleeding events appears to have decreased substantially with lower dosage of the agent. A prospective randomized study comparing the catheter-directed thrombolysis with anticoagulation and anticoagulation alone is on-going.

Efforts are underway to find percutaneous mechanical alternatives for thrombus removal that would be free of the risks of lytic therapy.[26] We have limited experience with two such devices, one purely mechanical (Angiojet® Peripheral, Possis Medical, Inc., Minneapolis, MN) and another, which combines mechanical action with a lytic agent (Trellis® Reserve, Bacchus Vascular, Inc., Santa Clara, CA). With the latter device the lytic agent is sequestered between occlu-

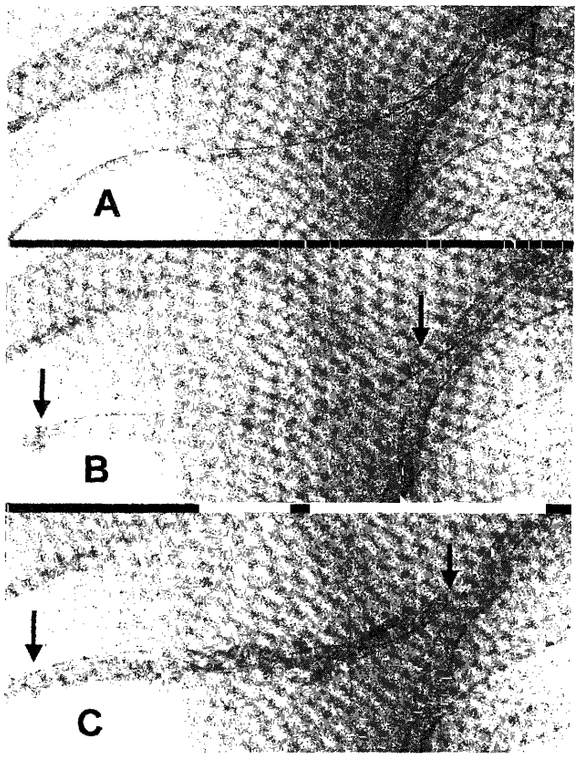

Figure 6. This is an axillary vein thrombus transversed by a guidewire (A). The Trellis® device sequestrates an area between two balloons (arrows), where the thrombus is lodged (B). A lytic agent is administered into the isolated area and the wire is twirled around until the clot has liquidified and is possible to aspirate (C). The balloons are placed to minimize the systemic effect of the lytic agent and prevent embolization.

sive balloons to prevent systemic dissipation of the agent (Fig. 6). Initial favorable results encourage continued evaluation of the devices for long term efficacy.

It appears prudent to remove an acute DVT involving the iliofemoral venous segment. Appropriate candidates for this treatment are individuals, who desire to pursue an active life style devoid of post-thrombotic syndrome. This is particularly true for the younger patients, who are at higher risk of developing symptoms because of the chronology of its evolution. Treated patients should have a life expectancy exceeding 10 years.

Summary

New technology is transforming our approach to venous disease. Once considered taboo for fear of causing deep venous thrombosis, surgical or endovenous intervention in the deep venous system is now known to be safe. Newer techniques allow minimally invasive procedures, many carried out on an outpatient basis. Traditional conservative regimens to treat acute ilio-femoral DVT are yielding to more aggressive interventional approaches to minimize the high incidence of postthrombotic syndrome with the former. Stent technology can safely and effectively relieve many of the disabling symptoms of chronic venous obstruction. Stent patency is high and morbidity low. Knowledge of venous pathophysiology has also advanced, though much remains to be learned. The beneficiaries are the large patient population with DVT and chronic venous insufficiency, which is estimated to be at least three times as large as patients with arterial disease. Unlike arterial disease, venous pathology afflicts the younger working age population in large numbers at enormous direct and social costs. In the older patient, deep venous disease is common, but seldom suspected. The symptoms are often ascribed to systemic causes. A thorough venous investigation is the key to proper diagnosis and treatment. Often, a minimally invasive procedure such as EVLT or stent insertion can offer surprising symptom relief with significant improvement in the quality of life during the twilight years.

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