Endovenous treatment of patients with iliac-caval venous obstruction

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Liberal use of intravascular ultrasound in symptomatic chronic venous disease (CVD) patients and the advent of venous stent technology have introduced a new paradigm of treatment for these conditions that often required open surgery in the past. Iliac outflow obstruction is present in >90% of limbs with CVD symptoms including in “primary” cases. In the latter, the obstructive lesion appears to function as a permissive lesion, provoking symptoms when additional secondary pathology is added. Like other known permissive lesions in human disease, symptom relief occurs after correction of the permissive lesion with a stent even when the secondary pathology is left uncorrected. Long-term stent patency is astonishingly high in “primary” disease and only slightly less in post-thrombotic subsets. Totally occluded veins, including those involving long segments of the ilio-femoral vein and vena cava, can be successfully recanalized with stent technology. The technique is minimally invasive and is carried out on an outpatient basis. Morbidity and mortality are minimal. Clinical results are excellent, including rather unexpected sustained healing of stasis ulceration in about 60% of patients. Later open surgery of the traditional types is not precluded should the stent were to fail. These attributes hold the promise of wider application of stent technology to a class of symptomatic CVD patients than was possible with open surgical techniques.

Key words: Ultrasonography, interventional, utilization - Vascular diseases - Surgical procedures, minimally invasive - Femoral vein, surgery - Vena cava, surgery.

Deployment of endovenous devices has a long history, with the first vena cava filters introduced in 1969. The excellent long-term patency of IVC filters, despite functioning as flow traps in a thrombogenic environment, was a harbinger of the astonishing patency of the flow-optimized stents in current use. Today venous stents are deployed in a broad spectrum of chronic venous diseases (CVD), with different clinical, etiologic, and pathologic features.

A brief review of current state-of-the-art including indications, diagnosis, technique and long-term results follows.

Indications

Generally symptomatic patients, CEAP class 3 and higher, who have failed conservative therapy are candidates for potential stent placement. Some class 0-2 may also be considered if they have venous pain (visual analogue scale >5 or requiring narcotics for control). About 5% to 10% of CVD patients have venous pain as the sole manifestation of the disease without any other signs. Pain disproportionate to clinical signs of CVD should also arouse suspicion of underlying outflow obstruction. Patients with severe stasis skin changes or ulceration are obvious candidates. Conservative therapy will fail in half or more of the patients in this category. Venous stenting after investigation should be considered in patients after conservative therapy has been unsuccessfully tried for a reasonable period, say 6 months to a year.

A CVD subset that is enlarging because of changing demographics is that of elderly patients, particularly women with leg swelling. The deterioration in quality of life from reduced mobility and ability for self-
care that leg swelling imposes in this geriatric group who are living alone is easily underestimated. Often the swelling is not investigated adequately and diuretics are prescribed on an empiric basis without effect. A venous basis for the swelling, even when bilateral, is often found on adequate investigation. Conservative measures may be difficult or impossible in this subset because of frailty of age, comorbidities or fragility of skin. Successful relief with a stent procedure may mean the difference between continued self-care and institutionalization.

Another CVD subset worth mention is that of patients with onset of leg swelling at an early age: these cases are often misdiagnosed as lymphedema, without benefit of a full venous and lymphatic investigation. A venous obstructive lesion may underlie the presentation. Lymphangiolegiogram may be surprisingly normal or may show delayed flow from lymphatic exhaustion or damage as a result of long-standing venous obstruction and resultant lymphatic overload. Lymphatics may recover after successful venous stenting in such cases.

**Clinical assessment**

The introduction of CEAP classification and the adjunctive clinical severity scoring system has simplified and standardized clinical assessment of CVD. Routine use of these tools amplified with a visual analogue scale for pain measurement is recommended for initial and follow-up assessment of CVD patients undergoing conservative or invasive interventions of any type. Improvement and regression in the clinical status of patients being followed quickly becomes clear when such standardized assessment tools are routinely used. Quality of life assessment tools are now available for long-term assessment of venous patients.

Assessment of limb edema remains imprecise. The venous clinical scoring system recommends the time of day (a.m., noon or p.m.) when swelling becomes maximal as reported by the patient. Patients become more aware of limb swelling when it is associated with pain and may be oblivious to it when it is painless. Thus the above method of grading has drawbacks. Grading swelling by physical examination (pitting, ankle edema, gross) is the current method of choice. This methodology too has a wide scale; for example, limb swelling that improves from involving the entire extremity to below the knee following intervention will not be marked as improvement by this technique despite obvious clinical benefit. Because limb edema is variable throughout the day, limb measurements should be carried out at the same time of day for progressive monitoring. Plethysmographic techniques for limb measurement are more reliable but are cumbersome and not amenable to easy clinical application.

**Etiology of venous outflow obstruction**

It has long been considered that post-thrombotic etiology largely represents most venous obstructions that come to clinical attention, with congenital, neoplastic or other causes being relatively rare in practice. This concept is undergoing some reappraisal as a result of current clinical stent experience. Since the original description of "primary" (non-thrombotic) iliac vein obstruction by McMurrich in 1908, a number of autopsy studies have confirmed the presence of a silent form of the lesion in 20% to 50% of the general population. The lesion is in the form of an intraluminal web; extrinsic compression by the artery may also be present. The term non-thrombotic iliac vein lesion (NIVL) has been suggested to denote either form, whether intrinsic or extrinsic. Modern imaging techniques estimate the prevalence of NIVL in the general population at about 60%. It is also well established that some of these lesions (probably 2% to 3%) become pathogenic, causing symptoms (May-Thurner or Cockett syndrome). The lesion may be associated with, or perhaps even trigger, iliac vein thrombosis in some patients. With the use of intravascular ultrasound (IVUS) for iliac vein assessment in symptomatic patients, it has become clear that the proportional incidence of NIVL and post-thrombotic cases is now 1:1, i.e. NIVL is found as often as post-thrombotic lesions in symptomatic patients. Routine use of IVUS in symptomatic CVD patients reveals either post-thrombotic or NIVL lesions in >90% of examined limbs. NIVL occurs on both sides (more often left), in both sexes (more often women) and in all age groups. The large prevalence of NIVL in silent form in the general population, and the even higher incidence in symptomatc patients, suggest a permissive role for the lesion in CVD patients. Permissive lesions that often remain silent but predispose to symptoms with onset of secondary
pathologies are ubiquitous in human disease. Some well known examples include patent foramen ovale and stroke, ureteral reflux and pylonephritis, esophageal reflux and asthma, colon polyps and cancer, obesity and diabetes and diabetes and neuropathy. In such complex pathologies, correction of the permissive lesion alone often results in symptom remission, even when the secondary associated pathology is not directly addressed. As a permissive lesion, NIVL may remain silent until additional secondary pathology/factors such as reflux, trauma, cellulitis, venosclerosis, arteriosclerosis of the overlying artery, immobility of the limb or prolonged limb dependency add to precipitate symptoms. In some cases, no such secondary pathology is apparent; it is assumed that further progression of stenosis is the basis for onset of symptoms. NIVL is associated with reflux (a third of it axial) in about half the stented limbs. Like other permissive lesions, correction of NIVL results in symptom remission; stent correction of NIVL results in symptom remission even when associated reflux remains uncorrected.14, 19 The very high prevalence of NIVL or post-thrombotic lesions in symptomatic CVD patients means that stent technology will be applicable in many, or indeed most, of these patients. That associated pathology can be ignored with expectation of remission indicates that stenting can be the initial, and often the definitive, approach in the majority of these patients. The minimally invasive and safe nature of this technique only enhances its attractiveness and potential for wide application. Later open techniques are not precluded if the initial stent procedure should fail.

Hemodynamics of venous obstruction

The hemodynamic importance of a segmental venous obstruction, and hence its propensity to produce symptoms, will depend upon its level (central or peripheral), presence of collaterals and additional pathology such as coexisting reflux. There are wide segmental variations in these attributes. Inferior vena cava and femoral obstructions appear to be well collateralized from naturally-occurring collaterals that have an embryonic basis.25, 26 Curiously, in vena cava obstructions only one limb is often symptomatic. The natural collaterals are present in putative form and enlarge rapidly once the main channel is obstructed. The flow within these collaterals is in the same direction as before and flow reversal against valves is not required for their function. Perhaps for this reason, "natural" collaterals are efficient; inferior vena cava (IVC) and femoral obstructions that remain clinically silent because of excellent natural collateralization are well known. Most of the IVC collaterals arise from the iliac vein. IVC obstructions tend to become symptomatic when the iliac veins are compromised by disease or occlusion.26 The iliac veins themselves appear to have few natural collaterals. When the iliac vein is obstructed, collateralization occurs via former tributaries with reversal of flow. This situation is inefficient. Furthermore, collateralization may be retarded by a perivenous sheath that develops in post-thrombotic cases.27 Iliac vein occlusions are much more frequently symptomatic than not, even when collaterals appear to be profuse on venography.28 Post-thrombotic obstructions are frequently disseminated with involvement of a combination of proximal and distal segments. The therapeutic focus in such cases should be the iliac vein segment for symptom relief as other segments are generally well compensated.

In NIVL only the iliac vein segment is involved in the obstructive process and collateral development is variable. A combination of obstruction and reflux is the dominant pattern in post-thrombotic disease;29 and a similar combination is increasingly recognized in "primary" disease as well, with use of IVUS.19, 30-32 Intuitively, such a combination would appear to present greater hemodynamic severity than either pathology alone; however, there are no reliable metrics currently available to quantitate hemodynamic severity of either pathology. Correction of obstruction alone in combined disease results in symptom remission including healing of stasis ulceration;19 conversely, abolition of reflux in the presence of obstruction results in symptom remission as well.33, 34 Segmental correction of reflux even at a single level results in symptom remission when the reflux involves multiple levels and systems.35, 36 Partial correction of venous pathology is, therefore, often clinically effective. A greater understanding of involved hemodynamics will not be possible until more accurate quantitative measurements become available.

Investigations

Duplex is widely available and remains the initial screening technique of choice. In the University of
Mississippi's clinical series, approximately a quarter of patients with CVD symptoms show little or no duplex abnormalities in the limb below the groin. The iliac vein segment should definitely be investigated in this subset and in all others as well to complete a comprehensive examination. While duplex can be employed to examine the iliac veins with special techniques, the methodology is still evolving and cannot be considered definitive. Venography has been widely used but has drawbacks. Ascending venography by pedal injection of contrast is unreliable, as adequate opacification of the iliacs may not be achieved for proper interpretation. Transfemoral venography is more satisfactory in this respect but has a diagnostic sensitivity of only about 50%, owing to the fact many iliac vein lesions are sagittal and are missed in the traditional frontal projections. Webs and membranes are easily obscured by contrast. Absence of collaterals does not rule out a significant obstructive iliac vein lesion; only about a third of clinical cases present with collaterals. IVUS does not suffer from such deficiencies and has a diagnostic sensitivity of >90%. Essential features of venous pathology such as wall fibrosis, trabeculae, and lumen size are more readily visible on IVUS than with contrast venography. IVUS has become the gold standard for definitive assessment of the iliac vein segment. Venous stenting is generally carried out at the same sitting as diagnostic IVUS. IVUS has been found invaluable during stent deployment to accomplish the many necessary technical steps in a more precise fashion than is possible with radiologic guidance alone. It is also free of radiation exposure hazard, still another benefit.

**Technique of venous stenting**

Venous stenting is performed with the patient in the supine position. General anesthesia is preferable as iliac vein balloon dilatation can be painful and better cardiopulmonary control and oxygenation are achieved particularly in the elderly patient. About a quarter of stented patients are geriatric; there have been no anesthetic deaths. After successful stenting, patients are discharged after overnight observation (23 h stay).

Femoral vein access is obtained at the mid thigh level under ultrasound guidance. Maneuverability of guidewires and other endovenous implements is superior to the popliteal approach, which requires a proper position a drawback in obese or elderly patients. Because of ultrasound control, low pressure in the venous system and routine use of a sealing device, access complications are extremely rare. The femoral, iliac and IVC segments are assessed by on-table venography (optional to provide a guide map) and definitively by IVUS. Lesions greater than 60% lumen stenosis are considered significant. They are dilated by balloon to normal lumen size (12 mm common femoral, 14 mm external iliac, 16 mm common iliac and 21-24 mm IVC). Similar size stents are necessary as smaller size stents may thrombose or may not adequately decompress the limb, even if they remain patent. The upper landing site is the IVC, usually about 3-4 cm above the common iliac confluence (or even higher in the case of IVC involvement). Extension of the stent into IVC is necessary as the iliac-IVC junction is a choke point and will otherwise tend to squeeze the stent distally over time and result in recurrence. Contralateral iliac vein flow is seldom affected. The stent(s) should be extended distally to cover lesions without skip areas; skip areas between stents tend to become stenotic over time. A distal NIVL at the external-common iliac junction is frequently present in patients and is a source of recurrent stenosis or residual symptoms. Less commonly, retroinguinal lesions are present as well. The tendency to extend the stent (self-expanding, braided Wall stent®) below the inguinal ligament into the common femoral vein is becoming increasingly common; no stent thromboses, compression, fractures or erosions have been observed because of such infrainguinal extensions. The procedure is covered by preoperative and postoperative low-molecular-weight heparin in prophylactic dosage. Only aspirin is used long-term after discharge, except in cases of thrombophilia, certain high risk groups or in recurrent previous thromboses when long-term warfarin anticoagulation is resumed/started.

Venous stenting can be combined with laser or other forms of minimally invasive saphenous ablation in the same session, to treat combined superficial and deep venous pathology. Totally occluded veins can be successfully recanalized by an extended technique by guidewire manipulation and passage through the occlusion, after which progressive balloon dilatation and stent deployment can take place. Procedure success and cumulative long-term patency as well (74% at 4 years) in such cases is surprisingly good. Long occlusions involving the entire IVC have been treated successfully in...
this fashion.26, 45 No clinical vein ruptures have occurred from aggressive balloon dilatation required in these and the other >1500 stenotic cases as well, presumably because of the low pressure in the venous system and containment of any subclinical rupture by perivenous tissues.

Because of the routine vena caval extension of the stent, fenestration of the stent is required during subsequent contralateral stenting, when needed. The two stents are joined assuming the form of an inverted "Y". This is generally accomplished with high procedure success, although special techniques are necessary to perform the fenestration in some. If performed simultaneously, bilateral stents can stretch side by side ("double barrel") into the vena cava and fenestration is not required.

The voluminous use of IVC filters poses special difficulties when some of these patients present with post-thrombotic syndrome later. The filter may be thrombosed, or even if patent, may be associated with stenosis of the vena cava at the placement site and beyond. Authors have succeed in pushing away the stent with balloon dilatation and stent across the compacted filter in most such cases without apparent complications.

**Results**

Reported morbidity is negligible and mortality minor.14, 32, 41 Early and late deep vein thrombosis is comparable to other vascular procedures.14 Cumulative long-term stent patency is astonishingly high in "primary", and only slightly less in post-thrombotic subsets in the University of Mississippi Medical Center, as shown in Figure 1.

Clinical results in terms of relief of pain and swelling track the excellent stent patency as shown in Figures 2, 3. Surprisingly, 58% of ulcers heal (cumulative) after stenting and remain healed long-term with little degradation of the survival curve (Figure 4). This observation calls into question the long-held belief that stasis ulcers are primarily a result of reflux. Quality of life is significantly improved.
Figure 4.—Long term cumulative rate of ulcer healing in stented limbs. Deep venous reflux present in many limbs was left uncorrected.

Evolving stent technology thus appears to hold the promise of a simpler more effective technique that can be widely applied in a broad spectrum of patients with symptomatic CVD.

References

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