Ten Lessons Learned in Iliac Venous Stenting

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Iliac vein stenting is an extension of arterial stent technology. The two share some technical similarities and much of the hardware; however, the indications for and purpose of iliac vein stenting are fundamentally different from arterial practice. Pathophysiologic differences require specific modifications of techniques as well. The clinical outcome of iliac vein stenting has been surprising in some aspects, challenging long-held core concepts.

VENOUS OBSTRUCTION IS WIDELY PREVALENT

Reflux has been the dominant concept in the pathology of chronic venous disease (CVD) for over a century. Much of the venous literature was and still is devoted to this concept. In a landmark article published in 1995, Johnson and colleagues showed that postthrombotic syndrome (PTS) is pathologically caused by a combination of obstruction and reflux.[1] At that time, reflux was still considered the main pathology in nonthrombotic CVD. An obstructive component related to CVD (May-Thurner syndrome) was recognized in a small subset of patients (approximately 3%), largely found in the left lower extremity of young women.[2] With the advent of intravascular ultrasound (IVUS), the clinical picture has dramatically changed. We now know that nonthrombotic iliac vein lesions with advanced clinical features are widely prevalent in the CVD population.[3] Both sexes, both sides of the body, and all age groups are affected.

AN ILIAC VEIN OBSTRUCTION IS A PERMISSIVE LESION

The occurrence of iliac vein obstructive lesions in otherwise asymptomatic individuals has long been a source of controversy. There is no question that these lesions are often found in symptomatic CVD limbs and clinical relief is provided when corrected.[4] One way to resolve this paradox is to consider iliac vein stenosis as a permissive lesion.[3] Permissive lesions are a frequent source of a wide variety of human disease. Initially silent, such lesions trigger symptoms when an additional injury or insult is superimposed. A well-known example is stroke from patent foramen ovale, which is silent in about 20% of the general population. Other examples include obesity and diabetes, carotid plaque and stroke, and ureteral reflux and pyelonephritis. In general, correction of the permissive lesion alone is curative when symptoms develop. With regard to iliac vein obstruction, it is a common clinical experience for joint replacement, other trauma, or cellulitis to precipitate limb swelling in patients with apparently long-standing silent iliac vein lesions. The onset of new reflux or deep vein thrombosis, immobility of age, and edematogenic medications are precipitating events as well.[5]

CONTRAST VENOGRAPHY IS POORLY SENSITIVE TO ILIAC VEIN OBSTRUCTION

In detailed studies of iliac vein obstruction in the 1950s, Cockett and colleagues showed that the lesions were detectable on venography in only about 50% of cases.[6] The continued reliance on venography to diagnose this lesion has been the main impediment in recognizing the wide prevalence of these lesions in limbs affected by CVD. Venography is not sensitive because the iliac vein lesions are often two dimensional ("compressive") rather than circumferential and may be easily missed in frontal projections. However, "iliac vein compression" is a misnomer because compression is only one characteristic of the lesion; transmural fibrosis with luminal webs and membranes may also be found.[7] In some limbs affected by PTS, the iliac veins are diffusely stenotic without focal cues. Lacking an internal scale, the venogram may look deceptively normal despite a narrowed lumen.[8]

IVUS CAN BE USED FOR DIAGNOSIS AND STENT PLACEMENT

Most iliac vein pathology is detectable on intraluminal imaging with IVUS; the integrated pixel-based scale provides area measurements crucial for diagnosis and proper stent technique. The instrument is superior to venography because area metrics are important in iliac vein stenting. IVUS can be used repeatedly throughout the procedure without the radiation hazard. IVUS-guided stenting can be

TABLE 1. OPTIMAL POSTSTENT DIAMETER AND AREA IN ILIAC VEIN STENTING		
	Diameter (mm)	Area (mm^2)
Common femoral vein	12	125
External iliac vein	14	150
Common iliac vein	16	200
Inferior vena cava	18–24	300–400

performed under fluoroscopy without contrast in patients allergic to contrast or with renal failure.

A more compelling reason to utilize IVUS over venographic guidance is that venography is inferior in identifying major anatomic features essential for accurate stenting. In an analysis of 162 limbs that underwent iliac vein stenting, the level of iliac–inferior vena cava (IVC) confluence, the location and degree of maximum stenosis, and the optimal landing zone for the stent were assessed by venography and IVUS by independent teams in blinded fashion.[9] Compared to the IVUS standard, the level of iliac confluence estimated by venography differed by as much as one vertebra. The lesion was completely missed by venography in 25% of patients, and the site of maximum stenosis was incorrect in 67% of patients. Venography underestimated the degree of stenosis in 69%.

WHAT IS CRITICAL STENOSIS IN THE ILIAC VEIN?

In arterial lesions, the critical element is downstream perfusion, whereas the pathogenic element in iliac vein stenosis is upstream (peripheral) back pressure. The factors controlling peripheral venous pressure are complex, but the caliber (absolute cross-sectional area) of iliac vein outflow has a major influence.[10] Iliac vein stenting to correct stenosis has been shown to decompress the peripheral venous bed, thus lowering the pressure.[10,11] For this reason, it is important to use large-caliber stents to achieve poststent cross-sectional areas mirroring normal anatomy. The optimal poststent diameter and areas (IVUS planimetry) for the various vein segments are shown in Table 1. It is common practice in arterial stenting to slightly undercorrect stenotic lesions ("perfect is the enemy of good") to avoid dissection or rupture. Undersizing stents in iliac veins results in residual symptoms, even though the stent may remain patent. For example, placement of a 14-mm stent in the common iliac vein, seemingly a minor downsizing, represents an iatrogenic area stenosis of 25% at the outset, disregarding any in-stent restenosis (ISR) that may develop (25% is common). Severe undersizing (Figure 1) results in severely symptomatic iatrogenic stenosis that is nearly impossible to rectify.

HIGH STENT PATENCY, LOW MORBIDITY

A major surprise from our iliac stenting experiences was the unexpectedly high long-term patency (Figure 2) in a

Figure 1. Stents used in iliac veins should mirror normal anatomical size. An 8-mm stent (half the recommended size) was inserted in the iliac vein. Severe symptoms persisted although the stent was "patent." Note the size discrepancy between the femoral vein and the iliac stent; such undersizing results in an iatrogenic stenosis that is nearly impossible to correct.

vascular bed prone to thrombosis with low-pressure, slow flow.[11] The overall stent thrombosis rate (noncumulative) was < 5% and was almost exclusive to postthrombotic limbs and extremely rare in nonthrombotic limbs.[12] The metal load was well tolerated and was not thrombogenic per se, thus allowing extensive stenting of long lesions involving the IVC and both iliac veins.[13] Aspirin appears to be adequate for long-term stent maintenance, with long-term anticoagulation reserved for postthrombotic limbs with traditional indications. Complications such as vessel ruptures, hemorrhage, stent fractures, and erosions (even when crossing the joint crease) appear to be rare with braided stents.[14] This is noteworthy because large-sized balloons and stents (16–18 mm) are routinely used in iliac venous stenting. The incidence of severe ISR (> 50%) is < 5%.[15]

HOW IMPORTANT IS STENT SURVEILLANCE?

In addition to ISR, iliac vein stents are prone to stent compression from the outside at anatomical choke points or from recurrent postthrombotic stenosis.[8] Stent compression is detected by reduced diameters with duplex ultrasound or IVUS; it is virtually impossible to identify with venography (Figure 3). Periodic surveillance with duplex

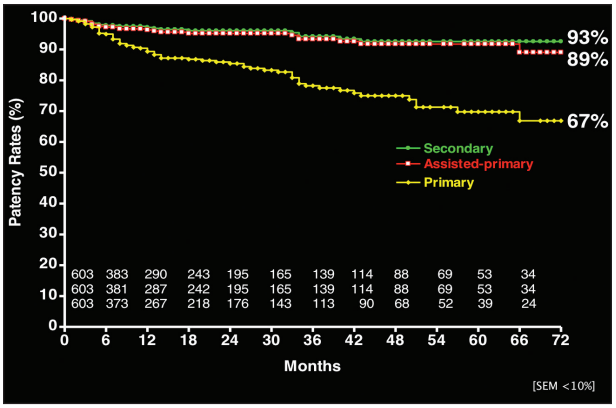

Figure 2. Patency rates of iliac vein stents (includes postthrombotic and nonthrombotic limbs). Cumulative secondary patency of 93% was recorded at 6 years. Reprinted with permission from Neglén P, Hollis KC, Olivier J, Raju S. Stenting of the venous outflow in chronic venous disease: long-term stent-related outcome, clinical, and hemodynamic result. J Vasc Surg. 2007;46:979-990.

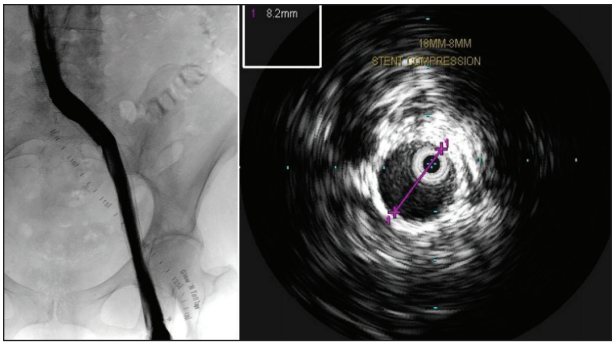

Figure 3. Stent compression is unique to venous stenting. It is difficult to detect on venography (left). In this instance, IVUS shows a 16-mm stent compressed to an 8-mm diameter (right). Reprinted with permission from Raju S, Davis M. Anomalous features of iliac vein stenosis that affect diagnosis and treatment. J Vasc Surg Venous Lymphat Disord. 2014;2:260-267.

ultrasound is desirable to identify and correct stent malfunction if there are recurrent or residual symptoms. Because these symptoms are more frequent in limbs affected by PTS, particularly after chronic total occlusion recanalization, monthly surveillance may be appropriate, at least initially, until stability is reached. For patients with May-Thurner syndrome, surveillance of limbs at 3 or 6 monthly intervals may be adequate if symptom resolution is maintained.

CLINICAL RELIEF CAN BE ACHIEVED WITH STENTING

Commensurate with the high patency rate with iliac stenting, a significant improvement in pain was reported in 74% of limbs (cumulative), with complete relief in 65% at 5 years. Swelling improved significantly in 62% of limbs, with complete relief in 32% at 5 years, and 58% of ulcers (cumulative) healed at 5 years.[11] These results are as good or better than historical results with alternative treatment approaches. Because of the easy percutaneous technique and acceptable safety and efficacy, iliac vein stenting is the preferred approach in most patients with advanced disease, even in the frail and elderly population.[16]

DOES REFLUX MATTER?

Another surprise to come out of our iliac vein stenting experiences was the clinical relief obtained in patients with combined obstruction/reflux.[17] Substantial clinical relief was obtained with stent correction of the obstruction alone, even when the associated reflux was severe and remained uncorrected. In an analysis of 168 limbs with venous stasis ulcers, there was no difference in ulcer healing with stent correction alone between limbs that had axial reflux and those without (Figure 4).[18] Limbs with a reflux segment score ≥ 3 appeared to have a lower rate of healing ($P < .03$), but cumulative healing even in this disadvantaged subset was 60% at 5 years. The limbs were mostly postthrombotic with multisegment reflux. A remarkable feature of ulcer healing curves in the ulcerated limbs, with or without reflux,

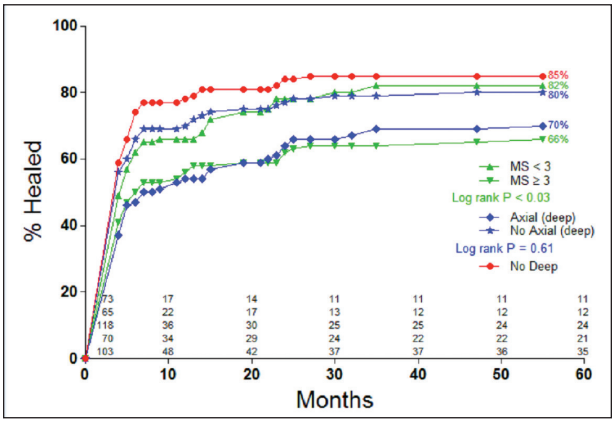

Figure 4. Cumulative ulcer healing after iliac vein stenting. There is no difference in the rate of healing between limbs with and without axial reflux (blue). When the number of reflexive segments is > 3, the healing rate is slower ($P < .03$), but two-thirds of limbs in the disadvantaged subset were still healed at 5 years. Note the stable cumulative healing curves (ie, few recurrences). Healing curves with other treatment approaches generally display a steady decline over time. Reprinted with permission from Raju S, Kirk OK, Jones TL. Endovenous management of venous leg ulcers. J Vasc Surg Venous Lymphat Disord. 2013;1:165-172.

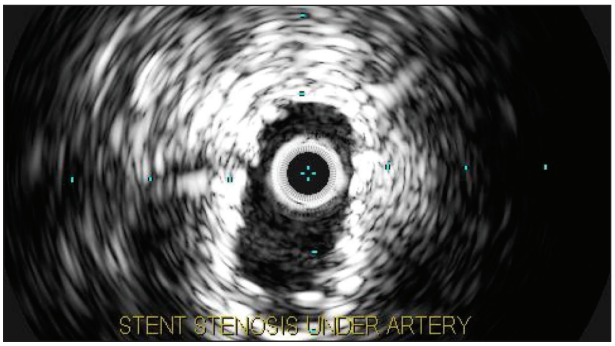

Figure 5. Compression of an iliac stent behind the artery, which is a common choke point.

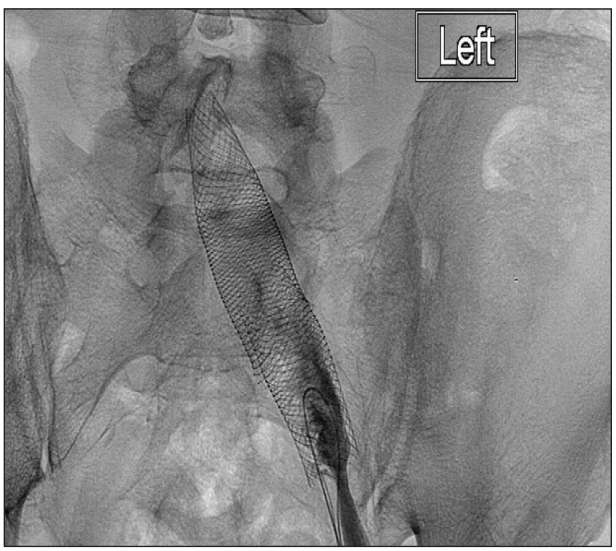

Figure 6. It is generally impossible to precisely place a stent at the iliocaval junction. Often, the stent will not completely traverse the lesion because of its spiral orientation, which may extend into the IVC. A short extension of the stent into the IVC displays thrombosis from coning due to adjacent compression by the choke point.

is their flat nature with little decline over time (ie, healing is durable). This is in contrast to historical experiences with valve reconstruction techniques.[19] This experience raises fundamental questions regarding the relative importance of obstruction versus reflux in ulcer pathology.

DO WE NEED A DEDICATED VENOUS STENT?

The iliac vein stent experience outlined previously is with off-label use of a Wallstent endoprosthesis (Boston Scientific Corporation), which is designed for extravascular use. Although it has performed better than anticipated, certain deficiencies, some specific to the iliocaval anatomy and others more general, have come to light. About 25% of the stents require reinterventions to correct ISR/stent compression.[20] The natural history of ISR related to venous stenting may be different as compared with arterial stenting.[21] Stent compression at the iliac arterial crossover point has been a problem (Figure 5); for unknown reasons, it is associated with a higher incidence of deep vein thrombosis in the limb (unpublished data). A 3- to 5-cm stent extension into the IVC is often required to traverse the lesion completely and minimize end effects (eg, coning) (Figure 6) and distal migration of the stent. This poses a potential risk of partial jailing of contralateral iliac flow. Simultaneous or sequential bilateral stenting with current stent designs are unsatisfactory and may be technically difficult or impossible.[22,23] Although we can improvise to counter these problems, a dedicated venous stent with improved performance in these areas is clearly desirable.[23] ■

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