Intravascular ultrasound scan evaluation of the obstructed vein

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Purpose: **The purpose of this study was the comparison of intravascular ultrasound scanning (IVUS) with transfemoral venography in the assessment of chronic iliac vein obstruction.**

Methods: **IVUS and standard, single-plane, transfemoral venography were performed in 304 consecutive limbs during balloon dilation and stenting of an obstructed iliac venous segment. The appearance of the obstruction was described, and the degree of stenosis (maximal diameter reduction) was estimated with venography and IVUS. The stenotic area was derived with diameter calculations (πr^2) and also was measured with the built-in software of the IVUS apparatus before and after dilation and stenting in 173 limbs. Preoperative hand/foot differential pressure and preoperative dorsal foot venous and intraoperative transfemoral hyperemia-induced pressure elevations after intra-arterial injection of papaverine hydrochloride were measured.**

Results: **With IVUS, fine intraluminal and mural details were detected (eg, trabeculation, frozen valves, mural thickness, and outside compression) that were not seen with venography. The median stenosis (with diameter reduction) on venographic results was 50% (range, 0 to 100%) and on IVUS results was 80% (range, 25% to 100%). In a comparison with IVUS as the standard, venography had poor sensitivity (45%) and negative predictive value (49%) in the detection of a venous area stenosis of >70%. The actual stenotic area was more severe when measured directly with IVUS (0.31 cm^2; range, 0 to 1.68 cm^2) versus derived (0.36 cm^2; range, 0 to 3.08 cm^2; $P < .001$), probably as a result of the noncircular lumen geometry of the stenosis. No correlation was found between any of the preoperative or intraoperative pressure measurements and degree of stenosis with or without collaterals. When collaterals were present, a more severe stenosis (median, 85%; range, 25% to 100%) was observed (versus a 70% stenosis in the absence of collaterals; range, 30% to 99%; $P < .001$), along with actual stenotic area (with collaterals: median, 0.24 cm^2; range, 0 to 1.18 cm^2; without collaterals: median, 0.45 cm^2; range, 0.02 to 1.68 cm^2; $P < .01$) and a higher rate of hyperemia-induced pressure gradient (≥2 mm Hg; with collaterals, 34%; without collaterals, 11%; $P < .05$).**

Conclusion: **Venous IVUS appears to be superior to single-plane venography for the morphologic diagnosis of iliac venous outflow obstruction and is an invaluable assistance in the accurate placement of venous stents after venoplasty. No preoperative or intraoperative pressure test appears to adequately measure the hemodynamic significance of the stenosis. In lieu of adequate hemodynamic tests, IVUS determination of morphologically significant stenosis appears to be presently the best available method for the diagnosis of clinically important chronic iliac vein obstruction. Collateral formation should perhaps be looked on as an indicator of a more severe stenosis, although significant obstruction may exist with no collateral formation. (J Vasc Surg 2002;35:694-700.)**

Venoplasty and stenting of the iliac vein is evolving as a safe alternative to open bypass grafting surgery and, at least in the short term, as an effective method in the treatment of iliocaval chronic venous obstruction.[1-9] In this process, the inaccuracy of transfemoral venography in the delineation of the iliac venous outflow obstruction has been increasingly recognized. The extent and severity of the obstructive lesion appear to be worse on intravascular ultrasound scan (IVUS) results as compared with venographic findings, and even severe obstructions may go undetected with venography.[7,8] To our knowledge, however, no reports describe the use of IVUS in the venous system in more detail. This study aims to illustrate intraluminal and mural morphologic observations with IVUS and to compare the assessment of the degree of stenosis with venous IVUS investigations and single-plane transfemoral venography in limbs with chronic iliac vein obstruction.

MATERIALS AND METHODS

From March 1997 to August 2000, 345 consecutive limbs were investigated with transfemoral venography and IVUS on suspicion of chronic iliac vein obstruction. The findings were recorded prospectively in a set protocol. The number of investigated limbs corresponded to approximately 17% of the new patients who underwent evaluation for chronic venous insufficiency by the authors during the same time period. As is the routine in our service, a com-

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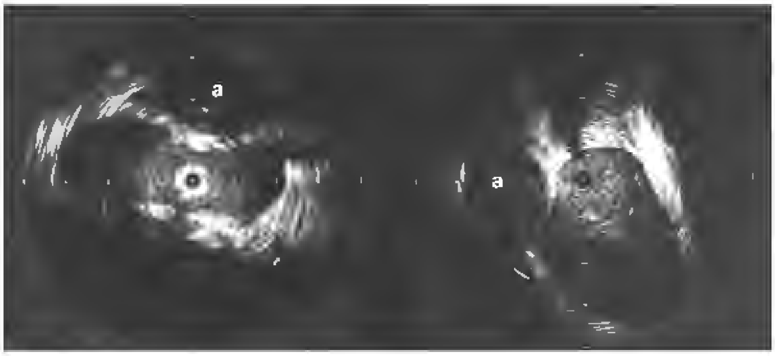

Fig 1. Intravascular ultrasound scan images show different degrees of outside compression of left common iliac vein as it is crossed by right common iliac artery *(a)*. Position of iliac artery depends on orientation of catheter *(black circle inside vein)* and does not necessarily reflect anatomic topography.

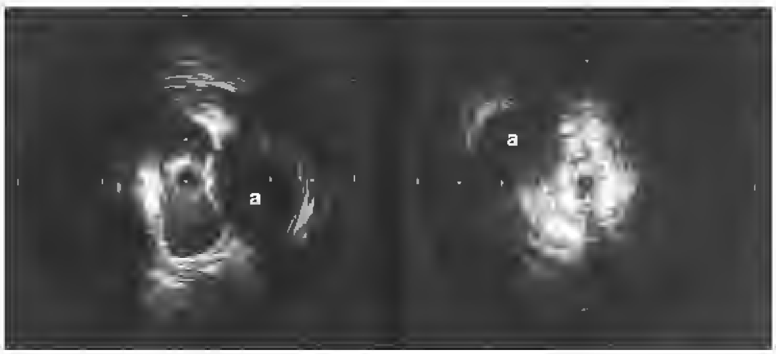

Fig 2. Intravascular ultrasound scan images show different degrees of outside compression of left common iliac vein as it is crossed by right common iliac artery *(a)*. Position of iliac artery depends on orientation of catheter *(black circle inside vein)* and does not necessarily reflect anatomic topography.

prehensive work-up was performed in all the patients before the intervention and included the following examinations: ascending, descending, and antegrade transfemoral venography; ambulatory venous pressure measurement; hand/foot venous pressure differential at rest and after tourniquet ischemia-induced hyperemia; air plethysmography; and erect duplex Doppler scan investigation with standardized compression. The technical aspects of these investigations have been detailed in previous publications.[10,11]

The following preoperative parameters suggestive of iliac vein obstruction were used: limbs with 25% or greater stenosis on the preoperative ascending or antegrade transfemoral phlebographic results, radiographic visualization of pelvic collaterals with or without visualized iliac vein obstruction, or positive pressure test results with arm/foot pressure difference of 4 mm Hg or more or reactive hyperemia pressure rise of 8 mm Hg or more.[12] With these criteria for the performance of IVUS investigation, a healthy vein was found in 35 limbs (10%). The obstructed iliac vein segment could not be recannalized and transversed with a guidewire and therefore was not dilated in six limbs (2%). The remaining 304 limbs (88%) in 294 patients underwent balloon dilatation and stent insertion of the iliac vein. In 10 patients, the iliac veins were stented bilaterally. Because the procedures were performed at different time points and in the contralateral limb, each stent procedure was considered an independent event and is statistically treated as such. In these 304 limbs, femoral venous pressures were measured and the appearance of the obstruction and the degree of stenosis were described with venography and IVUS investigations before and after stenting.

The details of the intervention have been outlined previously.[7,8] The authors performed all the procedures in an operating room with ceiling-mounted International Surgical Systems, Inc, equipment (Phoenix, Ariz). After the cannulation of the femoral vein, a guidewire was inserted and a sheath was introduced. Antegrade single-plane phlebography then was performed according to a standardized manner. For this purpose, a power injector (Medrad Mark V Plus, Medrad, Inc, Indianola, Pa) was used, set at an ejection rate of 8 mL/s, an injection volume of 15 mL, and a pressure of 900 psi, and images were acquired continuously. The degree of stenosis was mea-

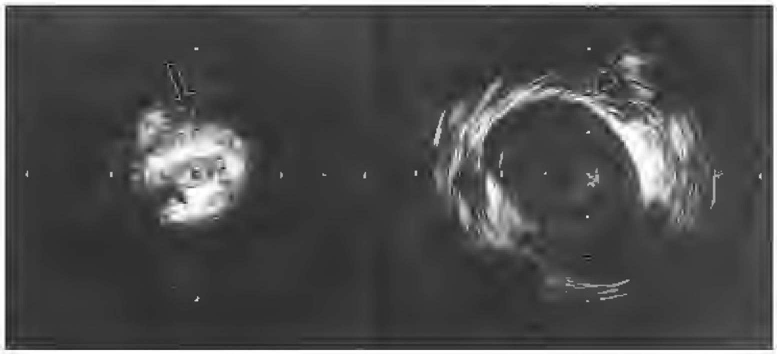

Fig 3. Highly echogenic, thick wall of narrowed postthrombotic vein *(left, arrow)* compared with thin-walled healthy vein with low echogenicity *(right, arrow)* as shown with intravascular ultrasound scanning.

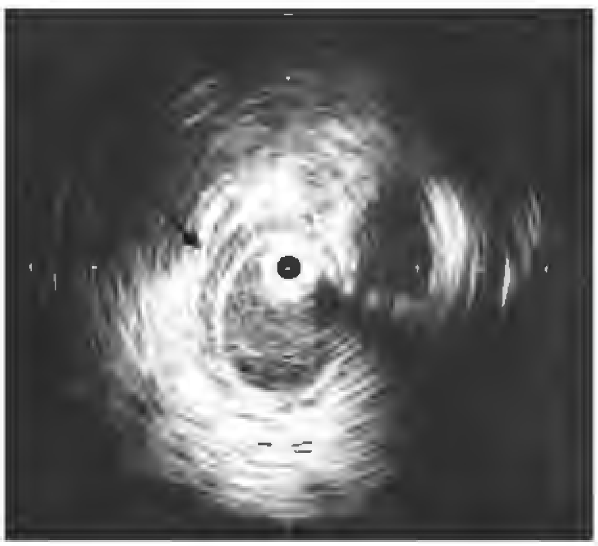

Fig 4. Intravascular ultrasound scan image shows "double-contoured" wall of vein *(arrow)*, which may indicate periphlebitic edema.

sured as the diameter of the stenotic area divided by the diameter of the healthy vein below the stenosis multiplied by 100 (%). Obstructions were not always obvious with venography. Some limbs had subtle radiologic findings (eg, some broadening or translucency of the vein). These limbs were considered to have no radiologic stenosis. The presence or absence of collaterals was noted. Collateralization was determined as one or more obvious collateral vessels of any size with upper or lower transpelvic or axial course or contrast filling of ascending lumbar vein with paravertebral vessels.

Subsequently, an over-the-wire IVUS investigation was performed (SONOS Intravascular Diagnosis System M2400A, Hewlett-Packard, Andover, Mass; with Sonicath Ultra 6 imaging catheter, 6F, 12.5 MHz, Boston Scientific Corp, Watertown, Mass; or with EndoSonics In-Vision Gold Imaging System with ChromaFlow with Visions PV Five-64, 8.2F imaging catheter, Jomed, Rancho Cordova, Calif). With the built-in software program, the degree of obstruction could be recorded as the greatest diameter of the stenotic area divided by the greatest diameter of the healthy vein below the stenosis multiplied by 100 (%). The area of the stenosis could be derived with diameter calculations (Tcr^2). Later in the study, the actual transverse lumen area was outlined and measured in 173 limbs. Obvious close axial collaterals were noted, but otherwise no directed attempt was made for the assessment of transpelvic or ascending lumbar vein collaterals with IVUS.

The femoral vein pressure below the obstruction was recorded with an external transducer (Transpac IV Monitoring Kit, Abbott Critical Care Systems, North Chicago, Ill). The transducer was calibrated and kept at the level of the right atrium as in measuring central vein pressure. The femoral pressure distal to the obstruction was obtained before and after the injection of 30 mg of papaverine hydrochloride in the ipsilateral femoral artery to increase the venous outflow.[13] If possible, intraoperative pull-through pressure from the inferior vena cava to the femoral vein then was obtained. Venography, IVUS investigation, and venous pressure measurements were repeated after the completion of dilation and stent insertion.

Wilcoxon rank sum paired and unpaired nonparametric tests were used in the appropriate setting for the evaluation of statistical significance. The χ^2 test was used for the comparison of frequencies. Standard methods were used in the calculation of correlation coefficient. A *P* value of less than .05 was considered significant.

RESULTS

The IVUS investigation may reveal intraluminal and mural details that were undetected with venography (Figs 1 to 7). The left iliac vein may be compressed by the right iliac artery as it transverses the vein, a so-called May-Thurner syndrome. With venography, such a compression may be

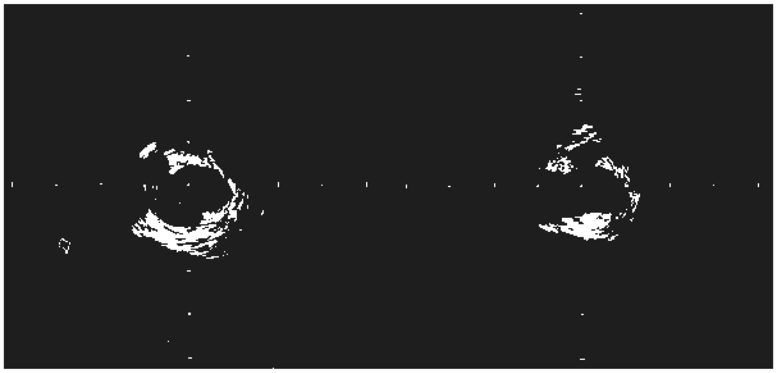

Fig 5. Intravascular ultrasound scan image shows axial collaterals surrounding postthrombotic stenotic vein.

Table I. Degree of obstruction, diameters, and calculated and actual transverse lumen areas (median [range])

Obstruction (n = 304)		*Before stenting (n = 173)*			*After stenting (n = 173)*		
With venography	*With IVUS*	*Diameter (cm)*	*Calculated area (cm²)*	*Actual area (cm²)*	*Diameter (cm)*	*Calculated area (cm²)*	*Actual area (cm²)*
50% (0 – 100%)	80% (25% – 100%)*	0.67 (0 – 1.98)	0.36 (0 – 3.08)	0.31 (0 – 1.68)†	1.48 (0.85 – 1.91)	1.72 (0.56 – 2.86)	1.67 (0.65 – 2.60)†

*$P < .001$, compared with obstruction on venographic results.
†$P < .001$, comparison of actual area with calculated area.
IVUS, Intravascular ultrasound scanning.

indirectly suggested with the appearance of a widening of the iliac vein, a "thinning" of the contrast dye resulting in a translucence of the area, and the presence of transpelvic collaterals, sometimes despite the healthy appearance of the iliofemoral vein. With IVUS, this compression can be clearly delineated and may sometimes result in an hour-glass deformity of the vein of different degrees. This discrepancy was found in 21% of the limbs (62 of 304). IVUS results can also show the degrees of echogenicity, both of the vessel wall and of the intraluminal thrombi, which may indicate varying degrees of wall thickness and may correlate with the age of the thrombosis. This detection was not possible with venography. Fig 4 illustrates another example of venous wall alteration observed in a patient after thrombolysis for acute iliac vein thrombosis. The "double-contour" may indicate a periphlebitic edema. Axial collateral formation in close proximity to the native vein may not be separated with venography but could be seen with IVUS. Finer intraluminal details, such as webs, frozen valves, and trabeculation, could be detected with ultrasound scanning but may be "hidden" in the injected contrast dye.

With diameter measurement, the median degree of stenosis with transfemoral venography was 50% (range, 0 to 100%) as compared with 80% (range, 25% to 100%) with IVUS (Table I). In 42% of the venograms as compared with only 10% of the IVUS investigations, the stenosis was less than 50%. On the other hand, the venous stenosis was greater than 70% in 32% of venograms and in 63% of IVUS investigations. With the IVUS result as the standard, venography had poor sensitivity (45%) and negative predictive value (49%) in the detection of an obstruction of greater than 70% (specificity, 95%; positive predictive value, 94%). When the stenosis on venographic results was found to be ≥70%, the stenosis on IVUS investigation results was also ≥ 70% in 77% of the limbs. On the other hand, when the venographic stenosis was <70%, the IVUS findings only corresponded in 20% of the limbs. Thus, the degree of iliac vein stenosis was substantially underestimated with venography. Although its findings were not measured and compared in this study, the IVUS also appeared to more accurately show the extent of the lesion.

The discrepancy between the findings with venography and with IVUS is illustrated in Fig 8. The median transverse lumen area was derived with calculation (ie, πr^2) and was found to be significantly larger than the actual area measured with outlining the true lumen (Table I). In many cases, the vein was deformed with scarring or outside compression as illustrated previously. This irregular shape negated the assumption of a circular shape, which was necessary for accurate results with the previous calculation. Only in 15% of the veins was the difference of the actual area and the calculated area less than 10%, which

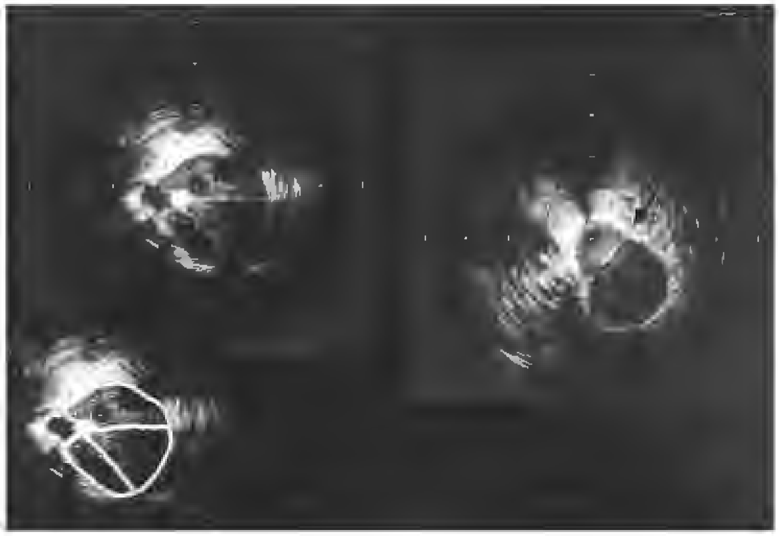

Fig 6. Intraluminal details visualized with intravascular ultrasound scanning. Postthrombotic trabeculation (*left,* trabeculae and vein wall artificially enhanced in *lower image*) and intraluminal web *(right, arrow).*

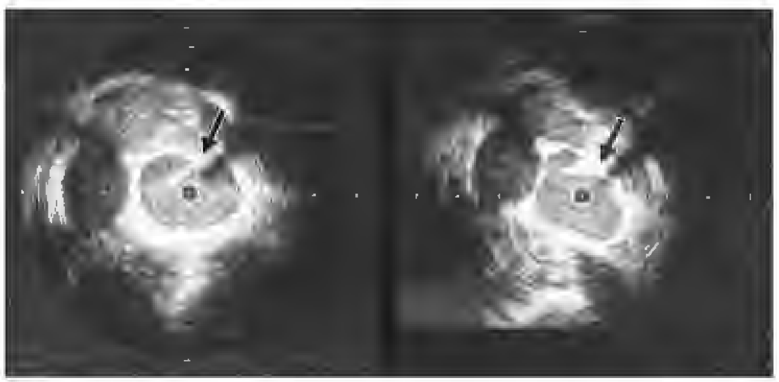

Fig 7. Intravascular ultrasound scan images show thickened valve leaflet *(left, arrow)* and frozen valve *(right, arrow).*

Table II. Degree of original stenosis

	Diameter after stenting	*Calculated area after stenting*	*Actual area after stenting*
Median (range)	53% (-20% – 100%)	78% (-45% – 100%)	80% (20% – 100%)
Mean ± standard deviation	52% ± 25%	71% ± 27%	76% ± 19%

indicates that in most stenosis the narrowing was not concentric. The importance of shape was obvious when the degree of stenosis was evaluated in relation to the achieved dilation of the vein (Table II). The maximal lumen diameter could actually decrease after dilation as a markedly compressed, flattened vein with one long diameter reverted to a more circular shape with a shorter diameter after stenting. Similarly, the calculated area with the greatest diameter before and after stenting could also numerically decrease as the diameter decreased. This paradoxic observation was entirely the result of the change of vein geometry and numeric calculation without any physiologic base because the greatest diameter was always used.

Before intervention, only 6% of the limbs had significant hand/foot pressure difference (≥4 mm Hg) and 25% had a significant reactive hyperemia pressure rise (≥8 mm Hg). Thus, 26% of the limbs had an obstruction grade of 2 to 4 according to the Raju classification.[5] Similarly, a more than 2 mm Hg pressure gradient on pull-through and on intraarterial injection of papaverine hydrochloride was found in 22% and 28% of the limbs, respectively. These intraoperative findings, however, were not necessar-

Table III. Findings in limbs with iliac venous obstruction and radiologically visualized collaterals compared with limbs with noncollateralizing venous obstruction

	With collaterals (n = 122)	*Without collaterals (n = 51)*
Obstruction grade > 2 (Raju classification)	26%	27% (NS)
Pressure gradient with intraarterial papaverine hydrochloride injection of >2 mm Hg	34%	11%*
Median stenosis as per IVUS diameter (range)	85% (25% – 100%)	70% (30% – 99%)‡
Median actual transverse lumen area (cm^2; range)	0.24 (0.00 – 1.18)	0.45 (0.02 – 1.68)†

$^*P < .05$.
$^†P < .01$.
$^‡P < .001$.
NS, Not significant; *IVUS,* intravascular ultrasound scan.

ily found in the limbs with preoperative positive pressure measurements. At least one of these tests had positive results in 42% of the limbs.

Collateral formation was seen in 71% of the limbs (122 of 173). Transpelvic collaterals were most frequently seen (89%), one third of which were combined with axial or ascending lumbar vein and paravertebral collaterals. The visulatization of axial or ascending lumbar collateralization alone was rare, 5% and 6%, respectively. There was no statistically significant correlation between preoperative hand/foot venous pressure differential and foot venous pressure hyperemia increase or between intraoperative basal femoral pressure, transiliac pressure gradient, and femoral pressure increase after papaverine hydrochloride injection and degree of stenosis measured with IVUS or venography, with or without the presence of collaterals (range from 0.02 to 0.24; all *P* values > .05). However, there were some surprising findings in the comparison of limbs with and without radiographically visualized collaterals (Table III). Limbs with iliac venous outflow obstruction and collateral formation had significantly tighter stenosis than did limbs without collateralization, measured either as actual cross-cut area or as percent stenosis as per IVUS diameter measurement. Although the frequency of limbs with preoperative obstruction grade of 2 or more was approximately 26% in both groups, the rate of limbs with femoral pressure increase of more than 2 mm Hg with intraarterial injection of papaverine hydrochloride was more than three times more common in patients with collaterals. Collateral formation appeared to be more common with more severe morphologic and significant hemodynamic obstruction.

Fig 8. Several iliac venous intravascular ultrasound scan (IVUS) images *(left)* and transfemoral venogram *(right)* obtained in postthrombotic limb. On IVUS images, iliac artery *(a)* is in similar position and catheter can be seen in vein *(black circle)*. *Arrows* on venogram indicate levels where IVUS images were obtained. With transverse orientation of stenosis with IVUS, venogram appearance may be near normal despite severe stenosis *(top)* as compared with sagital orientation of the stenosis, when findings on IVUS and venogram correspond *(bottom)*. *Middle images* show nonstenotic vein on both investigations.

DISCUSSION

IVUS investigation yielded findings that were not obvious on transfemoral venographic results. Injection of contrast dye can hide details (eg, intraluminal webs) that were revealed with IVUS. Axial collateral formation in near proximity to the postthrombotic main vein may be differentiated from intraluminal trabeculation. External compression and the resulting deformity of the venous lumen could be directly visualized. Most importantly, IVUS appears to be superior to standard single-plane venography for the estimation of the morphologic degree of iliac vein stenosis. On average, the transfemoral venogram results significantly underestimated the degree of stenosis by 30%. Venography was inaccurate in the detection of obstruction of greater than 70% as compared with IVUS. Adequate information of extent and degree of the obstructive lesion is of particular importance in the choice of the length and size of stents to be inserted during balloon dilation and stenting. IVUS was superior to single-plane venography in providing adequate morphologic information. The accuracy of transfemoral venography may improve if multiple side views are obtained. This is, however, not usually performed in standard practice at this time.

The determination of the hemodynamic significance of a venous stenosis is difficult. This is not specific for this study. In most papers that describe venous stenting, venous hemodynamic assessment is lacking.[1-4,6] The significance of the stenosis is commonly determined with the presence of stenosis and the corresponding clinical signs and symptoms. Although positive hemodynamic test results (eg, decreased plethysmographic ouflow fraction, increased hand/foot pressure differential, increased hyperemia pressure differential, pull-through gradient of > 2 to 3 mm Hg, and increased pressure after intraarterial papaverine hydrochloride injection) may indicate hemodynamic significance, healthy test results do not exclude it.[12,14,15] At least one of these tests had positive results in 42% of the limbs in this study. Despite the lack of positive hemodynamic results with available methods, balloon dilation and stenting of stenotic iliac veins guided with morphologic area stenosis of more than 50% on IVUS results appear to have apparent clinical benefits for the patients.[7,8] High rates of healing of ulcers, resolution of edema, and relief of pain have been objectively shown. No available preoperative or intraoperative pressure tests appeared to adequately measure the hemodynamic significance of a venous stenosis. No correlation was found between the morphologic degree of stenosis and the preoperative and intraoperative tests, whether or not collaterals were present. It is apparent that our methods for the assessment of hemodynamic stenosis in the venous system are not optimal. The concept of a significant obstruction being a stenosis of >70% to 80% is derived from observations on the arterial system. These conclusions may, however, not be applicable in the venous system because there are many fundamental differences. An arterial stenosis has high peripheral resistance downstream, and the iliac vein stenosis has low resistance. The effects of the venous obstruction are upstream (lack of emptying) rather than downstream (lack of perfusion), which results in a different set of signs and symptoms. The contralateral veins converge beyond the iliac stenosis, which may mitigate any pressure gradient at rest. Finally, the venous velocity is lower at rest and the geometry of the narrowing may be more important in the venous system.[16] When a venous stenosis should be considered "critical" is not known. In lieu of adequate hemodynamic tests, it appears that IVUS determination of morphologic significant stenosis is presently the best available method for the diagnosis of clinically significant chronic iliac vein obstruction.

Collaterals may look impressive on venographic results, but they may be of little functional value. In this study, the collateral flow did not appear to adequately compensate for the outflow obstruction in many instances. Despite the presence of collaterals, the rate of a significant obstruction as per preoperative pressure measurements were the same as in limbs without collaterals. One third of the limbs with collateral formation still had increased pressure gradient on papaverine hydrochloride injection during surgery, and on average, these limbs had a tighter area stenosis than did the limbs without collaterals. The presence of collaterals should perhaps be looked on as an indicator of a more severe stenosis, although significant obstruction may exist with no collateral formation.

In conclusion, venous IVUS appears to be superior to standard single-plan venography for morphologic diagnosis of iliac venous outflow obstruction, and it is an invaluable aid in the accurate placement of venous stents after venoplasty. Better tests for the evaluation of hemodynamic significance of venous obstruction must be developed.

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