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Relative importance of iliac vein obstruction in patients with post-thrombotic femoral vein occlusion

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Background: **Patients with femoral vein occlusion rapidly develop collateral flow through the deep femoral vein, an embryonic collateral. In contrast, iliac vein collateralization is sparser and functionally poorer. It is not uncommon to have femoral vein occlusions associated with iliac vein obstruction, even though the femoral vein occlusion is often more readily apparent on venograms and duplex scans, whereas the iliac vein obstruction may remain occult. We examined whether percutaneous stent correction of iliac vein obstruction associated with femoral vein occlusions would yield symptomatic relief.**

Methods: **During a 13-year period, 39 patients with femoral vein occlusions underwent stenting of associated iliac vein stenoses.**

Results: **Median age was 51 years (17-86 years). The male-to-female and right-to-left ratios were 1:3 and 1:2, respectively. The clinical class of the Clinical, Etiologic, Anatomic, and Pathologic (CEAP) classification was as follows: C0-2 (with pain), two of 39 (5%); C3, 19 of 39 (48%); C4, 10 of 39 (26%); C5, one of 39 (3%); and C6, seven of 39 (18%). Concurrent ablation of a refluxive saphenous vein was performed in seven of 39 (18%). Reintervention was carried out in 14 of 39 limbs (36%). Median follow-up was 26 months (1-154 months). Median iliac vein stenosis was 80% (40%-100%). Primary, primary assisted, and secondary patency rates at 2 years were 57%, 88%, and 96%, respectively. Pain grade (visual analog scale, 0-10) improved from median 5 (0-9) to 3 (0-8) after stenting ($P < .03$); 12% were completely relieved of pain. Cumulative improvement in pain (≥3 of 10 on the visual analog scale) was 87% at 2 years. Median swelling (grade 0, none; grade 1, pitting; grade 2, ankle edema; grade 3, gross) improved from median 3/3 (0-3) to 2/3 (0-3) ($P = .09$, NS). Among 22 of 39 limbs (56%) with grade 3 swelling before stenting, seven of 22 limbs (32%) with grade 3 swelling improved (≥1 grade) after stent placement. In the 15 of 22 limbs (68%) with residual grade 3 swelling after stenting, subjective improvement was reported by all. Four of seven active ulcers (54%) healed. There were no obstructive sequelae after concurrent saphenous ablation. Saphenous flow in the erect position was not different from that of controls with patent femoral veins.**

Conclusions: **Percutaneous stenting of associated iliac vein obstruction in symptomatic limbs with femoral vein occlusion yields satisfactory clinical relief. The saphenous vein has little collateral role in this pathologic process and can be safely ablated if it is refluxive, in line with prior observations. (J Vasc Surg: Venous and Lym Dis 2015;3:161-7.)**

Deep venous thrombosis is a multisegment disease; often the iliac, femoral, and crural segments are involved.[1] When post-thrombotic syndrome develops, either obstruction or reflux or commonly both may be evident in all three segments. As duplex ultrasonography has emerged as the initial and often the only diagnostic tool in many centers, the femoral vein pathologic changes are often the most clearly detected. Chronic total occlusions (CTOs) of the femoral vein occur in a small fraction of cases with chronic venous disease (CVD) but often are the main focus of attention. Iliac vein obstruction is relatively impervious to duplex ultrasonography and even to contrast venography with only ≈50% sensitivity.[2,3] Hemodynamically, iliac vein lesions, whether they are stenoses or CTO lesions, are likely to be more important than the more obvious femoral vein CTOs because the iliac vein lesions are more central and have inferior collateralization.[4] The question then arises if active investigations for the detection and correction of iliac vein lesions should not be carried out routinely before considering correction of more readily apparent femoral vein CTO lesions. This has some practical significance as iliac vein lesions can now be successfully relieved by percutaneous techniques in an outpatient setting, whereas open surgical correction (Husni bypass) is still practiced for the treatment of symptomatic femoral vein occlusions.[5,6] Some patients who will not be candidates for open procedures because of comorbidities can be readily considered for the minimally invasive iliac vein procedure. There is little published experience with the utility of recanalization of chronic femoral vein occlusions (CTOs).

A controversial unresolved question related to the management of femoral vein CTO lesions is the role of the saphenous vein. If the saphenous vein is refluxive, should it be ablated or preserved because of its collateral contribution? Traditional teaching holds that such "secondary" varices should not be removed. Our earlier

From the Rane Center at St. Dominic.

Author conflict of interest: S.R. has stock in Veniti and holds a U.S. patent for intravascular ultrasound diagnosis in veins.

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Methods: During a 13-year period, 39 patients with femoral vein occlusions underwent stenting of associated iliac vein stenoses.
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experience contradicts the traditional view. In the current analysis, we extended prior findings with saphenous flow measurements in femoral CTO limbs with comparison to controls with nonoccluded femoral veins.

The aim of this report was to present the clinical results in a subset of 39 femoral vein CTO lesions in which targeted preoperative assessment led to the diagnosis of coincident iliac vein obstructive lesions that were corrected by percutaneous stenting. Ancillary data relevant to the potential collateral role of the saphenous vein in femoral vein CTO lesions are also presented.

METHODS

Iliac vein stenting to correct coincident obstruction in 39 limbs with femoral vein CTO was performed during a 13-year period (2000-2013). This represented 1.6% of all iliac vein stents (n = 2475) to correct obstructive lesions during the same period. Demographics and Clinical, Etiologic, Anatomic, and Pathologic (CEAP) classification of clinical material are shown in Tables I and II. Concurrent ablation of a refluxive saphenous vein was carried out in seven of 39 limbs (18%) in which saphenous reflux was thought to be contributory to the symptom complex.

Duplex ultrasound examination for reflux. Duplex ultrasound measurement of reflux in the superficial and deep systems was performed in the erect position with automated quick inflation/deflation cuffs. For perforator reflux, the patient was examined in the sitting position with the cuff around the foot, supplemented by manual squeezing of the foot as needed. Reflux thresholds reported in this manuscript conform to current guideline recommendations.[7]

Saphenous flow. Duplex saphenous flow data from 21 limbs with femoral vein occlusions in this series were compared with data in normal limbs (n = 21) as well as in 30 randomly selected (every third limb in the last 90) CVD limbs with patent femoral veins in our laboratory database. Saphenous size and time-averaged velocity in the erect position were measured 2 cm below the saphenofemoral junction by standard technique with color duplex ultrasound (Logiq 9; GE Healthcare, Fairfield, Conn). Volumetric flow/second was calculated from these measurements.

Clinical assessment and iliac vein stenting technique with intravascular ultrasound (IVUS) guidance, stent surveillance, and follow-up protocols have been described in detail elsewhere.[8,9] Briefly, clinical assessment was based on CEAP classification and Venous Clinical Severity Score and entered into a time-stamped electronic medical record program contemporaneously. This system scores subjective severity of swelling on the basis of time at onset as assessed by the patient in the working day. In addition, swelling was graded objectively by physical examination from 0 to 3 (none, pitting, ankle edema, or gross swelling, respectively). Pain was scored 0 to 10 on the visual analog scale (VAS).[10] Iliac vein lesions were diagnosed and confirmed on IVUS examination and stented during the same sitting under general anesthesia. Patients were seen on follow-up for clinical assessment with concurrent duplex examination of stent patency at 6 weeks, 3 months, 6 months, and yearly thereafter. Interval symptoms prompted additional clinical evaluation and duplex assessment of stent patency as needed. Interval symptoms were commonly due to stent malfunction (in-stent restenosis or stent compression, sometimes associated with inflow and outflow problems).[11] Reintervention was based on severity of interval symptoms. Asymptomatic in-stent restenosis of up to 25% lumen reduction was common and was not an indication for reintervention.[12] Correctional reintervention consisted of balloon dilation of the stent to clear the lesions with simultaneous stent correction of inflow and outflow problems, if any.

IVUS guidance with planimetry (to gauge stenosis and restenosis) was used heavily with fluoroscopy during the initial and reinterventional procedures. The diagnostic sensitivity of IVUS to iliac vein lesions is ≈ 80%, with some lesions at tributary junctions escaping detection (or only partially visible) because the IVUS probe is not centered.[13,14] These lesions can be uncovered by waisting of the balloon during routine "sizing" of the iliac vein segments.

Wallstents (Boston Scientific Inc, Marlborough, Mass) were exclusively used in this experience. All patients in this subset received warfarin anticoagulation postoperatively.

Statistics. Past data were retrieved from electronic medical records and the venous laboratory database and analyzed. Paired and unpaired two-tailed *t*-tests were used for comparison where appropriate. Significance was defined as $P < .05$. Stent patency, pain, and swelling are presented as cumulative curves. Left and right sides were combined, neglecting left and right side interaction, if any,

Table I. Demographics of 39 femoral vein chronic total occlusion (CTO) lesions with concurrent iliac vein obstructive lesions

Age, years	51 (17-86)
Male:female	1:3
Right:left	1:2
Median iliac vein stenosis	80% (40%-100%)
Concurrent saphenous ablation	7 (18%)

Table II. Clinical classification of 39 femoral vein chronic total occlusion (CTO) lesions with concurrent iliac vein obstructive lesions

CEAP clinical class	*No. (%)*
0-2 (with pain)	2 (5)
3	19 (48)
4	10 (26)
5	1 (3)
6	7 (18)

CEAP, Clinical, Etiologic, Anatomic, and Pathologic classification.

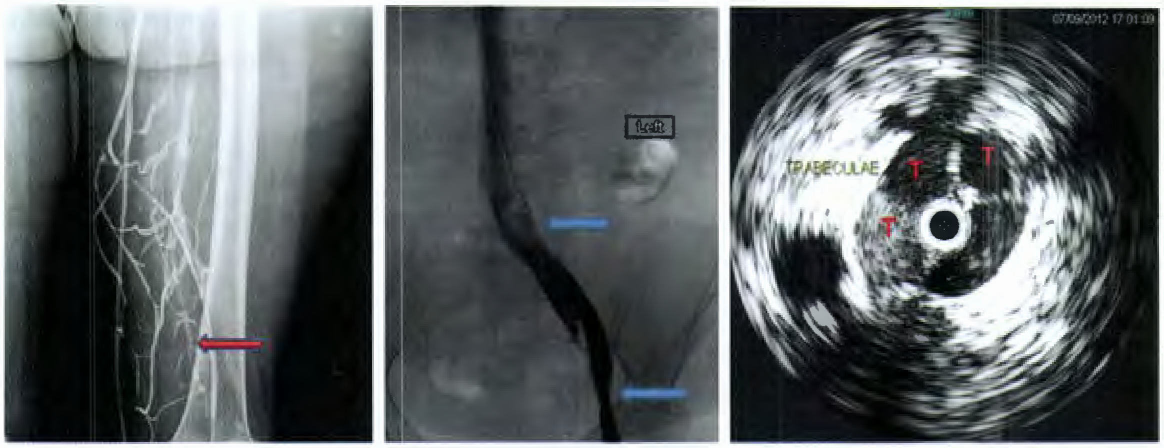

Fig 1. Post-thrombotic femoral vein occlusion (*left*) with suspected concurrent iliac vein lesions shown by *arrows* (*middle*). Extensive trabeculations (*T*) were seen in the external iliac vein on intravascular ultrasound (IVUS) examination, which was not suspected on the venogram. The IVUS catheter can be seen in the center (*right*).

on survival estimates. All analyses were performed with Prism software (Prism Software Corporation, Irvine, Calif).

Institutional Review Board permission was obtained in acquiring data in normal limbs. Informed consent was obtained from patients for indicated clinical interventions at the time. Institutional Review Board permission was also obtained for publication of past clinical data in anonymous aggregate fashion.

RESULTS

Femoral vein occlusion in the subset (n = 39) was documented by on-table venography and confirmed by duplex examination (Fig 1). An enlarged profunda femoris vein is the main outflow tract in these limbs (Fig 2). A coincident iliac vein lesion was suspected on preoperative venography in only 29 limbs. In the remaining 10 limbs, the occult iliac vein lesion was detected on IVUS examination or balloon sizing of the segments (Fig 3).

Reflux detail is shown in Table III. Of note, no perforator reflux was found in any of the limbs. Proximal saphenous reflux was present in nine limbs. Of these, concurrent saphenous ablation with stenting was carried out in seven limbs (two ulcers; four dermatitis/lipodermatosclerosis; one swelling with large great saphenous vein). Concurrent saphenous ablation was not carried out in two other limbs (<4 mm saphenous in one limb; unclear reason in one limb).

There was no procedural mortality (30 days). Morbidity included recurrent deep venous thrombosis in two limbs (<30 days). Stents occluded in two limbs (at 5

Fig 2. A 60-year-old man with post-thrombotic occlusion of the right femoral vein (*left*) and a "normal"-appearing iliac vein on venography (*middle*). A Greenfield filter can be seen in the vena cava (*arrow*). On intravascular ultrasound (IVUS) examination (*right*), there was no stenosis at the filter site, but a long diffuse stenosis was present in the common iliac vein. The lumen area measures 78.5 mm^2 (61% stenosis) compared with a normal expected lumen area of 200 mm^2.

Fig 3. Chronic femoral vein occlusion (*left arrow*) with excellent collateralization through profunda femoris vein (*right arrow*). The enlarged profunda femoris vein can be easily mistaken for the femoral vein because of comparable lumen size and anatomic course.

and 25 months, respectively), of which one was reopened by lysis. Median iliac vein stenosis was 80% (40%-100%). These IVUS planimetry data include four limbs in which the lesion was only partially visible with area values of <50% stenosis.

Reintervention to correct stent malfunction suspected from recurrent or residual symptoms was carried out in 14 of 39 limbs (36%), which occurred without mortality. The two occluded stents are included in the 14 limbs that had reinterventions. Reintervention in nonoccluded stents consisted of balloon dilation of in-stent restenosis or stent compression alone in eight limbs and with correction of associated inflow or outflow by stent extension in four limbs. Clinical results presented here reflect status after reinterventions. Median follow-up was 26 months (1-154 months).

Table III. Reflux detail in limbs with occluded femoral vein (n = 37)[a]

Segment	*No. (% reflux)*
Proximal GSV	9 (24)
Distal GSV	8 (22)
SSV	10 (28)
Perforator	0 (0)
Profunda	1 (3)
Popliteal	13 (35)
Posterior tibial	4 (11)
Gastrocnemius	9 (24)
Superficial only	8 (22)
Deep only	3 (8)
Superficial/deep combination	11 (30)
No reflux	15 (40)

GSV, Great saphenous vein; *SSV*, small saphenous vein.
[a]Data missing in two limbs.

Primary, primary assisted, and secondary patencies at 2 years were 57%, 88%, and 96%, respectively.

Pain grade (VAS, 0-10) improved from median 5 of 10 (0-9) to 3 of 10 (0-8) after stenting ($P < .03$). Four of 33 limbs (12%) were completely relieved of pain. Cumulative improvement in pain, (≥3 of 10 on VAS) was 87% at 2 years.

Median objective swelling improved from grade 3 (0-3) to grade 2 (0-3) by physical examination after stenting ($P = .09$, NS).

Among 22 of 39 limbs (56%) with grade 3 swelling before stenting, seven of 22 limbs (32%) were objectively improved in the degree of swelling (≥1 grade) by physical examination. Subjective improvement was reported by the patient in all of the remaining 15 of 22 limbs (68%) after stent placement ($P < .0001$). Objective confirmation was not possible because the swelling was technically still grade 3, although the patient perceived it to be less severe than preoperatively.

Four of seven active ulcers (54%) healed.

Saphenectomy and saphenous flow. There was no statistical difference (underpowered) in clinical outcome by the addition of saphenectomy to iliac vein stenting ($P = .25$ for pain and $P = .79$ for swelling). There were no obstructive sequelae (phlegmasia, increased swelling above baseline, venous gangrene) in the seven of 39 limbs (18%) specifically related to saphenous ablation (collateral function) even though the femoral vein was occluded. The saphenous flow (mL/s) in 21 limbs in this series in which it was measured was not significantly different from that of 21 normal controls and 30 randomly selected CVD limbs without femoral vein obstruction; the saphenous vein was also of similar size (Table IV).

DISCUSSION

Post-thrombotic chronic occlusions of the femoral vein (CTOs) are readily found on duplex or venographic examination. It is intuitive to attribute symptoms in this clinical context to the femoral vein occlusion. The data presented herein suggest that a concurrent overt or occult iliac vein lesion should be considered as a contributor of the symptom complex in this setting. The iliac veins are often omitted in duplex examination, and where it is carried out in "routine" fashion, diagnostic accuracy is probably not similar to that of venography. IVUS examination remains the ultimate diagnostic tool to unearth occult iliac vein lesions.[2] A high diagnostic yield can be expected with IVUS use.[15]

There are several pieces of ancillary evidence to suggest that the iliac veins are hemodynamically and pathophysiologically more important than the accompanying femoral

Table IV. Erect saphenous size and flow

	Normals (n = 21)	*CVD limbs with patent femoral vein (n = 30)*	*Occluded femoral (n = 21)*	P[a]
GSV diameter, cm	0.63 (0.3-0.8)	0.6 (0.4-1.5)	0.69 (0.23-1.11)	.67, .14 (NS)
GSV flow, mL/s	0.85 (0.21-3.09)	0.85 (0.2-5.3)	1.22 (0.12-5.8)	.36, .11 (NS)

CVD, Chronic venous disease; *GSV,* great saphenous vein; *NS,* not significant.
[a]*P* vs normal and CVD limbs with patent femoral veins, respectively.

vein CTO. The iliac vein is more central and carries about four times the flow of the femoral vein. The development of post-thrombotic syndrome has been related to involvement of the iliac veins in deep venous thrombosis and also positively correlated with failure to recanalize this central venous segment.[16-18]

Furthermore, excellent collateralization through the profunda femoris vein is the rule in femoral vein CTO lesions, whereas iliac vein collateralization is typically less efficient.[19-21] The profunda femoris vein is the embryologic axial vein, with the femoral vein replacing it in later development. The connection between the two at the popliteal vein level persists in adulthood as a putative collateral connection, explaining the rapid evolution of the alternative profunda pathway in case of femoral vein occlusion. Collateral flow direction in the profunda femoris is the same as valve orientation, whereas iliac collateral flow occurs through tributaries against valve orientation. The profunda femoris rapidly enlarges in chronic femoral vein occlusions to resemble the caliber of the femoral vein.[21] It is not unusual at this stage to mistake the dilated profunda femoris for the femoral vein proper (Fig 2). In an estimated 20% of post-thrombotic limbs in our experience, the profunda femoris is also involved in the post-thrombotic process, in which case its collateral potential to carry femoral vein flow is likely diminished. If the lesion involves only the profunda femoris orifice per IVUS or venography, the iliac-femoral stent can be extended into the profunda femoris vein with good patency (unpublished data). If the profunda femoris involvement is more extensive, adequate inflow in the common femoral vein may not be available to sustain the stent as the femoral vein is also occluded. Fortunately, this appears to be a rarity. We have stented iliac vein lesions even when inflow seems questionable on venography. Most such stents have remained open, and there has been no clinical worsening beyond original baseline when stent occlusion has occurred. At present, there is no reliable preprocedural or intraprocedural way to reliably estimate inflow adequacy at the common femoral vein level.[22]

The saphenous size remains relatively small in comparison after femoral vein occlusions. Any diversion of flow from deep veins to the saphenous has to be through enlarged perforators. Because such flow has to occur against valves and the additional resistance ($\approx \pi r^4$) offered by the relatively small caliber of the perforators, their collateral potential (even if enlarged to, say, 3 or 4 mm) is limited per the Poiseuille equation. Disregarding the resistance to outward flow offered by the perforator valves, 81 perforators of 3-mm size will be required to equal the conductance of a 9-mm femoral vein, and about 400 perforators each 2-mm in size will be required to replace femoral vein flow. Normally, there are about 80 to 150 perforators each 1- to 2-mm in size. Larger perforators in such profusion are seldom seen on venography or duplex ultrasonography in limbs with femoral vein CTO, as was the case in the current subset. Perforator valve incompetence is a requirement for their collateral function; this was noticeably (and surprisingly) absent in this subset. The venographic appearance of a seemingly "wiped out" deep system with all of the contrast material flowing through the superficial network is often a venographic artifact preventing entry of contrast material into the deep system with higher pressures. With direct introduction of contrast material into the deep system, profuse intramuscular collaterals can be visualized (Fig 4). Saphenous flow measurements in this series confirm their limited collateral function. Saphenous size and volumetric flow in this subset are not different from normal or CVD limbs with patent femoral vein. We have previously shown that saphenous vein can be safely ablated if it is refluxive with little clinical risk and often to the patient's benefit.[23] There is little increase in calculated outflow resistance after saphenous ablation or manual occlusion in the presence of deep venous obstructive disease.[23,24]

Symptomatic relief of pain, swelling, and healing of stasis ulceration after iliac vein stenting appear to be satisfactory enough to warrant consideration of the minimally invasive procedure in CVD.[25] Nevertheless, the degree of relief with iliac vein stenting does seem less (anecdotally) in the current subset with femoral vein CTO compared with historical experience in limbs without concurrent femoral vein occlusion. Possible explanations include that femoral vein involvement indicates a more widespread and severe disease than in segmental iliac vein stenoses; involvement of the profunda femoris collateral in the thrombotic disease; and presence of high-pressure bottleneck in the critical profunda-popliteal connection, reducing collateral efficiency. Another negative is the relatively high percentage of reinterventions (36%) in this experience compared with historical norms of $\approx$20%.[11] Whereas the small numbers in this subset may have resulted in some data skewing, incomplete resolution of swelling in many patients also prompted more reinterventions than usual to improve the clinical outcome.

Limb swelling extends into the thigh in many cases in this series. A symptomatic improvement after stenting where the swelling recedes from the thigh to below the

Fig 4. Descending venogram (*left*) shows multiple deep venous collaterals in a limb with occluded femoral vein (*arrowhead*), yet ascending venogram (*right*) opacifies only the superficial venous network, with the deep system seemingly "wiped out." This is due to failure of the contrast material to enter the higher pressure deep venous system in such limbs.

knee, although significant from the patient's point of view, will still be classified as grade 3 by objective grading and will not be adequately reflected in the current classification system. Whereas the current report documents subjective improvement as reported by the patient in these cases, it remains subject to the vagaries of the placebo effect. A classification with better resolution of swelling severity is needed. Gross swelling extending to the thigh deserves a higher grade in the classification system than one confined to below the knee. Plethysmographic techniques, which are notoriously cumbersome, are virtually impossible when swelling extends to the thigh.

Study limitations. Small sample size, retrospective analysis, and imprecise swelling metrics are major limitations in this study.

CONCLUSIONS

It is worthwhile to search for a coincident iliac vein stenosis in cases of post-thrombotic femoral vein occlusions. IVUS is the optimal tool of choice in the diagnosis and stenting of iliac vein lesions. Satisfactory clinical relief and avoidance of an open venovenous bypass are potential benefits of this approach. Clinical relief, although adequate to warrant intervention, appears to be less than historical experience in larger subsets without femoral vein occlusion.

AUTHOR CONTRIBUTIONS

Conception and design: SR
Analysis and interpretation: SR
Data collection: SR, MW, MD
Writing the article: SR
Critical revision of the article: SR
Final approval of the article: SR
Statistical analysis: SR, MW, MD
Obtained funding: Not applicable
Overall responsibility: SR

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