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Endovascular Surgery in the Treatment of Chronic Primary and Post-thrombotic Iliac Vein Obstruction*

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Objectives: *to compare the results and complications of endovascular surgery in limbs with post-thrombotic and non-thrombotic disease and to detail some technical aspects of the procedure.*
Design: *a single centre, prospective study.*
Materials and methods: *between March 1997 and August 1999, 139 consecutive lower extremities with chronic iliac venous obstruction (61 limbs with primary disease [MTS] and 78 with post-thrombotic disease [PTS]) were treated by balloon dilation and stenting. History, clinical examination, procedure and follow-up data were recorded.*
Results: *mortality was zero. Non-thrombotic complication rate was only 3%. Postoperative (8%, 6/78) and late occlusion (3%, 2/69) occurred only in post-thrombotic limbs. Primary, primary-assisted and secondary cumulative patency rates of the stented area at 2 years were 52%, 88% and 90%, respectively, in the PTS group as compared to 60%, 100% and 100% in the MTS group. Clinical improvement in pain and swelling was significant in both groups. Half of active venous ulcers healed after the procedure.*
Conclusions: *chronic iliac vein obstruction appears to be a symptomatic lesion that can be treated safely and effectively by endovascular surgery regardless of aetiology. Generous use of IVUS is suggested in both diagnosis and treatment since phlebography is unreliable. The clinical improvement was significant in both groups; however, more excessive neointimal hyperplasia and a higher early and late occlusion rate were observed in post-thrombotic disease. Stenting after balloon dilation is advised in all venoplasties; stents should be inserted well into the IVC when treating iliocaval junction stenosis. A wide-diameter (16 mm) stent is recommended. The stent should cover the entire lesion as outlined by the IVUS.*

Key Words: Iliac vein obstruction; Stent; Venoplasty; Balloon dilation; Post-thrombotic; May–Thurner syndrome.

Introduction

Venous insufficiency of the lower extremity is a complex disease with a number of contributing factors, including valve reflux, venous outflow obstruction, diseased vein walls and poor calf mechanics. Recent studies have suggested that the role of obstruction is underestimated and that it is a feature in the majority of post-thrombotic limbs, most often in combination with reflux.[1,2] Furthermore, the interest in primary and secondary chronic venous insufficiency has focused mainly on the formation, healing and treatment of stasis ulcers. A substantial number of patients with ambulatory venous hypertension, however, complain of disabling limb pain and swelling without skin changes.[3] These symptoms and signs are not always improved by wearing compression stockings. In these patients it is possible that the symptoms may be caused by outflow obstruction. The introduction of percutaneous iliac vein balloon dilation and insertion of a stent[4] has made it possible to correct pelvic vein obstruction and thus avoid major invasive surgical procedures with uncertain long-term outcome.[5–7]

The present study describes and compares the results and complications of endovascular treatment in limbs with post-thrombotic and primary disease, details some technical aspects of the procedure, and emphasises the importance of intravascular ultrasound in diagnosis.

Materials and Methods

Between March 1997 and August 1999, a total of 139 lower extremities in 137 consecutive patients (left/right ratio = 105/34; male/female ratio = 50/89; median age: 48 years [range: 14–77]) underwent femoral

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vein cannulation and percutaneous balloon dilation and stenting of the iliac vein. This number represents approximately 9% of patients evaluated for venous disease by the authors during the same time period. The patients had chronic symptoms with a median duration of complaint of 60 months (range: 1–480) before treatment. In 32 patients previous interventions had been performed, including long saphenous vein stripping in 12, venous valvuloplasty in 15, failed Palma bypass operation in two, and thrombolysis in three limbs. All patients were screened for thrombophilia. Predisposing conditions for the development of venous thrombosis were observed in 74 patients. A history of trauma to the lower extremity or pelvis (14) or previous surgery (29) was found in 43 patients, in combination with thrombophilia in 10. Only one patient had been operated for a malignancy (breast cancer) and was free of recurrence. None of the obstructions were caused by local compression of malignant tumours. An additional 31 patients had only thrombophilia. The majority of patients with procoagulant conditions had protein C, protein S and/or Antithrombin III deficiency (73%, 30/41).

The degree of pain was evaluated using a visual analogue scale from 0–10, wherein 10 is the most severe pain.[8] Swelling was assessed as grade 0 (absent), grade 1 (pitting, not obvious), grade 2 (visible ankle oedema), and grade 3 (massive oedema, encompassing the entire leg). As is the routine in our service, a comprehensive workup was performed in all patients prior to the intervention, including ascending, descending and antegrade transfemoral phlebographies; ambulatory venous pressure measurement; hand/foot venous pressure differential at rest and after tourniquet ischaemia-induced hyperaemia; air plethysmography; and erect duplex Doppler investigation with standardised compression. The technical aspects of these investigations are detailed in previous publications.[9,10]

Post-thrombotic disease (PTS group)

Of the total, 78 patients had verified post-thrombotic disease, i.e. known occurrence of deep vein thrombosis diagnosed with duplex ultrasound or ascending phlebography and subsequently treated with heparin and oral anticoagulants; or findings on phlebography (occlusion, stenosis or collaterals) and/or duplex ultrasound indicating previous deep vein thrombosis below the inguinal ligament (direct visualisation of thrombus or indirect indication by partial or total inability to compress the vein) (PTS group).

Table 1. Rate of primary complaint of the individual patient and prevalence of pain and swelling in all 139 limbs with chronic venous outflow obstruction.

Primary complaint	Post-thrombotic limbs ($n = 78$)	Limbs with primary disease ($n = 61$)
Pain	19 (24%)	16 (26%)
Swelling	34 (43%)	40 (66%)
Dermatitis/pigmentation	3 (4%)	1 (1%)
Active ulcer	23 (29%)	4 (7%)
Prevalence of symptoms		
Pain	73 (94%)	45 (74%)
Pain scale ≥5	27 (35%)	23 (38%)
Swelling	76 (97%)	58 (95%)

May–Thurner syndrome (MTS group)

The remaining 61 limbs had no previous history of deep vein thrombosis. Ascending and transfemoral phlebography and duplex ultrasound showed no evidence of previous event of deep vein thrombosis of the calf, popliteal, femoral and iliac veins. The iliac obstruction in this group of patients was considered to be of primary aetiology. The majority of these (77%, 47/61) had a localised narrowing at the vessel crossing at the left common iliac vein, a so-called May–Thurner syndrome (MTS group).[11]

The median age was similar in both groups, 47 years [range: 18–77] in the PTS group vs 50 years [range: 14–77] in the MTS group. Distribution according to sex was equal in the PTS group, while primary disease was four times more common in females. The post-thrombotic disease was only twice as common in the left iliac vein, whereas the primary disease was five times more common in the left than in the right side.

The presenting limb complaints are shown in Table 1. One third of the patients with post-thrombotic disease had severe signs and symptoms of chronic venous insufficiency with active/healed ulcer or dermatitis, while this was uncommon in limbs with primary disease. The majority in the latter group complained of pain and swelling. The distribution of severe limb pain (pain scale ≥5, 35–38%) and the prevalence of swelling (95–97%) were similar in the two groups. Only 6% and 26% of the PTS and MTS groups, respectively, were completely free of dependent pain prior to the intervention.

Following completion of tests the lower extremities were classified according to the CEAP classification as

Table 2. CEAP score of 139 limbs with chronic venous outflow obstruction.

	Post-thrombotic limbs ($n=78$)	Limbs with primary disease ($n=61$)
Clinical score		
2	0	4
3	39	44
4	9	7
5	6	2
6	24	4
Etiology		
Primary	0	61
Secondary	78	0
Anatomy		
Deep	33	43
Deep/superficial	45	18
Pathophysiology		
Obstruction	25	42
Reflux/obstruction	52	19

Table 3. Comparison of preoperative haemodynamic test results in obstructed post-thrombotic limbs and limbs with primary disease.

	Post-thrombotic limbs ($n=78$)	Limbs with primary obstruction ($n=61$)
Ambulatory venous pressure drop, %	57 [13–99]	61 [31–92]**
Venous recovery time, s	19 [1–108]	34 [3–150]***
Venous filling index$_{90}$, ml/s	2.8 [0.2–12.1]	1.0 [0.1–9.0]***
Hand/foot pressure differential, mmHg	1 [0–5]	1 [0–8]^{ns}
Hyperaemia pressure elevation, mmHg	6 [0–48]	4 [0–16]*
Multi-segment score	3 [0–6]	0 [0–3]***
Kistner's axial reflux score	2 [0–4]	0 [0–4]***

Median [range], * $p<0.05$, ** $p<0.01$, *** $p<0.001$, ns = no significance.

per the guidelines of the SVS/ISCVS[12] (Table 2). The clinical severity score largely reflects the distribution of primary complaints. PTS limbs more frequently had higher clinical severity scores (≥4; 50% vs 21%), involvement of superficial in combination with deep system (58% vs 30%), and both reflux and obstruction on preoperative evaluation without IVUS (67% vs 31%) than did MTS limbs. The reflux observed in the latter limbs was mainly isolated superficial insufficiency, i.e. only long saphenous vein incompetence with no deep involvement. The results of the haemodynamic studies performed before surgery are outlined in Table 3. The differences in the haemodynamics of the two groups of limbs reflect the more extensive iliac disease combined with a higher rate of significant deep and superficial reflux observed in the PTS limbs. In these limbs,

Table 4. Distribution and combination of parameters leading to performance of iliac IVUS investigation in 78 post-thrombotic limbs and 61 limbs with primary obstruction.

	Post-thrombotic limbs ($n=78$)	Limbs with primary obstruction ($n=61$)
Phlebographic occlusion/stenosis		
alone	21	17
with collaterals only	23	20
with collaterals and positive pressure test	13	4
with positive pressure test only	6	3
Pressure test positive (no phlebographic obstruction)		
without collaterals	2	4
with collaterals	9	2
Collaterals only (no phlebographic obstruction, normal pressure test)	4	11

average ambulatory venous pressure drop is less, venous recovery time shorter, reflux flow higher, multi-segment and Kistner's axial reflux score higher, indicating significant reflux, and the hyperaemia pressure elevation is greater, indicating more severe stenosis.

Recognising the inaccuracy of phlebography in determining the degree of stenosis,[4] generous criteria were used to perform transfemoral intravascular ultrasound (IVUS) investigation in patients with suspected iliac lesion. The following preoperative parameters suggestive of iliac vein obstruction were used: limbs with 25% or greater stenosis on the preoperative ascending or antegrade transfemoral phlebography, radiographic visualisation of pelvic collaterals with or without visualised iliac vein obstruction, and a positive pressure test with arm/foot pressure difference ≥4 mmHg or reactive hyperaemia pressure rise ≥8 mmHg[13] were used. With these criteria for performance of IVUS investigation a normal vein was found in 13% of limbs.[4] The distribution and combinations of these preoperative parameters are shown in Table 4. Positive pressure measurement was found more frequently in PTS (38%) than in MTS limbs (21%) preoperatively. The rates of radiological obstruction and visualisation of collaterals were similar in the two groups (81% vs 72% and 63% vs 61%, respectively, in PTS vs MTS group).

Procedure

The authors performed all the procedures in an operating room with ceiling mounted ISS equipment

(International Surgical Systems, Inc., Phoenix, AZ, U.S.A.), which was dedicated to combining percutaneous endovascular and open surgical interventions. The interventions were done under general anaesthesia or local infiltration analgesia in combination with monitored sedation. Cannulation of the femoral vein was initially blind, but later it was performed under ultrasound guidance (Site-Rite® Mark II 21000 Series, Dymax Corp., Pittsburgh, PA, U.S.A.). After cannulation and guidewire insertion followed by introduction of a sheath, an antegrade phlebography (Figs 1A, 2A) was performed and subsequently an over-the-wire intravascular ultrasound (IVUS) investigation (SONOS® Intravascular Diagnosis System M2400A, Hewlett-Packard, Andover, MA, U.S.A., with Sonicath Ultra® 6 imaging catheter, 6F, 12.5 MHz, Boston Scientific Corp., Watertown, MA, U.S.A.). Using the built-in software program the lumen transverse area could be measured and the degree, length and site of obstruction were recorded (Figs 1C, 2B). The presence or absence of collaterals was noted. If possible, intraoperative pull-through pressure from the inferior vena cava to the femoral vein was then obtained using standard equipment. Femoral pressure distal to the obstruction was obtained before and after injection of 30 mg papaverine intra-arterially to increase the venous flow.[14] The obstruction was dilated with a balloon (Medi-Tech XXL®, 12–20 mm diameter, 4–6 cm length, Boston Scientific Corp., Watertown, MA, U.S.A.). A stent of appropriate length and diameter (most commonly 16 mm) (Wallstent® endoprosthesis, Schneider, [U.S.A.] Inc., Pfizer Medical Technology Group, Minneapolis, MN, U.S.A.) was then inserted, covering the dilated area. The phlebogram, IVUS investigation and pressure measurements were repeated to assess the final result (Figs 1B,C, 2A,B). The sheath was removed and pressure applied for 10 min. The patients received dalteparin sodium 2500 units preoperatively and 3000–5000 units heparin and 30 mg ketorolac (Toradol®, Roche Laboratories Inc., Nutley, NJ, U.S.A.) intravenously during the procedure. Simultaneously, additional surgery was performed in 21 patients. Stripping of an incompetent long saphenous vein was added in 14 limbs with primary disease and in six limbs with post-thrombotic disease. A temporary arteriovenous fistula was created in one limb with post-thrombotic obstruction.

Postoperatively, a foot compression device was used; dalteparin sodium (2500) units was administered subcutaneously in the recovery room and again the following morning. The ketorolac injection was repeated the next morning before discharge. A daily 81 mg dose of aspirin was started immediately after the procedure and continued indefinitely. Only patients already on warfarin preoperatively owing to prior deep vein thrombosis and thrombophilia were anticoagulated postoperatively. Warfarin was not routinely discontinued in these patients prior to the endovascular procedure. All patients were admitted for less than 23 h.

The patients have been followed clinically after 6 weeks and intermittently until March 2000, with repeat ascending or antegrade transfemoral phlebography, ambulatory venous pressure measurement, hand/foot venous pressure differential at rest and after tourniquet ischaemia-induced hyperaemia, air plethysmography; and erect duplex Doppler investigation.

Definitions and Statistical Analysis

Intraoperative treatment success was defined as <20% residual stenosis as compared to maximal expected dilation and elimination of pressure gradient. Postoperative treatment failure was defined as occlusion of the stent on phlebography or a recurrence or deterioration of the clinical condition. Wilcoxon rank sum paired and unpaired non-parametric tests were used in the appropriate setting to evaluate statistical significance. A p-value of less than 0.05 was considered significant. Primary, assisted primary (patency after pre-emptive intervention) and secondary patency rates (patency after intervention for occlusion) as defined by the reporting standards of the SVS/ISCVS[12] were calculated using survival analysis with the Kaplan–Meier method.

Results

The percutaneous balloon dilation and stent insertion were performed with no mortality. The non-thrombotic complication rate was low (3%, 4/139). Blind cannulation prior to ultrasound guidance availability resulted in two complications: a retroperitoneal bleeding in one limb, which was successfully treated conservatively with blood transfusion; and an injury to the superficial femoral artery in one limb, which was repaired by insertion of an interposition graft. One limb had an immediate postoperative swelling of unknown origin despite a patent stent. The swelling subsided gradually within a few weeks. In one limb the guidewire became caught in a stent, necessitating the removal of both the stent and wire by an open femoral venotomy. All complications occurred among

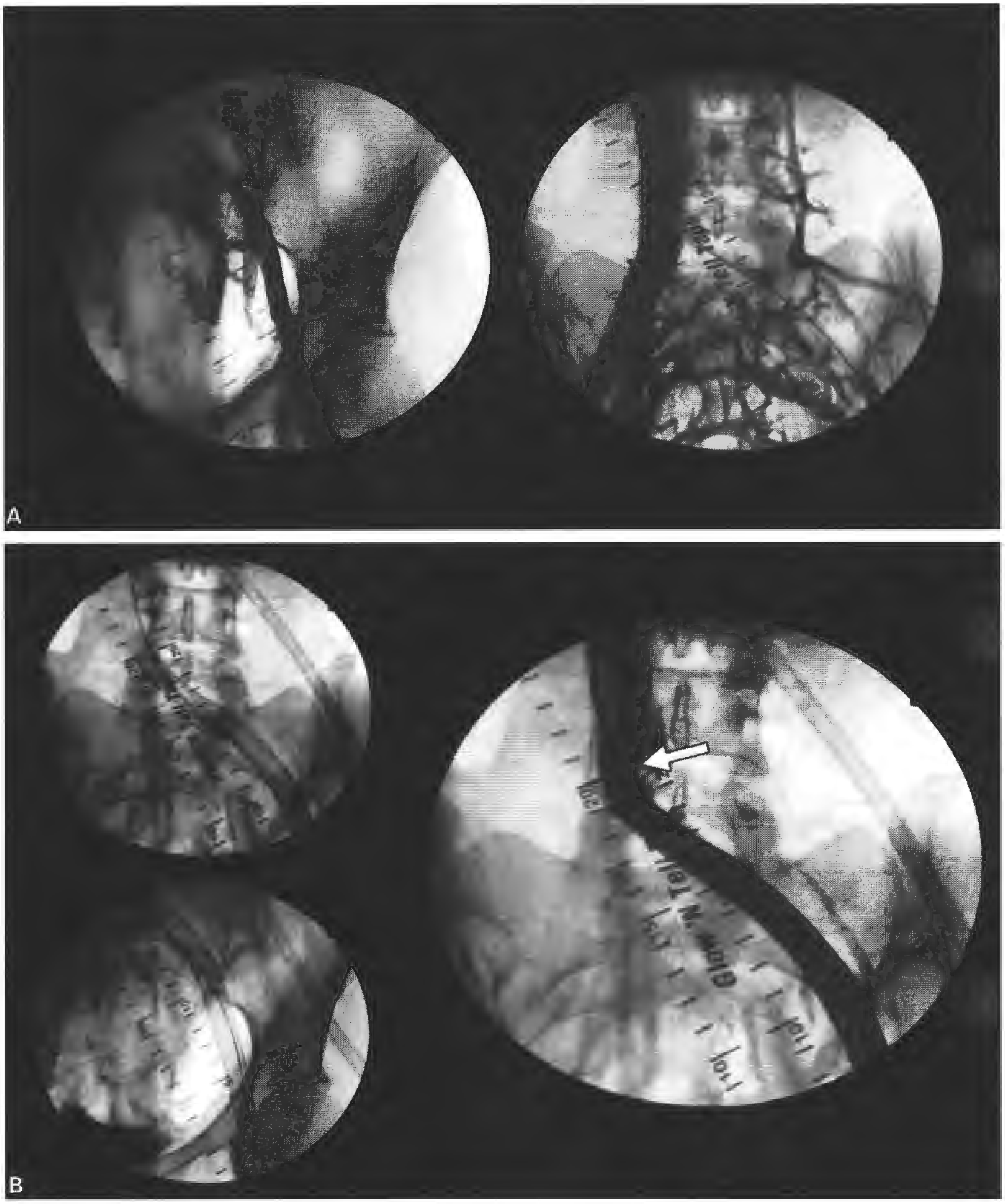

Fig. 1A. Intraoperative transfemoral ascending phlebogram prior to balloon dilation and stenting in a patient with PTS disease and common iliac vein near-occlusion and external iliac vein stenosis. Note the filling of the ascending lumbar vein and the marked transpelvic collateral circulation.
Fig. 1B. Status following insertion of two overlapping stents (diameter 12 mm) placed well into the IVC and covering the entire left iliac vein (left). Repeat phlebogram show an uninterrupted flow through the iliac vein into the IVC (proximal end of stent at arrow). No collateral circulation is visualised (right).

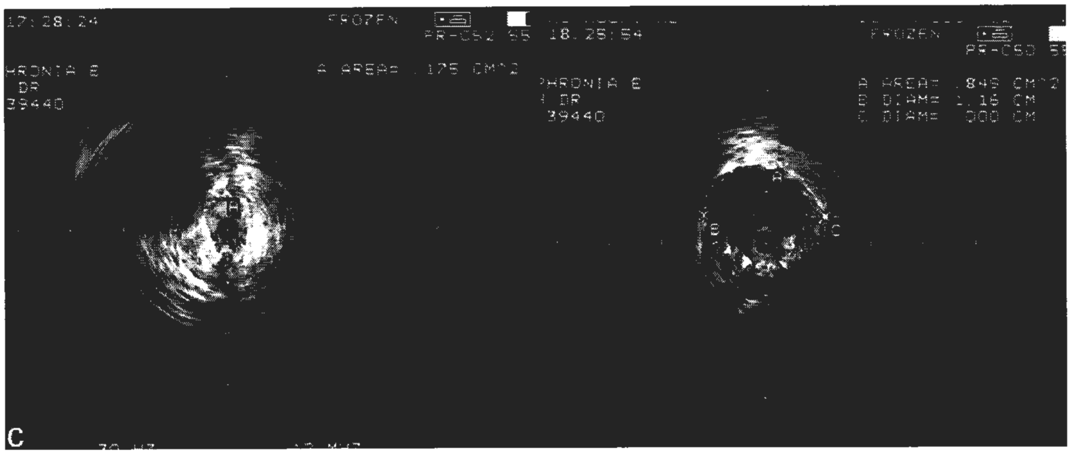

Fig. 1C. IVUS investigation before (left) and after (right) insertion of stent. Note area increase from 0.175 to 0.849 cm^2 and the surrounding high echogenicity indicating phlebosclerosis.

the first 29 insertions and before ultrasound guidance was used for cannulation of the femoral vein. There were no procedure-related complications in the subsequent 110 cases.

A postoperative thrombosis occurred in six post-thrombotic limbs within 3 weeks (6/78, 8%). None of the limbs treated for primary disease occluded, i.e. total postoperative thrombosis rate of 4% (6/139). Three patients received only anticoagulation. Two limbs were treated with catheter-directed thrombolysis. One case was successfully lysed, but a Palma crossover bypass was performed in the other to relieve the chronic obstruction. One limb rethrombosed 3 weeks after an open thrombectomy. The iliac stenosis could not be fully distended in five PTS limbs with post-thrombotic, highly resistant vein, leaving a narrowing of more than 20% post-stenting. In three limbs this also resulted in a remaining pressure gradient. The balloon dilation and stenting was successful in all MTS limbs. Thus, the postoperative occlusion rates were 8% (6/78) and 0%, and the technical success rate 94% (73/78) and 100%, respectively, in the PTS and MTS groups.

Several observations were made during the procedure (Table 5). There was a marked discrepancy in assessment of the degree of stenosis between the intraoperative phlebogram and IVUS investigation. The phlebogram significantly underestimated the degree of obstruction (by 20% and 28% in the PTS and MTS groups, respectively). On IVUS, 90% of all limbs had >50% stenosis and 61% had >70% stenosis. Compared to IVUS as the standard, the transfemoral phlebogram had poor sensitivity (51%) and negative predictive value (40%) to detect a vein stenosis of >70% (specificity 91%, positive predictive value 88%). When the actual stenotic area was measured by IVUS before and after stenting ($n = 46$) and compared to area derived by diameter calculations (πr^2), the severity of stenosis increased by a further 5–10%, probably owing to the irregular lumen geometry of the stenosis (Table 6). The extent of the lesions was greater in the PTS limbs. Almost the entire iliac vein was involved in 41% of these limbs as compared to 15% of MTS limbs. The obstruction was confined to the common iliac vein in 72% of these limbs as compared to 45% in the PTS group. The presence of collaterals on intra-operative iliac phlebography was similar in both groups (75%), but post-stenting they disappeared more often in PTS (72%) as compared to MTS limbs (43%) (Table 5). Femoral pressure was significantly more increased at rest and after intra-arterial injection of papaverine in PTS limbs. More than half of these limbs (52%) had a pressure increase >2 mmHg, a finding that was noted in only 22% of the MTS limbs. The recoil after balloon dilation was significant and similar in the two groups. Total recoil was observed in 7/10 and >50% recoil in 9/10 of limbs (Table 5).

A number of additional intraoperative data were collected prospectively (Table 6). Owing to the more extensive lesions seen in PTS, it was nearly twice as common to insert more than one stent in these limbs compared to MTS limbs (41% vs 23%, respectively) and three times more frequent with a total stent length of more than 10 cm (35% vs 13%, respectively). The average diameter of the stented PTS veins at the point of stenosis was approximately 2 mm smaller than that of the MTS veins (14.9 mm $\pm$ 2.2 vs 16.7 mm $\pm$ 1, respectively [mean $\pm$ SD]). Measurement of the actual transverse area of the lumen by IVUS showed a 33% less increase on average in the PTS as compared to MTS limbs (Table 6).

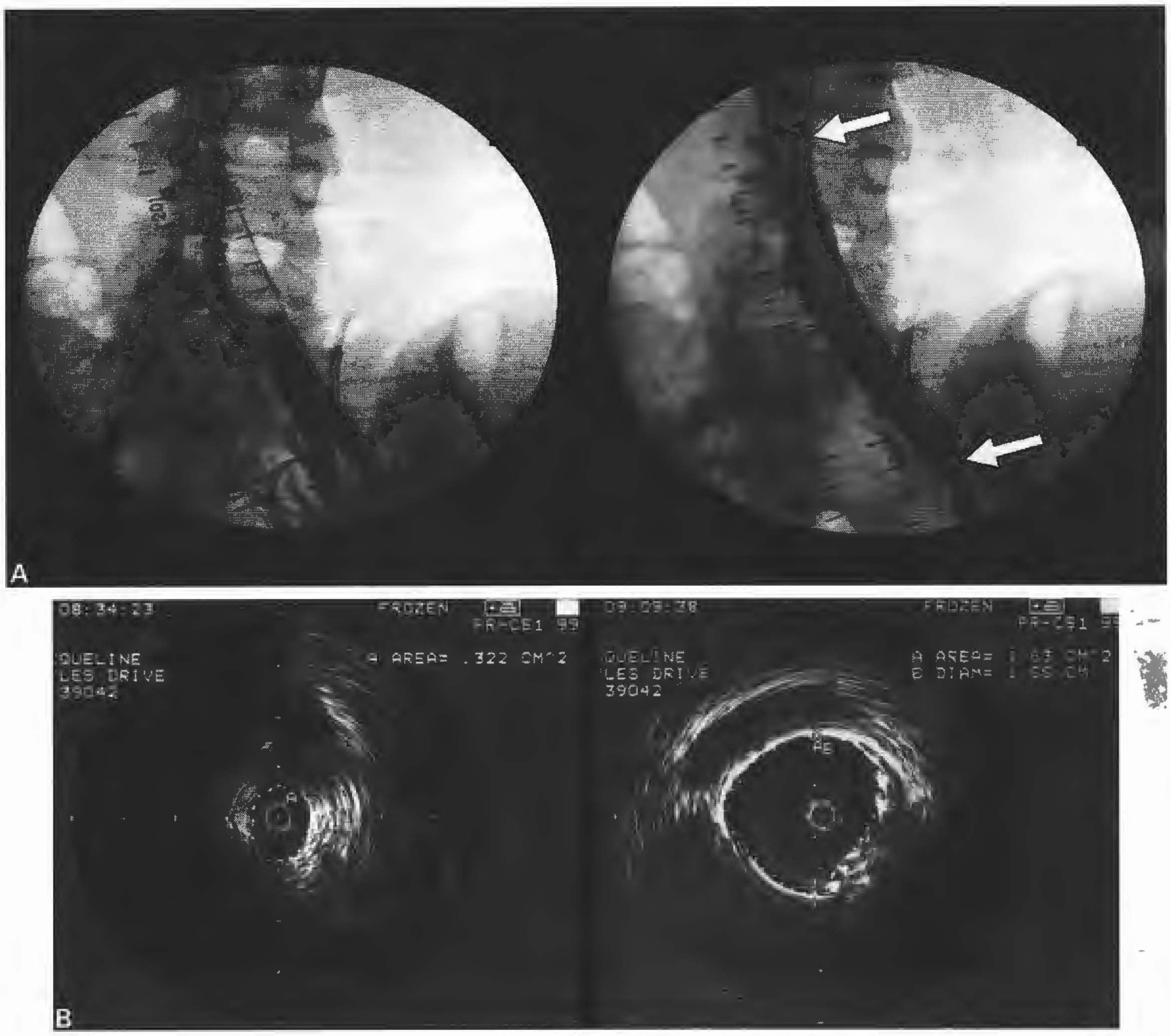

Fig. 2A. Intraoperative transfemoral ascending phlebogram before (left) and after (right) balloon dilation and insertion of stent (16 mm) in a patient with MTS. The transluscent common iliac vein with collaterals is typical. No collateral circulation is visualised after stenting (stent extending between arrows).
Fig. 2B. IVUS investigation before (left) and after (right) insertion of stent. Note area increase from 0.322 to 1.63 cm^2 and the relatively low echogenicity surrounding the lesion.

Follow-up was available in 95% of PTS limbs (69/73) and 87% of MTS limbs (53/61); the median follow-up was 13 months (range 2–36) and 10 months (range 2–35), respectively. The five patients with persistent early occlusion have been excluded as treatment failures. Primary, primary-assisted and secondary cumulative patency rates of the stented area as per phlebography at 2 years were 52%, 88% and 90% in the PTS group as compared to 60%, 100% and 100% in the MTS group (Figs 3 and 4).

During the follow-up, restenosis of the iliac segment was found in 22 limbs. The rate of restenosis was 17% regardless of the aetiology of the obstruction. In 14 limbs the recurrence was found proximal to, in seven distal to, in one in between previously inserted stents, and in one limb within the stent. When the first 25 limbs were stented for stenosis of the common iliac vein, the stent was inserted just beyond the narrowing at the iliocaval junction to ensure minimal or no projection of the stent into the inferior vena cava. All proximal stenoses in the entire series occurred in these initial 25 limbs and none occurred in the later part of the series when the stent was deliberately inserted to project well into the vena cava. All of these patients had become symptom-free after stenting and had re-investigations performed because of recurrence of

Table 5. Observations during iliac vein stenting in post-thrombotic limbs vs. limbs with primary obstruction.

	Post-thrombotic limbs ($n=78$)	Limbs with primary disease ($n=61$)
Site of obstruction		
IVC+CIV	4	4
CIV	35	44
CIV+EIV	32	9
EIV	4	1
Mid IV	3	3
Degree of stenosis		
on phlebogram, %	60 [0–99]	50 [0–99]
with IVUS, %	80 [25–99]	70 [40–99]
Presence of collaterals		
Pre-stenting	78% (61/78)	75% (46/61)
Post-stenting		
None	72% (44/61)	43% (20/46)
Less	17% (10/61)	30% (14/46)
Unchanged	11% (7/61)	27% (10/46)
Femoral pressure, mmHg		
At rest	12 [5–25]	11 [4–20]*
Pull-through gradient	0 [0–6]	0 [0–9]^{ns}
Increase after papaverin inj.	2 [0–22]	1 [0–4]**
Increase after tourniquet	0 [0–4]	0 [0–4]^{ns}
Recoil after dilatation, %	100 [20–100]	100 [40–100]

IVC = inferior *vena cava*, CIV = common iliac vein, EIV = external iliac vein, IV = iliac vein.
Median [range], * $p<0.05$, ** $p<0.01$, ns = not significant.

Table 6. Observations during stent insertion for iliac vein obstruction in post-thrombotic limbs and limbs with primary disease.

	Post-thrombotic limbs ($n=78$)	Limbs with primary disease ($n=61$)
Number of stents		
1	46	47
2	25	10
3	5	2
4	1	2
6	1	0
Total length of stented segment		
4 cm	10	7
6 cm	19	20
8–10 cm	22	26
11–17 cm	22	6
20–26 cm	5	2
Diameter of inserted stent		
10 mm	4	0
12 mm	11	0
14 mm	19	15
16 mm	34	33
18 mm	9	19
20 mm	1	4
Transverse lumen area, cm^2	($n=28$)	($n=18$)
Pre-stenting	0.32 [0.05–1.18]	0.24 [0.05–0.84]^{ns}
Post-stenting	1.56 [0.73–2.15]	1.73 [1.16–2.50]^{ns}
Pre/post increase	1.06 [0.50–1.97]	1.41 [1.04–2.31]**

Median [range], ** $p<0.01$, ns = not significant.

symptoms. Subsequently, 13 limbs with proximal stenosis have been successfully restented with placement of an additional stent proximally, well into the inferior *vena cava*. One patient refused restenting. After becoming aware of this complication, all proximal stents have been inserted well into the inferior vena cava. Neither secondary thrombosis of the contralateral limb nor any recurrent stenosis of the common iliac vein has occurred by extending the stent into the vena cava. When recalculated as if all limbs had stents inserted well into the inferior vena cava, primary cumulative patency increased to 70% (from 52%) in the PTS and to 90% (from 60%) in the MTS limbs at 2 years. The remaining limbs with recurrence of the stenosis below or between stents were successfully treated by balloon dilation (one limb) or restenting (seven).

One limb had a 60% stenosis within the stent owing to neointimal hyperplasia and underwent balloon dilation successfully. Follow-up phlebography revealed the development of intra-stent hyperplasia in seven limbs in the PTS group (7/69, 10%) and four in the MTS group (4/53, 8%). However, most stents (8/11) had minimal hyperplasia formation with <10% stenosis and no clinical consequences. In two PTS limbs, the gradual development of neointimal hyperplasia was resistant to balloon dilation and led to late occlusion at 8 and 12 months post-stenting (2/69, 3%). No late occlusion developed in limbs with primary disease.

Substantial alleviation of symptoms was achieved in both groups following endovascular surgery. In particular, the relief of pain was impressive. The rate of patients completely free of pain rose from 6% and 26% pre-stenting to 60% and 59% in the PTS and MTS groups, respectively. The average pain score was more than halved in both groups (Table 7). Similarly, the rate of limbs with no swelling increased from 3% and 5% pre-stenting to 42% and 43% post-stenting in the PTS and MTS groups, respectively. The average degree of swelling decreased significantly. An unexpectedly high rate of ulcer healing from this intervention alone was demonstrated. In the entire series, 28 limbs had a history of chronic recurrent ulcer disease for 90 months (median; range: 12–320) and an active ulceration for 12 months (median; range: 1–96). In the MTS group, four limbs had active venous stasis leg ulcer and all healed. However, one recurred during the observation period. Twenty-four of the PTS limbs had active leg ulcers: 12 (50%) healed and remained healed throughout the observation period; three healed but later recurred; five never healed; and four were lost to follow-up.

Discussion

Several successful small case experiences of balloon dilation and stenting of obstructed iliac veins have

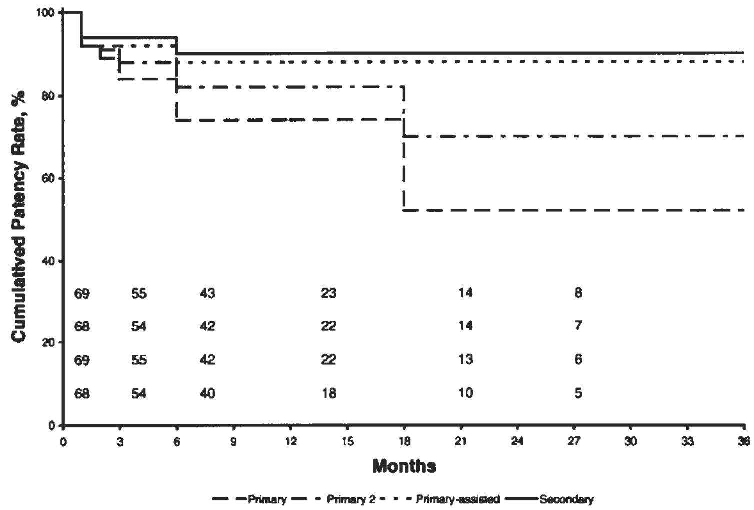

Fig. 3. Cumulative primary, primary-assisted and secondary patency rates following iliac vein balloon dilation and stent insertion in PTS limbs. In addition, primary patency rate (primary 2) is shown if all limbs had adequate proximal stent insertion into the IVC.

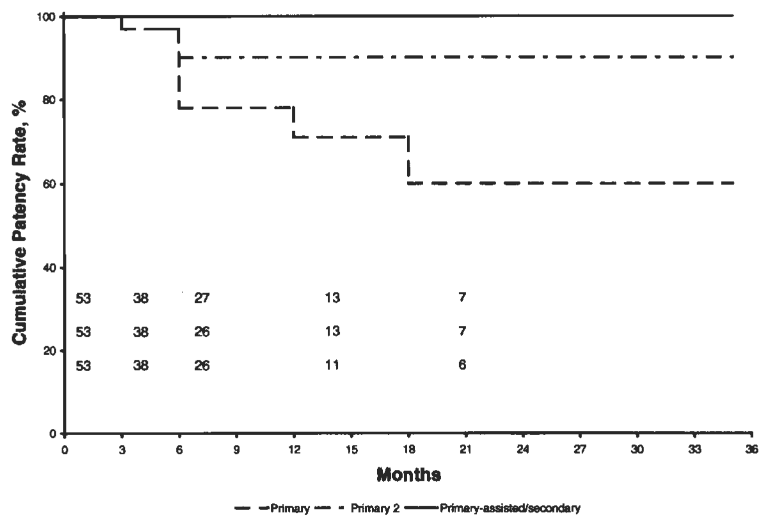

Fig. 4. Cumulative primary, primary-assisted and secondary patency rates following iliac vein balloon dilation and stent insertion in limbs with primary disease. In addition, primary patency rate (primary 2) is shown if all limbs had adequate proximal stent insertion into the IVC.

previously been reported.[15–20] To our knowledge, no comparison of different aetiology of chronic non-malignant iliac venous obstruction or longer follow-up has been previously reported. There are obvious differences in presentation, pathology, treatment and result in patients with lower extremity venous outflow obstruction due to post-thrombotic (PTS) and primary (MTS) disease. Regardless of aetiology, however, chronic iliac vein obstruction in itself may result in leg pain and swelling.

Obstruction due to MTS showed 4:1 preponderance for the female sex and 5:1 preponderance for the left limb, as compared to 1:1 and 2:1 preponderance, respectively, in PTS. The disease was clinically more severe in the PTS limbs as indicated by the CEAP score, because the occlusive disease was more extensive and more often combined with deep venous reflux than in the MTS limbs. The line of separation between PTS and MTS with regard to aetiology of obstruction has some overlap and limitations. May–Thurner Syn-

Table 7. Pain score using visual analogue pain scale (1–10) and degree of swelling (1–3) in limbs with primary disease and post-thrombotic obstruction.

	Post-thrombotic limbs	Limbs with primary disease
Pain	($n=67$)	($n=48$)
Pre-stenting	4 [1–9] (mean 4.4)	5 [1–9] (mean 4.9)
Post-stenting	0 [0–9] (mean 2.2)***	0 [0–6] (mean 1.4)***
Swelling	($n=75$)	($n=57$)
Pre-stenting	1 [1–3] (mean 1.6)	1 [1–3] (mean 1.5)
Post-stenting	1 [0–3] (mean 0.9)***	1 [0–3] (mean 1.2)*

Comparison of post-stenting and pre-stenting values (median [range], * $p<0.05$, *** $p<0.001$).

drome[11,21–23] may result in secondary thrombosis to the iliac vein segment or even more extensively, involving the entire limb.

The major problem is the lack of a gold standard to detect and assess the degree of outflow obstruction preoperatively. At present, there is no reliable non-invasive study available. Duplex Doppler and plethysmography have been helpful in the diagnosis of acute complete obstruction. Ultrasound investigation and outflow fractions obtained by air and strain gauge plethysmography have been shown to be unreliable and play a limited role in detection of chronic venous obstruction, especially of intra-abdominal stenosis. Even the invasive pressures, i.e. hand/foot pressure differential and reactive hyperemia pressure increase, and indirect resistance calculations are insensitive and do not define the level of obstruction.[24,25] Only 38% and 21% of the PTS and MTS limbs, respectively, had a positive pressure test preoperatively. Until an accurate haemodynamic test has been found, it is necessary to base the diagnosis of symptomatic iliac vein obstruction on clinical signs and symptoms and a high index of suspicion. Unfortunately, even pre-operative transfemoral phlebogram was "normal" in 19% of PTS and 28% of MTS limbs. Limbs with May-Thurner syndrome may have subtle radiological findings (e.g some broadening or translucency at the vessel crossing), which are easily overlooked. Intraoperative intravascular ultrasound often showed a short but very significant stenosis in these limbs. The phlebogram significantly underestimated the degree of stenosis, as compared to IVUS, which appeared superior to any other means to estimate the degree of a chronic venous obstruction. In addition, IVUS detects fine intraluminal and mural details, such as trabeculation, frozen valves, mural thickness and outside compression. IVUS also provides accurate measurements for selection of stent and confirms good wall apposition of the stent after insertion. Therefore, the authors recommend that IVUS be used generously in diagnosis and treatment.

The intraoperative pressure measurement was not helpful in assessment of severity of borderline obstruction. Pull-through pressure differential or pressure increase on exercise or hyperaemia of venous obstructions is much lower than in the arterial system.[26–28] Only small pressure increases at rest may be significant and these were probably not detected with the present methods. In a supine position during surgery, it is difficult to increase the venous outflow sufficiently to detect a haemodynamic obstruction. The results of transfemoral pull-through pressure measurement were equivocal, and hyperaemia induced by intra-arterial injection of papaverine increased the pressure in only 52% of post-thrombotic limbs and 22% of limbs with primary disease. In this study, morphological iliac vein stenosis assessed by IVUS diameter was >50% in 9/10 and >70% in almost two-thirds of limbs. In addition to the arithmetically increased severity of stenosis following conversion of diameter into area, the non-circular nature of the lesions results in even greater stenosis.

The concept of "critical" stenosis is based largely on work in the arterial system and is derived from the finding that distal flow volume and pressure do not diminish until the stenosis is 60–70% or greater. In lesser degrees of stenosis, flow volume and pressure are maintained at nearly original levels by increasing velocity across the stenosis in response to transient increased pressure gradient. In the arterial system, collaterals as well as the peripheral resistance influence the behaviour of the stenosis. Clinical features referable to the arterial stenosis are related to lack of downstream perfusion. In contrast, in venous stenosis peripheral resistance is not a factor, the collaterals may be inefficient due to valve orientation, and the symptoms are due to upstream effects (lack of emptying). Tributaries, e.g. the opposite iliac vein, may minimise or erase a developing pressure gradient across the stenosis, thus suppressing the compensatory flow increase.[29] Because of these differences between venous and arterial stenosis, the concept of critical stenosis probably cannot be transposed. The degree of stenosis that becomes "critical" in the venous system is not known.

Following dilation and stenting of an iliac vein obstruction, 80% of collaterals disappeared completely or markedly decreased. This observation has caused us to question the present view of pelvic collateralisation. Although collaterals may theoretically help to compensate an outflow obstruction, no relationship has been shown between the degree of collateralisation phlebographically and haemodynamic significance of venous obstruction.[30] The presence of collaterals should perhaps instead be looked upon as an indicator of a significant stenosis. Significant obstruction may exist, however, with no collateral formation and this has been described previously.[4]

Primary, primary-assisted and secondary cumulative stent patency rates at 2 years were 52%, 88% and 90% in the PTS limbs as compared to 60%, 100% and 100% in MTS limbs. If the patency is recalculated for patients with adequately placed stents (IVC extension), cumulative primary patency rates improve substantially to 70% in the PTS and 90% in the MTS limbs. Early thrombosis (<30 days) and late occlusion of the stents occurred only in post-thrombotic limbs (6/78, 8%), all of which had longer and smaller diameter (12 mm) stents inserted owing to the severity and extent of blockage. No relationship was found to the presence of thrombophilia.

The extent of the lesions were greater in the post-thrombotic limbs, while the vein was stenotic to a similar degree, regardless of aetiology. However, the stenoses of the post-thrombotic limbs were more rigid owing to the thick, dense periphlebitic fibrosis as compared with the more compliant, thinner wall in MTS as observed by IVUS though. The recoil was similar in both groups of limbs, but the resistance to dilation was markedly greater in the thrombotic limbs. This probably explains the 33% lesser increase of the crosscut area following stenting of the post-thrombotic vein. In this study Wallstent® endoprosthesis was used in all limbs. The spiral configuration and the inherent somewhat weak radial force of this self-expanding stent may explain the proximal restenosis in limbs with stents not placed well into the IVC[4] and the inability to force the thick-walled post-thrombotic vessels to fully expand. Stronger balloon expandable stents of the appropriate length and width are, however, not yet available. The two limbs with late occlusions were both in the PTS group and were preceded by neointimal hyperplasia within the stent. However, the rate of neointimal hyperplasia was similar in the two groups of limbs (8–10%), but appeared to be more excessive in the patients with post-thrombotic disease.

Several technical aspects are important. Simple balloon dilation leads to immediate recoil in the majority of limbs. Therefore, stenting is advised in all cases. The stent insertion in venous disease should be considered a different concept than stenting in arterial disease. When using the Wallstent® endoprosthesis, the stents should be inserted well into the IVC to prevent proximal restenosis. "Kissing" balloon technique at the confluence of the common iliac veins or insertion of bilateral stents is not necessary. We recommend using as wide-diameter a stent as possible (14–18 mm), and the stented area should always be re-dilated after insertion to achieve a good wall apposition. It is important to cover the entire obstruction as delineated by the IVUS. Although there is a natural tendency to insert as short a stent as possible, it is better to overstent than understent a lesion in terms of length. The occlusion rate does not appear to be related to the length of stent or metal load *per se* but to incomplete treatment.

The clinical outcome in the short-term was favourable. The method used to assess pain is reproducible and has been validated.[31] There was a statistically significant improvement in the pain and swelling scores of both groups. Moreover, the frequency of limbs with no pain whatsoever increased substantially in both groups, from 6–26% prior to stenting to 59–60% after intervention. Similarly, the rate of limbs with no swelling at all increased in both groups of patients from 3–5% before to 42–43% after the procedure. In addition, an unexpected high rate of ulcer healing after the procedure (50%) was observed with no additional reflux surgery. Patients with recurrence of obstruction also had recurrence of symptoms after a symptom-free period. These observations not only support the significant symptom relief after dilation and stenting of iliac vein obstruction, but may also indicate that outflow obstruction is a more important and frequent component in the treatment of chronic venous insufficiency than previously recognised.

In conclusion, chronic iliac vein obstruction can be treated safely in the short-term by venoplasty and stenting regardless of aetiology. After the initial learning period with 29 treated limbs and the introduction of ultrasound-guided cannulation of the vein, no procedure-related complications occurred. It is probably frequently overlooked, especially in patients with no previous history of deep vein thrombosis. Unfortunately, no accurate pre- or intraoperative tests exist to measure haemodynamic significance; therefore, generous use of IVUS is suggested in both diagnosis and treatment. There are obvious differences in presentation, treatment and results in patients with chronic iliac obstruction caused by post-thrombotic (PTS) and primary (MTS) disease. Although the clinical improvement is significant in both groups, more excessive neointimal hyperplasia and a higher early and late occlusion rate are observed in post-thrombotic disease.

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