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A 16-Year Haemodynamic Follow-up of Women with Pregnancy-related Medically Treated Iliofemoral Deep Venous Thrombosis

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Objectives: *to evaluate clinical and functional long-term outcomes following pregnancy-related medically treated iliofemoral deep venous thrombosis (DVT).*
Design: *retrospective follow-up of patients identified through a registry search.*
Material and methods: *twenty-five women underwent clinical examination, colour duplex ultrasound and computerised strain-gauge plethysmography on two occasions a mean of nine and 16 years after DVT.*
Results: *40% of the patients were completely asymptomatic and 52% had no clinical signs of venous disease after a mean follow-up of 16 years. The clinical signs were in general mild, and none of the 25 patients had skin changes or ulcers. Deep venous reflux was found in 36% of the patients; the same percentage at nine- and 16-years follow-up, and 24% had normal ultrasonographic appearance of all deep veins. None of the patients had plethysmographic evidence of outflow obstruction. There was a significant relationship between measures of venous reflux and the presence of leg swelling, but there was no clear relation between functional abnormalities and the extent of the initial DVT.*
Conclusion: *even after 16 years there are relatively mild symptoms and signs of venous disease in women with medically treated pregnancy-related iliofemoral DVT. Our results do not support earlier stated opinions that these patients represent a particular risk group for developing post-thrombotic syndrome.*

Key Words: Deep venous thrombosis; Pregnancy; Post-thrombotic syndrome; Ultrasonography; Strain-gauge plethysmography.

Introduction

The incidence of deep venous thrombosis (DVT) in the general population is around 1.4–1.8 per 1000 inhabitants.[1,2] The incidence of DVT during pregnancy or in the early puerperium is reported to be around 0.5–1.0 per 1000 live births.[3] There is an increased risk for iliofemoral DVT during the last trimester and shortly after delivery, possibly due to obstruction of iliac veins by the enlarged uterus in combination with hypercoagulability induced by pregnancy. These DVTs often arise in the iliac veins, propagate distally and will sometimes involve the whole limb if not diagnosed and treated at an early phase. Pregnancy-related DVT is of particular clinical importance as it involves fertile women with long life expectancy during which the post-thrombotic syndrome may develop. Earlier studies suggested that this group has a higher rate of long-term symptoms and signs compared with other groups of patients with previous DVT.[4,5]

In an earlier study, we compared the outcome after nine years for women with pregnancy-related iliofemoral venous thrombosis who had undergone surgical thrombectomy, with those who had received only medical treatment.[6] In that retrospective non-randomised comparison we found no evidence for surgical treatment being superior to conservative therapy. Somewhat surprisingly, we found only mild functional abnormalities and few post-thrombotic signs in both groups, and about 50% of the patients were completely asymptomatic.

In the present study, we have focused on the earlier described group of women with iliofemoral DVT treated non-surgically, to evaluate whether the relatively beneficial clinical outcome of conservative treatment after nine years is also maintained for a mean follow-up of 16 years. Furthermore, we aimed to relate the clinical and functional results to the extent of the initial thrombosis, to evaluate whether a beneficial clinical outcome was particularly common

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in women with DVT limited to the iliac veins above the groin.

Materials and Methods

Patients

A search from a registry of patients with venous thrombosis during pregnancy or puerperium in the Stockholm area from 1978 to 1989 was performed in the early 1990s. The search identified 37 women with conservatively treated iliofemoral DVT (i.e. with no surgical interventions), and 25 of these women could be traced and agreed to take part in a long-term follow-up study. Seven of the 37 could not be reached, and five women declined to participate. Eighteen of the 25 DVTs were diagnosed during pregnancy, and seven were diagnosed during puerperium. Twenty of the 25 DVTs were left-sided ($p<0.001$). Two of the patients had a history of previous DVT, in both cases affecting the contralateral limb.

During pregnancy or puerperium, the women had been treated with heparin from the time of diagnosis, initially given as a continuous i.v. infusion. This was continued for 5–10 days with s.c. injections. The heparin dose was generally adjusted to give an APT-time of one and a half to twice the prolongation of the normal time. Nineteen women were transferred to oral anticoagulants post partum. Two of the seven women with post-partum thrombosis received streptokinase. Elastic stockings and early mobilisation were used for general treatment. Further data concerning this group has been presented earlier.[6]

All patients gave their consent to participate in the investigation and the follow-up was approved by the local ethics committee.

Follow-up 1

This follow-up was performed during a 14-month period (November 1992 to January 1994) and consisted of a clinical examination, colour duplex ultrasound and computerised strain-gauge plethysmography. The mean age of the patients at this follow-up was 37 years (range 25–48) and the mean follow-up time was nine years (range 4–17). Since most of the results from follow-up 1 have been presented earlier,[6] this report focuses on results from follow-up 2 and the changes occurring from follow-up 1 to follow-up 2.

Follow-up 2

During the period February to October 2000, all 25 patients were seen at the Vascular Laboratory at Stockholm Söder Hospital, and underwent colour duplex ultrasound and computerised strain-gauge plethysmography, followed by a clinical examination by a vascular surgeon (ST) including a detailed CEAP-classification.[7] The clinical examination was performed without knowledge of results from the preceding tests. The CEAP-scoring included clinical classification (0–6), scoring for each symptom (0, no symptom; 1, mild/moderate; and 2, severe) and disability score (0–3).[7] The mean follow-up time was 16 years (range 10–24).

Before this visit at the hospital, all charts, including reports from phlebography and computerised tomography, were re-evaluated to obtain a definite and reliable description of the extent of the initial thrombus. The subjects were then classified into three groups depending on the degree of extension of the thrombus: Group 1, from iliac vein to groin ($n=8$); Group 2, from iliac vein to femoral vein ($n=8$); Group 3, from iliac vein to below the knee ($n=7$). Two women could not be classified reliably: one had the initial diagnostic procedures done in Mexico, and the diagnostic reports for the other could not be found. This classification was done by one of the authors (RH), who was not involved in the clinical or functional follow-up.

Clinical examinations as well as plethysmography and ultrasonography were performed and interpreted without knowledge of the group assignment. The same equipment was used for both follow-up examinations. Mean ages and mean follow-up times were not significantly different between the three groups (Table 1: see Statistics, below).

Colour duplex ultrasound

Duplex scanning was performed with a colour flow duplex imager (Acuson 128 XP, Mountain View, CA, U.S.A.). Depending on the depth of the vessel to be examined, an imaging transducer of 4, 5 or 7 MHz was selected in conjunction with pulsed and colour flow Doppler.

The patients were examined in the morning following overnight fasting. Venous flow was evaluated, with the patient in the supine position, in the inferior vena cava, iliac veins, femoral and popliteal veins, using a low velocity gain setting of the duplex imager. The occurrence of vessel wall abnormalities (irregularities, wall-thickening, decreased lumen) and flow in abnormal collateral veins were denoted and

Table 1. Clinical data at 16 years' follow-up for 25 patients with proximal deep venous thromboses during pregnancy. Results are shown as means (range) or numbers of patients (%). Extent of the initial thrombus: Group 1, iliac vein to the groin; Group 2, iliac to femoral vein; Group 3, iliac to below-knee veins.

	All patients ($n=25$)	Group 1 ($n=8$)	Group 2 ($n=8$)	Group 3 ($n=7$)
Mean age at follow-up (years)	43 (32–55)	43 (39–48)	44 (37–51)	43 (32–55)
Mean follow-up time (years)	16 (10–24)	16 (12–20)	17 (12–24)	15 (10–19)
Side of DVT (right/left)	5/20	3/5	1/7	0/7
New DVT during follow-up	6 (24%)	1 (12%)	2 (29%)	2 (29%)
Ipsilateral leg	3 (12%)	0	0	2 (29%)
Contralateral leg	3 (12%)	1 (12%)	2 (29%)	0
Symptomatic	15 (60%)	3 (37%)	6 (75%)	4 (57%)
Leg swelling	13 (52%)	3 (37%)	4 (50%)	4 (57%)
Venous claudication	8 (32%)	3 (37%)	3 (37%)	2 (29%)
Disability score, mean (range)	0.76 (0–2)	0.50 (0–2)	1.12 (0–2)	0.57 (0–1)
Total clinical score, mean (range)	2.0 (0–7)	1.75 (0–4)	2.5 (0–7)	1.9 (0–5)

Two patients could not be classified into a group, as the extension of the initial thrombus could not be verified.

used to identify post-thrombotic changes. Valvular function in veins between the groin and the knee was evaluated with the patient in a standing position. Veins below the knee were evaluated with the patient in a sitting position with the leg dependent. Reflux for a duration of more than 0.5 s following distal manual compression was considered significant.[8]

The following 16 segments were used for anatomic CEAP-classification,[7] and either post-thrombotic changes or valvular reflux were considered a positive finding: reticular veins; great saphenous vein above the knee; great saphenous vein below the knee; short saphenous vein; other superficial vein; inferior vena cava; common iliac vein; external iliac vein; other pelvic veins; common femoral vein; superficial femoral vein; popliteal vein; posterior tibial or fibular veins; calf muscular veins; thigh perforators, and calf perforators.

Computerised strain-gauge plethysmography

This procedure included two parts: a static measurement of venous volume and outflow capacity and a dynamic measure of volume changes following muscular exercise, using a computerised strain-gauge plethysmograph (Phlebotest™, Eureka AB, Sweden).

Venous outflow capacity and venous volume were measured with the patients laying supine with their heels resting on a heel support that elevated the calves 40 cm above bed level. The inflatable cuffs were wrapped around the thighs and the strain-gauge wires were placed around the largest diameter of each calf. Temporary venous occlusion was established by inflating the thigh cuffs to a pressure of 60 mmHg. When a volumetric plateau was established in both legs (detected by the instrument when venous filling was less than 0.1 ml/100 ml over 20 s), the cuffs were rapidly released, allowing outflow of the accumulated blood and a fall in the volumetric curve. Variables describing the volumetric curve were simultaneously calculated for each limb by the software of the unit using the DVT mode as follows:[9]

Venous volume (VV, ml/100 ml): the maximum volume change during the occlusion phase.
Venous emptying (VE, ml/100 ml per min): the outflow rate during the first second after deflation.
EV_4/VV: the volume of blood expelled during the initial 4 s divided by the maximum venous volume.

We used our earlier described diagnostic criteria for interpretation of plethysmographic evidence of outflow obstruction with this equipment.[10,11] These include a decision graph with three interpretations written out as "obstruction" (VE $\leq$50 and EV_4/VV $\leq$0.60), "free flow" (VE >50 and EV_4/VV >0.60) or "equivocal" (all other results).

The same equipment was used to measure volume changes during and after a standardised muscular exercise of 15 knee bends, but now using the software program "Venous insufficiency mode" (VI mode). For this part of the procedure, the patient stands with the wires applied just proximal to the malleolus. During calf muscle exercise, venous blood is expelled from the foot and the calf. Afterwards the volume is gradually restored by arterial inflow and, in patients with venous valvular insufficiency, this is accompanied by reflux of venous blood. A short time for refilling indicates venous reflux and a low refilling volume is usually supposed to indicate abnormal muscle pump function. Half-refilling times ($T\frac{1}{2}$) and refilling volumes (RV) were automatically calculated and printed out numerically and graphically by the unit's software.[12] The test was then repeated after occlusion of the superficial

veins using a below-the-knee cuff inflated to 80 mmHg.

Reproducibility of the plethysmographic procedures was tested by repeated studies in the following sequence: DVT mode, VI mode and repeated DVT mode for odd-numbered patients, and VI mode, DVT mode and repeated VI mode for even-numbered patients. The repeated studies did not include occlusion of superficial veins.

Statistics

If not otherwise stated, numerical data are presented as means and 95% confidence intervals (CI). Differences of means were tested for statistical significance by a one-way analysis of variance when three groups were compared, and by two-sided Student's *t*-tests when the comparison was restricted to two groups. Changes between follow-up 1 and follow-up 2, and between plethysmographic measures with and without superficial venous occlusion, were analysed by two-sided paired *t*-tests. Linear regression or Spearman's rank correlation were used to analyse relationships between different variables. Differences between proportions were analysed by Chi-square test. Statistical significance was assumed if p was less than 0.05.

The standard error (s) of a single plethysmographic determination was estimated from duplicate measurements and calculated as: $s = SD_{diff}/\sqrt{2}$. The coefficient of variation (CV) describes the variation as a percentage of the pooled mean values (x) and was calculated according to the formula: $CV\ (\%) = s/x \times 100$.

Results

Clinical examination at 16 years follow-up

Six patients had been treated for re-thrombosis during follow-up (Table 1). However, none of these did affect group belongings based on initial thrombus extension, since ipsilateral re-thrombosis was seen only in two patients in Group 3 with initial thromboses in the whole leg. These two patients suffered from ipsilateral re-thromboses in the calf.

Thirteen of the 25 patients (52%) were in CEAP clinical class 0 (no signs of venous disease); six patients were in class 1, and six patients were in class 2 (varicose veins >4 mm). None of the patients had ulcers or trophic skin changes. Three of the patients had undergone surgery for varicose veins during the follow-up; all of these were still in CEAP clinical class 2. There was no significant relation between clinical class and initial thrombus extension, but the percentage of patients lacking signs of venous disease decreased as thrombus extension increased. Thus, five of eight patients (62%) in Group 1, four of eight patients (50%) in Group 2 and three of seven patients (43%) in Group 3 were in class 0.

There was no significant difference between the groups regarding the frequency of symptomatic patients. The most common symptom was mild to moderate degree of leg swelling. Eight patients experienced pain during walking (venous claudication); this was mild in six of these patients, and severe in two (one patient in Group 2 and one in Group 3). Severe claudication was defined as pain emerging during exercise that was not relieved spontaneously shortly after exercise and which limited the patients walking ability. One of them sometimes used anagetics to relieve the pain. Symptoms in relation to initial thrombus extension are shown in Table 1.

Disability score was in general low, as 21 of 25 women reported that they were functioning in daily activities without the need for a support device (scores 0–1). Four patients scored 2 as they were symptomatic, but undertaking full daily activity with stockings. The disability score did not differ significantly between the groups. Group assignment did not significantly influence the total clinical score (i.e. the sum of scoring for symptoms and disability score).

Colour duplex ultrasound at 16 years follow-up

One patient in Group 3 still had occluded iliac veins. The prevalence of deep venous reflux in patients with DVT above the groin (Group 1) did not differ from that seen in those patients with DVT extending to below the groin (Groups 2–3) ($p = 0.47$).

Six of the patients (24%) had normal ultrasonographic appearance of all deep veins (i.e. no reflux and no post-thrombotic changes): two of these belonged to Group 1, three to Group 2 and one to Group 3. Three of the patients in Group 1 had post-thrombotic changes in the superficial femoral vein, although this segment was supposed to be unaffected. In two of these three cases, venous reflux was detected in deep veins below the groin.

There was a slight increase in the mean number of involved segments from Group 1 to Group 3; however, the overlap was large and there was no statistically significant relationship between extension of DVT and number of involved segments (Table 2).

Table 2. Duplex results at 16 years' follow-up in 25 patients with proximal deep venous thrombosis during pregnancy. Results are shown as numbers of patients (%) or numbers of venous segments involved (range) for all patients and in relation to extent of the initial thrombus.

	All patients ($n=25$)	Group 1 ($n=8$)	Group 2 ($n=8$)	Group 3 ($n=7$)
Post-thrombotic changes	19 (76%)	6 (75%)	5 (63%)	5 (71%)
Reflux in any deep vein	9 (36%)	2 (25%)	3 (38%)	3 (43%)
Reflux in:				
Femoral vein	8 (32%)	2 (25%)	3 (38%)	2 (29%)
Popliteal vein	7 (28%)	1 (13%)	3 (38%)	2 (29%)
Posterior tibial veins	8 (32%)	2 (25%)	2 (25%)	3 (43%)
Great saphenous vein	6 (24%)	1 (13%)	2 (25%)	2 (29%)
Number of segments involved	3.3 (0–7)	2.1 (1–3)	3.6 (0–7)	4 (1–7)

For definitions of Groups 1–3, see Table 1. Two patients could not be classified into a group, as the extension of the initial thrombus could not be verified.

Table 3. Plethysmographic results at 16 years' follow-up, in 25 patients with proximal deep venous thrombosis during pregnancy. Results are shown as means and 95% confidence intervals for all patients and in relation to extent of the initial thrombus.

	All patients ($n=25$)	Group 1 ($n=8$)	Group 2 ($n=8$)	Group 3 ($n=7$)
Venous emptying, VE (ml/100 ml per min)	95 (87–104)	99 (86–111)	92 (73–112)	101 (91–112)
Venous volume, VV (ml/100 ml)	5.6 (5.1–6.0)	5.5 (4.8–6.1)	5.7 (4.7–6.8)	5.9 (5.5–6.4)
EV_4/VV	0.62 (0.59–0.65)	0.63 (0.59–0.68)	0.63 (0.56–0.70)	0.59 (0.54–0.65)
Half-refilling time, $T\frac{1}{2}$ (s)*	8.3 (5.9–10.7)	10.5 (4.5–16.5)	4.7 (2.5–7.0)	9.7 (6.0–13.4)
$T\frac{1}{2}$ after occlusion of superficial veins*	7.4 (5.9–8.9)	8.6 (5.2–11.9)	5.6 (4.3–7.0)	7.9 (4.7–11.0)
Refilling volume, RV (ml/100 ml)*	1.06 (0.80–1.32)	1.40 (0.85–1.95)	0.77 (0.51–1.01)	1.04 (0.55–1.53)
RV after occlusion of superficial veins*	1.08 (0.80–1.35)	1.44 (0.86–2.02)	0.74 (0.37–1.11)	1.09 (0.57–1.60)

For definitions of Groups 1–3, see Table 1. Two patients could not be classified into a group, as the extension of the initial thrombus could not be verified.
* These measures include only 24 patients (7 patients in Group 2) since one recording was technically inadequate.

Computerised strain-gauge plethysmography at 16 years follow-up

One plethysmographic study during knee bends ($T\frac{1}{2}$ and RV from one patient in Group 2) was excluded because of technically inadequate recordings.

No significant differences were found between the groups regarding outflow capacity, venous volume or indices of venous reflux/muscle pump function (see Table 3). Neither were there any significant differences when subjects with DVT above the groin (isolated iliac DVT, $n=8$) were compared with those with DVT both above and below the groin (Groups 2–3, $n=15$). Half-refilling times were unaffected by the occlusion of superficial veins in Groups 1–2, while in Group 3 there was a significant decrease in $T\frac{1}{2}$ after occlusion of superficial veins ($p<0.05$). Refilling volume did not change significantly following occlusion of superficial veins in any of the groups.

None of the patients had plethysmographic evidence of outflow obstruction (VE ≤ 50 and $EV_4/VV \leq 0.60$). Fourteen patients had results compatible with "free flow" and 11 were classified as "equivocal". In all of the latter cases VE >50, but $EV_4/VV \leq 0.60$. Three patients in Group 1, three patients in Group 2 and four patients in Group 3 were classified as "equivocal".

We have no internal established reference values for measures of venous reflux or muscle pump dysfunction. With the use of the same equipment, another group has suggested a lower normal limit for $T\frac{1}{2}$ of 7 s.[12] Using this limit, 13 patients (52%) had "normal $T\frac{1}{2}$" and three patients in Group 1, five patients in Group 2 and two patients in Group 3 had "reduced $T\frac{1}{2}$".

There was a significant negative relationship between $T\frac{1}{2}$ and presence of leg swelling ($r=-0.53$, $p<0.01$). Leg swelling, however, was not significantly related to variables measuring outflow capacity. Spearman's rank correlation between the degree of venous claudication (0–1–2) and plethysmographic measures demonstrated significant correlations between claudication and $T\frac{1}{2}$ ($r=-0.64$, $p<0.001$) and RV ($r=-0.64$, $p<0.001$). There was a borderline significance between degree of claudication and EV_4/VV ($r=-0.39$, $p=0.056$).

Measures of reproducibility assessed from duplicate measurements are shown in Table 4. Generally, measurements of volume changes during and after knee bends were less reproducible than static measurements of volumes and outflow capacity.

Table 4. Measures of reproducibility for computerised strain-gauge plethysmography.

	Standard error of a single determination (s)	Coefficient of variation (CV)
Venous emptying, VE	9 ml/100 ml per min	10%
Venous volume, VV	0.4 ml/100 ml	8%
EV_4/VV	0.05	7%
Half-refilling time, $T_{\frac{1}{2}}$	3.0 s	30%
Refilling volume, RV	0.22 ml/100 ml	24%

Changes during follow-up: comparison between findings at follow-up 1 (9 years) and follow-up 2 (16 years)

The mean time difference between follow-up 1 and follow-up 2 was 6.8 years (median 7, range 6–8 years). Fourteen patients (56%) were symptomatic at follow-up 1 compared with 15 patients (60%) at follow-up 2.

The number of patients with deep venous reflux (any vein) at duplex examination was the same on both occasions. There were similar results at follow-up 1 and follow-up 2 regarding valvular function at femoral and popliteal levels; however, there was a significant increase in the number of patients with reflux in the posterior tibial veins (follow-up 1 = 1 limb, follow-up 2 = 8 limbs, $p = 0.01$). Newly developed posterior tibial vein reflux was seen in two patients in Group 1, one patient in Group 2 and three patients in Group 3.

VE increased with 22 ml/100 ml per min (CI 16–28, $p<0.01$) and VV increased with 1.0 ml/100 ml (CI 0.7–1.3, $p<0.01$) from follow-up 1 to follow-up 2, although EV_4/VV remained unchanged [0.60 (CI 0.56–0.63) vs 0.62 (CI 0.59–0.65)]. This pattern was in seen in all three groups, and the increase was statistically significant in Groups 1 and 2 ($p<0.01$ for both EV and VV in both groups). There were no significant changes in $T_{\frac{1}{2}}$ or RV from follow-up 1 to follow-up 2.

From the measures of reproducibility for plethysmographic variables, the 95% confidence interval for the error-free value of a single measurement can be calculated (2 s) and used to estimate when a change in a variable between to observations is likely to represent a true alteration. Applied to our data, a change in $T_{\frac{1}{2}}$ of more than 6 s (see Table 4) between follow-up 1 and follow-up 2 will indicate a true alteration. By this approach, the results show an increase in VE in 60% of the patients and no true alteration in the remaining 40%. Results for patients in the different groups are shown in Table 5.

Table 5. Change in plethysmographic variables from follow-up 1 to follow-up 2.

	Number of patients with increase	Number of patients with decrease	Number of patients with no true alteration
VE:			
Group 1	5 (62%)	0	3 (38%)
Group 2	6 (75%)	0	2 (25%)
Group 3	2 (29%)	0	5 (71%)
VV:			
Group 1	3 (38%)	0	5 (62%)
Group 2	6 (75%)	0	2 (25%)
Group 3	3 (43%)	0	4 (57%)
EV_4/VV:			
Group 1	3 (38%)	1 (12%)	4 (50%)
Group 2	2 (25%)	0	6 (75%)
Group 3	1 (14%)	0	6 (86%)
$T_{\frac{1}{2}}$:			
Group 1	1 (12%)	1 (12%)	6 (75%)
Group 2*	0	1 (14%)	6 (86%)
Group 3	0	0	7 (100%)
RV:			
Group 1	1 (12%)	1 (12%)	6 (75%)
Group 2*	1 (14%)	2 (29%)	4 (57%)
Group 3	2 (29%)	2 (29%)	3 (43%)

See Table 1 for definition of Groups 1–3 and Table 4 for definition of plethysmographic variables.
* These measures include only seven patients since one recording was technically inadequate.

Discussion

In this study there was no progression of venous symptoms from 9 years to 16 years follow-up, and only in a few cases could haemodynamic deterioration be documented. There was no clear relation between functional abnormalities and the extent of the initial DVT.

Clinical findings and symptoms

Forty per cent of the patients were completely asymptomatic and 52% had no clinical signs of venous disease after a follow-up of 10–24 years. The clinical signs were in general mild, and none of the 25 patients had skin changes or ulcers. A mild degree of swelling was the most commonly found symptom, and exercise-limiting venous claudication was described by two patients. Both of these patients had initial DVT extension below the groin, and deep venous reflux were found in both popliteal and posterior tibial veins. One of them had still an occluded iliac vein segment. Thus, signs and symptoms generally attributed to the post-thrombotic syndrome were seen in less than 10% of the patients. This contrasts for example to the follow-up study by Saarinen *et al.*[13] reporting chronic skin

changes in 71% after 10 years in a mixed population of patients with DVT.

The results from the present study clearly indicate that even after 16 years follow-up, conservatively treated iliofemoral thromboses during pregnancy do not carry a high risk for post-thrombotic complications as reported in some other studies for iliofemoral DVT in general or in relation to pregnancy.[4,5,13,14] On the contrary, we found fewer complications than in most other studies. These results do not support pregnancy-related iliofemoral thrombosis as a particular risk group for developing post-thrombotic syndromes.[4,5] One possible explanation is that regular supervision, more extensive use of compression stockings and prophylactic treatment for recurrent DVT have provided more beneficial long-term outcomes when compared with earlier series. This has also been suggested by other authors who have demonstrated fewer post-thrombotic complications than expected.[15–17] We chose to include two patients who, in addition and prior to anticoagulation, also received streptokinase post-partum. These patients belonged to Group 1 and Group 2, respectively, and did not show any better outcome than the rest of the patients. Both these patients were symptomatic with swelling and mild degree of venous claudication.

We were not able to prove that isolated iliac DVT had a better prognosis compared with more extensive ones. There was, however, a clear trend supporting this hypothesis and a larger series of patients might have given more clear conclusions. This highlights the problems in gathering large samples for this kind of long-term follow-up, as our material includes two-thirds of all conservatively treated pregnancy-related iliofemoral DVTs in the whole of the Stockholm area over 12 years.

Duplex ultrasound results

We found deep venous reflux in 36% of the patients: the same percentage at nine- and 16-years follow-up. The number of patients with reflux in the posterior tibial veins increased during the follow-up. This might represent valvular dysfunction secondary to progressive dilatation of distal deep veins in patients with reflux in more proximal veins. In some cases, a distal re-thrombosis possibly explains this finding.

It was interesting to note that a detailed ultrasonographic examination performed by highly experienced operators failed to demonstrate any venous abnormalities in a quarter of the patients, even in patients with prior DVT engaging the whole limb. Another finding was that definite abnormalities (vessel wall changes and reflux) could be demonstrated in venous segments without any previously known DVT. This observation has also been described by other authors,[18,19] and mechanisms such as dilatation due to inflammatory mediators have been discussed as a cause of valvular dysfunction. This does not, however, explain the occurrence of post-thrombotic vessel wall changes, which are more likely to be the result of silent re-thromboses during follow-up or to thrombus progression during treatment.[20] The latter situation has been described to occur in up to 30–40% of patients, using serial ultrasound examination,[21,22] and can contribute to the lack of obvious relation between initial thrombus extension and markers of post-thrombotic syndrome both in the present study and that of other authors.[16]

Computerised strain-gauge plethysmography

Venous emptying increased during follow-up. Since the relation between measures of outflow capacity and venous volume was essentially unchanged, the increase in venous emptying can be largely explained by an increase in venous volume. This is possibly an effect of dilatation of deep veins and collaterals. However, no outflow obstructions of importance were noted, but 11 of the patients had somewhat reduced EV_4/VV, which might represent minor degrees of relative outflow obstructions. In contrast to VE and VV, this quotient showed some, although weak, correlation to symptoms (i.e. degree of venous claudication, $p = 0.056$).

Stronger relationships to symptoms were found for measurements during knee bends, which highlights the importance of using dynamic methods to study functional abnormalities in the venous system. Our findings corroborate earlier observations, using plethysmography, stating that most sequelae of the post-thrombotic syndrome can be attributed to loss of valvular function rather than to outflow obstruction.[23]

One natural drawback to using dynamic measurements, rather than static, is the low reproducibility found for most variables measured during and after exercise. For example, we found a CV for T_2^1 of 30%. Similar findings have also been described earlier for healthy subjects.[24] This factor makes this method rather insensitive for detecting minor differences from one examination to another. Nevertheless, we could demonstrate both functional deterioration and functional

improvement in individual patients during follow-ups, regardless of the initial thrombus extension, implicating a complex and possibly multifactorial cause for the development of post-thrombotic sequelae.

Regarding $T_{\frac{1}{2}}$, we found a decrease following occlusion of superficial veins in patients with initial DVTs extending into veins below the knee. This possibly indicates more serious abnormalities in deep veins below the knee.

Conclusions

Even after 16 years, there were relatively mild symptoms and signs of venous disease in this group of women with medically treated pregnancy-related iliofemoral DVTs. This contrasts with some earlier reports and supports the idea of a non-surgical, but aggressive medical approach regarding treatment of this important group of patients. It could indicate an improvement of the clinical outcome of DVT with more active treatment, prophylaxis and follow-up. There was no progression in signs or post-thrombotic symptoms between nine- and 16-years follow-up. Although there were relatively few patients in each group, there were no obvious relations between long-term outcome and the extent of the initial thrombosis.

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