The postthrombotic syndrome in relation to venous hemodynamics, as measured by means of duplex scanning and strain-gauge plethysmography

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Purpose: **Venous hemodynamics were evaluated in relation to the postthrombotic syndrome (PTS) 7 to 13 years after deep venous thrombosis (DVT).**
Methods: **The presence of flow, reflux, and compressibility of 1394 vein segments in 82 patients was assessed by means of duplex scanning. The venous outflow resistance was measured by means of strain-gauge plethysmography. The venous hemodynamics were related to the clinical severity of the PTS, characterized by the CEAP (clinical, etiologic, anatomic, pathophysiologic) classification.**
Results: **In patients with severe clinical symptoms of PTS, the prevalence of reflux was significantly higher. There was no relationship between the severity of the PTS and the noncompressibility or the combination of reflux and noncompressibility or an increased venous resistance. By means of multiple regression analysis with the variables of age, gender, reflux, and venous resistance, age and reflux were shown to be the main contributors to the severity of PTS. Significantly more patients (64%) with severe signs of PTS had a combination of deep and superficial reflux. In each of the traceable vein segments, the mean of the CEAP classification was calculated for the vein segments with and without reflux. In the proximal superficial femoral vein ($P < .001$), distal superficial femoral vein ($P < .05$), and popliteal vein ($P < .05$), a significantly higher mean CEAP classification was found in the veins with reflux, whereas in the distal, long, and short saphenous veins, no such relationship was found.**
Conclusion: **Most patients with severe PTS had a combination of deep and superficial reflux. Reflux in the deep proximal veins contributes significantly to the PTS. (J Vasc Surg 1999;29:1071-6.)**

Deep venous thrombosis (DVT) may cause persistent venous abnormalities, resulting in postthrombotic syndrome (PTS). Venous hypertension caused by a persistent venous obstruction, valve incompetence, or a combination of the two is considered to be the major cause of PTS.[1-4] It is unclear whether an obstruction, reflux, or a combination of the two provides the main contribution to PTS. The presence of reflux in the popliteal vein is considered to be important in the pathophysiology of PTS,[5-7] but the influence of venous abnormalities in other areas is less clear.

In this study, the venous hemodynamics, in relation to the severity of the PTS, were evaluated in patients 7 to 13 years after DVT. Local venous compressibility, reflux, and the presence of flow were measured by means of color flow duplex scanning, and the venous resistance in the postthrombotic extremity was measured by means of strain-gauge plethysmography. Because duplex scanning provided a local evaluation of the veins, the venous resistance of the entire leg was measured by means of plethysmography.

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Table I. The number of patients in each classification of chronic lower extremity venous disease, the CEAP (clinical, etiologic, anatomic, pathophysiologic) scale

Class	*Signs of chronic lower-extremity venous disease*	*Patients (n)*
0	No visible or palpable signs of venous disease	22
1	Telangiectases, reticular veins, malleolar flare	11
2	Varicose veins	11
3	Edema without skin changes	10
4	Skin changes ascribed to venous disease (pigmentation, lipodermatosclerosis)	24
5	Skin changes with healed ulceration	4
6	Skin changes with active ulceration	0

Table II. Characteristics of the patients at follow-up examination for the different CEAP (clinical, etiologic, anatomic, pathophysiologic) classifications

CEAP classification	*0 (n = 22)*	*1 to 3 (n = 32)*	*4 to 6 (n = 28)*
Mean age (years) ± SD	45 ± 9	50 ± 15	64 ± 14
Mean body mass index (kg/m^2) ± SD	24 ± 3	27 ± 6	25 ± 4
Men (%)	55	66	82
Prevalence abnormal venous resistance (%)	5	6	21
Reflux			
Not present(%)*	32	22	4
Only deep (%)	41	41	29
Only superficial (%)	4	3	3
Superficial + deep (%)†	23	34	64
Location of thrombi at initial phlebography			
Proximal (%)	4	6	7
Proximal and distal (%)	17	21	24
Distal (%)	6	12	2
Deep (%)	13	28	21
Deep and superficial (%)	13	11	13

*$P < .05$, †$P < .01$ (Chi-square test).

METHODS

The records of all the patients at our institution who had DVT between 1983 and 1989 were reviewed. DVT was diagnosed by means of phlebography. Of the 256 patients, 92 died, 33 were unable to return for reexamination, 26 could not be traced, and 23 refused to participate in the study. The remaining 82 patients were reexamined 7 to 13 years (mean, 10 years) after the initial DVT. The study was approved by the ethics committee of the hospital, and informed consent was obtained from the participants.

All patients had been treated with heparin, administered intravenously for 5 to 10 days during the acute phase, and with oral anticoagulants for at least 12 weeks. All patients had been instructed to wear graduated compression stockings.

A physician, unaware of the findings of the duplex scanning and plethysmography, classified the patients according to the seven-point CEAP scale (clinical, etiologic, anatomic, pathophysiologic, class 0 to 6) of the update of the Ad Hoc Committee on Reporting Standards in Venous Disease.[8] For the sake of simplicity, the tables and figures were presented in three categories: (1) patients with no signs of PTS (class 0); (2) patients with mild signs of PTS (classes 1 to 3); and (3) patients with severe signs (classes 4 to 6) of PTS.

The venous resistance in the postthrombotic extremity was measured by means of strain-gauge plethysmography, as described previously.[9-11] The patients were examined in the supine position with pneumatic cuffs around the thighs and strain-gauges around the calves. After inflating the cuffs, the venous volume increased. When the maximum volume was reached, the cuff-pressure was released, resulting in a volume decrease measured by means of plethysmography. The tangent to the slope of the volume decrease was drawn 0.5 seconds after pressure release, and the slope was converted into a venous flow rate. This procedure was performed at five different cuff pressures. The corresponding venous flow rates were plotted against the effective cuff pressures. The slope of the line straight through

the points gave an angle β, and by means of analogy with Ohm's law, the venous resistance could be calculated as 1/tangent β. A venous resistance exceeding 0.8 mm Hg/min was considered abnormal.[10,11]

Duplex scanning was performed by two experienced vascular technicians using a Toshiba SSA 270A scanner with a 3.75 or 5 MHz probe on the low-flow setting. The vascular technicians scanned the patients without knowledge of the original location of the thrombosis. All veins were examined with the patient in a 45-degree sitting position, with the knees flexed and the feet resting on a footstool. The veins examined were the common femoral vein, the superficial femoral vein (proximal, middle, and distal), the long saphenous vein (proximal, middle, and distal), the popliteal vein, the short saphenous vein, and the posterior and anterior tibial, peroneal, and gastrocnemial veins. In the calf, each artery is accompanied by two veins. The two veins were numbered; number 1 was the most superficial vein, and number 2 was the deeper vein.

In the longitudinal plane, the presence of venous flow and reflux was measured. Proximally, reflux was measured after the Valsalva maneuver in the distal veins by means of distal manual compression with sudden release. Pathological reflux in the proximal veins was defined as a reversed flow duration of more than 1 second; in the distal veins, pathological reflux was defined as a reversed flow duration of more than 0.5 second, as described previously.[12] This previous study showed that our method with the patient in the sitting position is compatible with the method with patients in an upright position and the cuff deflation technique. Superficial or deep reflux was defined as the presence of abnormal venous reflux in at least one vein segment. Combined superficial and deep reflux was defined as the presence of abnormal venous reflux in at least two vein segments. Compressibility was assessed in the transverse plane. A vein was considered noncompressible when it was not totally compressed under gentle pressure of the duplex probe applied to the skin overlying the vein.

The relation between the seven-point CEAP scale and the presence of an abnormal venous resistance and body mass index (BMI) was studied with the chi-square test. The relation between the seven-point CEAP scale and the outcome of the venous evaluation by means of duplex scanning was studied at patient level, adjusted for age with multiple regression. The contribution of age, gender, reflux, and the venous resistance to the seven-point CEAP scale was also studied with multiple regression. The results were considered significant when $P \leq .05$ (two-sided).

RESULTS

The characteristics of the 82 patients are shown in Tables I and II. At the time of admission to the follow-up study, the mean age of the patients was 53 years (range, 21 to 80 years), their mean BMI was 26 kg/m^2 (SD ± 5); 56 patients (68%) were men, and 26 (32%) were women. The DVT was located in the right leg in 48 patients (59%) and in the left leg of 34 patients (41%). There was no significant relationship between the seven-point CEAP scale and the BMI.

The venous resistance, as measured by means of strain-gauge plethysmography, was abnormal in only nine patients (11%). The prevalence of an abnormal venous resistance was not significantly higher in patients with severe clinical symptoms of PTS. Significantly more of the patients (64%) with severe signs of PTS had a combination of deep and superficial reflux (Table II).

The duplex findings for all the 1394 vein segments of the patients were related to the clinical findings (Fig 1). Because the classification of PTS increased with age, an adjustment was made for age in the statistical analysis. It was shown by means of regression analysis that only reflux could explain the PTS classification. No relation was found between PTS and noncompressibility or a combination of reflux and noncompressibility. Flow was present in almost all noncompressible vein segments (93%). The nontraceable veins were almost all located distally (95%). These nontraceable veins were not included in further analysis.

Because only reflux was shown to have a significant relationship to the CEAP classification, reflux was evaluated more extensively. In each of the traceable vein segments, the mean of the CEAP classification was calculated for the vein segments with and without reflux (Table III). In the proximal superficial femoral vein ($P < .001$), distal superficial femoral vein ($P < .05$), and popliteal vein ($P < .05$), a significantly higher mean CEAP classification was found in the veins with reflux, whereas in the distal, long, and short saphenous veins, no such significant relationship was found.

After testing the contributions of the factors age, gender, reflux, and the venous resistance to the PTS by means of multiple regression, age ($P < .001$) and reflux ($P < .01$) appeared to be the main contributors to the severity of PTS .

DISCUSSION

It is possible to detect venous abnormalities by means of duplex scanning, sometimes even better than with invasive tests such as phlebography.[13,14]

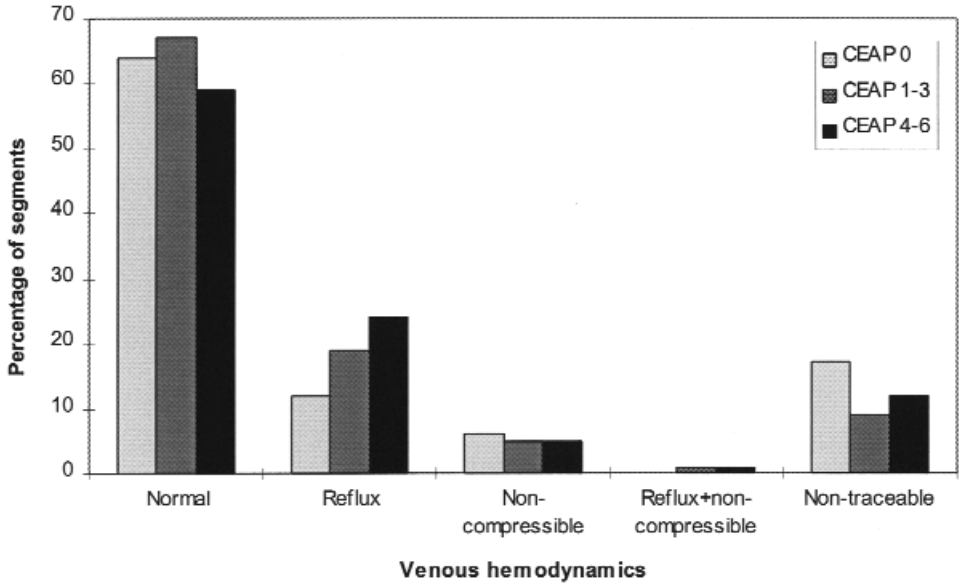

Fig 1. The relationship between venous hemodynamics in all segments and the CEAP (clinical, etiologic, anatomic, pathophysiologic) classification.

Table III. The mean of the CEAP (clinical, etiologic, anatomic, pathophysiologic) classification in the traceable veins, with and without reflux

Traceable veins	*n*	*Mean CEAP in veins with reflux*	*n*	*Mean CEAP in veins without reflux*
Proximal superficial femoral*	40	2.78	42	1.61
Middle superficial femoral	30	2.56	52	1.96
Distal superficial femoral*	19	2.71	58	1.93
Popliteal*	24	2.72	56	1.88
Proximal long saphenous	8	3.03	63	2.26
Middle long saphenous	26	2.29	56	2.13
Distal long saphenous	12	2.56	47	2.32
Short saphenous	15	2.67	62	1.96
Posterior tibial 1	17	2.17	51	2.16
Posterior tibial 2	14	2.62	35	2.27
Anterior tibial 1	25	2.21	51	2.10
Anterior tibial 2	21	2.43	55	2.14
Peroneal 1	5	1.12	61	2.26
Peroneal 2	4	1.08	55	2.23
Gastrocnemial 1	5	1.60	44	2.23
Gastrocnemial 2	7	1.56	37	2.17

*$P < .05$.

Descending phlebography underestimates severe reflux and is usually used as a means of evaluating deep vein reflux,[13] whereas the presence of superficial reflux seems also to be important.[15-17]

In a previous study,[18] the relationship between the initial phlebography and the outcome measured by means of duplex scanning was evaluated in the same patient database (except for the 10 patients with recurrent thrombosis). In the current study, the definition of pathological reflux for the distal veins was restricted from 1 second to 0.5 second; this definition was derived from another study.[12]

Duplex scanning provides local information on the veins. The consequences of these local abnormalities to the entire leg are uncertain and can be measured with plethysmography.

The prevalence of an abnormal venous resistance was not significantly higher in patients with severe clinical symptoms of PTS. This lack of statistical significance might be caused by the small sample size.

But because, in contrast to other studies,[4] no relation was found between (reflux and) noncompressibility and the clinical signs of PTS either, another explanation might be that in our patients almost all noncompressible vein segments were partially occluded because flow was present in almost all (93%) noncompressible veins.

Reflux was shown to be the main contributor to the severity of PTS by means of multiple regression analysis, in accordance with other studies.[2] As clearly shown in Table II, only a minority of the patients with severe signs of PTS had an abnormal venous resistance, whereas most of these patients had reflux.

Other studies showed that in patients with severe signs of PTS the involved incompetent segments were the superficial femoral, popliteal, and the long and short saphenous veins.[19,20] Although in our study the superficial femoral and popliteal veins showed a statistically significant increased prevalence of reflux with an increasing severeness of PTS, for the long and short saphenous veins this relationship showed a trend without being statistically significant.

This study corroborates the findings of others,[21] because it indicates that isolated deep reflux in itself does not always cause severe signs of PTS. Perhaps the superficial veins can take over the drainage of venous blood as long as there are sufficient perforating veins. If the perforating veins become insufficient, the venous pressure in the superficial veins might increase and possibly cause an overload of the superficial system, resulting in a gradually developing insufficiency of the superficial veins. When the superficial veins also become insufficient, PTS develops. We did not evaluate the presence of insufficient perforating veins. Other studies[22] have shown that duplex scanning misses a substantial number of incompetent perforating veins and therefore is unreliable in these evaluations. The patients in Table II with isolated deep vein reflux and severe signs of PTS might, therefore, have incompetent perforating veins, with an increased venous pressure in the superficial venous system, which is yet not insufficient.

In contrast to other studies,[17,23,24] no relationship was found between reflux limited to the superficial veins and the PTS classification. This may be caused by the small number of patients with reflux limited only to the superficial vein segments.

The influence of the calf veins on the PTS is still controversial, with some studies reporting a relationship between reflux and PTS in the distal veins[6,15] and others not reporting this.[25] In our study, not only the presence of reflux was analyzed, but also the traceability. Previously, we demonstrated that the nontraceable veins are probably occluded.[18] No relationship was found between reflux or traceability in the distal calf veins and an increased severity of PTS. Presumably because of the number of distal veins, reflux or an occlusion of one or more distal veins does not seem to contribute significantly to the presence of PTS. The other distal veins can probably drain away enough venous blood to prevent PTS.

Scott et al[26] revealed that many of the previously suggested associations with chronic venous insufficiency were in reality caused by the older age of the patients. In the present study, the severity of PTS also increased with age. Therefore, the statistical analysis was adjusted for age. Scott also found that patients with chronic venous insufficiency were men and were obese. The BMI of 21 of our patients was more than 27 kg/m^2, but these 21 patients were equally distributed among all classes of the CEAP scale. Perhaps our group of patients did not contain enough patients with severe obesity for us to uncover a relationship between obesity and PTS. In Scott's study, the mean BMI (30 kg/m^2) was much higher than in our patient population.

A problem with our study is that it is retrospective. This might incorporate a selection of patients, causing a bias in the data, because the patients lost to follow-up could be different than those actually examined. Selection, although present, is minimized in our study because almost 80% of the patients that we invited took part; therefore, not only successfully or unsuccessfully treated patients have been included. Also, patients of different ages were included, with a variation of the location of the thrombi at initial phlebography.

In conclusion, patients with severe PTS most frequently have a combination of deep and superficial reflux. Reflux in the deep proximal veins contributes significantly to PTS. Because not all patients with deep and superficial reflux had severe signs of PTS, mechanisms other than reflux must be involved in the development of PTS.

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