# Late hemodynamic sequelae of deep venous thrombosis

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**Twenty-nine limbs in 19 patients who had deep venous thrombosis documented by phlebography were studied by hemodynamic techniques 2 to 13 years later (mean, 7 years). Two limbs were found to be "normal." Nine limbs were hemodynamically obstructed; the remaining 18 limbs had developed reflux abnormality. All of the nine limbs with obstruction demonstrated symptoms of severe swelling or ulceration. In contrast, limbs with valve reflux were either asymptomatic or had only mild to moderately severe symptoms. Correspondingly, the reflux hemodynamic derangement was also mild, with reflux confined to a single level (commonly the popliteal valve). The implications of the differences in clinical presentation and hemodynamic profile between this group with postthrombotic valve reflux and the typical patient with stasis caused by chronic venous insufficiency are explored. The natural history of stasis sequelae of deep venous thrombosis has apparently changed somewhat since the introduction of anticoagulation therapy. (J VASC SURG 1986; 4:73-9.)**

The natural history of untreated deep venous thrombosis was carefully studied by Bauer[1] before heparin or other forms of anticoagulation became available for treating this condition. He reported a steady incidence of stasis ulceration in this patient population, approaching 80% when patients were followed up for a period of 10 years. Although this bleak outcome is repeatedly emphasized in the literature dealing with the subject, it is our impression, and that of others as well,[2] that the outlook for patients with deep venous thrombosis treated by anticoagulation has been much better than depicted in the early literature. In addition, the widespread availability of phlebography and other new diagnostic techniques would appear to have favorably influenced the outcome of deep venous thrombosis by allowing early detection and institution of anticoagulant treatment. Concrete data to support these clinical impressions are needed.

There are many other unresolved questions and controversies with regard to deep venous thrombosis and its sequelae. For example, attention has recently focused on a group of patients with deep venous insufficiency that is apparently nonthrombotic in origin.[3] This group with possible developmental or congenital reasons for deep venous insufficiency may be larger than previously suspected.[4,5] Even among patients clearly suffering from postthrombotic venous dysfunction, the relative incidence of obstructive and refluxive venous insufficiency is unknown and remains a matter of controversy.[4] Among patients with clearly established valvular insufficiency, some authorities have concentrated on the importance of the popliteal valve,[6] whereas others have emphasized the valve in the superficial femoral vein.[4,7,8] It appeared that a hemodynamic study of patients previously proved to have suffered from deep venous thrombosis could shed some light on many of these issues. Coincidentally, many techniques that assess venous hemodynamics, such as photoplethysmography (PPG), venous Doppler examination, and others described in this report, have become available for use only recently. With these techniques in hand, venous hemodynamics can be studied to an extent that was not possible only a few years ago.

## MATERIAL AND METHODS

### Patients

A search of the radiologic records of the University of Mississippi Medical Center identified 19 patients who had phlebograms that indicated deep venous thrombosis. Altogether, 29 limbs in 19 patients with a minimum follow-up of 2 years since phlebography were available for hemodynamic study. Mean follow-up after phlebography was 7 years (range, 2 to 13 years). The anticoagulation regimen used in these 19 patients consisted of varying combinations of heparin and warfarin.

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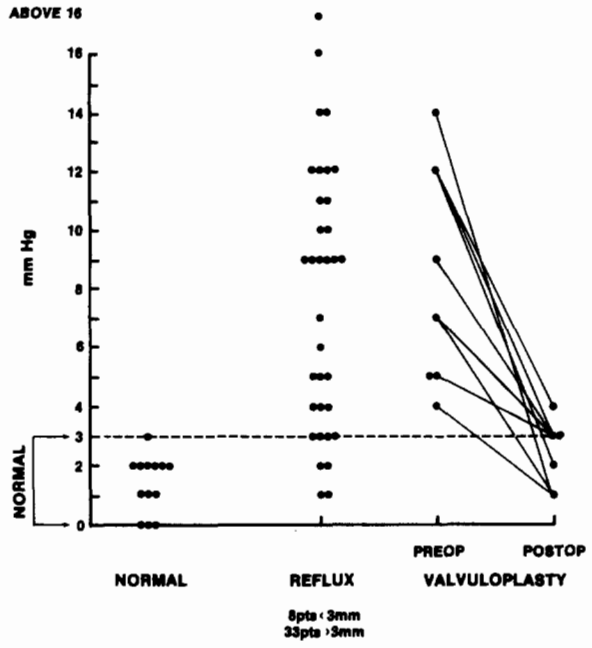


**Fig. 1.** Foot venous pressure elevation in supine patient with maximum Valsalva's maneuver in 13 "normal" volunteers, in 41 patients with venous reflux, and in 10 patients before and after valve reconstruction. Pressure value depicted represents difference between resting foot pressure and maximum pressure reached during Valsalva's maneuver.

## Symptomatology

Symptoms of the entire patient group were graded from 1 to 4 as follows: grade 1, mild swelling and/or pain; grade 2, moderate pain or swelling; grade 3, severe swelling; and grade 4, skin ulceration or stasis dermatitis.

## Hemodynamic study

The following techniques were used in each patient studied.

**Venous Doppler examination.** A 5 MHz probe was used to examine the common femoral, superficial femoral, popliteal, posterior tibial, and saphenous veins for signs of obstruction or reflux with proximal and distal compression maneuvers. Valsalva's maneuver with manual abdominal compression was used to monitor reflux at the common femoral level.[4] Phasic changes with respiration were also monitored to detect obstruction.

**PPG.** The technique was as described previously.[4] A tourniquet was used to differentiate superficial from deep venous insufficiency.

**Ambulatory venous pressure measurements.** The standard technique was modified to use manual calf compression rather than exercise to eliminate the variable of patient cooperation. Values were recorded with and without a tourniquet applied below the knee to identify superficial venous component.

**Table I.** Late hemodynamic sequelae of deep venous thrombosis (29 limbs in 19 patients)

| | *Incidence* % | *No.* |
|---|---|---|
| Normal venous profile | 7 | 2 |
| Reflux | 62 | 18 |
| Obstruction | 31 | 9 |

NOTE: Incidence of bilateral deep venous thrombosis, 53%.

**Arm/foot venous pressure differential and reactive hyperemia for detection of obstruction.** A hemodynamic technique to detect venous obstruction was developed on the basis of the peripheral venous pressure differential in the supine patient between the arm and the foot in the limb suspected to harbor obstruction. When hemodynamic obstruction was present at rest in the lower limb, a higher foot venous pressure would be present. If collaterals had developed that were hemodynamically adequate at rest, there would be no arm/foot venous pressure differential at rest. The adequacy of such collaterals during periods of increased flow could be assessed by inducing reactive hyperemia while monitoring foot venous pressure. If the collaterals were hemodynamically adequate during reactive hyperemia, foot venous pressure would not change with reactive hyperemia; if the collaterals were inadequate, a significant increase in foot venous pressure could be expected after induction of reactive hyperemia. The foot venous pressure change induced by reactive hyperemia is influenced by the presence or absence of an arm/foot venous pressure differential at rest. When a significant differential exists at rest, indicating uncompensated hemodynamic venous obstruction, venous pressure changes induced by reactive hyperemia may be absent, indicating a severe form of venous obstruction. At the other end of the spectrum, venous obstruction may be fully compensated by development of adequate collaterals during rest and with reactive hyperemia, indicated by a normal arm/foot venous pressure differential at rest and the absence of significant foot venous pressure changes during reactive hyperemia.

In between these two extremes, partial gradations of venous obstruction can be perceived. Arm/foot venous pressure differential at rest may be normal, but significant foot venous pressure increments may

be obtained with reactive hyperemia, indicating the presence of venous collaterals that are adequate at rest but insufficient during reactive hyperemia. The next gradation of hemodynamic venous obstruction would be indicated by the presence of an arm/foot venous pressure differential at rest and also a significant foot venous pressure change with reactive hyperemia. Hemodynamic venous obstruction is partially decompensated in this group, indicating the presence of venous collaterals that are inadequate during rest and reactive hyperemia. The method of assessment and gradation of venous obstruction is more fully detailed elsewhere.[9]

These two techniques were evaluated in 24 limbs with "normal" phlebograms and 20 limbs with phlebographically demonstrated obstruction. An arm/foot venous pressure differential of more than 4 mm Hg in the supine patient was found to denote the presence of hemodynamic obstruction at rest. A foot venous pressure elevation of greater than 6 mm Hg in the supine patient with reactive hyperemia indicated obstruction. With these benchmark values, the two techniques had a combined sensitivity of 90%, a specificity of 93%, positive predictive value of 95%, and negative predictive value of 94% in the 44 limbs evaluated.[9]

**Foot venous pressure with Valsalva's maneuver.** The foot venous pressure is monitored in the supine patient before and during maximum exertion with Valsalva's maneuver. Venous reflux is indicated by significant foot venous pressure elevation with application of Valsalva's maneuver. The foot venous pressure changes reflect the composite effect of the functional integrity of the venous valves cephalad to the monitoring needle in the foot. The principle is akin to the two-cuff technique described by Barnes et al.[10] to measure venous reflux. Unlike this technique, the Valsalva maneuver encompasses femoral valve reflux. In addition, venous pressure rather than calf volume is the hemodynamic variable monitored for venous reflux, greatly simplifying the technique. The Valsalva technique for reflux was evaluated in 13 "normal" limbs and 41 refluxive limbs. The presence or absence of reflux in these limbs was established by a complete Doppler examination, PPG, and ambulatory venous pressure measurements. The foot venous pressure elevation induced by Valsalva's maneuver from resting levels in "normal" and refluxive limbs is shown in Fig. 1. On the basis of this evaluation, a foot venous pressure elevation of 4 mm Hg or greater was considered significant for reflux. Twelve of 13 "normal" limbs had a value of 2 mm Hg or less. Fig. 1 also depicts the favorable change in this variable in 10 patients treated by valve reconstruction procedures for reflux.

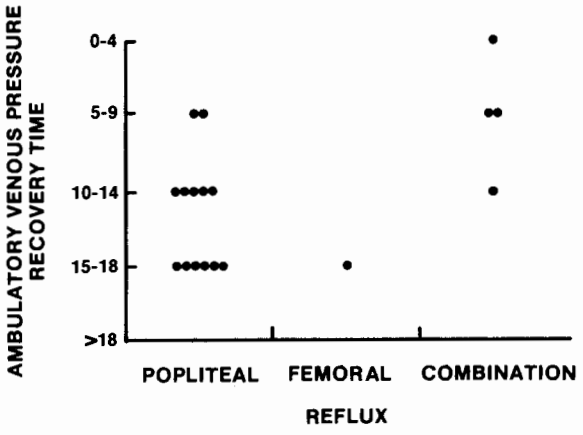


**Fig. 2.** Ambulatory venous pressure recovery times in this series of patients. Note commonality of isolated popliteal reflux and relatively moderate derangement as measured by recovery times.

## RESULTS

### Pathologic features and hemodynamics

Of the 29 limbs studied, two (7%) had virtually normal hemodynamics, indicated by normal PPG and phlebographic pressure measurements. The only hint of abnormality in these two limbs was the indication of minimal reflux with venous Doppler examination. These two limbs have been classified as "normal" hemodynamically. Hemodynamically significant obstruction was evident in nine limbs, and in 18 others venous reflux was the primary pathologic condition (Table I). The incidence of bilateral deep venous thrombosis in this group of 19 patients was 53%. Thus, among the 29 limbs all but two showed hemodynamic derangement of either obstruction or reflux.

**Hemodynamic reflux.** Of the 18 limbs exhibiting venous reflux, the incidence of bilaterality was 94%, although the opposite refluxive limb was implicated in previous deep venous thrombosis in only half the cases (discussed earlier). The 18 limbs exhibiting reflux by Doppler examination surprisingly showed only mild or moderate derangement of ambulatory venous pressure and PPG values (Fig. 2). Only one limb had venous pressure recovery time of less than 5 seconds; most of the remaining limbs had recovery time of more than 10 seconds. The Valsalva-induced measure of reflux at the foot level was similarly only mildly deranged, if at all (Fig. 3). The relatively mild reflux abnormality could be explained by the preponderance of single level valve reflux (Fig.

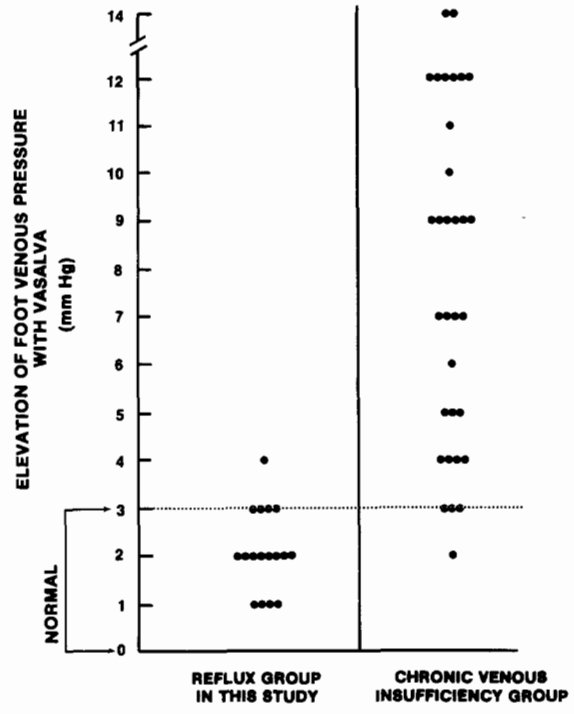


**Fig. 3.** Foot venous pressure induced by Valsalva's maneuver in limbs with reflux in this series compared with typical values obtained in patients with chronic venous insufficiency. Values for 32 patients investigated for venous insufficiency are shown at right.

2). Only 4 of 18 limbs had multilevel valve reflux. As a general rule, therefore, the hemodynamic severity of postthrombotic reflux was mild and tended to involve single level valve segments only. The tourniquet test was used to identify superficial and deep venous insufficiency by ambulatory venous pressure measurement in 11% and PPG in 50% of the refluxive limbs, respectively. The remainder had pure deep venous insufficiency (Table II).

**Hemodynamic venous obstruction.** Of the nine limbs with hemodynamic obstruction, previous phlebography had demonstrated iliofemoral obstruction in 44%, femoral or popliteal obstruction in 34%, or multilevel obstruction in 22% of the cases (Table II).

**Symptomatology.** The relationship between severity of symptoms and the hemodynamic abnormality is shown in Fig. 4. The more severe symptoms were invariably associated with hemodynamic obstruction. The anatomic site of obstruction was irrelevant; obstruction at any level caused severe symptoms, provided the hemodynamic criteria for obstruction were satisfied. In contrast, the patients with reflux had only mild to moderate symptoms. Four limbs with hemodynamic reflux were actually asymptomatic; seven had grade 1, or mild, symptoms, and seven others had grade 2, or moderate, symptoms. There were no refluxive limbs with severe swelling or stasis dermatitis or ulceration (grade 3 or 4 symptoms).

**Table II.** Hemodynamic venous reflux and obstruction

| | % |
|---|---|
| Reflux (18 limbs) | |
| Bilaterality | 94 |
| Superficial and deep venous reflux | |
| PPG | 50 |
| Venous pressure | 11 |
| Deep venous reflux | 100 |
| Obstruction (9 limbs) | |
| Iliofemoral | 44 |
| Femoropopliteal | 34 |
| Combination | 22 |

## DISCUSSION

The natural history of deep venous thrombosis appears to have changed since the gloomy report of Bauer[1] in 1942, who noted an extremely high incidence of stasis ulceration and dermatitis in his patients. Since then, the introduction of anticoagulation treatment and a generally more aggressive approach to the diagnosis and treatment of this disease appears to have reduced, but not eliminated, the more severe forms of postphlebitic syndrome. Only 10% of patients in our series had stasis ulceration. Nevertheless, the problem of postphlebitic syndrome has not disappeared and a substantial number of patients continue to suffer less severe forms of this impairment, despite recent advances in therapy and management of venous thrombosis.

Only 21% of the limbs in our study were asymptomatic; another 23% were mildly symptomatic, leaving 56% of the limbs with either moderate or severe disabling symptoms (Fig. 4). Roughly similar incidences of symptom expression have appeared in other reports dealing with this problem as well.[2,11] The incidence of hemodynamic abnormalities in our patient population was even more striking than the incidence of postphlebitic symptoms. Only 7% of the patients were "normal," the remainder being hemodynamically compromised at the time of study. Therefore, 14% of patients were free of symptoms although they demonstrated hemodynamic abnormalities. The type of hemodynamic abnormality was significant in symptom expression. If the hemodynamic abnormality was obstruction (9 of 29 limbs), symptoms were severe; all patients in this group

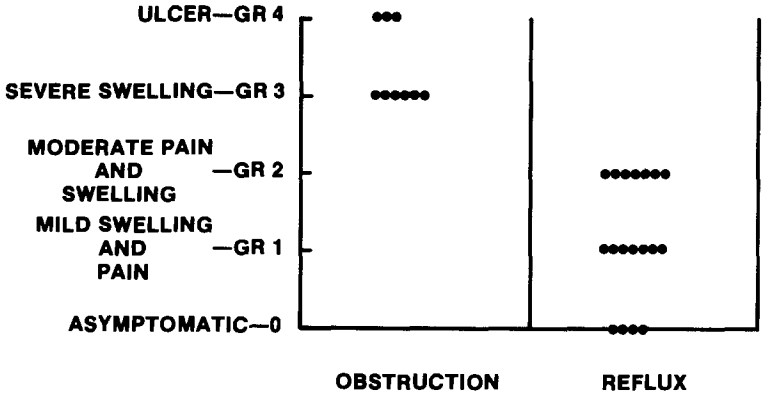


**Fig. 4.** Segregation of patients according to severity of symptoms. More severe symptomatology was confined to obstruction.

evinced either grade 3 or 4 symptoms. On the other hand, hemodynamic reflux was mild, involving more often than not single level valves and the corresponding symptoms were less severe. All patients in the latter group had grade 2 or lesser degrees of symptom classification (Fig. 4). No patients in the reflux group expressed grade 3 or 4 symptoms (severe swelling, stasis dermatitis, or ulceration). Such clear segregation of symptom expression according to pathophysiologic abnormality of either obstruction or reflux has not been reported previously. This may be due to the vagaries of case selection or perhaps more likely to the special hemodynamic criteria of obstruction used in this study. In the present study, of the nine patients with hemodynamic obstruction, the actual anatomic site of obstruction was widely varied (Table II). Regardless of the site of obstruction, all patients expressed severe forms of postphlebitic syndrome with either swelling or pain. Therefore, it appears that the presence of hemodynamic obstructive pressure criteria is more important than the actual site of anatomic obstruction per se in the production of stasis changes. Even distal forms of venous obstruction at the popliteal level could result in severe stasis changes if hemodynamic criteria of obstruction were present. Two such patients with popliteal level obstruction were identified in the present study. It has been generally believed that iliofemoral thrombosis more often than not resulted in obstructive stasis changes because of incomplete resolution of the thrombosis. Although it may be true that iliofemoral thrombosis is predisposed to result in obstruction, it has not been adequately emphasized or appreciated that thrombosis in other locations, even in distal venous sites, can result in severe stasis changes if hemodynamic obstruction is present.

Several other authors have reported on the late hemodynamic sequelae of deep venous thrombosis, using different techniques and methodologies. Lawrence and Kakkar,[12] using foot volumetry, reported 100% incidence of hemodynamic abnormalities at 24 months after "major" venous thrombosis. The incidence was only 55% when thrombosis was confined to the calf veins. Halstuk, Mahler, and Baker,[2] with strain-gauge plethysmography, have reported similar results. Latter authors also quantified reflux, with the isolate limb technique described by Barnes et al.[10] Killewich and Strandness,[11] using PPG and mercury strain gauge, have correlated symptomatology with hemodynamic parameters. It is difficult to relate the findings of these various studies to our own, primarily because of differences in methodology and technique; resort to some nonstandard techniques for hemodynamic study in this investigation was prompted by the reconfirmed inadequacies of currently available "standard" techniques in assessing the postphlebitic limb. Plethysmography or pressure-based techniques that assess the venous circulation in the erect limb (foot volumetry, PPG, or ambulatory venous pressure measurements) do not adequately separate hemodynamic obstruction from reflux. Even in instances of pure reflux, these techniques are unlikely to be sensitive to minor changes, because only maximal reflux under the effects of full gravity in the erect limb are measured. The innovative technique of Barnes et al.[10] to measure reflux in an isolate limb unfortunately does not encompass femoral valve function, because of the placement of the thigh cuff. The mercury strain gauge can be sensitive to numerous operator and machine-introduced variables; it measures venous outflow only under resting conditions.

The lack of correlation between phlebographic appearance and postphlebitic changes, as noted by

some authors,[13] should not be surprising. Assessment of venous function on the basis of phlebographic appearance can be grossly misleading.[9] Normal-looking phlebograms can mask severe hemodynamic abnormalities; conversely, in the presence of grossly abnormal phlebographic appearance, hemodynamic venous function may be essentially within normal limits.

There is a better correlation between postphlebitic symptomatology and hemodynamic variables than with phlebographic appearance.[9] As already stated, in sharp contrast to hemodynamic obstruction, the postphlebitic limbs suffering from hemodynamic reflux in this study provide a relatively benign form of sequelae. Viewed as a group, the postphlebitic reflux limb in our study evinced only mild to moderate symptoms, had reflux at only one valve level (usually the popliteal valve), and the hemodynamic reflux derangement as measured was correspondingly mild. We were surprised to encounter such a relatively mild reflux abnormality in this group of patients, since the picture of "postphlebitic reflux" one derives from seeing patients with chronic venous insufficiency in the clinic is that of a much more severe form of reflux abnormality. Typically, the patients in the latter group have a multilevel valve reflux with severe stasis changes, including ulceration, and demonstrate grossly deranged hemodynamic parameters of reflux (Fig. 3)[4]; the recovery time on ambulatory venous pressure measurements is frequently less than 5 seconds.

Several explanations could be offered for this disparity between the study group and the typical postphlebitic limb with reflux seen in the clinic: (1) Case selection, inevitable in retrospective studies of the type presented here; (2) time factor: the reflux abnormality could grow more severe with passage of time. It is well known that this patient population is subject to recurrent, overt, and covert deep venous thrombosis. Preexisting reflux may predispose to thrombosis from stasis, which may in turn further aggravate the reflux abnormality.[4,8] In addition, the incidence of severe stasis changes is a function of time passage[1]; (3) the possibility that a good many clinic patients who are labeled postphlebitic may, in fact, suffer from a congenital or developmental venous insufficiency of nonthrombotic origin.[4,5] It is commonly believed that stasis ulceration is invariably due to deep venous thrombosis. This belief may not be true. Kistner[3] was among the first to describe a group of patients who appeared to have a developmental rather than thrombotic cause for deep venous reflux. This group may be larger than previously suspected.[5] In patients undergoing primary valve reconstruction procedures in our institution at the present time, a postthrombotic origin cannot be established in more than half of the patients. The phlebograms do not show evidence of previous phlebitis and at the time of surgery no evidence of previous phlebitis is demonstrated, either outside the vein or inside on the valve cusps themselves. Other circumstantial evidence to support a nonthrombotic cause of reflux in these patients includes the invariable presence of reflux in the opposite "normal" limb and the surprising presence of reflux in the axillary vein valve in several patients. In addition, the femoral valve is more commonly involved than the popliteal valve.[4] The popliteal valve was the most commonly involved valve structure in the present study, no doubt because of the proximity of these valves to the calf, which provides the origin of thrombosis in most instances. The hemodynamic differences between the two groups have already been stressed.

Nicolaides et al.[6] have emphasized the functional importance of the popliteal valve in preventing the postphlebitic syndrome. In their experience, postphlebitic syndrome was prevented, even in the presence of proximal venous obstruction, provided the popliteal valve was intact. These findings are in sharp contrast to our experience reported here. Most of the refluxive limbs in our group did, in fact, have popliteal valve reflux, but their symptoms and hemodynamic abnormalities were quite mild. We believe that this can be attributed to the fact that in most of these limbs with popliteal valve reflux, multiple level valve reflux was absent. There is evidence[3-5,7,8] that *any* intact valve in the femoropopliteal venous segment, including the highest superficial femoral vein valve, can prevent the more severe forms of postphlebitic syndrome. However, other authorities hold quite the opposite view, ascribing a great deal of importance to the valves in the calf veins and the popliteal vein.[14,15] Nevertheless, the data presented here are quite supportive of the former view.

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