J CARDIOVASC SURG 1995;36:225-31

Compliance of the normal and post-thrombotic calf

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Objective. **In addition to degree of outflow obstruction and reflux and poor calf muscle pump function, vein wall compliance changes are important in understanding pathophysiology of venous disease. This study compares the pressure/volume relationship in post-thrombotic and healthy legs.**
Experimental design. **Prospective and comparative study.**
Setting. **Vascular laboratory.**
Participants. **Investigations were performed on 24 apparently normal legs and 30 post-thrombotic limbs as confirmed by phlebography.**
Method. **Dorsal vein pressure and absolute calf volume decrease were recorded simultaneously during outflow form the leg after release of the cuff during venous occlusion air-plethysmography with and without reactive hyperemia. The slope of the pressure/volume outflow curve was calculated. In addition, the distensibility (=collapsibility) was determined as % volume decrease/mmHg. The popliteal and femoral vein diameters were measured in supine and erect position by ultrasound.**
Results. **With and withouth induced hyperemia the mean slope coefficients of post-thrombotic legs were significantly higher (0.52±0.22 and 0.53±0.18) than in normal (0.15±0.10 and 0.29±0.11), i.e., the curve steeper since the calf was stiffer, less compliant. The degree of outflow obstruction and severity of skin changes did not affect the slope measurement substantially. Collapsibility during venous outflow was significantly less in post-thrombotic legs. The post-thrombotic veins were less distended on standing.**
Conclusions. **Post-thrombotic calfs are less compliant than normal legs mainly due to less compliance of the vein wall, although theoretically reduced venous volume may contribute.**

KEY WORDS: Veins - Compliance - Leg, post-thrombotic - Plethysmography.

Presented at the 4th Annual Meeting of the American Venous Forum, San Diego, February 26-28, 1992.

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The geometry of the low pressure venous system is much more influenced by vein wall compliance and surrounding tissue forces than the high pressure arterial system.[1] This may be important in understanding venous function and in treatment of venous disease. Compliance may change in different types of venous diseases and its effect on calf muscle pump function and different hemodynamic tests are poorly known. It is probably of much greater importance than previously thought.[2] Matching mechanical properties of graft to host vessels in arterial surgery have been emphasized repeatedly and should be of no less importance in venous reconstructive surgery.[3]

Earlier attempts to assess compliance in the post-thrombotic calf have yielded conflicting results.[4-7] These early studies utilized indirect strain gauge methods without any venous pressure measurements. The post-thrombotic state in the population was not always confirmed by phlebography in the earlier studies. Attinger has emphasized the importance of simultaneous volume and pressure measurement in the determination of venous compliance.[1] Norgren and Thulesius demonstrated decreased compliance of the foot in chronic venous insufficiency utilizing a combination of foot volumetry and simultaneous pressure measurements.[8]

The authors have validated a method using occlusion air plethysmography and simultaneous dorsal vein pressure measurement to assess the

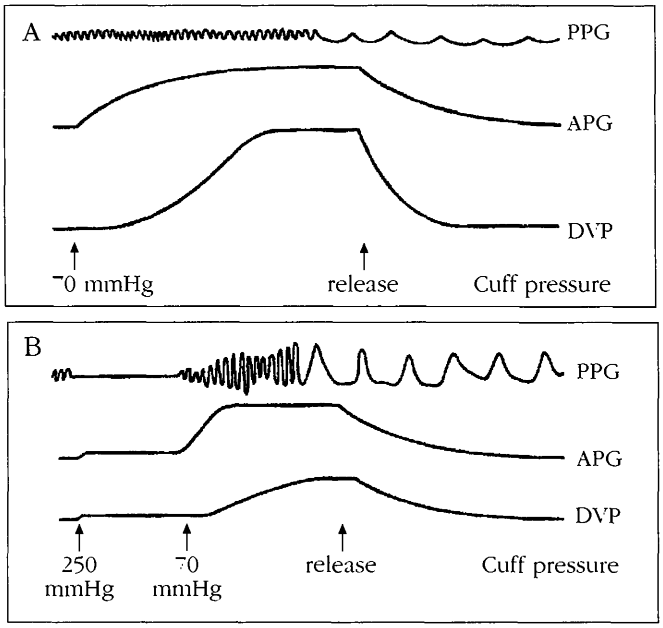

Fig. 1.—Qualitative tracings of arterial pulse (PPG), volume (APG) and dorsal vein pressure (DVP) of a healthy leg obtained simultaneously. Group A curves depict venous occlusion only, while group B curves are recorded during initial ischemia followed by venous occlusion before the release of the cuff. Although the volume is the same in both situations the pressure build up is less following ischemia despite hyperemia flow (increased pulse amplitude). Just before cuff release the recording paper speed was increased (from 10 mm/min to 10 mm/s).

pressure/volume relationship of the calf.[9] The present study is based on that technique and had a two-fold objective. On one hand, to compare the pressure/volume relationship in normal and post-thrombotic limbs; on the other, to evaluate the influence of arterial inflow, outflow obstruction or local skin changes on the plethysmographic outflow curve, i.e., potential pitfalls of the method.

Materials and methods

The control group consisted of 24 legs in 13 healthy persons with no signs or symptoms of vascular disease. The patient group comprised 30 lower limbs in 27 patients with previous deep venous thrombosis verified by ascending and transfemoral phlebogram. Radiologically, the thrombus was shown to extend proximally involving at least the superficial femoral vein segment in all cases. All patients had chronic venous insufficiency, often with a combination of reflux and obstruction. The degree of obstruction according to Raju's classification [10] was Grade 1 (no hemodynamic obstruction) in 13 legs. In 10 lower limbs the hyperemia stress test was positive (Grade 2). Six patients (7 legs) had a severe outflow obstruction (Grade 3 and 4) with a hand/foot pressure difference of more than 5 mmHg. According to the classification of chronic venous insufficiency by the Ad Hoc Committee, [11] 8 legs were only slightly symptomatic (Class 1), while 5 had signs and symptoms corresponding to Class 2. Active or recent ulceration was observed in 17 lower limbs (Class 3). No patient was completely asymptomatic.

Venous pressure measurement and calf volume determination were performed simultaneously. Venous pressure was measured through a 23-gauge scalp needle inserted into a dorsal foot vein. This was connected to a transducer (P 10 EZ, Gould Inc., USA) placed at the level of the insertion and the signal continuously displayed on a polygraph (Model 7E, Grass Instrument Co., USA).

The calf volume was measured with an air plethysmograph (APG-1000, ACI Medical Inc. USA). The patient was supine throughout the procedure. Initially the leg was emptied by elevation to at least 45 degrees. The air bag was adapted on the leg and the foot lowered to 30 degrees five minutes later. An occlusive cuff was fixed around the thigh. Volume changes were measured during venous occlusion at cuff pressure 70 mmHg (inflow) and after sudden release of the cuff (outflow). After a 5 minute rest, the measurements were repeated following induced hyperemia, a technique previously described.[12] An arterial occlusion pressure of 250 mmHg was applied for 2 minutes. The cuff pressure was suddenly decreased to the level of venous occlusion, i.e., 70 mmHg. When the sudden increase in venous volume due to hyperemia had leveled off, the cuff was instantaneously emptied and the resulting outflow recorded. The initial arterial ischemia and the later hyperemia were monitored by a photoplethysmography probe (Photopulse Sensor Model PH 77, MedaSonics, USA) tracing the arterial pulse wave attached to the big toe (Fig. 1).

As the calf volume and the dorsal vein pressure curves were recorded simultaneously on the multichannel polygraph, the volumetric and pressure curves could directly be compared and used for

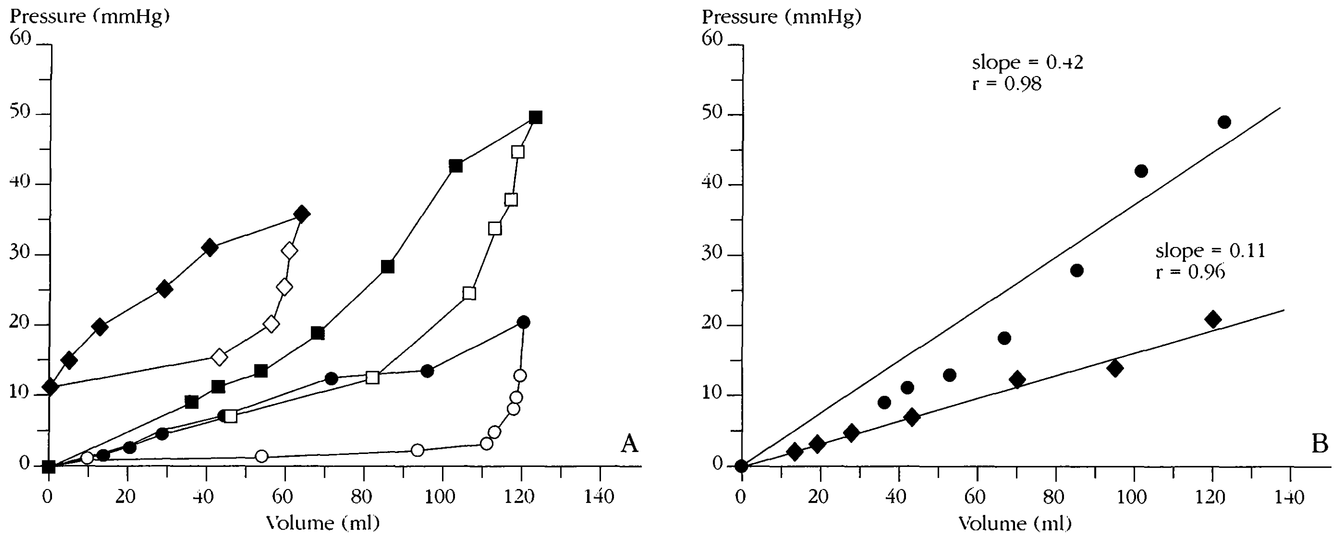

Fig. 2.—A) Typical filling and outflow pressure/volume loops during venous occlusion in three individual legs. Each loop is traced counterclockwise and consists of inflow curve (open) and outflow curve (filled). The lower half of the loop representes pressure-volume relationship during inflow portion of the occlusion plethysmography and is strongly curvilinear with concavity facing pressure axis. The outflow curve starts at the maximum volume reached at end of inflow curve and traces from right to left. Note the outflow of the loop is much less of a curve than the inflow portion. B) Two sets of pressure/volume points during outflow registration the fitted line is superimposed and r-values and slope coefficients are given.

estimation of the pressure-volume relationship during expansion (inflow) and collapse (outflow) of the calf. The inflow and outflow curves are plotted as counterclockwise loops in Figure 2. The lower portion of the loop represents inflow and the upper outflow. The ending inflow volume and the beginning outflow volume are the same and are plotted as a single point to the top right.

The up-slope was curvilinear and varied markedly, likely influenced by the individual variation in arterial inflow and induced outflow obstruction. The down-slope starting from a maximum volume was considered to better reflect a comparable point of full vein distention. Contrary to the inflow curve, the outflow curve exhibited a very gentle curve, which significantly related to a straight line ($r=0.98\pm0.03$, range 0.94-1.00, $n=54$). Therefore, the outflow curve could for practical purposes be described by a linear regression analysis using the formula: $P=kV+c$, where P is venous pressure, k is the slope coefficient, V is calf volume, and c a constant (the y axis intercept) equal to zero, when the line passes through origo (Fig. 2).

Each pressure/volume outflow curve could be characterized by the slope coefficient, which was used in comparison between different individuals and groups of patients. A higher slope coefficient indicated steeper curve and less vein compliance. This technique of assessing compliance has previously been validated by comparing to other techniques not dependent on the outflow curve.[9]

In addition, distensibility (or collapsibility) was calculated as percent volume decrease per mmHg during 0.5 and 1 second increments during the first 5 seconds after cuff deflation. The resulting curve is a different way to express compliance.

Using duplex Doppler ultrasound (Acuson 128 PV, probe 531 Linear) the sagittal and transverse diameters of the common femoral and popliteal veins were measured in the supine and erect position. In both positions measurements were performed with and without a standardized Valsalva's maneuver (blowing into a mercury manometer at a pressure of 40 mmHg).

Wilcoxon-Rank unpaired and paired non-parametric tests were used for statistical analysis in the appropriate situations. A p-valve of <0.05 was considered significant. Standard methods were used to calculate correlation coefficient and perform linear regression analysis. All values are given as mean ± SD, unless otherwise indicated.

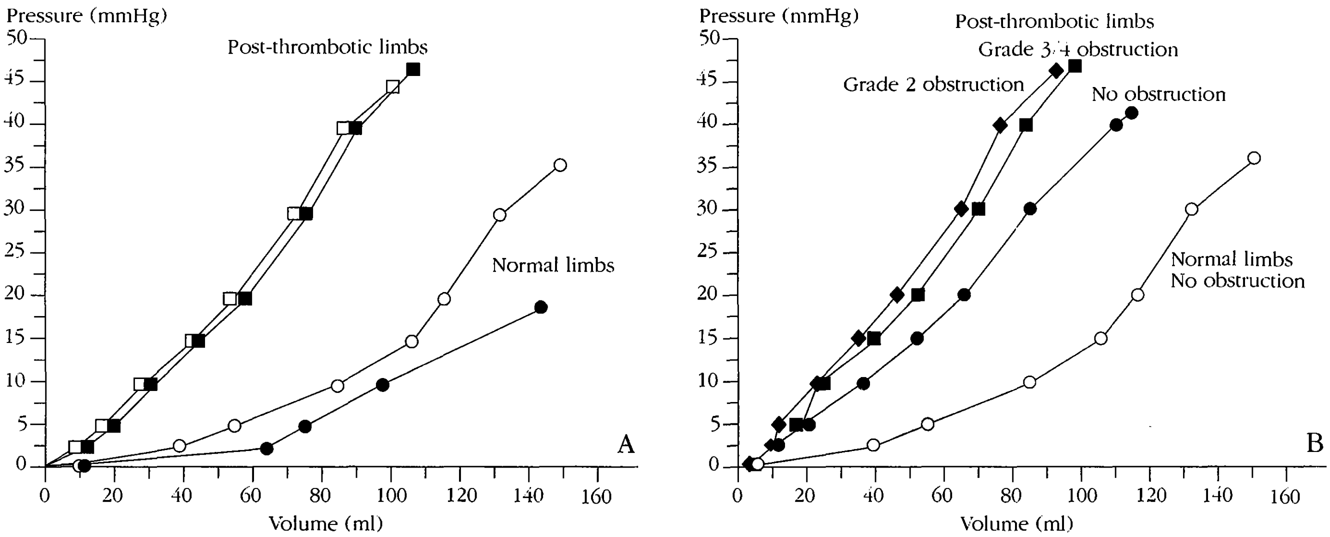

Fig. 3.—A) Mean pressure/volume curve during outflow in post-thrombotic (n=30) and normal (n=24) legs without previous ischemia (open) and following ischemia (filled). B) The average pressure/volume outflow curve in normal legs (O—O; n=24), in legs with previous deep vein thrombosis but without hemodynamic obstruction (Grade 1; ●—●; n=13), in legs with Grade 2 outflow obstruction (♦—♦; n=10), and in legs with Grade 3/4 obstruction (■—■; n=7). For definitions of degree of obstrucion see text.

Results

Average pressure/volume outflow curves in patients and healthy persons are depicted in Figure 3 A. The mean slope coefficient of post-thrombotic legs with or without ischemia was higher (0.48±0.20 and 0.49±0.16, respectively) than in normal (0.15±0.10 and 0.29±0.11, respectively), i.e., the curves were steeper. Unlike healthy controls the patients slopes were unaffected by the induced ischemia and hyperemia. The abnormal pressure/volume relationship in the post-thrombotic calf was not influenced by any outflow obstruction since there was no significant difference in slope between the different degrees of hemodynamic obstruction. Even the curve describing the post-thrombotic legs with no obstruction (Grade 1) was significantly steeper than the healthy legs (slope coefficient 0.41±0.12 vs. 0.19±0.11, respectively, $p<0.05$) (Fig. 3 B).The slope coefficient of normal (Grade 0) and post-thrombotic legs stratified according to clinical class (Ad Hoc Committee[11]) are shown in Figure 4. Again the difference between normals and diseased limbs is apparent, but no differences were observed among classes of various severity of chronic venous insufficiency. The average slope coefficient value was 0.29±0.11 in Class 0 (normal calfs), 0.56±0.22 in Class 1, 0.50±0.27 in Class 2, and 0.44±0.17 in Class 3. Despite advanced calf tissue involvement including lipodermatosclerosis in Class 3, the calf pressure/volume relationship was similar to Class 1 with only mild swelling.

The post-thrombotic legs had less tendency to collapse following cuff release. The curve depicting collapsibility (% volume decrease/mmHg) was higher in normal legs (Fig. 5). Collapsibility as measured is a different way to express compliance. It was the same regardless of the degree of presenting outflow obstruction, i.e., no differences among post-thrombotic limbs with or without outflow obstruction were found.

The sagittal and transverse diameters of the common femoral vein were not significantly different in the supine position (11.5±2.1 vs 11.8±2.1 mm, respectively). This suggests that the vein was fully extended in the this position. In the popliteal vein the transverse diameter was constantly slightly longer than the sagittal regardless of posture or Valsalva's maneuver (in supine position, 9.2±1.6 vs 7.8±1.2 mm, respectively). This might be due to compression by surrounding structures. No substantial collapse of any vein was observed in any position used.

The influence of Valsalva's maneuver and change

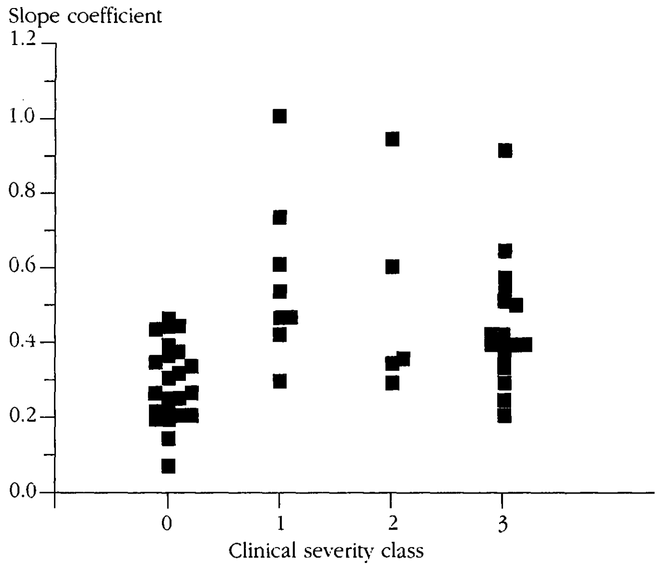

Fig. 4.—Pressure/volume slope coefficients (compliance) in 24 controls (Class 0) and 30 post-thrombotic limbs distributed according to clinical severity Class 1-3. No compliance difference was observed between classe 1-3 (for definitions of clinical severity classification see text).

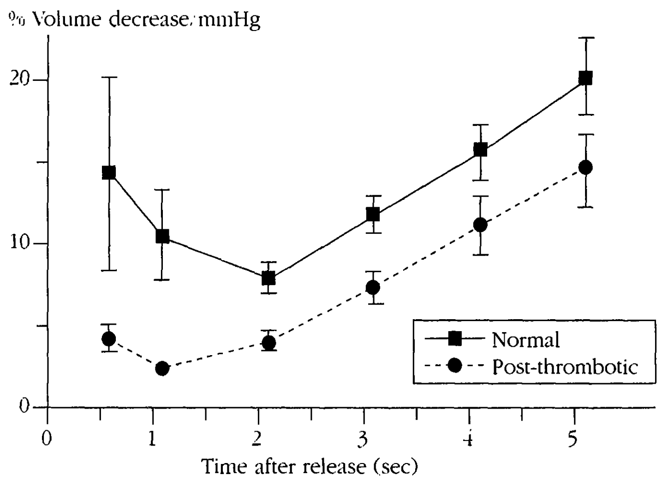

Fig. 5.—Collapsibility (% volume decrease/mmHg) following release of venous occlusion in post-thrombotic (n=16) and apparently healthy legs (n=16) (Mean±SD).

of posture on the common femoral and popliteal vein sagittal diameters in controls and patients is shown in Figure 6. This diameter was chosen since it was technically easier to delineate and thus better reproducible. The measurement provides an

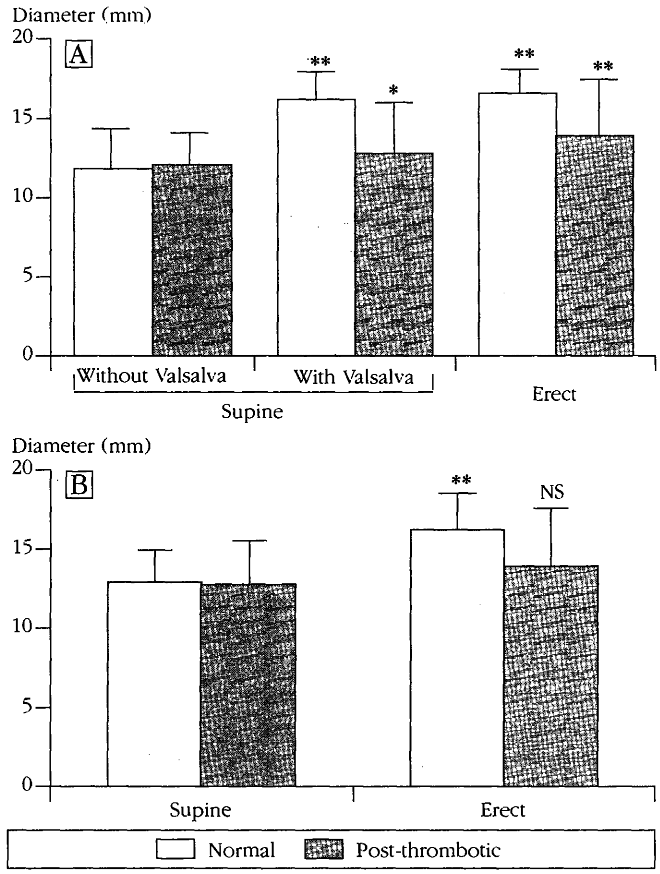

Fig. 6.—Diameter of the post-thrombotic (n=19) and normal (n=23) common femoral (A) and popliteal (B) veins in supine position with and without Valsalva's maneuver and erect position. The post-thrombotic vein dilates significantly less than the normal vein (Mean±SD; NS = no significance, * p<0.05, ** p<0.005; see text for details).

index of venous distensibility. The common femoral vein of both the normal and post-thrombotic limbs dilated significantly on assuming the erect position, but the latter dilated less on standing compared to controls (2.4±1.6 mm and 4.9±2.2 mm, respectively, p<0.05). A similar difference was observed following Valsava's maneuver in supine position. While the post-thrombotic vein changed very little, the normal vein dilated markedly (1.0±1.7 mm and 4.9±2.6 mm, respectively, p<0.001). The healthy popliteal vein dilated significantly on standing (7.8±1.2 to 9.8±1.4 mm, p<0.001), but the post-thrombotic popliteal vein did not (7.7±1.6 to 8.3±2.1 mm, no significance).

Discussion and conclusions

The method to assess the pressure/volume relationship of the apparently healthy and post-thrombotic limbs in this report has been validated in a previous study.[9] It showed that the degree of venous reflux has no influence on the pressure/volume curve, which is theoretically not expected since the subject is in supine position with elevatd leg. Although plethysmographic outflow pressure/volume curves are slightly curved (which physiologically is expected) the practical approximation into a straight line was shown to be acceptable for the purpose of this study. With this method only relative volume changes are measured. A potential pitfall is the inability to measure baseline venous volume of the whole leg and the distribution between superficial and deep systems. To our knowledge no practical method to do so is available. Other potential pitfalls, e.g., influence of outflow obstruction, local skin and subcutaneous changes, and arterial inflow, are evaluated in this study.

The patients with leg ulcers, scar tissue or lipodermatosclerosis in clinical severity Class 2 and 3 had the same range of slope coefficients, i.e., compliance, as the patients with very slight or no local calf signs of chronic venous insufficiency. As venous wall changes probably precedes tissue compliance changes, the authors speculate that the latter are preempted from being manifest in pressure/volume curves that are already abnormal from venous wall changes. Also, local skin changes and lipodermatosclerosis are confined to the gaiter area and less commonly involve the bulky more proximal portion of the calf enclosed in the plethysmography.

As expected, a severe outflow obstruction did not affect the pressure/volume outflow slope following the release of the occluding cuff. An significant outflow obstruction resulted in a higher dorsal vein pressure at a smaller calf volume, but the pressure/volume curve slope was not affected. Post-thrombotic legs without any hemodynamical obstruction were significantly stiffer than the healthy. Thus, an outflow obstruction did not substantially influence the pressure/volume relationship.

Hyperemic flow induced elevation of the dorsal foot vein pressure has successfully been used previously to detect and classify venous outflow obstruction.[10 12] In order to accentuate or precipitate any «critical» outflow obstruction the occlusion plethysmography was also performed during hyperemia induced by ischemia. Since dorsal foot vein pressure was simultaneously recorded, pressure/volume outflow curves were obtained with and without ischemia. Unexpectantly, the compliance of the calf did not change after ischemia in the post-thrombotic legs, but increased in the normal. The mechanism for this is unknown. After a deep venous thrombosis a process of repair with an inflammatory response and invasion of granulation tissue starts in the valve and vein wall.[13 14] The ultimate result is often valve destruction, vein wall thickening and endothelium injury. To explain the unresponsiveness to ischemia it can be speculated that endothelium mediated relaxing factors may be deficient in the post-thrombotic vein. It can also be due to a pure mechanical problem, i.e., the post-thrombotic vein wall is so stiff that it is unable to dilate. The technique of occlusion plethysmography itself or the metabolites produced during the ischemic occlusion period may have had a differential effect on venous compliance of normal and post-thrombotic calf. It is a novel observation, which needs further studies.

Several other observations supported the conclusion that previously thrombotic veins are «stiffer» than healthy. The collapsibility of the calf veins after release of the occluding cuff was significantly lower in the post-thrombotic legs compared with normal controls. The inability of the popliteal vein to fully dilate on standing denoted a stiffer wall. Interestingly, this was also seen in the common femoral vein, even if the previous thrombosis only reached a lower level and the ascending or transfemoral phlebography appeared normal in the examined segment. This suggests that the post-thrombotic inflammatory response can reach a higher level of the vein than radiologically expected. During the course of valve reconstructive surgery the authors have encountered post-thrombotic wall changes in veins, which appeared radiographically "normal". Contrast phlebography is sensitive to the technique used and can underestimate the extent of deep vein thrombosis.[15] The inability to dilate the post-thrombotic common femoral vein with Valsalva's maneuver in the supine position did not necessarily indicate a greater stiffness. The necessary pressure build up against a closed femoral valve does not occur since the valves often are incompetent resulting in reflux. However, incompetent valves do not affect the finding in the standing person.

It can be concluded that post-thrombotic calfs exhibit an abnormal pressure/volume relationship compared to normal controls under the conditions of the present study. It is likely that low compliance of the post-thrombotic veins are mainly responsible even though other factors may also contribute to the observed abnormal pressure/volume curves. A reduced venous volume may shift the curve to the left without any changes of vein compliance. On the other hand, large varicosities would lead to underestimation of any decrease of compliance of the deep veins.

The importance of vein wall properties in the etiology of chronic venous disease and how they influence presently used hemodynamic tests needs to be further studied. As in surgery on the arteries, the design of an adequate synthetic graft for venous reconstruction has to take mechanical wall properties into account to be successful. The substantial failure rate of a compliant axillary vein transplant to a «stiff» post-thrombotic popliteal may partly be explained by a compliance "mismatch", resulting in the observed late dilatation.[16]

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