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Validation of the supine venous pump function test: a new non-invasive tool in the assessment of deep venous insufficiency

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1. A new non-invasive test was developed to assess calf muscle pump function: the supine venous pump function test. The technique uses strain-gauge plethysmography and is performed in the supine position. The method is superior to other non-invasive methods because basically the most essential haemodynamic parameter, venous pressure decrease, is used by properly converting venous volume measurements into venous pressure. The validity of this test was established by comparison with invasive venous pressure measurements and by determining the reproducibility. Additionally, normal values were determined.

2. In 28 extremities the supine venous pump function test was performed simultaneously with invasive venous pressure measurements. The reproducibility of the test was assessed in 10 randomly chosen volunteers. In 34 volunteers normal values were obtained and 26 patients with clinical venous insufficiency were examined.

3. Comparison of the two methods revealed a correlation coefficient of $r=0.98$ ($P<0.001$). A mean difference of $3.9\%_{PF}$ between both methods was found with limits of agreement of $-6.3\%_{PF}$ to $14.1\%_{PF}$. The coefficient of repeatability was $13\%_{PF}$ and the coefficient of variation was 9% . The normal range was found to be $>60\%_{PF}$. The mean pump function in the patient group was $45\%_{PF}$.

4. The limits of agreement are small enough to be confident that the supine venous pump function test can be used instead of invasive venous pressure measurements to assess calf muscle pump function in clinical practice. The reproducibility of the test is good.

INTRODUCTION

Chronic venous insufficiency (CVI) is a poten-

tially disabling disease with a high prevalence and considerable socio-economic importance. In clinical practice CVI is divided into 'superficial' and 'deep' CVI. 'Superficial' CVI is due to dysfunction of the venous valves in the superficial veins, either primary (congenital) or secondary. It often presents itself as varicose veins with slight pedal oedema or corona phlebectasia, or clinical class 2 CVI according to the updated classification as proposed by Porter et al. [1]. 'Deep' CVI – insufficiency of the deep venous system – can be the result of a primary (congenital) dysfunction of deep venous valves, sometimes combined with superficial insufficiency. Deep CVI can also be secondary to deep venous thrombosis (DVT) and is then caused by venous hypertension due to thrombus-related valvular damage or insufficient recanalization and inadequate formation of collateral vessels after thrombosis. In this case, it is referred to as the post-thrombotic syndrome (PTS) [1]. Deep CVI often causes more severe oedema, trophic skin changes (class 4) and venous ulceration (class 5–6).

In deep CVI, persisting venous hypertension is the main pathophysiological feature [2, 3]. When a normal individual changes from the supine to the standing position, lower extremity venous pressure will increase from approximately 5 mmHg to about 80–110 mmHg, depending on the height of the subject. An intact calf muscle pump reduces this standing venous pressure to below 25 mmHg, thus removing the damaging effect of the hydrostatic pressure. In PTS and other forms of CVI, obstruction of the venous lumen in combination with destruction or primary dysfunction of venous valves compromise the venous pump, causing insufficient lowering of venous pressure. Through a mechanism, which has not been fully elucidated, a long-standing transmural venous pressure exceeding 20–30 mmHg gives

Key words: calf muscle pump function, chronic venous insufficiency, plethysmography, post-thrombotic syndrome, validation.

Abbreviations: CI, confidence interval; CVI, chronic venous insufficiency; DVT, deep venous thrombosis; IVP, Invasive dynamic venous pressure measurement; PF, pump function; PTS, post-thrombotic syndrome; SVPT, supine venous pump function test.

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rise to changes in the microcirculation [2–6]. Subsequently, these may lead to the various symptoms of CVI, such as oedema, trophic skin changes and venous ulceration.

In all cases, venous hypertension will be present before clinical symptoms are manifest, especially after a period of DVT. Therefore, a test that reliably measures venous pressure might identify high-risk patients at an early stage of their disease. Consequently, prophylactic therapeutical measures (elastic stockings, surgical correction) might prevent further progression.

The current gold standard in the diagnosis of venous disorders, the invasive dynamic venous pressure measurements (IVPMs) [7], is not suited for routine use on a large scale because of its invasive, time-consuming and rather cumbersome nature. For this reason several non-invasive techniques have been developed [8–12].

A non-invasive test has been in practice in our hospital for 30 years, which calculates venous pressure using strain-gauge plethysmography [13, 14]. Just like the IVPMs, it measures the reduction in venous pressure resulting from tiptoe movements in the upright position. Strain-gauges only measure volume changes; therefore this test requires determination of the relation between volume (V) and pressure (P) of the extremity. This is performed in the supine position using congestion by cuffs as a source of increased venous pressure. Its disadvantage lies in the change in posture from upright to supine, necessary to measure the pressure–volume (P – V) relation. This change in posture influences venous tone, unless the body is conditioned to a room temperature of $>28^{\circ}\text{C}$, which is a laborious procedure. We have therefore developed a new test that is fully performed in the supine position; the supine venous pump function test (SVPT). Dorsiflexion and tiptoe movements are performed against a congestion pressure produced by inflatable cuffs around the thighs. These cuffs effectively compress the superficial system of the upper leg, eliminating reflux in the greater saphenous vein. This allows us to test solely the deep venous system without having to use tourniquets to occlude the superficial venous system.

This SVPT is superior to other non-invasive methods because the haemodynamically most essential parameter, venous pressure decrease, is assessed by converting venous volume changes into venous pressure changes using the P – V relation. All other techniques only consider refill time or changes in venous volume rather than venous pressure itself.

To establish the validity of this SVPT we first compared it with IVPMs in healthy volunteers and patients. Secondly, we determined the reproducibility and finally we obtained normal values and compared them with values obtained in patients with different types of clinical CVI.

PATIENTS AND METHODS

Patients

The study was approved by the Ethics Committee of our hospital and informed consent was obtained from each subject.

The SVPT and IVPMs were compared in 16 volunteers (13 males and three females, mean age 30 years) without clinical signs or symptoms of venous insufficiency and 12 patients (five males and seven females, mean age 38 years) with clinical CVI. Normal values were obtained in 34 normal volunteers (16 males and 18 females, mean age 35 years). Of these, 10 randomly chosen volunteers participated in reproducibility studies. In addition, 11 extremities of eight patients (three males and five females, mean age 44 years) with PTS, 16 extremities of eight patients (two males and six females, mean age 64 years) with clinical CVI (without DVT in the past) and 20 extremities of 10 patients (two males and eight females, mean age 44 years) with only clinical superficial varicose veins were studied. Patients were diagnosed on the basis of history and physical examination. The severity of venous disease was classified using the updated consensus [1].

Patients with a clinical history of diabetes mellitus, hypertension (systolic pressure >160 mmHg, diastolic pressure >95 mmHg), severe oedema, lymphoedema or oedema resulting from diseases other than venous insufficiency, patients using calcium antagonists and patients with reduced or absent mobility of the leg (paresis or joint complaints) were excluded. In all patients the venous outflow resistance was also measured to exclude patients with venous obstruction (>0.80 mmHg \times min/%) [15]. The ankle–brachial index was measured to exclude patients with arterial disease (<0.9).

Methods

IVPMs. Venous pressure was obtained by inserting a 21-gauge needle into a dorsal vein of the foot. Venous pressure was recorded by a pressure transducer (Gould) connected to a pen recorder, which provided a continuous recording of the venous pressure. In this setting, IVPMs were performed simultaneously with the SVPT in the supine position. Thus, pressure changes as a result of exercise were directly recorded. Calf muscle pump function (PF) has been calculated as pressure decrease as a percentage of the initial pressure according to the formula: $\text{PF} = (P_1 - P_2/P_1) \times 100\%$, where P_1 is the initial venous pressure (depending on cuff pressure) and P_2 is the venous pressure directly after exercise. We have chosen to represent the value of PF as $\%^{\text{pf}}$.

SVPT. The tests were performed in a semi-climate-controlled room with little fluctuation of

temperature (23.5–25°C). The patient was supine with the knees slightly bent at an angle of 120° while the feet rested against a foot support 10–15 cm above the bed. The knees were supported laterally by foam pads. Inflatable cuffs (cuff size 14 × 90 cm) were placed around the thighs. Strain-gauges (SG-24 or SG-33; Medasonics Inc., Fremont, CA, U.S.A.) were strapped around the lower leg, 1–2 cm below the origin of the Achilles tendon. The strain-gauges were connected to a plethysmograph, and the cuffs to a pressure tank. Both were controlled by a personal computer.

Measurements began with inflation of the cuffs to 50 mmHg. This resulted in a gradual venous volume and pressure increase distal to the site of the cuff compression due to the venous occlusion. The volume changes were monitored by the plethysmograph. Maximum volume is achieved when the venous pressure equals the effective congestion pressure. Then, with the cuffs still inflated, the patient was instructed to perform maximum dorsiflexion movements of the feet, followed by maximum plantar flexion. A total of 10 such movements were made in 20 s. This muscle pump action causes blood to be squeezed beyond the cuff, resulting in a volume decrease in the limb which can be measured accurately. In the period of rest after the exercise, with the cuffs still inflated, venous volume and pressure return to their maximum value and the expelled volume can be measured. This procedure was repeated once at the same pressure of 50 mmHg and then twice at cuff pressures of 60 and 70 mmHg. The subsequent decreases in relative lower limb volume, after these exercises, were recorded.

Additionally, a P - V relation was determined by measuring the ensuing relative volume increase at five different cuff pressures. By plotting the volume changes against the congestion pressure, the P - V relation is found which is characteristic of the limb at that strain gauge location (Fig. 1; example of a P - V relation). With this P - V relation, the volume reduction during exercise can be converted to a pressure decrease. The initial pressure (P_1) is known because that is the congestion pressure. According to the P - V relation, volume V_1 belongs to this pressure. The expelled volume (V_e) is measured. V_2 is the volume after exercise. Following the P - V relation V_2 corresponds with a pressure P_2 , so P_2 is the residual pressure after exercise. Pressure decrease ($P_1 - P_2$) is expressed as a percentage of the initial pressure (P_1) before the exercise was started and is a measure of the calf muscle pump function [$PF = (P_1 - P_2/P_1) \times 100\% = \%PF$].

Statistical evaluation

Differences in groups were calculated using the paired Student t -test. A P -value less than 0.05 was considered significant. Correlation between data was

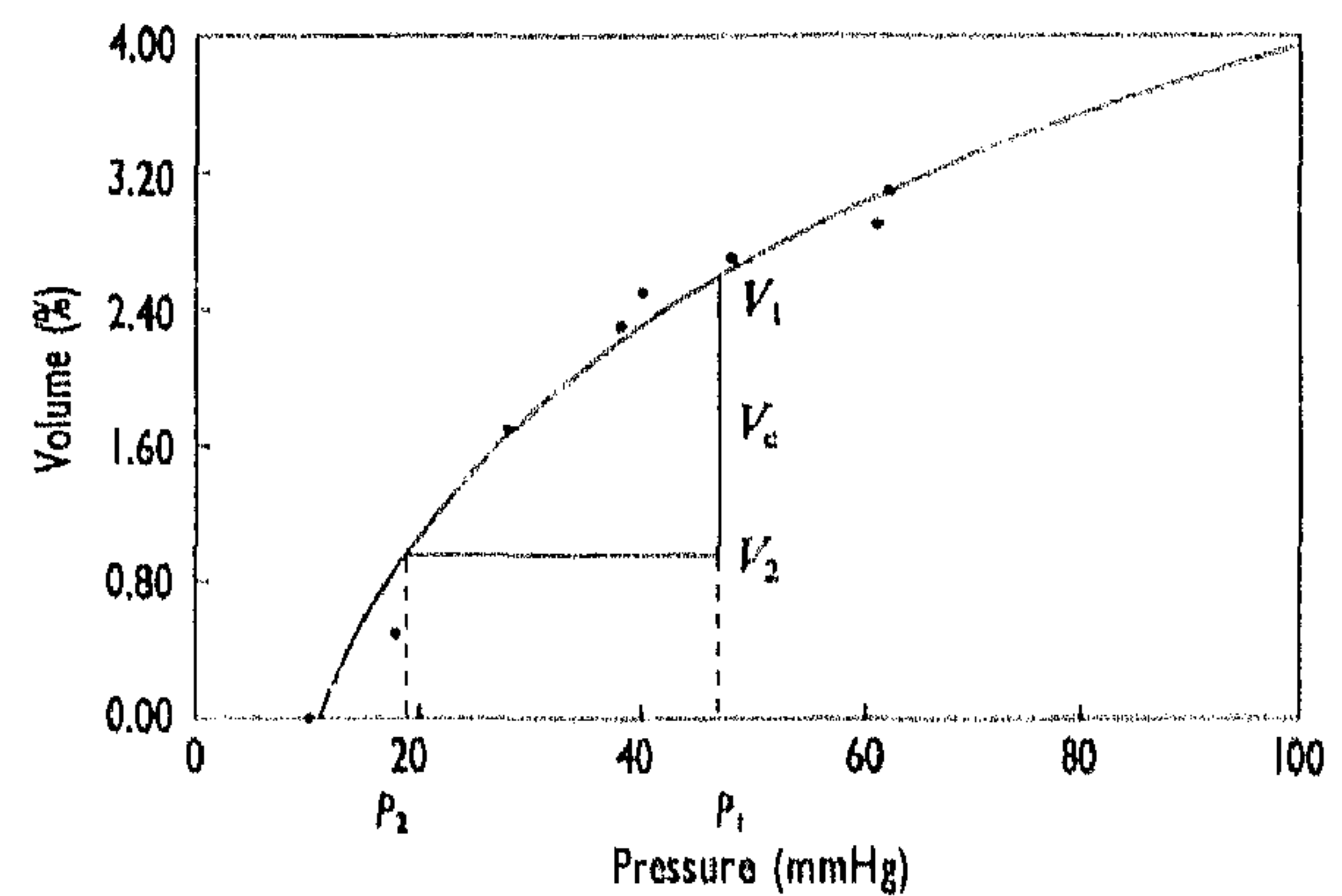


Fig. 1. Example of a P - V relation in a lower extremity. The measured volume increase (y-axis in %) is plotted against the used congestion pressure (x-axis in mmHg). The expelled volume (V_e) is converted into a pressure decrease ($P_1 - P_2$). V_1 , Initial volume; V_2 , volume after movements; P_1 , initial pressure; P_2 , pressure after movements.

calculated according to Pearson. Because the use of a correlation coefficient is not sufficient to compare two measurement techniques, additional statistical calculations were performed [16]. The bias was estimated by the mean difference and the SD of the differences. The limits of agreement and 95% confidence intervals (CI) of these estimations were calculated.

Twenty extremities of 10 randomly chosen volunteers were tested twice. The reproducibility of these repeated tests was calculated as the coefficient of repeatability. Three volunteers (six extremities) were tested five times, also at random intervals to determine the coefficient of variation.

RESULTS

Comparison with IVPs

A total of 28 paired venous pressure measurements and SVPTs were obtained in the supine position; 16 in normal, healthy volunteers and 12 in patients with clinical signs of venous insufficiency. Comparison of the PF values calculated from IVPs and the SVPT revealed a highly significant correlation coefficient ($r = 0.98$, $P < 0.001$). The mean difference was 3.9%^{PF} (CI 2.0–5.8) and the SD was 5.1%^{PF}. Figure 2 shows the plot of difference between the measurements against the invasive measurements. The calculated limits of agreement are -6.3%^{PF} (CI -9.5 to -3.1) and 14.1%^{PF} (CI 10.9–17.3).

Reproducibility

The coefficient of repeatability, expressed as %^{PF}, is 13%^{PF}. The coefficient of variation, which embodies the average SD of the test results, expressed as a percentage of their means, is 9%.

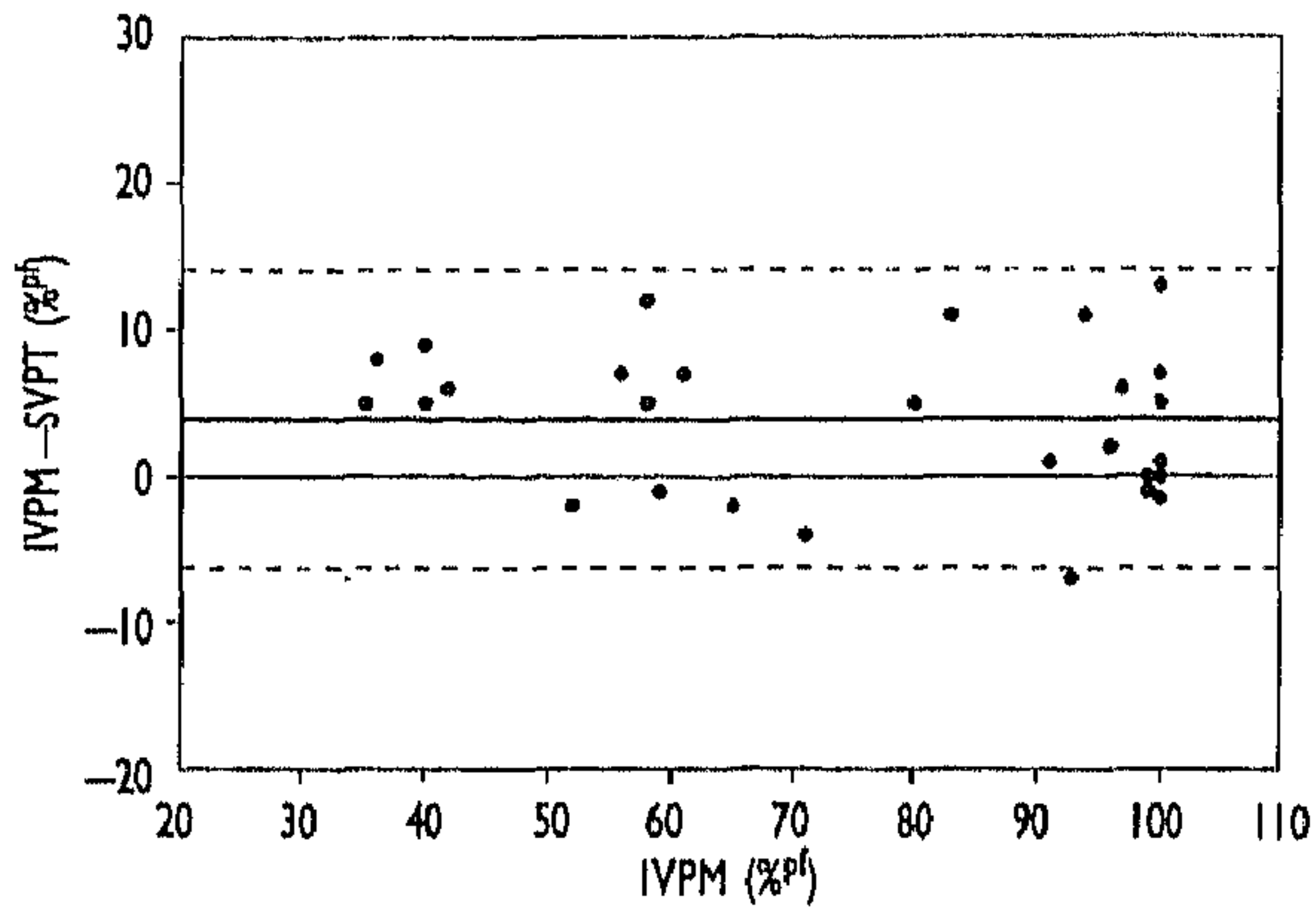


Fig. 2. Difference between IVPM and the non-invasive measured pump function (SVPT) is plotted against the gold standard (IVPM). The mean difference ($3.9\%^{pf}$) and limits of agreement ($-6.3-14.1\%^{pf}$) are also indicated in the figure.

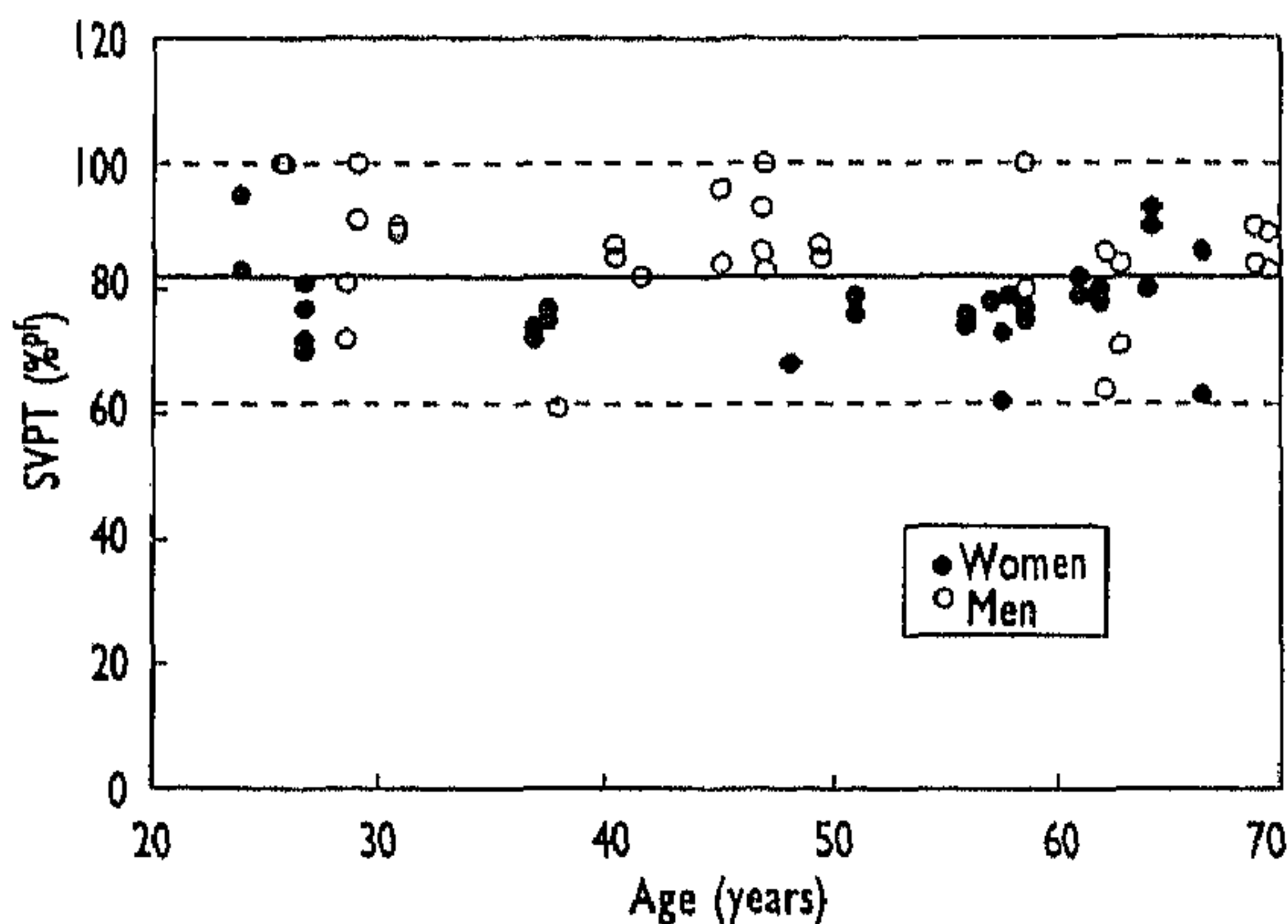


Fig. 3. Values of the SVPT plotted against age for a group of healthy volunteers (18 males and 16 females). Values are expressed in $\%^{pf}$. Mean values $\pm 2SD$ are indicated.

Normal values

Figure 3 shows the values of the SVPT in 34 healthy volunteers, 16 women and 18 men, plotted against age. Values are presented as mean $\pm 2SD$. Due to a technical failure, in six tests only one extremity could be evaluated. Therefore, the results of 62 instead of 68 extremities are presented. The average pump function in these normal subjects was found to be $82 \pm 10.2\%^{pf}$. When the results of men and women are compared, there is a difference of $8\%^{pf}$ (men scoring higher). The difference in pump function between men and women was strongest in the age group 40–60 years. There was no significant correlation between pump function and either age, body mass index or calf circumference.

Patients

Figure 4 shows the SVPT values in patients with CVI, PTS and varicose veins compared with normal volunteers. The average pump function in the group of patients with CVI ($n=16$ extremities of eight patients) is $46 \pm 12.9\%^{pf}$. The average pump function

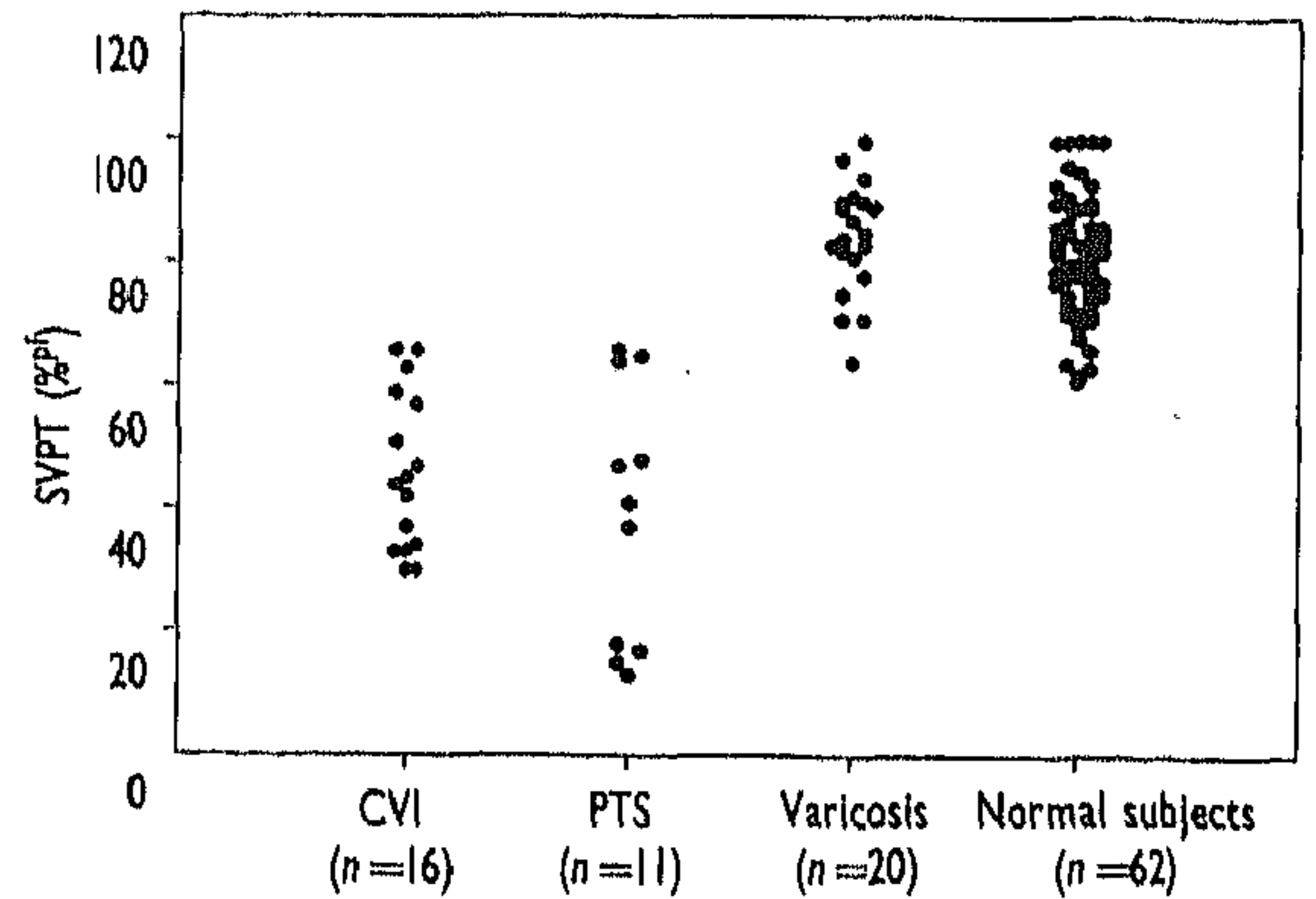


Fig. 4. Pump function values measured with the SVPT are indicated for patients with CVI, PTS and varicosis and for healthy volunteers. Values are expressed in $\%^{pf}$.

in patients with PTS ($n=11$ extremities of eight patients) is $45 \pm 19\%^{pf}$. Thus, both CVI and PTS patients had a significantly lower SVPT value ($P < 0.05$). The group of patients with superficial varicosities but no clinical venous insufficiency ($n=20$ extremities of 10 patients) show a normal average pump function of $84 \pm 9.5\%^{pf}$.

DISCUSSION

In this study we used a non-invasive method to evaluate changes in venous pressure in the assessment of calf muscle pump function. Since the IVPMs are invasive, they cannot be repeated frequently and cannot be used as a screening test. Various non-invasive tests have been developed [8]. However, IVPMs remain the gold standard, essential for the validation of the non-invasive tests.

With our method, changes in venous volume of the leg are measured, which are then translated into venous pressure changes. Furthermore, this method uses venous congestion by cuffs placed around the thigh as the source of venous pressure, rather than using orthostatic venous pressure. Theoretically, inflation of the cuffs (to a pressure below diastolic blood pressure) will compress both superficial and deep veins in the leg. This results in an increase in venous volume distal to the site of cuff compression. Volume increases until the concomitant rise in venous pressure equals the effective cuff pressure squeezing the veins: an equilibrium will then be established with venous outflow from the leg equalling arterial inflow. At this time the calf muscle pump is activated by movements of the feet and venous blood is expelled from the lower limb, resulting in a reduced venous volume and hence reduced venous pressure.

All these changes in volume can be recorded by strain-gauge plethysmography, a reliable technique to record volume changes [11, 17–19]. In addition, other newly developed plethysmographic techniques, such as air-plethysmography and photopleth-

ysmography, have been used in the diagnosis of venous insufficiency [10, 20–24]. All these non-invasive tests only consider changes in venous volume and flow or refill time, rather than venous pressure itself. It is assumed that the changes in venous volume represent changes in venous pressure [25]. This presumes that the relation between venous pressure and venous volume should be linear and identical for all subjects, i.e. a change in venous pressure causes an identical relative change in venous volume for all subjects. As the true $P-V$ relation is a linear and depends on the distensibility of the veins, this assumption may lead to serious miscalculations of venous pressure. Unique to our technique is the use of the $P-V$ relation to translate volume changes into pressure changes. By measuring variation in venous volume at different congestion pressures, the individual venous pressure–volume relation ($P-V$ relation) of the lower limb can be determined (Fig. 1).

We measured venous pressure directly using the invasive technique while simultaneously performing our non-invasive test. The results show a good correlation of calf muscle pump function assessed by these two techniques. The mean difference was 3.9%^{pf} with limits of agreement of –6.3 to 14.1%^{pf}. These limits of agreement are very acceptable for such a non-invasive technique. We therefore conclude that the concept of translating changes in venous volume to changes in venous pressure using the recorded $P-V$ relation, and subsequently calculating the calf muscle pump function, is justified.

This test is performed entirely in the supine position, which has several advantages. Firstly, both the exercises and the recording of the $P-V$ relation are performed in the same position. This abolishes reflex-mediated reactions in the lower limb (e.g. change in venous tone) resulting from a change in posture. Other benefits include increased patient comfort and a more reliable standardization of the movements, as the influences of weight and balance on the force of muscle contractions are avoided. Secondly the cuffs placed around the thigh make any reflux in the greater saphenous vein impossible. This will allow our technique to test only the deep venous system, without using tourniquets. The results of the 10 patients with superficial varicosis without deep insufficiency (on clinical grounds) support this assumption, as they all had values within the normal range.

The results of our test in the normal group allowed us to define a lower limit of normal venous pump function at 60%^{pf}. We found no correlation between the outcome of the SVPT and age, body mass index or calf circumference. We observed differences between men and women, but these were not consistent in all age groups and did not result in an altered value of the lower limit of normal values.

Repeated measurements in randomly chosen volunteers showed a very reliable repeatability coef-

ficient of 13%^{pf} and a coefficient of variation of 9%, satisfactory for an *in vivo* biological test. Figure 3 shows that there is no obvious relation between errors and the magnitude of the quantity measured. For this reason we considered the reproducibility studied in healthy volunteers as representative for the reproducibility of the test.

Almost all the patients tested, who had a clinically evident diagnosis of CVI or PTS, scored below the established lower limit of normal values of 60%^{pf}. A clinically relevant question in the assessment of the patient with CVI is the severity of the insufficiency. The relation we found between clinical degree of CVI and pump function seems to correspond to what was expected, with all class 4–6 patients scoring low, but class 1–3 patients scoring from normal to low. However, it must be stressed that the number of patients in the different subgroups is too low to draw major conclusions.

Some reservations regarding the SVPT must be made. In theory, this test can be expected to be less reliable in patients with (severe) oedema, as this will change distensibility and thereby the $P-V$ relation. Reduction of oedema using appropriate hosiery must be attempted before testing these patients. This also holds for all other non-invasive tests currently available. In this protocol the influence of muscle force (during movements) on venous pump function has not been established. Preliminary results of current investigations show almost no influence of muscle contraction force on the outcome of the pump function test.

This SVPT may have several indications. In patients with severe varicosis, if it is not clear whether the complaints are due to superficial or deep venous insufficiency, this test can be of use in deciding which therapy to choose. Also in patients with complaints suggesting venous insufficiency, but without clinical signs, this test can show if there is a degree of deep venous insufficiency. Finally the damage to the deep venous system after DVT can be tested. In this way the test might identify patients at risk for PTS, enabling early treatment.

In conclusion the SVPT correlates well with IVPs and may be a valuable tool in assessing calf muscle pump function. The test is simple and suitable for routine measurements; it is comfortable for the patient and does not create a potentially hazardous skin lesion. It might be a promising test in the management of CVI and PTS. Further long-term follow-up studies are necessary to evaluate its use in clinical settings.

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