# Comparison of new continuous measurements of ambulatory venous pressure (AVP) with conventional tiptoe exercise ambulatory AVP in relation to the CEAP clinical classification of chronic venous disease

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*Introduction:* **Quantitative measurements of chronic venous insufficiency (CVI) are sensitive in detecting the presence of CVI but have low specificity in differentiating clinical severities of CVI as defined by the CEAP classification. One possible reason for this is measurement techniques do not assess variables that reflect hemodynamic changes that occur during normal exercise. Our aim was to compare the association of variables determined from a new technique, continuous ambulatory venous pressure monitoring (CAVPM), and those of conventional AVP measurement with the clinical severity of chronic venous insufficiency in patients with primary venous reflux.**

*Methods:* **Fifty-four limbs of 49 patients with CVI and 15 healthy controls were studied. CVI clinical severity was classified according to CEAP as C2&C3 (mild disease), C4 (moderate disease), and C5&C6 (severe disease). All participants underwent duplex ultrasound scanning to rule out the presence of reflux in the control group and to confirm it in the patient groups. Conventional AVP measurements, including 90% refilling time (RT90), were compared with the new CAVP variables of mean walking pressure (MWP) and percentage fall in walking pressure (%FWP). Data were analyzed by analysis of variance using the Kruskal-Wallis test, and comparisons between groups were performed using Mann-Whitney tests. Discriminant analysis was used to determine the ability of a test to classify limbs into clinical classes.**

*Results:* **Conventional AVP measurements could not differentiate between the control group and the presence of mild disease ($P = .56$) but did differentiate between controls and severe disease as well as mild and severe disease ($P < .001$). RT90 detected differences between controls and reflux groups ($P < .001$) but not between moderate (C4) and severe (C5&C6) clinical groups ($P > .5$). MWP and %FWP showed significant differences between all clinical severities and controls ($P < .001$).**

*Conclusion:* **In the assessment of CVI, mean walking pressure and percent fall in walking pressure are more reliably associated with anatomic distribution of reflux and clinical severity of CVI than the gold standard investigations of conventional AVP and RT90. (J Vasc Surg 2006;44:794-802.)**

The pathophysiology of chronic venous insufficiency (CVI) is multifactorial. Prolonged elevation of venous pressure and the loss of exercise-induced venous hypotension are thought to be the most significant pathophysiologic processes in the development of CVI.[1-5] Significant contributors to venous hypertension, which may lead to the development of skin changes in patients with CVI, are increased age and duration of venous reflux,[1,3,6] disturbed gait and calf muscle pump failure,[2,7] impaired ankle range of movement,[8] and a history of deep venous thromboses or phlebitis.[3,6] In addition, some authors have implicated prolonged sitting and standing at work.[6,9-14]

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Competition of interest: none.

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Ambulatory venous pressure (AVP) measurement is the recognized gold standard in the quantitative assessment of lower limb venous incompetence.[15-18] The standard test involves measurement of dorsal foot vein pressure from a resting standing position and during 10 tiptoe exercises. The minimum pressure attained at the end of the tenth tiptoe is assumed for practical purposes to be identical to the mean venous pressure during walking.[15] This value of AVP will be referred to as $AVP_{10}$ in this report. The time taken for recovery of the pressure back to the standing resting level is also measured. From the recovery time (RT), the standard variable measured is the time taken for the pressure to return to 90% of the resting standing value (RT90). Despite the clear impact of elevated venous pressure on the development of CVI skin changes, a reliable correlation still does not exist between parameters of venous pressure and the clinical severity of CVI.

The aim of this study was to assess the association of AVP measurements and new variables determined from a technique of continuous ambulatory venous pressure monitoring (CAVPM) with the clinical severity of CVI using the

**Table I.** Inclusion and exclusion criteria

| |
|---|
| Inclusion criteria |
| All patients with lower limb venous disease, belonging to any of the clinical classes of the CEAP classification C2, C3, C4, C5 and C6. |
| All patients belong to CEAP EP and PR. |
| All CVI patients between ages 18 and 65 |
| Exclusion criteria |
| All patients belonging to CEAP $E_C$, $P_O$ and $P_{O,\ R}$ |
| A history suggestive of deep venous obstruction. |
| Peripheral arterial disease (defined by ankle-brachial pressure index < 0.9) |
| Any history of systemic diseases such as angina, myocardial infarction, asthma, chronic obstructive airway disease, chronic cardiac failure, hepatic failure, malignancy, and renal failure. |
| Current pregnancy. |
| Any history of musculoskeletal debilitating disease |

CEAP classification, which is the universally accepted classification of CVI.[19,20]

## METHODS

Ethics approval was obtained from the relevant governing bodies. Patients were recruited from vascular surgery outpatient clinics at Queen Elizabeth Hospital, Gateshead, and Freeman Hospital, Newcastle Upon Tyne. Healthy volunteers were recruited as controls and consisted of medical, nursing, laboratory, and clerical staff from the two hospitals. The inclusion and exclusion criteria are presented Table I. Fifty-four limbs of 49 patients and 15 normal controls were recruited from vascular clinics in both centers.

All participants underwent duplex ultrasound scanning to confirm normal venous function in the control group, to determine the anatomic extent of reflux in the patient group, and to rule out any congenital venous disorders and venous obstruction. The scans were performed with a Philips ATL HDI 3000 scanner (Bothell, Wash) using a 7-MHz to 10-MHz linear probe with participants in a standing position. Superficial, perforator, and deep reflux were defined as reversed flow lasting longer than 0.5, 0.35, and 1.0 seconds, respectively,[21] after ankle dorsiflexion/relaxation and manual calf compression/relaxation.

Clinical examination was performed by one observer (R. K. G. E.) to place subjects into CEAP clinical groups: (1) CO healthy controls (no skin changes of CVI); (2) C2&C3 (no skin changes and edema only, respectively), (3) C4 (venous eczema, pigmentation, lipodermatosclerosis), and (4) C5&C6 (healed or active venous ulceration).

Venous pressures were measured by insertion of a 20-gauge polytetrafluoroethylene cannula into the great saphenous vein (GSV) anterior to the medial malleolus (Fig 1). In instances where cannulation of the GSV under direct vision was not possible, the vein was cannulated under ultrasound guidance. The cannula is connected to a pressure transducer and pressure monitoring kit (Medex MX960PM and DPS720004 respectively; Medex Medical Ltd, Lancashire, UK) and the transducer attached to the leg at the same height of the cannula tip. Patency of the cannula was maintained by a continuous heparinized saline flush (concentration 10 U/mL) infused via a MS 16A syringe driver (Sims Graseby Ltd, Herts, UK) at 1 U/min.

**Fig 1.** The 20-gauge cannula in situ in the great saphenous vein anterior to the medial malleolus. The transducer is fixed at the level of the cannula tip with a Velcro strap.

The transducer was then attached to the CAVPM recorder. This is a microprocessor-based data logger that is primarily intended for use as a monitoring system for continuous AVP monitoring. It has been designed for ease of use with simple on-screen instructions and an event marker. There are no user adjustable controls. (Catheter offsets are measured, displayed and compensated for under software control.) Measurements were taken at a rate of 20 Hz.

Data were recorded onto a removable, industry-standard memory card–SRAM PCMCIA Memory card, typically 512 kB. This memory card allows quick and easy transfer of recorded data to a personal computer, which contains the download software AMBULOG (Medical Physics Dept., Freeman Hospital, Newcastle-Upon-Tyne, UK). Data was processed using MatLab 13 (MathWorks, Natick, Mass). The full CAVPM measuring kit is shown in Fig 2.

Three AVP recording were taken using the technique described by Nicolaides and Zukowski.[15] CAVPM was recorded during continuous walking on a treadmill at increasing speeds (at 3-minute intervals) from 0.5 mph to 3 mph. The CAVPM variables measured were the mean

**Fig 2.** The continuous ambulatory venous pressure monitoring data logger (black bag) and syringe driver (blue bag) fitted to a patient. It allows full mobility during continuous pressure measurement.

walking pressure (MWP) and the percentage fall in walking pressure (%FWP) from the resting standing value ($AVP_0$).

Statistical analysis was performed using nonparametric methods (Kruskal-Wallis and Mann-Whitney tests). Data are presented in median values and 95% confidence intervals (CI). Discriminant analysis was used to determine the sensitivity and specificity as well as the positive and negative predictive values of each test.

## RESULTS

A total of 69 limbs were studied from 15 controls and 49 patients (54 limbs). The four clinical groups were matched for age. There was a predominance of women in the C2&C3 group and men in the C4 and C5&C6 groups (Table II), which may be responsible for the differences in weight, height, and body mass index (BMI) between the groups. Advancing age and increased weight were weakly correlated with clinical severity of CVI ($r$ = 0.472, $P$ < .001; $r$ = .423, $P$ < .001, respectively). Increasing BMI was positively correlated with increasing clinical severity of CVI ($r$ = 0.507, $P$ < .001), but height and clinical severity were not correlated ($r$ = 0.068, $P$ = .544).

Limbs were grouped into different anatomical reflux groups as detailed in Table III as determined from ultrasound findings. The ultrasound-determined anatomic distribution of reflux in different CEAP clinical groups is detailed in Table IV. The control group did not have any lower limb venous pathology. Of 22 limbs in the C2&C3 group, 14 (64%) had superficial reflux only and 8 (36%) had superficial and perforator reflux. Of 20 limbs in the C4 group, 12 (60%) had superficial and perforator reflux and 4 (20%) had deep reflux with superficial reflux, perforator reflux, or both. Reflux anatomy was distributed similarly in the 12 limbs in the C5&C6 group, with 7 (58%) limbs having superficial and perforator reflux and 3 (25%) having deep reflux combined with superficial or perforator reflux.

There were no statistically significant differences in $AVP_{10}$ between the C0 and the C2&C3 groups ($P$ = .262) or between the C4 and the C5&C6 groups ($P$ = .471), nor was statistical significance found between these groups in the percent fall in $AVP_{10}$ (Figs 3 and 4). Fig 3 also demonstrates a linear relationship with $AVP_{10}$ and increasing clinical severity of CVI ($r$ = 0.507). Mann-Whitney tests among groups reveal that $AVP_{10}$ values were significantly different between the controls and the C4 group ($P$ = .0028; 95% CI, 6.7 to 28.7) and controls and the C5&C6 group (P = .0057; 95% CI, 8 to 34.6). Differences were also detectable between the C2&C3 group and more the severe C4 and C5&C6 groups ($P$ = .0008, 95% CI, 6 to 20.2; and $P$ = .016; 95% CI, 7.8 to 26, respectively).

The RT90 values fell exponentially with increasing clinical severity (Fig 5). RT90 values were significantly different between the controls and all patient groups ($P$ < .0001; 95% CI, 9.7 to 20.1) as well as between the C2&C3 group and more severe clinical groups ($P$ < .0002; 95% CI, 1.2 to 4.1). There was no significant difference in RT90, however, between the C4 and C5&C6 groups ($P$ = 0.68; 95% CI, −0.801 to 1.2).

The MWPs changed during walking at different speeds, falling gradually to a minimum pressure while walking at between 1.5 and 2 mph (Fig 6). For this reason, the MWP at 2 mph has been used for analysis. Values of MWP at 2 mph demonstrated more clearly defined distinctions between clinical groups and less overlap between 95% CI boxes (Fig 7). Furthermore, the median values of each clinical group were significantly different from other clinical groups. $P$ values between successive clinical groups are shown in Fig 7.

The distribution of anatomic reflux in the clinical groups is demonstrated in Fig 8. Limbs with superficial reflux only did not demonstrate any significant differences in the median MWP between clinical groups ($P$ > .05). There were no significant differences in MWP between limbs with superficial reflux and those with superficial and perforator reflux in clinical groups C2&C3 and C4. In the C5&C6 group, however, the presence of perforator reflux was associated with a significant increase in the MWP compared with limbs with superficial reflux only ($P$ = .022), despite equal proportions of incompetent perforators in each of the clinical groups (Table V). The presence of deep venous reflux significantly increased the MWP in the C4 and C5&C6 groups ($P$ = .04 and 0.02, respec-

**Table II.** Medians of age, weight, height and body mass index of participants and Spearman's correlation with clinical groups

| | | CEAP group | | | Spearman correlation | |
|---|---|---|---|---|---|---|
| *Characteristics* | *C0 (normal controls) n = 15* | *C2&C3 n = 22* | *C4 n = 20* | *C5&C6 N = 12* | *r* | P *value* |
| Sex (M:F) | 9:6 | 7:15 | 15:3 | 10:2 | | |
| Mean age (range) | 39 (26-44) | 45 (33-67) | 56 (34-63) | 45 (29-60) | 0.472 | <.001 |
| Weight (kg) | 76.8 | 69.7 | 86.7 | 96.7 | 0.423 | <.001 |
| Height (cm) | 168.3 | 156.1 | 168.2 | 172.3 | 0.068 | .544 |
| Body mass index (kg/M$^2$) | 27.1 | 28.7 | 30.8 | 32.5 | 0.507 | <.001 |

**Table III.** Anatomic grouping of limbs based on ultrasound findings

| *Scan finding* | *CEAP anatomic class* | *Anatomic group for analysis* |
|---|---|---|
| No lower limb venous pathology | As,p,d 0 | Normal controls (NC) |
| SFJ + GSV<br>SPJ + SSV<br>Non-saphenous reflux | As2r and As2, 3r<br>As4r<br>As5r | Superficial reflux only (S) |
| Presence of above or below knee perforators with superficial incompetence | Ap17r and/or Ap18r<br>PLUS<br>As2r to 5r | Superficial reflux with perforators (S&P) |
| Deep incompetence with any other incompetence | Ad11 to Ad16<br>PLUS<br>As2 to 5 and Ap17 to18 | Deep reflux and any other reflux (D&S/P) |

*SFJ,* Saphenofemoral junction; *GSV,* great saphenous vein; *SSV,* short saphenous vein.

**Table IV.** Anatomic distribution of reflux in CEAP clinical groups

| | *C0 (Normal controls) n = 15 (%)* | *C2&C3 n = 22 (%)* | *C4 n = 20 (%)* | *C5&C6 n = 12 (%)* |
|---|---|---|---|---|
| No reflux | 15 (100) | 0 | 0 | 0 |
| Superficial reflux only | 0 | 14 (64) | 4 (20) | 2 (16) |
| Superficial and perforator reflux | 0 | 8 (36) | 12 (60) | 7 (58) |
| Deep reflux plus any other reflux | 0 | 0 | 4 (20) | 3 (25) |

Data are presented as totals (%) for each clinical group.

tively). All patients in the C5&C6 group with deep venous reflux had femoropopliteal reflux. Three of four patients in the C4 group with deep reflux had posterior tibial ± gastrocnemius reflux and one had posterior tibial with popliteal reflux.

The extent of overlap in MWP is demonstrated in Fig 9, which compares the percentages of limbs from different CEAP classes with MWP in increments of 10 mm Hg. The total number of limbs in each clinical group is written in each of the boxes. Only controls were found to have a MWP <20 mm Hg, and the percentage of controls limbs fell in a linear relationship with increasing MWP. Furthermore, only limbs in the C5&C6 group were found to have MWP >80 mm Hg. Equal proportions of controls and C4 limbs had MWPs of 31 to 40 mm Hg and equal proportions of C2&C3 and C4 limbs had MWPs of 41 to 50 mm Hg.

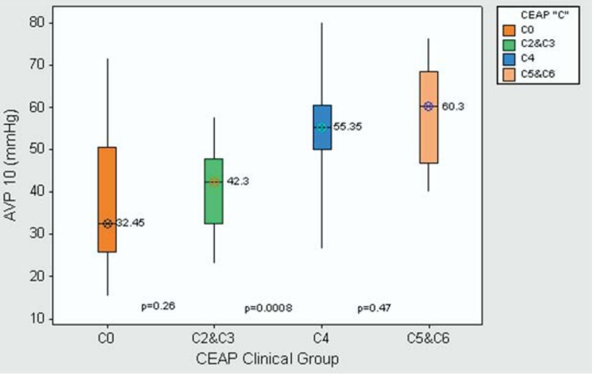


**Fig 3.** Box and whisker plots of ambulatory venous pressure at the 10th tiptoe exercise *($AVP_{10}$)* in different CEAP clinical groups. Boxes represent the 95% confidence interval limits.

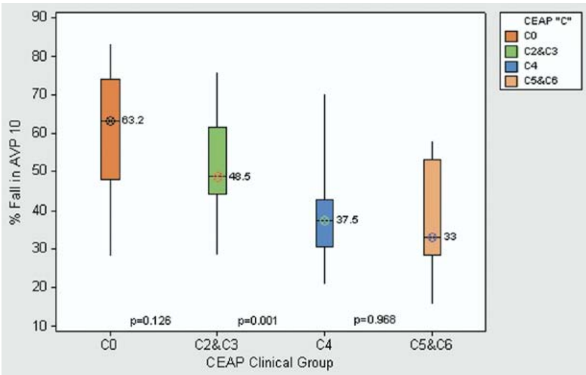


**Fig 4.** Box and whisker plots showing 95% confidence intervals of percent fall (%Fall) in ambulatory venous pressure (AVP) in different CEAP clinical groups. Boxes represent the 95% confidence interval limits.

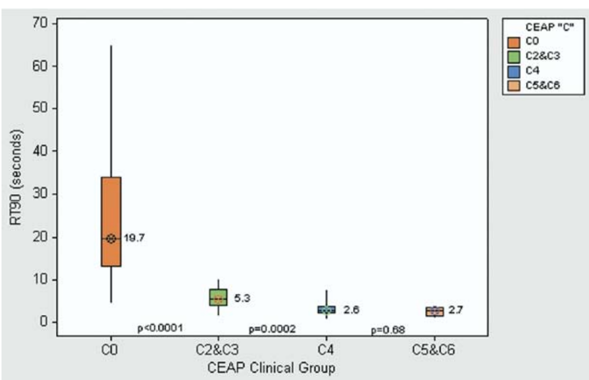


**Fig 5.** Box and whisker plots showing 95% confidence intervals of the refilling time to 90% of the resting standing value *(RT90)* in different CEAP clinical groups. Boxes represent the 95% confidence interval limits.

The percentage fall in $AVP_{10}$ and walking pressure from the resting standing value was calculated to take into account the differences in heights of the patients, which may affect the minimum AVP and mean walking pressures attained. Clinical groups that showed no statistical different in $AVP_{10}$, remained statistically indifferent. The statistical significance in MWP between clinical groups was mildly improved by values of %FWP.

The positive predictive (PPV) and negative predictive values (NPV) of tests to place a limb into the correct CEAP clinical group are shown in Tables VI and VII. Tests with the highest PPV and NPV in each clinical class are shown in bold type. RT90 accurately classified 100% of control limbs and also accurately classified the highest percentage of C2&C3 limbs (58%). The test with the highest PPV in C4 and C5&C6 groups is the MWP (57%).

The test with most significant NPV was %FWP in control limbs; RT90 in C2&C3 limbs, MWP in C4 limbs and %FWP in C5&C6 limbs for clarity. The PPV and NPV of tests to classify limbs into anatomic groups are shown in Tables VIII and IX. RT90 has the greatest PPV in classifying control limbs and limbs with superficial reflux only, but the PPV falls in limbs with superficial and perforator reflux and those with deep reflux. The %FWP has the greatest PPV in classifying limbs with superficial and perforator reflux and those with deep reflux. The %FWP also has the highest NPV for classifying limbs into each anatomic group.

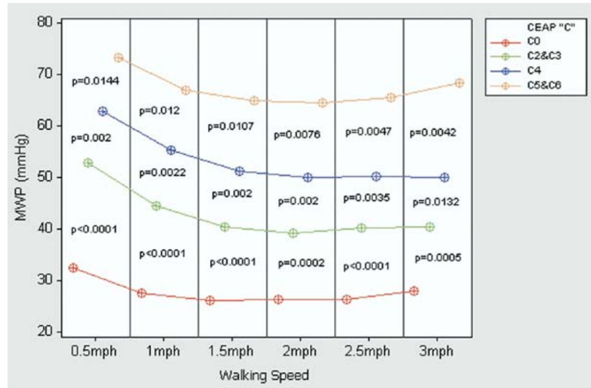


**Fig 6.** Mean walking pressure *(MWP)* at increasing speeds from 0.5 mph to 3 mph in different CEAP clinical groups. *P* values are shown between clinical groups at each walking speed.

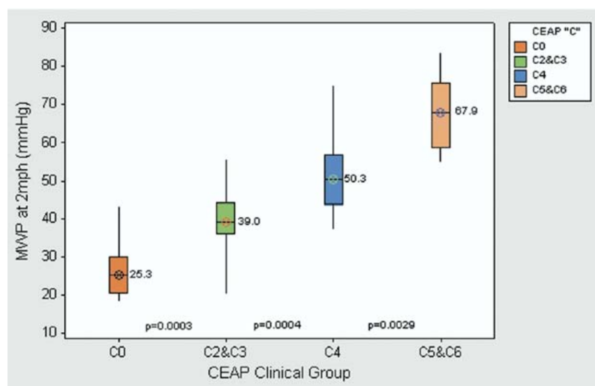


**Fig 7.** Box and whisker plots of mean walking pressure *(MWP)* at 2 mph in different CEAP clinical groups. Boxes represent the 95% confidence interval limits.

## DISCUSSION

Nicolaides and Zukowski[15] demonstrated a positive linear correlation between elevated $AVP_{10}$ and clinical severity. In their study, these authors found that provided the $AVP_{10}$ was <45 mm Hg, the incidence of venous ulceration was zero, and the incidence of ulceration was >80% with $AVP_{10}$ >80 mm Hg. Furthermore, these authors defined the 95% tolerance level of $AVP_{10}$ in normal limbs to be <30 mm Hg. In 1993, Nicolaides et al[22] went on to demonstrate a 100% incidence of venous ulceration in limbs with $AVP_{10}$ >90 mm Hg, fortifying the direct relationship between AVP and clinical severity of CVI. These

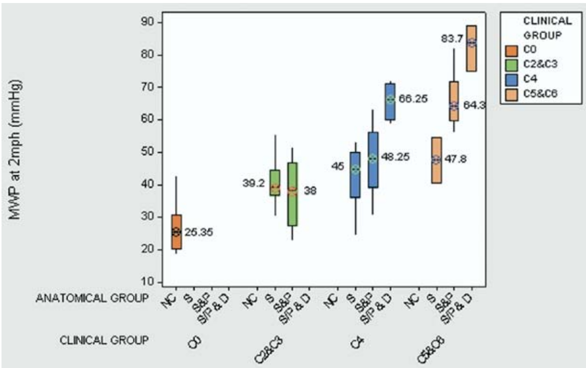


**Fig 8.** Impact of anatomical reflux groups on mean walking pressure *(MWP)* in different clinical groups. Boxes represent the 95% confidence interval limits.

**Table V.** Number of incompetent perforators in S&P anatomical group in each clinical group. Expressed as total limbs (%).

| *Number of incompetent perforators* | *C2&C3* | *C4* | *C5&C6* |
|---|---|---|---|
| 1 | 6(75%) | 9(75%) | 6(86%) |
| 2 | 2(25%) | 2(17%) | 1(14%) |
| 3 | 0 | 1(8%) | 0 |

Data are expressed as total number of limbs (%).

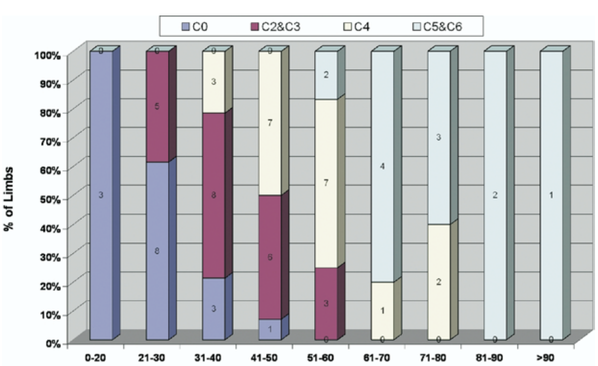


**Fig 9.** Mean walking pressure and CEAP clinical groups.

latter findings, however, were in patients with deep venous incompetence, and patients in the same study were also found to have venous ulceration with $AVP_{10}$ as low as 31 to 40 mm Hg. The same study demonstrated that the highest incidence of ulceration in limbs with superficial reflux only occurred in patients with $AVP_{10}$ between 71 and 80 mm Hg. In the group with deep venous reflux, the highest incidence of ulceration occurred at $AVP_{10}$ between 61 and 70 mm Hg.

In 1996, Payne et al[18] correlated ambulatory venous pressure with skin condition by dividing patients into four groups: those with venous reflux and healthy skin, mild skin changes (eczema and pigmentation), severe skin changes (lipodermatosclerosis), and history or presence of venous ulcers. AVP was assessed using the method described by Nicolaides and Zukowski.[15] These authors found a direct correlation between $AVP_{10}$ and clinical severity; however, there was significant overlap among results in the patient groups, and no significant differences were detectable among groups of progressive severity. $AVP_{10}$ values were significantly different between healthy individuals and patients and was mildly significant between those with mild skin changes those with ulcers.

Our study has similarly demonstrated a linear increase in $AVP_{10}$ with increasing clinical severity, with relatively strong correlation ($r = 0.52$; $P < .001$). There was, however, significant variation in 95% CIs and overlap between CEAP clinical groups. The PPV and NPV of $AVP_{10}$ and percent fall in $AVP_{10}$ were the lowest of all tests (Tables VI and VII).

Previous studies have demonstrated that no ulceration occurred in patients with RT90 >20 seconds and a 79% incidence of ulceration with RT90 <2.5 seconds.[22] The relationship between RT90 and the incidence of ulceration was exponential, and it was suggested that RT90 was of value in detecting the presence of CVI but not in grading its severity. The same authors assessed RT90 in relation to the anatomic distribution of reflux and found that RT90 was significantly different between controls and patients but not among groups with superficial reflux only, deep reflux, and combined superficial and deep reflux. These results are again similar to our measurements of RT90, demonstrating an exponential decrease in RT90 with increasing clinical severity (Fig 5) and a decreasing distinction between more severe clinical groups.

As a result of this exponential decrease, RT90 has strong PPV in classifying control limbs and those with mild disease (100% and 58%, respectively) but poor PPV in classifying limbs of clinical severities C4 to C6. Its NPV is also high in control and C2&C3 groups (94% and 82%, respectively). RT90 is a passive measure of venous refilling and does not take into consideration the influence of dynamic forces that will occur during normal ambulation. It is therefore understandable that RT90 has high PPV and NPV in classifying limbs with full venous competence (controls) and simple venous reflux (C2&C3) without the hemodynamic derangements necessary to produce the changes seen in limbs with C4 to C6 disease. The lower PPV and NPV in RT90 in limbs of C4 to C6 classes indicate that other factors in addition to venous reflux and hypertension influence the development of venous skin changes and progression to venous ulceration.

Payne et al[18] suggested several reasons for the lack of differentiation in $AVP_{10}$ and RT90 results between clinical classes of CVI. They noticed that some individuals attained minimum foot vein pressure after one or two tiptoe exercises, whereas others took longer to attain a minimum pressure (≥10 repetitions). It would follow from this observation that continuous measurements of venous pressure

**Table VI.** Positive predictive value of tests to classify limbs accurately into CEAP clinical groups

| | *CEAP C class* | | | |
|---|---|---|---|---|
| *Test* | *Control limb (%)* | *C2&C3 (%)* | *C4 (%)* | *C5&C6 (%)* |
| $AVP_{10}$ | 36 | 40 | 47 | 28 |
| % Fall in $AVP_{10}$ | 33 | 36 | 47 | 19 |
| RT90 | **100** | **58** | 37 | 21 |
| MWP | 55 | 50 | **57** | **57** |
| %FWP | 63 | 48 | 50 | 53 |

*$AVP_{10}$* Ambulatory venous pressure at the 10th tiptoe; *RT90*, refilling time to 90% of the resting standing value; *MWP*, mean walking pressure; *%FWP*, percentage fall in walking pressure.

**Table VII.** Negative predictive value of tests to classify limbs accurately into CEAP clinical groups

| | *CEAP C class* | | | |
|---|---|---|---|---|
| *Test* | *Control limb (%)* | *C2&C3 (%)* | *C4 (%)* | *C5&C6 (%)* |
| $AVP_{10}$ | 90 | 73 | 66 | 89 |
| % Fall in $AVP_{10}$ | 89 | 70 | 66 | 85 |
| RT90 | 94 | **82** | 63 | 88 |
| MWP | 95 | 79 | **70** | 95 |
| %FWP | **97** | 77 | 66 | **97** |

*$AVP_{10}$* Ambulatory venous pressure at the 10th tiptoe; *RT90*, refilling time to 90% of the resting standing value; *MWP*, mean walking pressure; *%FWP*, percentage fall in walking pressure.

**Table VIII.** Positive predictive value of tests to classify limbs accurately into anatomic groups

| | *Anatomic reflux groups* | | | |
|---|---|---|---|---|
| *Test* | *Normal (%)* | *S (%)* | *S&P (%)* | *D&S/P (%)* |
| $AVP_{10}$ | 35 | 51 | 0 | 6 |
| %Fall in $AVP_{10}$ | 33 | 44 | 0 | 9 |
| RT90 | **100** | **82** | 47 | 14 |
| MWP | 55 | 53 | 54 | 38 |
| %FWP | 60 | 59 | **73** | **78** |

*S*, Superficial reflux only; *S&P*, Superficial and perforator reflux; *D&S/P*, Deep reflux and any other reflux; *$AVP_{10}$*, ambulatory venous pressure at the 10th tiptoe; *RT90*, refilling time to 90% of the resting standing value; *MWP*, mean walking pressure; *%FWP*, percentage fall in walking pressure.

**Table IX.** Negative predictive value of tests to classify limbs accurately into anatomic groups

| | *Anatomic reflux groups* | | | |
|---|---|---|---|---|
| *Test* | *Normal* | *S* | *S&P* | *D&S/P* |
| $AVP_{10}$ | 88% | 82% | 59% | 88% |
| % Fall in $AVP_{10}$ | 89% | 73% | 59% | 90% |
| RT90 | **97%** | 79% | 62% | 93% |
| MWP | 95% | 81% | 63% | 97% |
| %FWP | **97%** | **85%** | **66%** | **98%** |

*S*, Superficial reflux only; *S&P*, Superficial and perforator reflux; *D&S/P*, Deep reflux and any other reflux; *$AVP_{10}$*, ambulatory venous pressure at the 10th tiptoe; *RT90*, refilling time to 90% of the resting standing value; *MWP*, mean walking pressure; *%FWP*, percentage fall in walking pressure.

during exercise would give a more accurate measure of minimum ambulatory venous pressure.

Our technique of measuring MWP and %FWP demonstrated the linear relationship between CEAP clinical groups and ambulatory venous pressure ($r$ = 0.76, $P <$ .001) more clearly than $AVP_{10}$ and revealed more reliable confidence limits for each clinical group. The PPV of MWP and %FWP were lower than RT90 in control and C2&C3 limbs, but these tests had highest PPV in classifying limbs from C4 and C5&C6 groups (57% in both groups). MWP and %FWP had the greatest NPV in all groups except the C2&C3 group, where the NPV (79%) was comparable with that of RT90 (82%).

After controlling for sex differences between groups, a positive correlation between BMI and clinical severity is apparent ($r$ = 0.507, $P <$ .001). This may reflect a role of obesity in the development of CVI skin changes. A positive correlation also exists between MWP and BMI ($r$ = 0.503, $P <$ .001).

We used the long saphenous vein for venous pressure measurement rather than a dorsal foot vein. The previously held belief that dorsal foot vein pressure reflected the global venous pressure at the same level[23,24] was refuted by Neglen and Raju[25] in 2000. These authors found that GSV, dorsal foot, and popliteal/posterior tibial veins exhibit different pressure waveforms in response to exercise. Furthermore, Amarigiri et al[26] measured the ambulatory venous pressures ($AVP_{10}$ and mean walking pressures) in GSV and dorsal foot veins of the same limbs and found that $AVP_{10}$ was lower in the dorsal foot vein than the GSV by an amount relative to the difference in height of the cannula. The overall percentage fall in pressure with exercise was greater in the GSV compared with the dorsal foot veins, however. The same authors found that the values of RT90 were indistinguishable whether measured in the GSV or a dorsal foot vein.

Other authors have noticed extravasation from dorsal foot veins during exercise,[27,28] possibly due to the small diameter of the veins and the position of a cannula on the dorsum of the foot not being suitable in patients undergoing pressure monitoring during continuous exercise. Cannulation of the GSV at the ankle did not hinder exercise and should have dealt with the possibility of extravasation.

There are variations of the exercise technique, such as calf compressions, knee bends, pressing on a foot pedal, or active plantar and dorsiflexion, and several authors have calculated different variables from these measurements (ie, RT50, rate of pressure increase over initial 4-second postexercise (4SR) and percent fall in $AVP_{10}$) in attempts to increase the specificity of the test.[27,29] They have not, however, demonstrated a significant correlation with the clinical severity of CVI.

We did not include measurements with tourniquets in attempts to occlude the superficial system because other authors have shown that lower limb tourniquets did not reliably occlude the superficial system[18] and that the required pressure to occlude the superficial veins was variable and unpredictable in different individuals.[30] Also, use of a tourniquet during continuous exercise was not feasible.

Like standard ambulatory venous pressure measurement, CAVPM is invasive and therefore is not easily repeatable. We do not advocate its use as a screening test, but it has clear value in venous research, in the validation of other quantitative tests of venous insufficiency, and in the assessment of the results of venous surgery in primary venous insufficiency. Further studies that include post-thrombotic limbs and limbs with deep venous obstruction are necessary before the results can be applied to such patients.

## CONCLUSION

Continuous ambulatory venous pressure monitoring (CAVPM) is more closely associated with the clinical severity of CVI than $AVP_{10}$. RT90 and MWP have high PPV in classifying limbs according to clinical groups, and RT90 and %FWP have greatest PPV in classifying limbs according to anatomic reflux groups. The strong association of a quantitative measure of CVI with severity as defined by the CEAP clinical classification enforces the value of this clinical classification in routine practice.

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## AUTHOR CONTRIBUTIONS

Conception and design: RE, HA, TL
Analysis and interpretation: RE, TL
Data collection: RE
Writing the article: RE
Critical revision of the article: HA, TL
Final approval of the article: RE, HA, TL
Statistical analysis: RE
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Overall responsibility: RE

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