Variability of venous hemodynamics detected by air plethysmography in CEAP clinical classes

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J Vasc Bras. 2007;6(4):359-65.

RESUMO

Contexto: A variabilidade hemodinâmica da pletismografia a ar é conhecida, mas o exato papel dessa variabilidade no cotidiano clínico não foi investigado, podendo ter algum significado clínico ainda não explorado. Sabe-se que há sobreposição entre as classes clínicas (C0 a C6) da classificação CEAP e mesmo entre membros inferiores de uma mesma classe clínica.

Objetivo: Avaliar a variabilidade hemodinâmica dos parâmetros da pletismografia a ar nas classes clínicas da classificação CEAP.

Método: Este estudo retrospectivo confronta a doença varicosa de membros inferiores classificada de C0 a C6 pela classificação CEAP com os parâmetros hemodinâmicos venosos obtidos pela pletismografia a ar. Os dados obtidos foram tabulados e analisados em suas classes clínicas pelos testes de variância de Kruskal-Wallys e Barllett.

Resultados: Foram realizados 310 exames em 230 pacientes cujas idades variaram entre 19 a 81 anos, com uma média de 46,2 anos. Os parâmetros índice de enchimento venoso e volume venoso funcional mostraram aumento da variabilidade hemodinâmica quando analisados na classe clínica C0 do CEAP, demonstrada por meio do coeficiente de variabilidade que, para o índice de enchimento venoso foi de 28,12% na classe clínica C0 e se manteve acima de 57% nas classes de C2 a C6. A fração de ejeção e a fração de volume residual não aumentaram a variabilidade quando comparados com a classe clínica C0 do CEAP.

Conclusão: O índice de enchimento venoso foi o melhor parâmetro para avaliação e triagem de pacientes com insuficiência venosa crônica, mas tem grande variabilidade nas classes clínicas C2 a C6 do CEAP.

Palavras-chave: Varizes, insuficiência venosa, pletismografia.

ABSTRACT

Background: The hemodynamic variability of air plethysmography is known in the literature, but the clinical significance of this event has not been investigated yet, and there may be some unexplored clinical meaning. There is known superpositioning of CEAP clinical classes (C0-C6) and even in lower limbs of the same clinical classes.

Objective: To evaluate hemodynamic variability of air plethysmography parameters in CEAP clinical classes.

Methods: This retrospective study compares lower limb varicose disease between C0 and C6 CEAP clinical classes with venous hemodynamic parameters obtained by air plethysmography. Data were tabled and analyzed according to their clinical classes by Kruskal-Wallys and Barllet variance tests.

Results: A total of 310 examinations were performed in 230 patients, aged between 19-81 years (mean = 46.2 years). Venous filling index and functional venous volume increased hemodynamic variability when compared with CEAP C0. This was demonstrated by the variability coefficient, which was 28.12% for venous filling index in C0 and higher than 57% between clinical classes C2 and C6. Ejection fraction and residual venous fraction had no increase in variability when compared with CEAP C0.

Conclusion: Venous filling index is the best parameter for assessment and screening patients with chronic venous insufficiency, but has great variability in C2 to C6 CEAP clinical classes.

Keywords: Varicose veins, venous insufficiency, plethysmography.

Introduction

In the study of venous diseases, phlebography is considered as the gold standard,[1] since it can provide high-quality anatomic images for most venous diseases. That examination, however, is invasive and can cause harm to the patient, which limits its use and leads researchers to study noninvasive methods.

Color-flow Doppler ultrasound has gained attention because it is reproducible and provides anatomic and hemodynamic data. For those reasons, it started being considered as the main examination for a proper venous assessment,[1] since even in C1 and C2 patients, it can bring essential information to characterize the disease and its treatment.[2] Thus, it has also been used in population studies.[3] However, it has limitations, such as low sensitivity to detect insufficient perforating veins,[4,5] and it is not able to provide an overall evaluation of venous hemodynamics, since it evaluates independent venous segments. For that reason, it is not able to distinguish overall lower limb hemodynamic changes during physical activity; some authors even suggest the need of associating a physiological test to measure severity of venous insufficiency.[6]

Introduction and development of air plethysmography in the diagnosis and prognosis of venous diseases by Christopoulos et al. in 1987[7] allowed venous hemodynamic evaluation under varied situations, reinforcing this method to be used in clinical practice.[8] Routine use of air plethysmography as a tool to assess venous function has not been properly studied by well controlled clinical trials. There are studies indicating that rates of air plethysmography may not be correlated with type of great saphenous vein reflux,[9] whereas others show a correlation with the great saphenous vein ostial reflux.[10] However, it is known that air plethysmography is a reproducible examination and that the parameter venous filling index (VFI) is a good predictor of venous reflux. However, it is not considered a proper parameter for the prognosis of disease severity or phlebopathic ulcer because it has high rates even in lower clinical classes, in which there are no ulcers.[11]

The present research study aimed at investigating hemodynamic variability that occurs in venous disease and better define the best criteria for its interpretation, using the parameters of air plethysmography as a study method.

Method

Air plethysmography was used in 230 patients, resulting in 310 lower limbs studied. The examinations were performed at the laboratory of vascular flow at Universidade Federal de São Paulo – Escola Paulista de Medicina (UNIFESP-EPM), between February 2002 to November 2003, following the method described by Christopoulos et al.[7] The patients were initially assessed clinically (anamnesis, general physical examination and specific vascular examination). We used the CEAP classification[12] to classify lower limbs in:

C0 -no visible or palpable venous disease;

C1 -telangiectasias or reticular veins;

C2 -varicose veins by a diameter of 3 mm or more;

C3 -belonging to C1 and C2 classes with edema;

C4 -hyperpigmentation, eczema, lipodermatosclerosis or white atrophy;

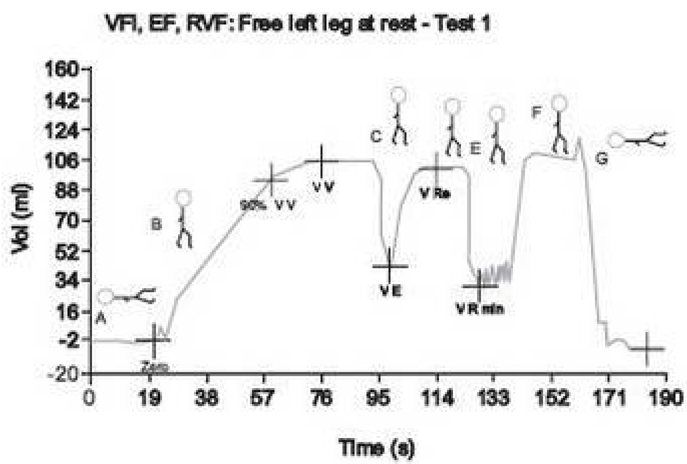
C5 -healed leg ulcers;

C6 -active (open) leg ulcers.

Inclusion criteria were outpatients, patients with lower limb varicose veins, who agreed to participate in the study, aged between 19-81 years. Thirteen of these patients had one lower limb without venous disease and were selected in clinical class C0. Exclusion criteria were patients with arterial and/or lymphatic diseases, pregnant women, psychiatric patients and those who could not collaborate to perform the examination. The research project was approved by the Research Ethics Committee at UNIFESP-EPM according to resolution 196 from 10.10.96 on research involving human beings. Statistical analysis was performed using the Kruskal-Wallys & Barllett variance tests.[13] $P \leq 0.05$ was considered significant (95% confidence interval).

Air plethysmography

Air plethysmography was performed according to the protocol proposed by Christopoulos et al.[7] (Figure 1), with the patient in the supine position, elevated leg and flexed knee. The foot was placed on a 20-cm support. The inflatable compartment was maintained at a constant pressure of 6 mmHg to allow a good contact with the skin and minimal occlusion of superficial veins. A first measurement was obtained (baseline value) and the patient was requested to stand up using only the unassessed limb, supporting himself with a walker. In the vertical position, increased leg volume was observed until curve stabilization, indicating vein filling. The difference between initial and plateau volume represents functional venous volume (VV). Conventionally, the time spent to reach 90% of total filling is defined as venous filling time 90 (VFT 90). The relation between variation in produced volume, divided by its corresponding time in seconds when changing from the lying to the supine position was then measured, obtaining VFI. That index is obtained by the formula VFI = 90% VV/VFT 90, and the values are expressed in mL/s.[14] Next, the patient was requested to stand on both feet and perform a single movement of plantar flexion, causing contracture in the calf muscle and, soon after, the patient should return to initial position. Deflexion in the obtained curve corresponded to ejection volume (EV), resulting from calf muscle contraction. After that movement, we waited for a new curve stabilization and the patient was requested to perform 10 plantar flexion movements, one at each second. Decreased volume was also recorded. Residual volume (RV) is calculated based on final basal value in relation to remaining volume at the end of movements. Ejection fraction (EF) was then calculated, based on EF = (EV/VV) x 100, and residual volume fraction (RVF) based on RVF = (RV/VV) x 100. When the test was over, the patient returned to standing rest position and, once the curve was stabilized, he returned to the supine position.[7,8]



VFI = venous filling index (90% VV/VFT90); VFT90 = 90% of venous filling time; VV = venous volume; EV = ejected volume; EF = ejection fraction [(EV/VV) x 100]; RVF = residual volume fraction [(RVmin/VV) x 100]; RVmin = minimal residual volume.

Figure 1 - Schematic representation of an air plethysmography record according to the protocol by Christopoulos et al.: A) patient in the supine position with leg to be assessed elevated at 45 degrees and supported; B) patient standing on the contralateral limb; C) plantar flexion; D) same as B; E) 10 plantar flexion movements; F) same as B; G) same as A

Results

CEAP classification

All 310 lower limbs were classified according to CEAP classification:

C0: 13 (4.2%)

C1: 15 (4.8%)

C2: 108 (34.8%)

C3: 44 (14.2%)

C4: 35 (11.3%)

C5: 19 (6.2%)

C6: 76 (24.5%)

Venous filling index. Figure 2 shows a curve with a growth tendency in VFI values in higher classes of the CEAP clinical classification. In intraclass analyses, VFI values were statistically different (Kruskal-Wallys test, $p < 0.0000$). Intraclass analysis also showed a tendency of higher data variation (box sizes) proportional to venous disease severity, considering that variances between CEAP clinical classes are statistically different between themselves, confirmed by Bartlett test for variance homogeneity ($p < 0.0000$).

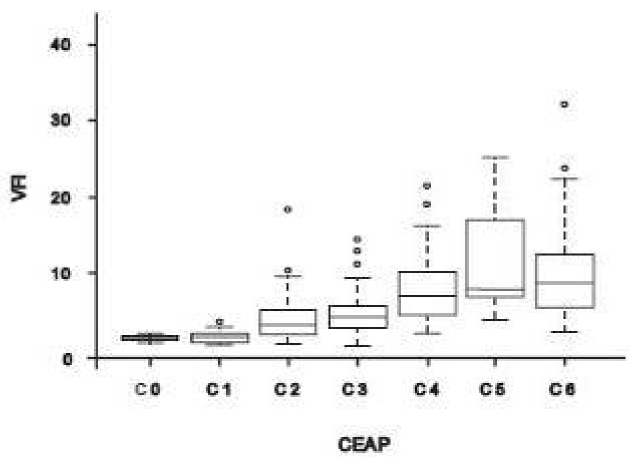


Figure 2 - Box diagram of venous filling index evolution as to CEAP classification

Venous volume. Figure 3 shows the growth tendency of VV values proportional to clinical severity, which is lower than that observed for VFI, but significant according to the Kruskal-Wallis test ($p < 0.0000$). Data variation (box size in the box chart) also had a slight tendency to increase proportionally to CEAP increase, considering that variation between CEAP classes were statistically different between themselves according to Bartlett test for variance homogeneity ($p < 0.0000$).

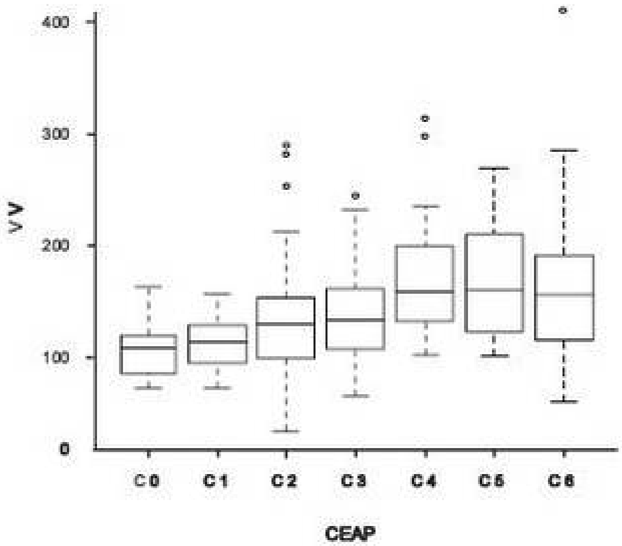


Figure 3 - Box chart of venous volume evolution as to CEAP clinical classification

Ejection fraction. Figure 4 shows the tendency of median EF values to remain constant with CEAP classification. Such tendency was confirmed by the non-significant result of the Kruskal-Wallis test, which does not indicate any difference between EF values in CEAP clinical classes ($p = 0.4177$).

Residual volume fraction. Figure 4 shows that there were no variations in median values and in RVF variability as to CEAP clinical classification. Differences in RVF variances as to CEAP classification were not significant according to Bartlett test ($p = 0.3595$), and the same occurred to the parameter values of RVF distribution location, whose differences were not statistically significant by the Kruskal-Wallis test ($p = 0.519$).

Figure 4 shows the comparison of air plethysmography parameter data (VFI, VV, EF and RVF) and the evolution of hemodynamic variability between CEAP clinical classes.

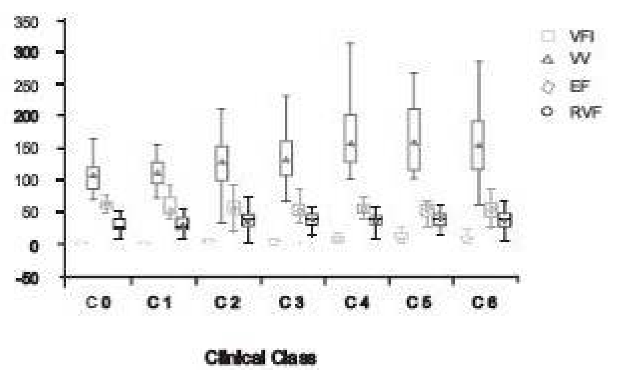


Figure 4 - Box chart showing evolution of venous filling index, venous volume, ejection fraction and residual volume fraction as to CEAP clinical classification (VFI = mL/s, VV= mL, EF = %, RVF = %)

We also analyzed the variation coefficient (VC) of each plethysmographic parameter. VC was obtained by the relation between standard deviation and mean of each parameter, multiplied by

100. Thus, an objective measurement of data variability can be obtained in each CEAP clinical class and for each parameter analyzed.

Figure 5 shows VC values for VFI, VV, EF and RVF measurements according to CEAP classification. VFI and VV had a quite similar VC in normal individuals (C0); however, as the disease became more severe (CEAP classification worsened), VFI VC increased up to 70% for CEAP C2. Such increase represents more than 200% in relation to CEAP clinical class C0. (For variables VV and EF there was also a small variation in VC as the CEAP classification increased, which was a discrete increase when compared with VFI. RVF VC remained the same between C0 and C3, falling a little in C4 and rising again for C5 and C6, but not being higher than the values for C0).

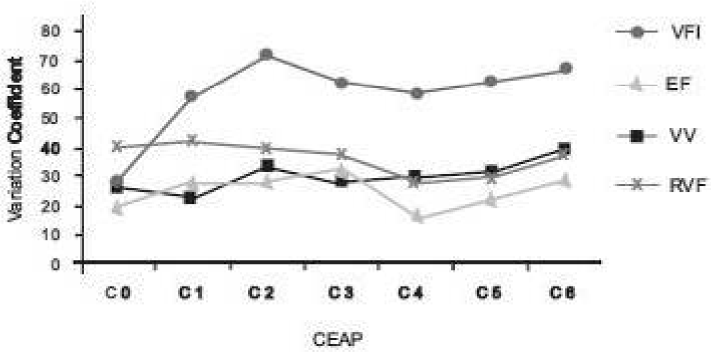


Figure 5 - Evolution of variation coefficient between CEAP clinical classes

Discussion

Despite CEAP classification being the most widely used for clinical classification of chronic venous insufficiency, it is still subject to criticisms because it does not answer all doubts by clinicians or surgeons.[15] It can have large interrater variability, requiring parameters that better standardize such situation, creating space for assessment through other complementary examinations.

Use of color-flow Doppler ultrasound has limitations of hemodynamic evaluation pertinent to that method.[16] After introduction of air plethysmography, VFI proved to be the plethysmographic parameter that best expresses clinical severity of chronic venous insufficiency.[11,17,18] Thus, this study is important to test possibilities of practical use of air plethysmography.

However, we can see in the present study a large variability of plethysmographic parameters, especially VFI, in all CEAP clinical classes when compared with CEAP clinical class C0 (Figures 2 and 5). VC, which was 28.12% in clinical class C0, went to 70% in clinical class C2, which had the highest VC, probably because it had the largest sample. This can make the association between VFI and disease severity difficult, since in this study we verified lower limbs of clinical class C2 with VFI similar to lower limbs of clinical class C6, and the opposite was also true.

Such variability is also seen in box charts (Figures 1 and 2), in which increase in box sizes and overlapping of plethysmographic values between several CEAP clinical classes demonstrated a large variability of VFI and VV values, since the box represents the distances between the first and the third quartile of the normal distribution curve.

There are still doubts as to factors and consequences of VFI variability in chronic venous insufficiency. There may be compensatory mechanisms to avoid formation of leg ulcers in lower limbs with varicose veins.[17,19] Such mechanisms can range from proper lymphatic drainage to efficient fibrinolytic activity, removing excess of extravascular fluid and fibrin deposits.[20] Another hypothesis is that the condition of high VFI is not present for a sufficient amount of time to cause skin lesions of chronic venous insufficiency.[21] But the causes of that large hemodynamic variability can be attributed to the examiner, patient, environment in which the examination is performed and to variability of venous disease.[22] Therefore, we believe proper examiner training, adequate patient collaboration, patient's age and control of room temperature are essential to standardize air plethysmography. Of those factors, patient collaboration is very important to determine EF and VFR, since these are dependent on muscle strength (plantar flexion). Thus, VFI and VV parameters are the most reliable in air plethysmography, since they depend less on patient collaboration.

Considering that VFI is an adequate plethysmographic parameter to classify severity of venous disease,[21] we have seen in this study that there is a considerable number of lower limbs that probably have higher risk than others of developing chronic venous insufficiency and ulcers. That index may suggest which patient, within the same clinical class, should be prioritized for surgical treatment of lower limb varicose veins before there are any complications.

When a given clinical class is studied, it can be observed that the mean obtained from plethysmographic values is little influenced by extreme values, and these are not good parameters for evaluation of variability.[23] Our study detected the following VFI extreme values: zero individuals in C0, one individual in C1, two in C2, three in C3, two in C4, zero in C5 and three in C6 (Figure 2). This justifies use of VC to make variability data of air plethysmography more understandable.

VC was not able to distinguish CEAP clinical classes C2 to C6 as independent groups, but VFI was the parameter with the highest variation, which makes it more reliable in the plethysmographic assessment of venous insufficiency.

It is worth remembering that air plethysmography can also provide data as to use of compressive measurements in the treatment of varicose disease[7,24,25] and even provide subsides for the prognosis of lower limb varicose vein surgery.[26,27]

Conclusions

Based on obtained data, we can conclude that VFI was the best plethysmographic parameter to assess patients with chronic venous insufficiency and has large hemodynamic variability in several CEAP clinical classes. Therefore, it can be said that, using air plethysmography, there are patients with more or less severity in the same CEAP clinical class, and these parameters can be used to prioritize lower limbs for surgery to repair chronic venous insufficiency of the lower limbs. This may imply that VFI is the prognostic factor for evolution of chronic venous insufficiency.

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This study is part of the master's thesis presented at Universidade Federal de São Paulo to obtain the title of Master in Vascular Surgery in the Graduate Program in Vascular, Cardiac, Thoracic Surgery and Anesthesiology, UNIFESP-EPM, São Paulo, SP, Brazil.

Manuscript received August 20, 2007, accepted November 21, 2007.