Noninvasive diagnostic methods to evaluate venous insufficiency of the lower limbs

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J Vasc Bras. 2007;6(3):266-75.

ABSTRACT

Clinical evaluation of lower limbs of patients with venous insufficiency alone may not identify involved systems or anatomical sites, thus complementary tests are needed. These tests can be invasive or noninvasive. Invasive tests, such as phlebography and ambulatory venous pressure, despite being accurate, may produce discomfort and complications. Some of the most used noninvasive tests are continuous wave Doppler ultrasound, photoplethysmography, air plethysmography and duplex scanning. Doppler ultrasound assesses blood flow velocity indirectly. Photoplethysmography assesses venous refilling time, providing an objective parameter of venous reflux quantification. Air plethysmography allows quantification of reduction in venous capacitance, reflux and performance of the calf muscle pump. Duplex is considered a gold standard among noninvasive methods, because it allows quantitative and qualitative evaluation, supplying anatomical and functional information, thus providing a more complete and detailed evaluation of both deep and superficial venous system.

Keywords: Diagnosis, venous insufficiency, ultrasonics, plethysmography.

RESUMO

A avaliação clínica dos membros inferiores na insuficiência venosa por si só não identifica os sistemas envolvidos ou os níveis anatômicos, sendo necessários exames complementares. Esses

exames podem ser invasivos ou não-invasivos. Os invasivos, como flebografia e pressão venosa ambulatória, apesar de terem boa acurácia, trazem desconforto e complicações. Dentre os não-invasivos, destacam-se: Doppler ultra-som de ondas contínuas, fotopletismografia, pletismografia a ar e mapeamento dúplex. O Doppler ultra-som avalia a velocidade do fluxo sangüíneo de maneira indireta. A fotopletismografia avalia o tempo de reenchimento venoso, fornecendo um parâmetro objetivo de quantificação do refluxo venoso. A pletismografia a ar permite quantificar a redução ou não da capacitância, o refluxo e o desempenho da bomba muscular da panturrilha. O dúplex é considerado padrão-ouro dentre os não-invasivos, porque permite uma avaliação quantitativa e qualitativa, fornecendo informações anatômicas e funcionais, dando avaliação mais completa e detalhada dos sistemas venosos profundo e superficial.

Palavras-chave: Diagnóstico, insuficiência venosa, ultra-som, pletismografia.

Venous insufficiency

Chronic venous insufficiency (CVI) can be defined as a set of alterations that occur in the skin and subcutaneous tissue, especially in lower limbs, resulting from a long-term venous hypertension caused by valve insufficiency and/or venous obstruction.[1]

In 1994, at the American Venous Forum held in Maui (Hawaii, USA), the CEAP classification of venous diseases was developed, based on clinical signs (C), etiology (E), anatomical distribution (A) and pathophysiologic dysfunction (P).[2] It is considered as the standard classification and allows uniformity in report and assessment of different modalities of diagnostic and treatment. In 2004, a modification to that classification was proposed, with the aim of enhancing it.[3] The changes regarding what is called CVI are those included in clinical classes 2 to 6 of CEAP classification.[2]

CVI is a very common disease and, although having mortality rate close to zero, it has important morbidity, leading to worsening of quality of life and has a large socioeconomic impact, including in our country.[1]

In an epidemiologic study carried out in Brazil by Maffei et al.[4] including patients who sought treatment at a Health Center in Botucatu (SP) for routine examinations, there was a 47.6% prevalence of varicose veins. After statistical correction, estimated prevalence for the population in the same socioeconomic level in that municipality was 35.5%, excluding cases of complaints regarding lower limbs.

González-Fajardo et al.[5] mention a study sponsored by the World Health Organization (WHO) in Spain, in which there was a 10.5% prevalence of lower limb venous diseases in a sample of 4,800 people aged between 30-65 years.

Barros Jr.[6] performed a study in pregnant patients at the prenatal care of Hospital Amparo Maternal, with the aim of analyzing prevalence of varicose disease, risk factors and symptoms during pregnancy. The study showed a high prevalence of varicose disease (72.7%), and the most prevalent risk factors were age and positive family history for varicose veins.

Scuderi et al.[7] assessed the clinical findings of venous diseases in 2,104 individuals, according to code C of CEAP classification. Individuals were classified as to gender and age, and women according to number of pregnancies. In the age group between 14 and 22 years, 46.42% had no

apparent symptoms or veins, whereas in the age group over 48 years only 4.67% had that condition. Most women (62.79%) had apparent symptoms and veins, whereas most men (65.54%) did not have apparent symptoms or veins. The authors concluded that prevalence is much higher in females than in males and that age and number of pregnancies were important factors in disease development.

Venous diseases have peculiar characteristics, since some of them, with superficial changes, can be perceived by patients themselves; however, other changes involving the deep venous system (DVS) in early stages frequently do not cause signs or symptoms that reveal its presence.[8]

Clinical assessment of individuals with venous insufficiency of the lower limbs, despite being important, does not independently identify affected systems or anatomic levels.[9,10] Ulcers caused by CVI can result from obstruction or reflux in the DVS, reflux in superficial system veins and in perforating veins, or from a combination of both.

To have a more detailed and accurate assessment, besides clinical examination, complementary examinations should be applied, which can use invasive or noninvasive tests or methods.

Invasive tests that have been used are phlebography and direct measurement of ambulatory venous pressure (AVP) by puncturing a vein on the back of the foot. Phlebography, which has been considered the gold standard method, allows visualization of the venous system and identifies morphological and functional alterations.[9,11] With that it is possible to obtain important anatomic and pathophysiologic information not only for diagnosis, but also for choosing surgical or endovascular techniques for CVI repair. AVP performs a global assessment of CVI, but does not identify whether changes are caused by obstruction or reflux in the DVS.[11] Phlebography and AVP, because they are both invasive, can bring discomfort and complications to patients. Therefore, such tests have low acceptance and their repetition is hard for patient follow-up or assessment of therapies for CVI.

With the aim of performing a noninvasive and reliable diagnosis, throughout the last decades of the past century, some noninvasive methods were developed to assess venous function in patients with venous insufficiency, such as continuous-wave Doppler ultrasound (CWD), photoplethysmography (PPG), air plethysmography (APG) and duplex scanning (DS), among others.[2,8,11-14]

Noninvasive tests are more economical, fast and do not bring much discomfort to patients when compared with invasive tests.[15]

Next, the main noninvasive methods and their capacities for CVI diagnosis are described.

Continuous-wave Doppler ultrasound

CWD was developed by Satomura & Kaneko in 1960.[16] It assesses arterial or venous blood flow velocity by detecting change or variation in frequency of reflected ultrasound beam based on moving red cells. The instrument produces an audible sound signal or a waveform that can be registered. Normal standard of venous flow is a spontaneous and phasic sound with breathing. It is audible with Doppler probe in all locations, except in superficial and small-caliber veins.[17]

The main advantages of CWD are its low cost, easy transportation and possibility of repeating the examination as many times as necessary. Its disadvantages are technique subjectivity, which demands much training time to make the examiner able to perform it accurately.[17,18] Since it is a

qualitative and non-quantitative method, when the follow-up is not performed by the same professional, assessment is even more difficult.[19-22]

Lucas et al.[23] assessed 210 lower limbs by auscultation of the great saphenous vein using Doppler during Trendelenburg maneuver. In 10 limbs with primary varicose veins, phlebography examinations were also performed, with the aim of comparing results, and the correlation was observed in all cases. One hundred lower limbs that had primary varicose veins were classified according to varicose vein extension and caliber; the other 100 lower limbs did not present clinically detectable varicose veins. The authors observed great saphenous vein insufficiency in 57.3% of 89 limbs with bilateral primary varicose veins and 18.18% in 11 normal limbs of patients with unilateral varicose veins. With regard to the 100 limbs without varicose veins, 2% had saphenous vein insufficiency on examination.

Bartolo et al.[24] studied 9,178 lower limbs and assessed venous pressure using CWD. They verified that venous pressure values at rest gradually increased from normal limbs to varicose limbs, reaching higher levels in patients with postphlebitic syndrome.

Menezes & Sales[19] assessed 96 lower limbs of 50 patients with venous insufficiency using CWD. They verified presence of changes in DVS in 14 patients (28%), three of whom had bilateral lesions, in a total of 17 limbs with alterations (17.7% of 96 limbs). Reflux was present in 9.37% of limbs, and was associated with presence of clinical complications of varicose veins; obstruction in 8.33% was not associated with a more severe clinical status.

Cheng et al.[25] used CWD and PPG to assess 1,583 limbs of 878 patients who presented CVI symptoms. Combination of valve insufficiency in superficial and perforating systems was found in most patients. The authors considered that the results of applied examinations were useful for patient assessment.

A study carried out at the laboratory of Hospital das Clínicas da Faculdade de Medicina de Botucatu (FMB) assessed 71 lower limbs of 50 patients with varicose veins and/or CVI using CWD compared with DS to assess venous reflux or valve incompetence.[26] Results were: sensitivity of 71 and 78%, specificity of 87 and 81% and accuracy of 84 and 79%, respectively, for popliteal and great saphenous veins.

Based on what has been described, CWD can be used in angiologists' and vascular surgeons' daily practice as an instrument to complement clinical examination of patients with venous insufficiency, allowing to select those who should be referred for more accurate diagnostic tests, such as DS. Therefore, CWD, when used by experienced examiners, may provide important information about presence of venous reflux.

Photoplethysmography

PPG, introduced in venous hemodynamic studies by Barnes et al.,[27] is a method to assess venous function that can be easily performed, does not require extensive training for the operator and evaluates venous filling time (VFT), providing an objective parameter to quantify venous reflux.[28] It is used in some services to diagnose venous diseases of the lower limbs and follow-up of candidates to varicose vein surgery before and after the surgery.[6,28-34]

Absolute values found in PPG examinations before and after the surgery are useful and objective quantitative measurements to verify change in venous hemodynamics resulting from varicose vein surgery. They allow verification of whether varicose vein surgery improved or not the patient's limb

hemodynamics.[28]

VFT is measured and registered in a curve based on a baseline. VFT value is an indirect measurement of venous reflux and valve incompetence.[35] Many researchers used PPG to assess venous disease of the lower limbs[31,34,36-39] and postoperative follow-up, with the aim of verifying surgical efficacy.[25,40-44] Most authors consider VFT values greater then 20 s as normal, such as Gaitini et al.,[45] Evangelista & Fonseca,[28] Sakurai et al.[33] and Welch et al.[11] Other researchers, such as Sanches & Gomes,[32] Gonzáles-Fajardo[6] and Lane et al.,[44] consider values above 23 s as normal.

In cases of venous system filling through incompetent valves (reflux), there is an abnormally fast return of the examination curve to the initial baseline.[35] PPG is useful to assess superficial venous system reflux in patients with normal DVS, since it does not assess well the degree of reflux in the DVS.[46]

This examination can also be performed by placing tourniquets or automatic pressure cuffs attached to the device, in a position that prevents reflux of the superficial venous system (short and great saphenous veins), obtaining predictive values for reduction in reflux with venous surgery in the superficial system.[46,47] Reflux measurement is based on venous emptying caused by calf contractions due to exercises, and it can be affected by the following factors:

-Obstructions in deep veins can prevent adequate calf emptying, which can cause a reduced filling time and will be interpreted as reflux.

-Patient's inability to perform the movements with his feet in the right position (neurological problems, arthritis, anchylosis, etc.) prevents adequate calf emptying, which will cause a reduced filling time, which can be interpreted as reflux.

-Patients with high levels of exercise-induced hyperemia will have a faster VFT, which may seem as reflux.[47]

Sarin et al.[30] compared PPG examination curves with clinical evaluation and with DS in patients with venous insufficiency and found a good correlation in observed results. Patients with severe venous insufficiency invariably had quite altered VFT data, and this assessment parameter was considered reliable.

Sanches & Gomes,[32] in 1991, studied 35 lower limbs of 18 individuals without previous history of venous disease, with the aim of establishing a clinical routine for the PPG examination. Stages were established according to VFT value, thus allowing estimate of venous sectors. Values ≥ 23 s were considered normal. The authors concluded that an elaborate clinical routine allows diagnosis of valve insufficiency when one or more segments are affected.

Tucker et al.[38] performed a study with PPG to assess normal patients, patients who had leg pain, with or without CVI. The method proved to be quite reproducible.

Dunn et al.[41] applied PPG to assess six patients submitted to valve transplantation of lower limbs before and after the surgery. Such patients had altered VFT (< 20 s) and, after the surgery, there was improvement in VFT of 100% or more.

Rodriguez et al.[43] used PPG in patients with venous ulcers of the lower limbs before and after external valvuloplasty. There was a significant increase in VFT after the surgery, when the ulcer was healed, between 18 and 35 days.

Froneck et al.,[39] in 2000, proposed a modification in the conventional technique of PPG, allowing to quantify drained blood flow induced by elevation of the lower limb above heart level, affecting hydrostatic pressure on the leg. When a plateau is reached in the graphic register, the limb is quickly lowered and left at a resting position, thus causing venous filling due to increased hydrostatic pressure. The authors concluded that this technique allowed assessment of presence or absence of deep venous thrombosis and valve insufficiency of the DVS.

PPG has been used as a follow-up method in many vascular laboratories because VFT is a sensitive indicator of reflux, but PPG is unable to distinguish degrees of clinical severity of the disease.[48]

Scriven et al.,[31] in a prospective longitudinal study, performed PPG examinations before and 30 days after the surgery to evaluate efficacy of perforating vein surgery. Seven ulcerated members with perforating and deep vein insufficiency were submitted to surgery. The authors observed that PPG showed abnormalities of venous reflux of the lower limbs before the surgery, which persisted after the surgeries, suggesting that perforating vein surgery alone does not adequately treat patients with lower limb ulcers and who have simultaneous deep vein insufficiency.

Based on what has been presented above, PPG is still being used and has proved to be a useful method for CVI assessment, as well as for assessment of surgical techniques or other procedures to treat venous insufficiency.

Air plethysmography

APG is a relatively new noninvasive method, used for quantitative assessment of the venous system of lower limbs and arterial perfusion[49] and that allows quantifying reduction or not of venous capacitance, and calf muscle pump reflux and performance.[50] APG devices perform such quantification by determining the following parameters: venous volume (VV), ejected volume by a *tiptoe* (EV), mean residual volume (RV) and filling time until reaching 90% of VV (VFT90). Based on those parameters, the following indexes are calculated: venous filling index (VFI), ejection fraction (EF) and residual volume fraction (RVF).

As advantages, this is an examination whose equipment and maintenance are not very expensive, it is less examiner-dependent, easier to be performed and, although it does not provide anatomic information as precisely as DS, it allows patient follow-up to evaluate performed treatment.[51,52]

Christopoulos et al.[53] compared APG with outpatient venous pressure measurement in a study to evaluate the effect of wearing medium and high compression stockings , respectively, for patients with superficial and deep venous insufficiency. The authors verified APG reproducibility and concluded that it is not only a method of diagnostic value, but also allowed evaluation of hemodynamic effects of different forms of elastic compression.

In another study, Christopoulos et al.[54] observed a good correlation ($r = 0.81$) of APG parameters with outpatient venous pressure measurement, analyzing 30 normal limbs, 110 with primary varicose veins and 65 with DVS occlusion of insufficiency. They concluded that APG is an accurate method to identify predominant hemodynamic factor (alteration of calf muscle pump and reflux or both), responsible for the patient's clinical status.

APG is also used to monitor outcomes of venous surgeries. Christopoulos et al.[55] evaluated the outcomes of surgeries in 42 limbs of 33 patients with primary varicose veins before and after the surgery between 8 and 10 days using APG. Control of venous reflux was observed in all patients, and the authors concluded that the method was objective and of great diagnostic value.

Gillespie et al.[56] also used APG to assess 25 lower limbs before and after varicose vein surgery, defined according to clinical examinations and DS. The method proved to be efficacious in the assessment of hemodynamic changes, especially regarding VFI and VV.

Studies have been performed with the aim of verifying correlation of APG and DS and phlebography.[11,13,14,57] Van Bemmelen et al.[13] assessed 32 lower limbs of 28 patients and obtained poor correlation between VFI findings of APG and presence of insufficient veins and their diameters measured by DS. However, Weingarten et al.[14] obtained good results with APG in the assessment of 122 limbs of 61 patients with different degrees of venous insufficiency, with statistically significant correlation between VFI of APG and reflux time determined by DS.

Welch et al.[11] concluded, in a study in 28 upper limbs, that APG, when compared with phlebography, was able to detect presence of venous insufficiency, but it was not able to distinguish severity degrees of the disease. Kalodiki et al.,[58] in a retrospective study in 224 limbs that had suggestive signs of deep venous thrombosis and 41 limbs without varicose veins and no evidence of DVT in venography, compared APG with the gold standard (phlebography) and observed that there was no difference between both methods.

Yang et al.[59] tested variability of APG parameters in patients with CVI by repeating examinations in patients at different times and observed that there were variations in determinations that were repeated in the same patient. According to those authors, this result suggests that APG is not likely to be able to detect small variations in evaluated parameters.

In our country, Engelhorn et al.,[60] in a study in 88 limbs of 48 patients, aimed at determining which APG parameters allowed differentiation of mild, moderate and severe CVI classes, according to CEAP clinical classification. The patients were divided into three groups: group A – mild venous insufficiency (classes 1 and 2); group B – moderate venous insufficiency (class 3); and group C – severe venous insufficiency (classes 4, 5 and 6). There was no statistically significant difference between mild and moderate CVI degrees, but there was difference between group C, when compared with groups A and B.

Seidel[61] studied 100 limbs of 81 patients to correlate APG examinations with clinical findings and with color-flow DS in the diagnosis of great saphenous vein insufficiency. It was not possible to assess APG correlation with clinical status, since most (61%) patients belonged to CEAP class 2. Correlation of APG results with DS was very weak.

Therefore, it could be seen that most studies using APG have shown that it is useful to assess CVI, despite some authors[13,59] still questioning its validity, since APG has not been a method able to identify small differences.

Duplex scan

DS is a combination of B-mode ultrasonography (US) and pulsed Doppler, thus allowing a simultaneous assessment of a bidimensional image of vessels and adjacent tissues and of flow characteristics through analysis of Doppler spectral curve.[62]

B-mode image is used for anatomic assessment of presence of intraluminal thrombus or changes in venous wall and valves, and pulsed Doppler allows detection of presence of reflux due to valve incompetence.[26] In lower limb varicose veins, DS examination allows assessment of changes in the DVS, superficial venous system and perforating veins. Thus, it allows differentiating patients with primary or essential varicose veins, whose alterations predominantly occur in the superficial venous

system, from patients with secondary varicose veins, in which the DVS is the site of pathological alterations. This diagnostic test has a potential of assessing both venous anatomy and physiology.[62]

In the color-flow DS, static tissues are shown in a gray scale, whereas the Doppler effect is codified in colors. Codification of flow colors, red or blue, is dependent on flow direction in relation to sound beam orientation.[17] This resource facilitates US examination, since it allows better vessel visualization, especially those of smaller diameter, making this examination faster.

DS has been considered an examination with similar accuracy to phlebography in the identification of venous reflux produced by valve insufficiency of the deep and superficial system and perforating veins or a combination of them.[57] It can also detect small refluxes in isolated segments in asymptomatic patients, and also whether the reflux is located in veins above or below the knee or whether it extends through the whole limb. In the absence of deep venous obstruction, limbs with reflux restricted to veins above the knee rarely develop skin alterations or ulcers. The standard of reflux involving at least two venous systems (superficial and deep; superficial and perforating; superficial, perforating and deep) is found in around 2/3 of patients with skin alterations or ulcers.[63] DS has been considered not only the most specific noninvasive examination, but also the most widely accepted by patients.

Neglen & Raju[64] assessed reflux in 56 limbs of patients with venous insufficiency using DS compared with phlebography. DS positive predictive value was 77%, compared with 35-44% of descending phlebography, which confirms better accuracy of the former. Baker et al.[65] compared the findings of reflux obtained by DS and ascending phlebography and concluded that DS was more sensitive to detect superficial and deep venous reflux and, at the thigh level, also allowed assessment of isolated segments with reflux, as well as great saphenous vein reflux.

Delis et al.[66] used DS for hemodynamic assessment of perforating veins in venous insufficiency of the lower limbs. Results of the examinations were related to CEAP classification levels. The authors claimed that neither perforating vein diameter, nor reflux time and other hemodynamic parameters investigated had correlation with CEAP classes, which indicates that severity of venous insufficiency does not primarily depend on perforating vein function alone, but on multiple factors, occurring simultaneously in the venous system.

Engelhorn et al.,[60] in a retrospective study in 500 limbs of 301 patients with primary varicose veins, performed DS examinations before the surgery, with the aim of analyzing a new classification of superficial venous insufficiency. The authors stressed the importance of standardizing the classification of superficial venous insufficiency for surgical planning, avoiding possible recurrences or unnecessary stripping of great saphenous veins.

DS is considered as the gold standard among noninvasive examinations, because it allows identifying and locating pathophysiological alterations, obstructions or refluxes, both in the DVS and in the superficial venous system. Over the past years, it has replaced phlebography in many of its indications.[62] However, it requires much time, is examiner-dependent, needs more training time and has a high cost, since the equipment is more sophisticated and its maintenance is more expensive. For that reason, its use for long-term follow-up of patients with CVI is difficult, especially if follow-up examinations should be performed frequently.

Final considerations

Any noninvasive diagnostic test performed independently allows a complete assessment of all

anatomic and functional parameters that should be considered in venous insufficiency of the lower limbs.

DS, which is considered the gold standard among noninvasive diagnostic methods for venous diseases of the lower limbs, is currently the most widely indicated because it allows qualitative and quantitative assessment. It provides both anatomic and functional information, thus allowing a more complete and detailed assessment of the venous system.

In cases in which it is not possible to perform DS, due to device inexistence or financial restrictions, practitioners should use PPG or APG to help diagnosis and follow-up of patients with venous disease. Such plethysmographies are a quite useful method to assess venous disease, as well as in the follow-up of lower limb surgeries.

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Manuscript received November 9, 2006, accepted June 14, 2007.