Bioimpedance spectroscopy in haemodynamic analysis

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Abstract. Venous insufficiency is estimated to affect between 10% and 35% of the population in the US with symptoms ranging from mild discomfort to chronic ulceration which may reduce quality of life. Early diagnosis is the key to pre-emptive treatment. We have previously reported [5] an impedance technique for measurement of calf muscle pump function although it was noted that the results could be confounded by change in limb geometry during the exercise protocol. We report here a modified protocol to account for change in limb geometry. Impedance of a 20 cm segment of the calf was continuously recorded using an SFB7 bioimpedance spectrometer whilst subjects performed a sequence of manoeuvres: a) supine with leg raised (for 10 min); b) standing (4 s); c) plantar flexion (tiptoe, 4 s); d) standing elevated on one leg removing tension on the measured leg with the foot horizontal (4 s); e) with the leg relaxed (4 s) and then the sequence repeated. The impedance ratio, k = (e-d)/(c-b), was the proportion of the impedance change, occurring during calf muscle pumping, due primarily to change in limb shape only, i.e. independent of the impedance change due to ejection of blood as a function of calf muscle pump action. Thus (1-k) can be used to correct the ejection fraction (%) calculated as (c-b)/(a-b)*100 for the confounding effect of change in limb geometry. Ejection fractions calculated by this method in 10 control subjects were 51.5 ± 30.1% with no values greater than 100% as found previously.

1. Introduction
Disorders of the peripheral vascular system are commonplace. Venous insufficiency is estimated to affect between 10% and 35% of the population in the US. Poor venous drainage results in venous hypertension, increased transmural pressure with consequent oedema that frequently leads to inflammation, infection and ulceration. Symptoms range from varicose veins, which are present in approximately 30% of adult women and 20% of adult men, to chronic ulceration, with a prevalence of ~1% [1]. These may result from deep vein thrombosis (DVT) which affects approximately 84 in every 100,000 adults [2]. The direct costs of venous disorders have been estimated at over $1 billion for the Unites States alone [3].

Since the venous system contains approximately 70% of the total blood volume, any alteration to the capacity or efficacy of the venous system can affect venous return and cardiac output which should be the same under steady state conditions. The compliance of deep veins of the legs is controlled by the surrounding skeletal muscles since the deep veins have little sympathetic innervation [4]. Venous valves, present in leg veins, assisted by the massaging effect of the calf muscle pump on the veins, ensure that there is a flow of blood towards the heart and reflux is prevented when changing posture from the supine position to standing. The action of the calf muscle pump (CMP) has been implicated as a critical “anti-oedema” mechanism by enhancing fluid flow to the lymphatics thereby decreasing tissue fluid pressures [4]. A deficient calf muscle pump has also been identified as probably the key factor in venous insufficiency in the elderly [1].

Various methods for haemodynamic analysis exist including, ambulatory venous pressure measurements (AVP), photoplethysmography, air plethysmography (APG), ambulatory strain gauge plethysmography (SPG), foot volumetry, continuous-wave Doppler or duplex scanning ultrasound and impedance plethysmography (IPG) with the latter having been identified as a potential criterion diagnostic method for DVT [2]. In the present study, we measured CMP activity by an IPG technique during a calf muscle pumping protocol modified from that used in APG and SPG.
2. Materials and methods

2.1. Principle of the method

In the normal upright posture, despite the venous return of the circulatory system, blood tends to pool in feet and lower portions of the leg due to gravity. When a supine position is assumed with the foot and lower leg elevated above the level of the heart (> 20 cm height difference), the blood is drained from the limb and attains a minimum volume (mv) after about 10 min. When the upright posture, without weight-bearing, is reassumed, blood volume rapidly achieves a maximum (MV) due to venous filling. The difference (MV-mv) represents the functional venous volume (VV). If the subject now undertakes a tip-toe manoeuvre, calf muscle contraction activates the muscle pump, ejecting blood from the lower leg, i.e. the ejected volume (EV). These volume changes can be measured as changes in impedance of the lower leg. However, the measured impedance is not solely a function of volume change but also the shape change of the calf associated with muscle contraction, confounding the measurements and potentially contributing to anomalous results noted previously [5] where the ejected volume exceeded the functional volume, i.e. EV > VV, in some subjects. We hypothesised that this shape change could be simulated under non-contracting muscle conditions (no CMP activity) by the relaxed leg with an unsupported downward hanging foot. Measurement of impedance under these conditions would approximate that due to geometric change alone and could be used to correct the impedance measured during the tip-toe manoeuvre.

2.2. Experimental

2.2.1. Subjects

Ten self-reported healthy volunteers (7 males and 3 females) with body mass indices (BMI) ranging from 21 to 28 kg/m² participated.

2.2.2. Impedance measurements

Impedance, deconvoluted into its components of resistance and reactance, was measured using an ImpediMed SFB7 impedance analyser modified to record impedance at a sampling rate of one reading per ms at a frequency of 5 kHz.

2.2.3. Protocol

Subjects were weighed and their height measured. While standing upright, the point of maximal calf circumference was determined and measured. Points 10 cm either side of this mid-point along the mid-line of the calf were located, the circumferences measured and sense electrodes (Ag-AgCl gel) applied. Current drive electrodes were located at the base of the fingers and toes. All measurements were performed on the right side. The subject reclined supine for 10 min with the foot raised 40 cm above heart level, supported on a box. Impedance was continuously recorded for 10 s after 1 min and 5 min recumbency and 10 seconds immediately before standing. After 10 min, the subject stood, initially taking their weight on the left foot and stabilising themselves with a walking frame until weight was evenly distributed on both feet. Measurement continued during attainment of the upright position and for a further 20 s after the stable standing position was achieved. The subject remained standing for 4 min and with impedance measurements again being made while the subject remained standing for 10 s and during tip-toe movements at approximately 2 s intervals. Measurements were performed in triplicate. The subject then stood on a box, again taking their weight on the left foot and supported on by the walking frame. The right leg was held horizontal for 5 s and then allowed to hang fully relaxed for 4 s over the side of the box whilst measurements were made. Measurements were made in triplicate at 5 s intervals.

2.2.4. Data analysis

Resistance data were processed through a Butterworth filter and plotted against time of measurement. The mean resistance was determined during: a) lying supine with leg raised; b) standing; c) plantar flexion (tiptoe); d) standing elevated on the opposite leg, thereby removing tension on the measured leg, with the foot horizontal and e) with the leg relaxed and foot hanging. VV is represented by (a-b) whilst (c-b) is the resistance change due to change in blood volume and segment...
shape. This was corrected for the proportion of the impedance change due primarily to change in limb shape only by the impedance ratio, \( k = (e-d)/(c-b) \). The volume of ejected blood (EV) may be calculated according to the well known Nyboer equation:

\[
EV = \frac{-\rho_b L^3 \Delta R}{R_0^2}
\]  

(1)

where \( \rho_b \) is the resistivity of blood (150 ohm.cm [6]); \( L \) is the length of the segment; \( \Delta R \) is the change in resistance related to the change in blood volume; \( R_0 \) is the resistance of the calf segment before the tip-toe manoeuvre. The volume (V) of the leg segment being measured was calculated from the measured circumferences using the equation for a truncated cone assuming that the calf was best represented by two opposed cones [5].

3. Results

A typical time course profile for the change in resistance of the calf is presented in Figure 1. Resistance decreased (i.e., volume increased due to venous filling) as the subject transfered from recumbency with the leg elevated to the fully upright standing position with the weight evenly distributed on both feet. Resistance increased with each tiptoe movement as CMP activity pumped blood from the calf. The resistance change during this manoeuvre was presumed to include a contribution due to geometric change estimated from the shape change occurring in the relaxed unsupported leg (figure 1 d).

![Figure 1](image)

**Figure 1.** Time course change in resistance (R, ohm) from supine (a) to standing (b), during tiptoe movements (c) and when the foot is relaxed and unsupported while standing (d). VV is the difference between the maximum and the minimum volumes. “EV” is the difference between the maximum volume and the mean volume of the tiptoe movements with the contribution due to shape change of the calf (d). Corrected EV = “EV” – “Geometry”.

Impedance profiles were reproducible within subjects, coefficients of variation for replicate measurements within subjects ranged from 1 to 5 %. Profiles were similar between subjects but varied in magnitude, e.g., supine impedance varied from 49 to 70 ohm, and were correlated with calf volume \( r = 0.7 \). Calculated CMP haemodynamic parameters, corrected for geometric change, are presented in Table 1. The maximum EF observed for any subject in any trial was 87%.
Table 1. Haemodynamic parameters (mean ± SD, n = 10) calculated from impedance measurements of the calf. Ejected volume data are corrected for changes in limb geometry.

| Venous volume (ml) | Ejected volume (ml) | Ejected fraction (%) | Ejected volume per 100 ml tissue (ml) |
|--------------------|---------------------|----------------------|--------------------------------------|
| 191.2 ± 56.1       | 93.7 ± 52.3         | 51.5 ± 30.1          | 4.1 ± 1.7                            |

4. Discussion
The quantitative measurement of CMP activity is notoriously difficult [2] and there are relatively few published data. Nevertheless, the ejection volumes and fractions are similar to those obtained by others using methods such as APG [7] and ejection volume per unit volume of tissue fall within the range expected for healthy subjects.

Change in limb shape and geometry are recognized to affect haemodynamic measurements. In an attempt to overcome these problems, measurement at the ankle rather than at the calf has been proposed [5]. In the present study, the alternative approach of correcting for shape change was adopted. A number of observations attest to the support of this approach. Firstly, data comparable to published normal data was obtained. Secondly, no ejection fractions greater than 100% were observed unlike previously where values of greater than 150% were found [5]. Thirdly, ejection volume was calculated from the total change in impedance during a tip-toe manoeuvre rather than proportion of this value [4] as used in standard APG and SPG protocols.

Calculation of volume from resistance was based on the Nyboer equation (equation 1). This equation has been criticized as not taking into account the non-homogeneous nature of limb tissue and should be corrected using the muscle volume to total limb volume ratio, ~0.6 [7]. Application of this correction decreases the mean ejected volume from 93.7 ml to 62.1 ml. However, application of both this and a geometric correction may lead to underestimation since it is likely that the volume correction partially corrects for geometric changes [7]. We used a value of 150 ohm.cm for blood resistivity, although widely used in the Nyboer equation, resistivity varies with haematocrit and blood flow. More recent estimates [8], suggest that a value of 135 ohm.cm may reflect better the value found in vivo. This would decrease the volume estimates proportionately.

In conclusion, with further development and validation, quantitative impedance plethysmography could become the preferred method for haemodynamic analysis due to its convenience and low cost.

References
[1] Nicolaides AN 2000 Investigation of chronic venous insufficiency. A consensus statement Circulation 102 e126-63
[2] Kearon C, Julian JA, Newman TE and Ginsberg MD 1998 Noninvasive diagnosis of deep vein thrombosis Ann. Intern. Med. 128 663-77
[3] Goddard AA, Pierce CS and McLeod KJ 2008 Reversal of lower limb edema by calf muscle pump stimulation J. Cardiopulmon. Rehab. Prevent. 28 174-179
[4] Buckley JC, Peshock RM and Blomqvist CG 1988 Deep venous contributions to hydrostatic blood volume change in the human leg Am. J. Cardiol. 62 449-53
[5] McCullagh WA, Ward LC, Shrier, W and Chetham S 2007 Bioelectrical impedance analysis measures the ejection fraction of the calf muscle pump Proc. XIII Int Conf Electrical Bioimpedance & VIII Conf on Electrical Impedance Tomography (Graz, Austria, 29 August - 2 September) IFMBE Proc 17 616-619
[6] Anderson FA 1984 Impedance plethysmography in the diagnosis of arterial and venous disease Ann. Biomed. Eng. 12 79-102
[7] Bermudez K, Knudson M, Marabito D and Kessel O 1998 Fasciotomy, chronic venous insufficiency, and the calf muscle pump Arch. Surg. 133 1356-61
[8] Traugott FM, Quail AWE and White SW 1981 Evaluation of blood resistivity in vivo for impedance cardiography in man, dog and rabbit Med.Biol. Eng. Comput. 19 547-52