Ultrasound: a reproducible method to measure conduit vein compliance

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Table 1. Subject characteristics of the spinal cord-injured individuals and the healthy controls

<table>
<thead>
<tr>
<th></th>
<th>SCI (n = 6)</th>
<th>C (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>32 (8)</td>
<td>34 (13)</td>
</tr>
<tr>
<td>Body mass, kg</td>
<td>67 (7)</td>
<td>75 (7)</td>
</tr>
<tr>
<td>Height, cm</td>
<td>176 (7)</td>
<td>180 (6)</td>
</tr>
<tr>
<td>Calf circumference, cm</td>
<td>30 (4)*</td>
<td>38 (4)</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>118 (7)</td>
<td>120 (6)</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>71 (8)</td>
<td>73 (12)</td>
</tr>
<tr>
<td>Resting popliteal vein diameter, cm</td>
<td>0.30 (0.11) †</td>
<td>0.53 (0.06)</td>
</tr>
</tbody>
</table>

Values are means (SD); n, no. of subjects. SCI, spinal cord-injured individuals; C, healthy controls. *P < 0.05. †P < 0.01.

METHODS

Subjects

Six able-bodied C subjects and six SCI individuals participated in the study. None of the subjects had a history of cardiovascular disease, diabetes mellitus, or deep venous thrombosis. None of the subjects used medication likely to interfere with the venous system. The SCI individuals had complete motor and sensor lesions (ASIA A) (17) at levels between C5 and L1 for at least 1 yr. The hospital ethical committee approved the study, and all subjects gave their written, informed consent before participating. Subject characteristics are presented in Table 1.

Protocol and Measurements

For at least 3 h before the tests, the subjects refrained from caffeine, alcohol, and smoking. The measurements were performed with the subjects in the supine position in a quiet room with a constant temperature between 21 and 23°C. Leg venous characteristics were assessed simultaneously, at the same horizontal level, with ultrasound and mercury-in-Silastic strain gauge VOP. The heels and feet rested on a foot support 23 cm above the examination table to empty the venous system and to enable measurements in the popliteal fossa. The upper legs were supported laterally by foam paths. After instrumentation of the subjects and a 15-min resting period with stable plethysmographic signals, test procedures were started. At first, two baseline images of the vena poplitea in the popliteal space were obtained and stored for offline analyses (Fig. 1). Then, the test protocol started with a venous occlusion of 20 mmHg followed by subsequent cuff pressures of 40, 60, and 80 mmHg. The effective pressure on the venous system was estimated as 0.8 times the cuff pressure (5). The occlusions of 20, 40, 60, and 80 mmHg were sustained for predefined durations of 2, 3, 4, and 5 min, respectively. We designed our protocol with relatively short venous occlusions to emphasize contribution of the venous filling to calf compliance and limit the time for capillary filtration. In virtually all cases, we achieved a plateau. One-minute breaks between occlusions allowed for new baseline formation and prevented excessive edema. During the last minute of each stage, when a plateau was reached in the plethysmography signal, two images of the diameter of the popliteal vein were obtained with ultrasound and stored for offline analyses (Fig. 1). Before and after the test, blood pressure was measured manually with a sphygmomanometer.

Short-term reproducibility (measurements performed on 1 day, separated by 1 h) as well as long-term reproducibility (same measurement performed after 1 wk) was assessed in the six healthy C subjects.

Measurements

VOP. Mercury-in-Silastic strain gauges were stretched around the largest part of the right calf. A pressure cuff (model SC12L, Hokanson, Bellevue, WA) was placed around the upper right leg and connected to a rapid cuff inflator (Hokanson Stopler E-20) to ensure rapid and accurate filling and deflating of the cuff.

Changes in limb volume were measured by VOP according to the principle of Whitney (31). Data signals were collected by a data acquisition system (Midaq, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands) and analyzed in Matlab 6.5 (Mathworks) with custom-written software (Fysiomon).

From the plethysmographic recordings, the venous volume variation (ml/100 ml), which is defined as the maximal volume increase at a certain cuff pressure, was determined. The venous volume variation for the cuff pressures of 20, 40, 60, and 80 mmHg was represented in a pressure-volume curve. Because the venous pressure-volume curves are nonlinear, we analyzed our VOP data in a curvilinear fashion according to the formula of the three-parameter model of Van Langen (27). The parameters of the Van Langen model were optimized individually with the Levenberg-Marquardt algorithm to achieve optimal fitting of the pressure-volume curve to the measured venous volume variations. The first derivative of the obtained formula was used to calculate the venous compliance at the different cuff pressures.

The Van Langen model uses three parameters, i.e., venous pressure (P0), resting compliance (C0), and the stiffness constant (k), and it has been demonstrated to give a proper description of the curvilinear venous-pressure relationship (27). The parameters P0, C0, and k were determined by the Levenberg-Marquardt algorithm. The principle of Whitney (31) was used to calculate the venous compliance at the different cuff pressures.

Ultrasound. All diameters (cm) of the popliteal vein were measured with an ultrasound device (Megas, Esaote, Firenze, Italy) by using a
Innovative Methodology

LEG VEIN COMPLIANCE ASSESSED BY ULTRASOUND

Fig. 2. Correlation between the compliance at the different cuff pressures as measured with ultrasound (x-axis) and venous occlusion plethysmography (VOP; y-axis) for all subjects. Data are from 6 control subjects and 6 spinal cord-injured (SCI) subjects.

Figures

5- to 7-MHz linear transducer. Two consecutive images of the baseline diameter and the diameters at cuff pressures of 20, 40, 60, and 80 mmHg were frozen in the end-diastolic phase of the cardiac cycle, immediately before the QRS complex (recognized by means of a simultaneous ECG signal). It is suggested that changes in vein geometry at low pressures may account for most of the change in volume and that this is not really a function of the elastic properties of the vein. Therefore, vein geometry was determined in a cross-sectional view. Subsequently, longitudinal images were stored for offline analyses (Fig. 1).

Measurements were performed at the same anatomic location of the vein in the popliteal space. Figure 1 depicts the sequence of longitudinal and cross-sectional ultrasound images (at baseline and at each venous occlusion pressure). Vessel margins of the longitudinal images were defined from leading edge to leading edge. Three measurements were performed per diameter image, and the average of six diameters represents the mean diameter. Because the obtained cross-sectional images provide evidence that the shape of the vein resembles a circle even at low venous pressure levels, the cross-sectional area (π radius²) of the vein at the different cuff pressures was used for further analyses to calculate the compliance according to the curvilinear Van Langen model (27). Moreover, a previous study has demonstrated that venous cross-sectional area can be calculated accurately with the diameters obtained from longitudinal images (16).

Statistics

A Pearson correlation coefficient was calculated between the compliance measured with VOP and the compliance measured with ultrasound. The CV was calculated following the classic approach on the basis of the pooled SD derived from ANOVA, as described previously (19).

CVs for compliance at the different cuff pressures were calculated for both methods. Additionally, for all cuff pressures, CVs were determined for the absolute popliteal vein diameters as measured with ultrasound and for the venous volume variations as measured with VOP. For biological variables, a CV of <10% is considered good and <20% acceptable (24). An unpaired Student’s t-test was applied to assess differences between SCI and C for subject characteristics, absolute diameters of the popliteal vein at different cuff pressures, and the venous volume variation at the different cuff pressures. Repeated-measurement ANOVA analyses were applied for venous compliance as measured with ultrasound and VOP (cuff pressure as within-subject factor and group as between-subject factor). Additional post hoc t-tests were applied to assess differences between groups at the different cuff pressures. The level of statistical significance for all tests was set at 5%. Data are presented as means with SD in parentheses, unless stated otherwise.

RESULTS

Age, body mass, height, heart rate, and blood pressure did not differ between the groups. Calf circumference and baseline popliteal vein diameter was significantly lower in SCI compared with C subjects (Table 1).

Ultrasound vs. VOP

A significant correlation coefficient of 0.624 ($r^2 = 0.39; P = 0.001$) was found between the calf compliance measured with VOP and the compliance of the popliteal vein measured with ultrasound for all subjects (Fig. 2).

Reproducibility

For the compliance data measured with VOP, short-term CV varied between 16 and 19% and long-term reproducibility between 16 and 20% (Table 2). Reproducibility of compliance measured with ultrasound varied from 9 to 13% for short-term reproducibility and from 10 to 13% for long-term reproducibility (Table 2). Short- and long-term CVs of the absolute diameters of the popliteal vein at baseline and at the different cuff pressures (ultrasound) varied between 2 and 9% (Table 2, Fig. 3A), and CVs for venous volume variation (VOP) ranged from 4 to 15% (Table 2, Fig. 3B).

Comparison of SCI With C Subjects

Diameter of the popliteal vein was significantly smaller in SCI compared with C subjects at baseline and at all subsequent cuff pressures ($P < 0.01$; Fig. 4A). The maximal volume variations as measured with VOP were significantly lower in

Table 2. Short- and long-term reproducibility for compliance measured by VOP and ultrasound, VVV measured by VOP, and diameter measured by ultrasound

<table>
<thead>
<tr>
<th>Venous Pressure, mmHg</th>
<th>Compliance VOP, %</th>
<th>Compliance Ultrasound, %</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Short term</td>
<td>Long term</td>
</tr>
<tr>
<td>16</td>
<td>19.3</td>
<td>19.9</td>
</tr>
<tr>
<td>32</td>
<td>16.3</td>
<td>16.9</td>
</tr>
<tr>
<td>48</td>
<td>16.9</td>
<td>16.4</td>
</tr>
<tr>
<td>64</td>
<td>17.7</td>
<td>18.7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Venous Pressure, mmHg</th>
<th>VVV VOP, %</th>
<th>Diameter Ultrasound, %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Short term</td>
<td>Long term</td>
</tr>
<tr>
<td>Baseline</td>
<td>4.7</td>
<td>8.8</td>
</tr>
<tr>
<td>16</td>
<td>8.8</td>
<td>15.7</td>
</tr>
<tr>
<td>32</td>
<td>14.1</td>
<td>10.2</td>
</tr>
<tr>
<td>48</td>
<td>5.3</td>
<td>14.9</td>
</tr>
</tbody>
</table>

Values are short- and long-term reproducibility (coefficient of variation) for compliance at the different venous pressures [as measured with venous occlusion plethysmography (VOP) ultrasound], for venous volume variations (VVV) at the various venous pressures (measured with venous occlusion plethysmography), and for absolute popliteal diameters at baseline and at the subsequent venous pressures (measured with ultrasound).
SCI individuals at venous cuff pressures of 32 ($P < 0.01$), 48, and 64 mmHg ($P < 0.05$) (Fig. 4B). Repeated-measurement analysis of venous compliance showed a significant interaction effect between group (SCI and C) and cuff pressure for both ultrasound measurements ($P < 0.01$) and VOP ($P < 0.01$). Additional post hoc tests revealed significantly lower popliteal vein compliance at all cuff pressures in SCI compared with C subjects (pressures of 16 and 32 mmHg: $P < 0.01$; pressure of 48 and 64 mmHg: $P < 0.05$; Fig. 5A), whereas for the VOP measurements, compliance in SCI subjects was significantly reduced at the lower pressure levels of 16 ($P < 0.05$) and 32 mmHg ($P < 0.01$) but not at the higher cuff pressures of 48 and 64 mmHg (Fig. 5B).

DISCUSSION

Ultrasound of the popliteal vein provides the possibility to specifically assess the compliance of one vein instead of whole calf compliance and appears to be a useful addition to the traditional VOP. The main results of the study are as follows. 1) A significant correlation exists between leg venous compli-

In this study, leg venous compliance was assessed noninvasively from ultrasound measurements of the popliteal vein diameter and from classical VOP measurements, which were performed simultaneously in one subject. Frequently, the relationship between venous volume variation and venous pressure is assumed to be linear. However, at low venous pressures, vascular compliance is high, whereas at high venous pressures compliance is low, which is clearly indicated by graphically representations of venous pressure volume relations (14, 21, 23). Therefore, the data of both ultrasound and VOP measurements were analyzed in a curvilinear fashion according to the recently described Van Langen model (27).
Although VOP and ultrasound assess different properties of the leg, i.e., whole calf vs. single vein compliance, respectively, a significant correlation coefficient was found, indicating that VOP and ultrasound compliance measurements are functionally related to each other (3). We reported an $r^2$ value of 39% between the ultrasound and VOP measurements, indicating that a moderate part of the variation in whole calf compliance may be attributed to variation in conduit vein compliance. This is supported by observations by Buckey et al. (6), who assessed the contribution of the deep veins to total leg venous compliance and reported that most volume changes at different venous occlusion pressures are attributable to deep venous filling (represented by the popliteal vein), i.e., 90% at 40 mmHg and 50% at 100 mmHg. Two aspects may explain the somewhat lower percent (39%) found in the present study, i.e., 1) the two methods measure different aspects of venous capacitance function and 2) the confounding effects of edema and hysteresis in the VOP measurements. The latter may especially hold for higher occlusion pressures, where a true plateau is often not reached in the plethysmographic signal. In a previous study using VOP, Gamble et al. (12) indicated that the time required for vascular volume filling ranges from 80 s to 3 min for cuff pressures from 20 to 40 mmHg, respectively; the subsequent volume changes are caused by fluid filtration. With our cuff inflation durations, we approached these time periods to have maximal contribution of venous filling and minimal contribution of capillary filtration to calf volume variation. In the ultrasound measurements, we observed a relatively large diameter increase shortly after occlusion with no more changes in the size of the popliteal vein after 30–60 s of occlusion. This supports the notion that ultrasound specifically assesses venous characteristics and not interstitial fluid accumulation.

Previously, the diameter of one single vein has been assessed in superficial cutaneous veins with various techniques such as an optical method (8), a photoelectric device (25) linear differential transformer and ultrasound (28). However, subcutaneous vein measurements are associated with a high degree of intersubject variability (1), and one should realize that responses in these subcutaneous veins are less representative for total vein compliance because their primary function is heat dissipation and not blood storage and conduction (18).

As a second aim of this study, we assessed short- and long-term reproducibility of both methods. For VOP, compliance reproducibility varied between 16 and 20%, and CVs for venous volume variations at the different cuff pressures ranged from 4 to 15%, which is more or less in line with previous VOP studies assessing reproducibility (4, 14, 26).

Using ultrasound, we reported CVs ranging from 9 to 14% for popliteal vein compliance and from 2 to 9% for popliteal vein diameters at baseline and at the subsequent venous occlusion pressures. One previous study reported a CV for resting diameter measurement of proximal veins of 15% (13), and a recent study evaluated the reproducibility of varicose vein diameters and reported a reproducibility error of 5 and 6% in supine and standing position, respectively (2). We are not aware of any study reporting on reproducibility of venous compliance assessed by ultrasound. For biological variables, the CVs as reported in our study for the ultrasound measurements may be considered as acceptable to good (24).

A third aim of our study was to assess leg venous compliance with both methods in a patient population (SCI) with known pathological changes in the venous vascular system. The 80% reduction in compliance of the popliteal vein and the 45% smaller diameter indicate that ultrasound is able to detect alterations in the venous vascular properties. These adaptations in the venous vascular bed in SCI individuals are most likely the result of marked muscle atrophy below the level of lesion with a concomitant vascular atrophy. The extensive muscle atrophy is illustrated by the significantly decreased calf circumference in SCI compared with C subjects observed in the present study and supported by other studies (15, 29).

Using VOP to assess venous characteristics in SCI, we demonstrated a significant reduction in venous volume variation in SCI individuals, ranging from 32 to 38% depending on the cuff pressures applied, which is in line with previous studies (11, 15, 29, 30). A possible explanation for the discrepancy in venous compliance between ultrasound (reduced compliance at all pressures) and VOP (reduced compliance only at lower cuff pressures) may be that venous volume variation (VOP) at higher cuff pressures is affected by the appearance of
edema and hysteresis, which is more pronounced in SCI than in C subjects. As a result, the differences in venous compliance between groups may be masked using VOP. In addition, previous studies suggest that calf compliance is inversely related to the leg muscle compartment and that a larger muscle mass may provide structural support, which limits vein expansion (9, 10). It is well known that SCI individuals suffer from dramatic reductions in leg muscle mass (7), which may contribute to an overestimation of calf compliance by VOP at the higher cuff pressures in SCI. Ultrasound measures the properties of one major vein and may, therefore, be less susceptible to factors that affect calf compliance such as muscle atrophy. Alternatively, muscle atrophy may affect compliance of venules more than of larger veins, suggesting that ultrasound specifically assesses the larger conduit veins and provides useful additional information to VOP.

In conclusion, we have presented a reproducible ultrasound technique for noninvasive assessment of venous function of one major vein of the leg in humans. This technique provides the possibility to specifically assess compliance of one vein instead of whole calf compliance and appears to be a useful complementary method to the traditional VOP.

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REFERENCES