Leg intravenous pressure during head-up tilt

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Departments of 1Physiology, 2Internal Medicine, 3Pharmacology-Toxicology, and 4Cardiology, Radboud University Nijmegen Medical Centre; and 5Department of Rehabilitation Medicine, Sint Maartenskliniek, Nijmegen, The Netherlands

Submitted 21 February 2008; accepted in final form 10 July 2008

Groothuis JT, Poelkens F, Wouters CW, Kooijman M, Hopman MT. Leg intravenous pressure during head-up tilt. J Appl Physiol 105: 811–815, 2008. First published July 17, 2008; doi:10.1152/japplphysiol.90304.2008.—Leg vascular resistance is calculated as the arterial-venous pressure gradient divided by blood flow. During orthostatic challenges it is assumed that the hydrostatic pressure contributes equally to leg arterial, as well as to leg venous pressure. Because of venous valves, one may question whether, during orthostatic challenges, a continuous hydrostatic column is formed and if leg venous pressure is equal to the hydrostatic pressure. The purpose of this study was, therefore, to measure intravenous pressure in the great saphenous vein of 12 healthy individuals during 30° and 70° head-up tilt and compare this with the calculated hydrostatic pressure. The height difference between the heart and the right medial malleolus level represented the hydrostatic column. The results demonstrate that there were no differences between the measured intravenous pressure and the calculated hydrostatic pressure during 30° (47.2 ± 1.0 and 46.9 ± 1.5 mmHg, respectively) and 70° head-up tilt (83.9 ± 0.9 and 85.1 ± 1.2 mmHg, respectively). Steady-state levels of intravenous pressure were reached after 95 ± 12 s during 30° and 161 ± 15 s during 70° head-up tilt. In conclusion, the measured leg venous pressure is similar to the calculated hydrostatic pressure during orthostatic challenges. Therefore, the assumption that hydrostatic pressure contributes equally to leg arterial as well as to leg venous pressure during orthostatic challenges can be made.

METHODS

Subjects. Twelve healthy individuals (6 men and 6 women) volunteered to participate in this study (Table 1). Subjects never smoked, were normotensive (<140/90 mmHg) and free of overt cardiovascular diseases, and did not report orthostatic intolerance. None of the subjects used any medication, except oral contraceptives in female subjects. The study has been carried out in accordance with the Declaration of Helsinki (2000) and was approved by the medical ethical committee of our institution. All subjects gave written informed consent.

Experimental procedures and protocol. All subjects refrained from caffeine-containing food and beverages, vitamin C supplements, and alcohol for at least 12 h before the experiment and refrained from heavy physical activity for at least 24 h before the experiment. Room temperature was controlled at 23 ± 1°C. After completing a health questionnaire, subjects were comfortably placed in the supine position on a manually controlled tilt table with footboard. A chest belt was used to prevent them from falling down in case of vasovagal syncope. The right leg was placed in such a way that the right medial malleolus was on heart level, midthoracically at the second intercostal space, in the supine position. The subjects supported their body weight during

THE INCREASE in leg vascular resistance, by a baroreflex-induced increase in sympathetic tone and by local mechanisms such as the venoarteriolar axon “reflex” (VAR) (10) and the myogenic response (12), are important to withstand orthostatic challenges (19). Peripheral vascular responses to orthostatic challenges, quantified by leg vascular resistance, have been studied in healthy individuals as well as in individuals with autonomic dysfunction (5, 7–9, 12–15, 20–23).

In supine position, leg vascular resistance is calculated as the arterial-venous pressure gradient (P_a – P_v) divided by blood flow. In supine position, most studies (7–9, 12, 13, 15) assume that venous pressure equals 0 mmHg and use mean arterial blood pressure (MAP) to replace the arterial-venous pressure gradient, while others (5, 20–23) have estimated venous pressure in the leg using venous occlusion plethysmography. During orthostatic challenges a hydrostatic pressure is added to leg arterial as well as to leg venous pressure due to gravitational translocation of blood (19, 24). One may question how upright posture will affect the arterial-venous pressure gradient. The veins have valves that close at the onset of orthostatic challenges and thereby interrupt the development of a continuous hydrostatic column. When an orthostatic challenge persists, the veins will continue to fill with blood, and consequently the venous valves will open to form a continuous hydrostatic column (17, 18, 24). At this time the assumption can be made that the hydrostatic pressure contributes equally to leg arterial as well as to leg venous pressure (24), and vascular resistance can be calculated as MAP (minus Pb, supine) divided by blood flow (5, 7–9, 12–15, 20–23).

Surprisingly, only a few studies have tested this assumption by measuring intravenous pressure. Unfortunately, these studies were done in a small number of individuals (16) and/or during relaxed (motionless) standing (11, 16), which still could cause considerable (in)voluntary muscle contractions (11). Recent studies on leg vascular responses use passive head-up tilt (HUT) to diminish these (in)voluntary muscle contractions. Others (5, 20, 21) have tested the assumption during passive HUT, but they used an indirect, noninvasive method (6) that could only be used in (HUT) angles up to 35°. The purpose of this study was, therefore, to measure leg venous pressure during 30° and 70° HUT. We hypothesized that the measured leg venous pressure is similar to the calculated hydrostatic pressure and, therefore, that the assumption can be made that the hydrostatic pressure makes an equal contribution to leg arterial as well as to leg venous pressure during orthostatic challenges.

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HUT by standing on the left leg, allowing the right leg to be relaxed for venous pressure measurements. The experimental procedures started after a supine resting period of at least 30 min after placement of an intravenous catheter in the right great saphenous vein.

First, baseline venous pressure was measured for 5 min in the supine position. Subsequently, subjects were tilted manually, within 5 s, to a passive 30° HUT position for 5 min, during which venous pressure was continuously measured. After returning to the supine position and venous pressure returned to baseline values, the same procedure was repeated with a passive 70° HUT.

Measurements. Blood pressure (BP) was measured auscultatory at the right brachial artery using a sphygmomanometer. MAP was calculated as diastolic BP.

A 20-gauge venous catheter was placed in the right great saphenous vein at the level of the medial malleolus and connected to a continuous pressure monitoring system (Edwards Life Sciences Services). Throughout the entire protocol, the venous catheter was fixed in the same position, e.g., in the saphenous vein at the level of the right medial malleolus. Figure 1 shows a typical intravenous pressure recording of one subject. Intravenous pressure (mmHg) was determined as the average of the last minute in each position. The time to reach a steady-state intravenous pressure was determined.

The hydrostatic column was determined by measuring the vertical height difference (cm) between heart level, midthoracally at the second intercostal space, and the right medial malleolus where intravenous pressure was monitored. To convert to units of millimeters Hg, the height difference was multiplied by a factor 0.766, which includes a correction for the specific gravity of blood (1.055) (4, 5, 22). The determination of the hydrostatic column was done in duplicate, with a coefficient of variation <4%.

Statistical analysis. Data are presented as means ± SE, unless otherwise stated. A paired Student’s t-test was used to determine the effect of HUT, and a Pearson correlation coefficient was calculated to determine the correlation between intravenous pressure and calculated hydrostatic pressure. Bland-Altman plots were constructed to show the distribution of the individual data. The level of statistical significance was set at α = 0.05.

RESULTS

Supine intravenous pressure. Venous pressure in the great saphenous vein in supine position varied between 6 and 13 mmHg and did not differ between supine positions before 30° and 70° HUT (Table 2). The mean value of supine venous pressure was 8.7 ± 0.3 mmHg, with a 95% confidence interval (CI) between 8.0 and 9.3 mmHg.

Intravenous and hydrostatic pressure during HUT. During both 30° and 70° HUT, the venous pressure increased in the great saphenous vein and reached steady-state levels (Table 2). The intravenous pressures during 30° HUT ranged from 41 to 51 mmHg and during 70° HUT from 80 to 91 mmHg. These steady-state levels were reached between 37 and 168 s for 30° and between 64 and 247 s for 70° HUT. The calculated hydrostatic pressures ranged from 39 to 55 mmHg during 30° HUT and from 79 to 93 mmHg during 70° HUT (Table 2). No differences were found between the measured intravenous pressure and the calculated hydrostatic pressure during both 30° HUT (47.2 ± 1.0 and 46.9 ± 4.5 mmHg, respectively) and 70° HUT (83.9 ± 0.9 and 85.1 ± 1.2 mmHg, respectively) (Table 2).

The measured intravenous pressure and the calculated hydrostatic pressure during 30° and 70° HUT correlated well, with a correlation coefficient (r) of 0.937 (P < 0.001) for 30° HUT and a correlation coefficient of 0.813 (P < 0.001) for 70° HUT (Fig. 2). In Fig. 3 Bland-Altman plots are shown for 30° and 70° HUT, demonstrating the distribution of the individual data.

DISCUSSION

The major finding of the present study is that the measured intravenous pressure in the great saphenous vein corresponds with the calculated hydrostatic pressure during 30° and 70° HUT. Thus the assumption that hydrostatic pressure contributes equally to leg arterial as well as to leg venous pressure during orthostatic challenges seems to be correct for both 30° and 70° HUT. Therefore, the arterial-venous pressure gradient during orthostatic challenges is equal to MAP, and leg vascular resistance can be calculated as MAP divided by blood flow.

Table 1. Subject characteristics

<table>
<thead>
<tr>
<th>Subject characteristic</th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
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<tbody>
<tr>
<td>Age, yr</td>
<td>22 ± 2</td>
<td>20–28</td>
</tr>
<tr>
<td>Height, cm</td>
<td>176 ± 6</td>
<td>168–187</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>69 ± 7</td>
<td>55–82</td>
</tr>
<tr>
<td>Calf circumference, cm</td>
<td>37 ± 1</td>
<td>35–39</td>
</tr>
<tr>
<td>Systolic BP, mmHg</td>
<td>119 ± 6</td>
<td>105–130</td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>72 ± 7</td>
<td>64–85</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>88 ± 7</td>
<td>78–97</td>
</tr>
</tbody>
</table>

Values represent means ± SD. BP, blood pressure; MAP, mean arterial blood pressure.
Supine intravenous pressure. Although most studies (7–9, 12, 13, 15) assume that supine leg venous pressure equals 0 mmHg, the results of the present study demonstrate that venous pressure ranges between 6 and 13 mmHg. This must be due to a combination of static and dynamic pressure (17), since the hydrostatic pressure component was alienated through placement of the right leg on heart level. The above-mentioned studies (7–9, 12, 13, 15), therefore, underestimate supine leg venous pressure and as a consequence overestimate leg vascular resistance, since vascular resistance is calculated as the arterial-venous pressure gradient divided by blood flow. The studies that indirectly derive supine leg venous pressure (5, 20–23) do not seem to underestimate leg venous pressure, as previously demonstrated by Christ et al. (4). The measured supine venous pressure in our study is in agreement with a recent study of Calbet et al. (3), who found a leg venous pressure of 7.1 ± 0.1 mmHg (mean ± SD). However, they measured venous pressure in the femoral vein, which may not be compared directly to venous pressures values in the saphenous vein.

Nevertheless, supine leg venous pressure can not be assumed to equal 0 mmHg because it was 8.7 (8.0–9.3) mmHg [mean (95% CI)]. A venous pressure within this 95% CI should be assumed when leg vascular resistance is calculated in supine position unless leg venous pressure is measured intravenously.

Intravenous pressure during HUT. Intravenously measured leg venous pressure corresponded and correlated well with the calculated hydrostatic pressure in 30° and 70° HUT. Average of measured venous pressure and calculated hydrostatic pressure (x-axis) plotted against difference of calculated hydrostatic pressure minus measured venous pressure (y-axis). The solid horizontal line indicates mean difference, and the dashed horizontal lines indicate ±2 SD.

### Table 2. HUT-induced changes in intravenous pressure, calculated hydrostatic pressure during HUT, and time until steady-state intravenous pressure

<table>
<thead>
<tr>
<th>Condition</th>
<th>Supine</th>
<th>30° HUT</th>
<th>70° HUT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venous pressure, mmHg</td>
<td>8.8±0.5</td>
<td>47.2±1.0*</td>
<td>83.9±0.9*</td>
</tr>
<tr>
<td>Hydrostatic pressure, mmHg</td>
<td>46.9±1.5</td>
<td>85.1±1.2</td>
<td></td>
</tr>
<tr>
<td>Time until steady state, s</td>
<td>95±12</td>
<td>161±15</td>
<td></td>
</tr>
</tbody>
</table>

Values represent means ± SE. HUT, head-up tilt. *Significantly different from supine.

![Fig. 2. Correlation for measured intravenous pressure and calculated hydrostatic pressure for 30° and 70° HUT. The dashed lines have been constructed to pass through the origin and have a slope of unity (slope = 1.0).](image)

![Fig. 3. Bland-Altman analysis of measured venous pressure and calculated hydrostatic pressure for each individual (n = 12) during 30° and 70° HUT. Average of measured venous pressure and calculated hydrostatic pressure (x-axis) plotted against difference of calculated hydrostatic pressure minus measured venous pressure (y-axis). The solid horizontal line indicates mean difference, and the dashed horizontal lines indicate ±2 SD.](image)
and a steady state, indicating equilibrium, was seen after 37–168 s during 30° HUT and after 64–247 s during 70° HUT. Thus the remark has to be made that the assumption can only be used when this equilibrium is achieved, because from that moment on, a continuous hydrostatic column has been formed in the veins.

Second, according to the assumption that during orthostatic challenges hydrostatic pressure contributes equally to leg arterial as well as to leg venous pressure, supine leg venous pressure should be added to the calculated hydrostatic pressure. The results of this study, however, demonstrate that leg venous pressure during orthostatic challenges equals hydrostatic pressure, without adding the supine leg venous pressure. A possible explanation could be that venous tone is reduced during HUT, although this seems unlikely and one would expect the opposite to occur during HUT. Another explanation could be that the decrease in leg blood flow during HUT (7–9, 14, 15) lowers venous pressure. Although this is an interesting question, the present study was not designed to answer that question.

Consequently, in the calculation of leg vascular resistance during orthostatic challenges, the arterial-venous pressure gradient can be replaced by MAP, without accounting for supine leg venous pressure.

Limitations. One may argue that the pressure in the great saphenous vein, a superficial vein, does not reflect the pressure in the deep veins (4), which drain most of the blood from the lower limbs (2). However, the pressure gradient between the deep and superficial veins is small, because blood is drained through low-resistance valves (1). Moreover, venous pressure measured at various cannulation sites varies by 1–2 mmHg, when measured after an equilibration time of 120 s (1). We therefore believe that the measured venous pressure in the great saphenous vein represents superficial as well as deep venous pressure.

From the Bland-Altman plot for 30° HUT (Fig. 3), one could argue that there might be an overestimation of intravenous pressure from the hydrostatic pressure for low pressures only (<48 mmHg). However, there were no differences between the intravenous and hydrostatic pressure and no systematic errors for both HUT positions. We are, therefore, convinced that the measured intravenous pressure corresponds with the calculated hydrostatic pressure during 30° and 70° HUT.

In this study we did not measure leg arterial pressure, because the hydrostatic column is immediately formed in the arteries (19, 24) and the added hydrostatic pressure to leg arterial pressure is calculated in the exact same manner as hydrostatic pressure is calculated in the present study for leg venous pressure (17).

Recommendations. From the results of this study, some important methodological recommendations can be made.

1) We recommend using a supine leg venous pressure of 8.7 (8.0–9.3) mmHg [mean (95% CI)] when the measured leg is placed on heart level.

2) The assumption that hydrostatic pressure contributes equally to leg arterial as well as to leg venous pressure during orthostatic challenges is correct. However, supine leg venous pressure should not be added to the hydrostatic pressure and the assumption can only be made after a continuous hydrostatic column is formed; for 30° HUT this is after 3 min and for 70° HUT after 4 min.

3) It is essential that arterial and venous measurements are at the same level compared with the heart; otherwise a correction equal to the hydrostatic column difference should be made. When these recommendations are taken into account, leg vascular resistance during orthostatic challenges can be calculated as MAP divided by (leg) blood flow.

Conclusion. During orthostatic challenges the leg venous pressure, measured intravenously in the great saphenous vein, is similar to the calculated hydrostatic pressure. Therefore, the assumption can be made that the hydrostatic pressure contributes equally to leg arterial as well as to leg venous pressure. Although this assumption can only be made when a continuous hydrostatic column has been formed in the veins, the time until this column has been formed is dependent on the performed orthostatic challenge.

REFERENCES


