Postural changes in capillary pressure in the hallux of healthy volunteers

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De Graaff, Jurgen C., Dirk T. Ubbink, Sjoerd M. Lagarde, and Michael J. H. M. Jacobs. Postural changes in capillary pressure in the hallux of healthy volunteers. J Appl Physiol 95: 2223–2228, 2003.—Capillary circulation is delicately regulated by microvascular constriction mechanisms, thereby controlling capillary perfusion and transmural pressure. The influence of posture on capillary flow has been investigated in both diseased and healthy people. However, its influence on capillary pressure has rarely been investigated. We measured capillary pressures in the supine and sitting positions in the hallux of healthy volunteers. The capillaries in the eponychium of the hallux were punctured by using a micropipette connected to a micropressure system (900A, WPI). Also, peripheral arterial and venous pressures were measured in both positions. The rise in systolic capillary pressure from supine to sitting position (32 mmHg; from 39 to 71 mmHg, respectively) was significantly (P < 0.001) smaller than the rise in systolic arterial toe pressure (57 mmHg, from 87 to 144 mmHg, respectively) and venous pressure (41 mmHg, from 26 mmHg to 67 mmHg, respectively). This study shows that the postural rise in precapillary arteriolar pressure is not completely transmitted to the capillaries, probably because of activation of peripheral vasoconstriction mechanisms.

CAPILLARY MICROCIRCULATION is essential for tissue nutrition, owing to transcapillary exchange of fluids and solutes. The fluid exchange across the capillary membrane of a single, short section of a capillary, as initially proposed by Starling (27), is dependent on the transmural pressure gradient, in which the capillary blood pressure is a crucial factor (19). Microcirculatory perfusion in the skin of fingers and toes is mainly regulated by local mechanisms (9), including the myogenic response of the precapillary arterioles after a change in transmural pressure (1) and the venuloarteriolar response, on the basis of a local axon reflex leading to arteriolar constriction when venular pressure is elevated (3, 11). Disturbed constriction responses, leading to capillary hypertension, may cause edema formation (9, 31).

Thus far the regulation of capillary blood pressure has been investigated in healthy and diseased subjects in the capillaries of the fingernail fold only, using a direct cannulation and a servo-nulling micropressure system (17). This direct method appeared to be a reliable technique to give valuable information about the (patho)physiology of microcirculatory perfusion (4, 23). Shore et al. (25) demonstrated that elevation of systemic blood pressure through exercise did not change capillary pressure in the hand and suggested that protective mechanisms minimize the transmission of changes in systemic blood pressure to the capillary bed, whereas an increase in venous pressure in the arm gave a pronounced rise in capillary pressure (18).

The regulation of capillary pressure in the foot is likely to be much more robust than in the hand to counteract the considerable changes in arterial and venous pressure on a change in posture. On the other hand, various diseases (arterial and venous insufficiency, diabetic microangiopathy, etc.) mainly affect, or are more pronounced in, the microcirculation of the foot (2, 22, 30). The regulatory mechanisms of capillary pressure in the foot have been investigated by Levick and Michel (14) by using a direct, static capillary pressure measurement technique. They showed that capillary pressure can rise up to 100 mmHg in standing position and that in the dependent extremity there is a tight control of capillary pressure probably by arteriolar vasoconstriction. Furthermore, they showed that capillary pressure approaches venous pressure in the dependent position (14). However, this work was performed only in two volunteers with a static measurement system and has never been confirmed by others. Jünger and colleagues (13, 28) have described the investigation of the capillary pressure in the foot in patients with venous insufficiency by using a dynamic micropressure system. Dynamic measurements allow for additional analysis of the capillary pulse pressure and capillary pressure waveform during the cardiac cycle and yield information about precapillary resistance (18, 26).
Knowledge about the regulation of the precapillary resistance in the foot may increase our understanding of the edema formation in patients suspected of capillary hypertension, e.g., venous insufficiency and diabetes mellitus, and the reappearance of postural vasoconstriction in the foot, e.g., after revascularization procedures that increase peripheral blood pressure. However, the (patho)physiological knowledge of capillary pressure regulation in health and disease is mainly derived from investigations performed in the fingers (21, 24–26). Therefore, in this study we investigated the effect of postural changes on capillary pressure and perfusion and in the hallux in healthy subjects by means of capillary microscopy, laser Doppler fluxmetry (LDF), and a servo-nulling micropressure system.

**SUBJECTS AND METHODS**

The left foot of 20 healthy volunteers was investigated after a 30-min acclimatization period in a temperature-controlled environment (25 ± 1°C). All measurements were performed in the sitting and the supine position with the measurement site at heart level. The order of the positions of investigation was chosen randomly. The height from toe to heart (represented by the fourth intercostal space) was measured in sitting position. Volunteers refrained from smoking and caffeine-containing drinks for at least 4 h before the measurement to avoid a possible effect on vascular tone. The investigation protocol was approved by the local medical ethical committee and conforms with the principles outlined in the Declaration of Helsinki. Written, informed consent was obtained from all volunteers.

Dynamic intracapillary blood pressure measurements were performed in the eponychium of the hallux of the left foot in the sitting and supine positions. LDF (PF 407, Periflux 4001, Perimed, Stockholm, Sweden; filter time 0.03 s) of the adjacent area, continuous blood pressure of the second toe (Finapres BP Monitor 2300, Ohmeda, Louisville, CO), and ECG were assessed simultaneously, to validate the capillary pressure. The laser Doppler was used to investigate total cutaneous perfusion (29), whereas the capillary red blood cell velocity was assessed to evaluate nutritive perfusion. Skin temperature of the toe (monitor 78342A, Hewlett-Packard, Amstelveen, The Netherlands) was monitored to evaluate a possible variability due to temperature changes (8, 14). All synchronous measurements (ECG, laser Doppler, temperature, capillary pressure, and continuous toe pressure) were sampled on-line and analyzed off-line by means of a data-acquisition and analysis system (AcqKnowledge III and MP 100WSW, Biopac System, Santa Barbara, CA). After this experiment, the brachial (Dinamap Plus; Criticon, Tampa, FL) and ankle pressures (highest of dorsal pedal artery and posterior tibial arteries at the level of the ankle) were measured with an 8-MHz Doppler probe (PV lab, Stöppler, Electric Diagnostic Instruments, Burbank, CA) and a cuff (12-cm width) just above the ankle. The toe pressure was measured on the hallux of the same foot as the capillary pressure by means of photoplethysmography (PV lab, Stöppler, Electric Diagnostic Instruments) and a digital cuff with a width depending on the diameter of the toe. A cuff width closest to 120% of the diameter of the hallux was chosen (cuff 1.5, 2.5, or 3.3 cm, Hokanson, Bellevue, WA) (5). The reproducibility of the brachial, ankle, and toe blood pressure measurements in our laboratory has been evaluated recently and appeared to be “good” (5). The reproducibility of the laser Doppler has been investigated previously by Lukkari-Rautiainen et al. (16).

Additionally, peripheral venous blood pressure was measured in the great saphenous vein at the foot by means of a 22-gauge Venflon connected to a pressure transducer (monitor 78342A, Hewlett-Packard) in eight subjects in the same positions in which the capillary pressure measurements were performed.

Intravital capillary microscopy. The capillaries of the hallux nail fold were visualized by means of a capillary microscope with motor focusing in combination with a video circuitry as described before (4, 30). Capillaries were punctured while visualized by use of a ×10 objective (PF Fluorat, 10/0.30 Leitz, Wetzlar, Germany) and a digital camera (Tm-6CN Pulnix America, Sunnyvale, CA), giving a total magnification on a monitor (PM 931, Ikegami, Maywood, NJ) of ∼×310 (screen 180 × 136 mm = 0.58 × 0.44 mm skin area). The images were stored on videotape for off-line analysis afterward. Capillary diameter (in μm), capillary density (in mm–2), and capillary red blood cell velocity (RBCV; in μm/s) during the capillary pressure measurement were assessed as described before (Cap-Image software, Zeintl, Biomedical Engineering, Heidelberg, Germany) (4, 32).

Capillary pressure. Capillary pressure was measured by a direct servo-nulling method. The principles of the measurement technique, circuit description, and calibration have been evaluated and described in detail before for the fingers but are essentially the same for the measurements in the toes (4). In short, the capillary loops were punctured in the apex with micropipettes (tip diameter varying between 3 and 4 μm), filled with a 2 M NaCl solution (with 10E/ml heparin to prevent plugging), connected to the servo-nulling micropressure system (900A World Precision Instruments, Sarasota, FL). The apparatus contains an electrical circuit and an air circuit, which regulates the pressure inside the pipette so that it equals the pressure outside the tip. The electrical circuit is formed by a Wein bridge oscillator, which generates a 1,000-Hz (sinusoidal voltage) constant carrier current through the microelectrode. An influx of blood into the capillary would change the impedance of the pipette. A pressure control driver will automatically adjust the microelectrode tip impedance to a change in pressure outside the tip of the probe (4, 6).

The cuticle and upper layer of the stratum corneum of the epidermis were removed to facilitate puncturing of the capillaries. The position of the tip of the pipette was adjusted so that flow through the capillary was visually unobstructed and a synchronous waveform was received (Fig. 1). A measurement was regarded valid when the capillary pulse pressure waves were in phase with the waveforms of the ECG, toe pressure, and laser Doppler while capillary flow was unobstructed for at least 5 s. The mean systolic, diastolic, and mean pressures were derived from the valid interval. The reproducibility of the capillary pressure measurement in two capillaries in the same digit was evaluated in fingers. The reproducibility using the present setup was expressed as the standard deviation of the difference between two paired measurements (n = 10) and was found to be small: 2.8 mmHg.

Furthermore, the capillary pulse pressure amplitude (CPPA), which can be used as a measure of the precapillary resistance, and the toe pulse pressure amplitude (TPPA) was defined as the pressure difference between the diastolic and systolic values (18). After the investigation, any remaining shards were removed by wiping with a paper tissue, and the puncture area was disinfected.
Statistics. The results are expressed in means with standard deviations after testing for skewness. Statistical analysis of possible differences between the sitting and supine positions in all measurements was evaluated by using the paired $t$-test. Power analysis revealed that 13 patients are required to refute the null hypotheses that the mean sitting and supine capillary pressures were not the same (minimum difference 8 mmHg, SD = 8 mmHg, power 0.8, and $P < 0.05$; two-sided, paired analyses). With 13 volunteers, the minimal size of differences that could be detected (to exclude type 2 errors) was, for ankle pressure, 7 mmHg; for toe pressure, 16 mmHg; for the mean toe pressure by Finapres, 15 mmHg; for capillary density, 11; for RBCV, 0.04 mm/s; for capillary diameter, 2 μm; for temperature, 2°C; and for LDF, 0.16 V.

RESULTS

In 13 of 20 (65%) volunteers (mean age 34 ± 10 yr; 4 men and 9 women), acceptable measurements could be obtained in both positions. The number of failures diminished with growing experience; these failures were caused by movement artifacts ($n = 5$) and thickness of the skin ($n = 2$). The duration of a complete investigation in both positions varied between 2 and 4 h. If the flow through the capillary was visually unobstructed, the pulse contour of the pressure could be visualized clearly, showing a steep upstroke in phase with the other recordings (Fig. 1). The difference in pulse contour between the sitting and supine positions due to a change in pre- and postcapillary resistance is clearly visible in these figures. The duration of one continuous pressure recording varied from 5 s to 6 min and was typically stable over time (Fig. 2).

Capillary pressure in the sitting position was significantly higher than in the supine position (see Table 1 and Fig. 3). The same was true for the toe, ankle, and venous pressures, whereas brachial pressures and skin temperature did not change significantly during the investigation. However, the rise in systolic capillary pressure (mean 32 mmHg) was significantly ($P = 0.001$) less than the rise in systolic ankle and toe pressures (both mean 57 mmHg, see Table 1) but less than the rise in venous pressure (mean 41 mmHg). There was a significant difference between the arterial-capillary blood pressure fall between supine and sitting position (56 and 81 mmHg, respectively). Capillary systolic pressure rose to up to 100 mmHg in the sitting position. However, the remaining microcirculatory parameters (CPPA, capillary density, RBCV, capillary diameter, LDF) did not change significantly on the change in posture, indicating that capillary volume flow and total skin flow did not alter substantially by the change in posture (Table 1).

DISCUSSION

This study shows that dynamic capillary pressure measurements are feasible in the capillary nail fold of the toe, in both the sitting and supine positions. Even the pulse contour of the blood pressure is clearly visible with this method. Second, this study confirms the observations of Levick and Michel (14) that the capillary pressure increases substantially in sitting position but not as much as arterial pressure increases. This is probably due to activation of precapillary (arteriolar) vasoconstriction mechanisms.

In this study, systolic capillary pressure in the toe during sitting was found to be rather high (70 up to 100

Fig. 1. Typical example of a recording of the laser Doppler flux, capillary and second toe pressure (Finapres), and ECG in sitting (A) and supine (B) position. Note the difference in (especially capillary pressure) waveforms between both positions.
mmHg), which is much higher than commonly known (19). Our results correspond with the static capillary pressure measurements using a manometric technique as performed by Levick and Michel (14), who found a capillary pressure of 67 mmHg when the hydrostatic pressure difference between heart and capillary was 80 mmHg and pressures up to 100 mmHg in the standing position. This increased pressure in the sitting position considerably influences the forces governing fluid movement across the capillary wall, because the capillary pressure is a crucial factor in this process and is bound to lead to interstitial edema formation. The fluid exchange across the capillary membrane of a single, short section of a capillary, as initially proposed by Starling (27), is dependent on the transmural pressure gradient (15, 19). An increase in hydrostatic pressure

Table 1. Measurement parameters in the sitting and supine positions

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Supine</th>
<th>Sitting</th>
<th>Sitting-Supine Difference</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brachial systolic, mmHg</td>
<td>117 ± 7</td>
<td>118 ± 8</td>
<td>2 ± 10</td>
<td>0.58</td>
</tr>
<tr>
<td>Brachial diastolic, mmHg</td>
<td>70 ± 7</td>
<td>73 ± 4</td>
<td>3 ± 7</td>
<td>0.12</td>
</tr>
<tr>
<td>Ankle systolic, mmHg</td>
<td>118 ± 7</td>
<td>175 ± 8</td>
<td>57 ± 9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Toe systolic, mmHg</td>
<td>87 ± 17</td>
<td>144 ± 18</td>
<td>57 ± 17</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Toe systolic Finapres, mmHg</td>
<td>98 ± 16</td>
<td>171 ± 25</td>
<td>73 ± 26</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Toe mean Finapres, mmHg</td>
<td>65 ± 15</td>
<td>126 ± 18</td>
<td>61 ± 16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Toe diastolic Finapres, mmHg</td>
<td>50 ± 16</td>
<td>106 ± 17</td>
<td>56 ± 14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TPPA, mmHg</td>
<td>47 ± 10</td>
<td>65 ± 18</td>
<td>18 ± 17</td>
<td>&lt;0.003</td>
</tr>
<tr>
<td>Capillary systolic, mmHg</td>
<td>39 ± 12</td>
<td>71 ± 11</td>
<td>32 ± 10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Capillary mean, mmHg</td>
<td>32 ± 8</td>
<td>63 ± 8</td>
<td>32 ± 7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Capillary diastolic, mmHg</td>
<td>28 ± 8</td>
<td>59 ± 8</td>
<td>31 ± 6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CPPA, mmHg</td>
<td>11 ± 7</td>
<td>12 ± 5</td>
<td>0.1 ± 3.1</td>
<td>0.50</td>
</tr>
<tr>
<td>Pressure fall, mmHg</td>
<td>56 ± 17</td>
<td>81 ± 20</td>
<td>25 ± 19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Capillary density, mm⁻²</td>
<td>55 ± 12</td>
<td>58 ± 14</td>
<td>3 ± 15</td>
<td>0.56</td>
</tr>
<tr>
<td>RBCV, mm/s</td>
<td>0.19 ± 0.04</td>
<td>0.19 ± 0.07</td>
<td>0.0 ± 0.06</td>
<td>1.0</td>
</tr>
<tr>
<td>Capillary diameter, μm</td>
<td>9.5 ± 1.7</td>
<td>9.1 ± 1.0</td>
<td>−0.4 ± 1.8</td>
<td>0.51</td>
</tr>
<tr>
<td>Temperature, °C</td>
<td>28 ± 2</td>
<td>26 ± 2</td>
<td>0.5 ± 1.3</td>
<td>0.28</td>
</tr>
<tr>
<td>LDF, volts</td>
<td>0.18 ± 0.17</td>
<td>0.22 ± 0.21</td>
<td>0.05 ± 0.25</td>
<td>0.50</td>
</tr>
<tr>
<td>High heart-toe, cm</td>
<td>0</td>
<td>79 ± 6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Venous pressure, mmHg</td>
<td>26 ± 3</td>
<td>67 ± 5</td>
<td>41 ± 4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>High heart-toe, cm</td>
<td>0</td>
<td>86 ± 6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SD, and differences are tested with the paired t-test. Pressure fall, pressure difference between toe systolic pressure and mean capillary pressure; TPPA, toe pulse pressure amplitude; CPPA, capillary pulse pressure amplitude; RBCV, capillary red blood cell velocity; LDF, laser Doppler fluxmetry.

Fig. 2. Typical example of the variation over a longer recording period of ECG, laser Doppler, capillary pressure, and second toe pressure (Finapres).

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causes extravascular fluid accumulation and edema formation. This process is linearly related to the ortho-

capillary pressure from 32 to 63 mmHg theoretically increases the fluid passage across the capillary wall (fluid filtration rate rises from 0.1 to ~0.4 \mu m^2/\mu m^3) (19). Under physiological situations, the orthostatic venous pressure is reduced by the calf muscle pump (12). This in turn might lower the capillary pressure and seems to be an essential factor in the prevention of edema formation, provided the venous valves are sufficient. Un-

fortunately, the effect of the calf muscle pump could not be evaluated in our setup, because even an isomet-

ric contraction of the calf muscle may cause movement artifacts that break the tip of the pipette.

The height difference between heart and toe was 79 cm, causing an orthostatic pressure equal to 58 mmHg, which corresponds with the increase in ankle and toe blood pressures (59 mmHg). Ubbink et al. (32) studied the effect of posture on skin capillary perfusion in the foot and concluded that postcapillary pressure appears to be an important factor in the regulation of capillary perfusion, because an increase in venous resistance mimics the effects of leg dependency. Previous investigations showed that microcirculatory perfusion in the foot changes on a change in posture, i.e., a reduced perfusion, because an increase in venous resistance outweighs pressure regulation in the microcirculation.

The mean capillary pressure increased in line with the increase in venous pressure. This is in agreement with previous observations showing that, with incremental elevation of venous pressure, pressure at the capillary apex approaches that in the veins (18, 32). After all, the postcapillary resistance is lower than the precapillary resistance. So changes in venous pressure (posture and breathing) can be easily transmitted to the capillary bed.

In summary, our results indicate that the systolic capillary blood pressure can rise substantially (up to 100 mmHg) on leg dependency but remains lower than the increase in toe systolic pressure. Apparently, activation of the peripheral vasoconstriction responses reduces the transmission of the arteriolar pressure to the capillaries and probably contributes as an edema-preventing factor. This technique seems suitable to provide valuable information about the pathophysiology of microvascular disorders in the foot.

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**DISCLOSURES**

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