Effects of posture on peripheral vascular responses to lower body positive pressure

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Nishiyasu T, Hayashida S, Kitano A, Nagashima K, Ichinose M. Effects of posture on peripheral vascular responses to lower body positive pressure. Am J Physiol Heart Circ Physiol 293: H760–H767, 2007. First published March 9, 2007; doi:10.1152/ajpheart.00462.2006.—We tested the hypothesis that peripheral vascular responses (in the lower and upper limbs) to application of lower body positive pressure (LBPP) are dependent on the posture of the subjects. We measured heart rate, stroke volume, mean arterial pressure, leg and forearm blood flow (using the Doppler ultrasound technique), and leg (LVC) and forearm (FVC) vascular conductance in 11 subjects (9 men, 2 women) without and with LBPP (25 and 50 mmHg) in supine and upright postures. Mean arterial pressure increased in proportion to increases in LBPP and was greater in supine than in upright subjects. Heart rate was unchanged when LBPP was applied to supine subjects but was reduced in upright ones. Leg blood flow and LVC were both reduced by LBPP in supine subjects [LVC: 4.8 (SD 4.0), 3.6 (SD 3.5), and 1.4 (SD 1.8) mL·min⁻¹·mmHg⁻¹ before LBPP and during 25 and 50 mmHg LBPP, respectively; P < 0.05] but were increased in upright ones [LVC: 2.0 (SD 1.2), 3.4 (SD 3.4), and 3.0 (SD 2.0) mL·min⁻¹·mmHg⁻¹, respectively; P < 0.05]. Forearm blood flow and FVC both declined when LBPP was applied to supine subjects [FVC: 1.3 (SD 0.6), 1.0 (SD 0.4), and 0.9 (SD 0.6) mL·min⁻¹·mmHg⁻¹, respectively; P < 0.05], but remained unchanged in upright ones [FVC: 0.7 (SD 0.4), 0.7 (SD 0.4), and 0.6 (SD 0.5) mL·min⁻¹·mmHg⁻¹, respectively]. Together, these findings indicate that the leg vascular response to application of LBPP is posture dependent and that the response differs in the lower and upper limbs when subjects assume an upright posture.

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ultrasound technique to measure the beat-by-beat changes in leg and upper arm blood flow evoked by application of LBPP, which enabled us to compare the changes in peripheral vascular conductance that occur when LBPP is applied to subjects assuming a supine or upright posture.

METHODS

Subjects

We studied 11 healthy volunteers (9 men and 2 women) with a mean age of 23 yr (SD 1), body weight of 61 kg (SD 3), and height of 169 cm (SD 2). None of the subjects was receiving medication, and none smoked. The study, which was in accordance with the Declaration of Helsinki, was approved by the Human Subjects Committee of the University of Tsukuba, and each subject gave informed, written consent.

Procedures

Experimental protocol. Before the experiment, we familiarized each subject with the procedures by providing them with an orientation session in which they experienced 90° HUT and LBPP. On the experimental day, each subject entered the test room, which was maintained at 25°C, and adopted a supine posture in an LBPP box (Taiseikouki), which could be tilted, and the waist was sealed at the level of the iliac crest. After measurements at supine rest were completed [baseline 1 (B1)], LBPP was applied at 25 and 50 mmHg (LBPP25 and LBPP50, respectively). The two levels of LBPP were applied sequentially, sustained for 3 min each, and followed by a 3-min recovery period. After a set of recovery measurements was taken, the subjects rested for at least an additional 5 min, and another set of “supine rest” measurements were taken (baseline 2). The subjects were then tilted to 90° HUT at a rate of 1° per second. The subject held this position while keeping his or her weight on a saddle with the left foot. No weight was applied to the right leg, where femoral artery blood flow was measured. After measurements at upright rest were complete [baseline 3 (B3)], LBPP25 and LBPP50 were sequentially applied and were again sustained for 3 min each and followed by a 3-min recovery period. Thereafter, the subjects were tilted back to 0° at a rate of 1° per second. Because all of the variables of interest could not be measured within a single performance of this protocol, measurements were repeated several times (separated by at least a 10-min recovery period). During a given performance of the protocol, we measured aortic blood velocity and diameter, brachial vascular diameter (BVDm), brachial artery blood flow velocity (Vb), femoral vascular diameter (FVDm), and femoral artery blood flow velocity (Vf). Measurements of aortic blood velocity and diameter and of BVDm, Vb, FVDm, and Vf were made on different days. The order of the measurements was randomly assigned.

Measurements. HR was monitored via a three-lead electrocardiogram. Changes in blood pressure were assessed by an automated blood pressure monitor (STBP-780; Nippon Colin) with the cuff placed around the upper arm and aligned at the level of the heart. A Doppler ultrasound system (HDI 3500; Philips) equipped with a transducer probe (model L12–5) with an operating frequency of 6 MHz was utilized to simultaneously measure two-dimensional artery transducer probe (model L12–5) with an operating frequency of 6 MHz. The video-taped records of the obtained vessel images were digitized by use of a digital video board (PCI-1411; National Instruments) and stored in a personal computer (ThinkPad T30; IBM) equipped with a computer program for vessel-diameter measurement. The artery diameters related to systole (Ds; mm) and diastole (Dd; mm) were taken as the largest and smallest diameters within each cardiac cycle, respectively. The mean diameter (Dm; mm) was calculated as

\[ D_m = \frac{D_s + 2 \times D_d}{3(23)} \]  

(F1)

FVDM and BVDm were calculated with the same formula.

The cross-sectional area of the artery (CSA; cm²) was estimated as

\[ CSA = \left( \frac{D_m}{2} \right)^2 \times \pi \]  

(2)

We calculated blood flow using the CSA obtained during the 3rd min of each stage (rest, LBPP25, LBPP50, and recovery).

Instantaneous mean blood velocity (MBV) was estimated with the use of a computer program developed with the aid of LabVIEW (version 6.0; National Instruments). Briefly, the frequency spectrum of the analog audio output signal of our Doppler ultrasound unit robustly reflects the Doppler shift frequency spectrum within the audio range (<7.5 kHz in this study). The analog audio output signal was digitized at a sampling frequency of 20 kHz through an analog-to-digital converter (DAQCard-6062E; National Instruments) for processing by a personal computer equipped with our program. The power spectrum of the digitized audio signal was obtained by fast-Fourier transform analysis techniques, employing a Hann smoothing window in 512 data-point segments. The mean frequency of the data segment was derived from the spectral data with the formula

\[ f_{\text{me}} = \frac{\sum_{i=0}^{N/2} (f_i \times P_i)}{\sum_{i=0}^{N/2} f_i} \]  

(3)

where \( f_{\text{me}} \) is the mean frequency, \( f_i \) is the spectral frequency, \( P_i \) is the power related to \( f_i \), and \( N \) is the number of data points. We then began an analysis of the next data segment of the digitized audio signal [which was advanced 200 data points from the beginning of the previous data segment, so that 312 data points (15.6 ms) overlapped]. Our program repeats the above processes in real time, continuously producing 100 values of \( f_{\text{me}} \) per second (100 Hz). The calculated \( f_{\text{me}} \) correlated very well with the actual mean Doppler-shift frequency when an electronically generated arbitrary ultrasound wave was transmitted to the transducer probe and measured using our Doppler ultrasound unit. We therefore regarded \( f_{\text{me}} \) as the mean Doppler shift frequency and used it to calculate instantaneous MBV (see below). The analog signals representing the ECG were digitized at a sampling frequency of 100 Hz and stored together with \( f_{\text{me}} \), which enabled all of the data to be analyzed together for the same time period. HR and MBV were calculated with an off-line data analysis program. MBV was derived from the stored \( f_{\text{me}} \) data using the formula

\[ \text{MBV} = \frac{f_{\text{me}} \times C}{2 \times f_s \times \cos \theta} \times 100 \]  

(4)

where \( f_s \) is the emitted frequency from the transducer probe (6 MHz for femoral and brachial blood flow and 2 MHz for aortic blood flow), \( C \) is the sound velocity in the tissues (we employed 1,530 m/s), and \( \theta \) is the angle between the blood flow direction and the ultrasound beam (we kept \( \theta \) below 60° for femoral and brachial blood flow and 20° for aortic blood flow). We applied the above formula to all of the stored \( f_{\text{me}} \) data and obtained an instantaneous MBV profile over the entire
RESULTS

During application of LBPP, the increase in MAP from the relevant baseline was proportional to the increase in LBPP in the two postures (Fig. 1). Moreover, the changes from each baseline during LBPP were greater \((P < 0.05)\) when subjects were supine than when they were upright [in mmHg: 7 (SD 3) during LBPP25 and 14 (SD 5) during LBPP50 in supine; 3 (SD 2) during LBPP25 and 8 (SD 4) during LBPP50 in an upright posture]. When subjects were upright, HR was higher \((P < 0.05)\) than when they were supine (Fig. 1). HR did not change when LBPP was applied to subjects assuming a supine posture, but it was reduced \((P < 0.05)\) when subjects were upright.

When subjects were at rest in an upright posture, SV, CO, and TVC were all lower \((P < 0.05)\) than when subjects were supine. Application of LBPP25 to subjects in a supine posture had no effect on SV or CO, but LBPP50 elicited a slight reduction \((P < 0.05)\) from baseline (Figs. 1 and 2). With subjects in an upright posture, LBPP25 elicited increases in SV and CO \((P < 0.05)\), and during LBPP50 those values increased \((P < 0.05)\) up to the levels seen with subjects in a supine posture. TVC declined in proportion to the increase in LBPP when subjects were supine but increased in proportion to the increase in LBPP when they were upright (Fig. 2).

When subjects were at rest in an upright posture, LBF, LVC, FVC, and FVDm were all lower \((P < 0.05)\) than when they were supine. LBPP25 had no effect on LBF in supine subjects, but LBPP50 elicited marked declines from baseline [in ml/min:...
354.6 (SD 240.5) at B1, 283.5 (SD 244.9) during LBPP25, and
103.9 (SD 118.4) during LBPP50; \( P < 0.05 \) (Fig. 3). By
counter, LBF increased during LBPP in upright subjects [in
ml/min: 173.4 (SD 103.9) at B3, 288.9 (SD 272.7) during
LBPP25, and 248.5 (SD 162.3) during LBPP50; \( P < 0.05 \)]
(Fig. 3). Application of LBPP reduced LVC in supine subjects
[in ml/min: 4.8 (SD 4.0) at B1, 3.6 (SD 3.5) during
LBPP25, and 1.4 (SD 1.8) during LBPP50; \( P < 0.05 \)]
but increased LVC in upright subjects [in ml/min: 2.0 (SD 1.2) at B3, 3.4 (SD 3.4) during
LBPP25, and 3.0 (SD 2.0) during LBPP50; \( P < 0.05 \)] (Fig. 4). It also reduced FVC
[in ml/min: 1.3 (SD 0.6) at B1, 1.0 (SD 0.4) during
LBPP25, and 0.9 (SD 0.6) during LBPP50; \( P < 0.05 \)] in
supine subjects but had no effect on FVC when subjects
were upright [in ml/min: 0.7 (SD 0.4) at B3, 0.7 (SD 0.4) during
LBPP25, and 0.6 (SD 0.5) during LBPP50] (Fig. 4). The pattern of the changes in FBF was similar to that
seen with FVC [in a supine posture, in ml/min: 91.3 (SD 46.6)
at B1, 73.3 (SD 33.4) during LBPP25, and 75.1 (SD 44.6)
during LBPP50; in an upright one in ml/min: 54.0 (SD 32.5) at
B3, 60.4 (SD 35.3) during LBPP25, and 57.3 (SD 47.2) during
LBPP50] (Fig. 3).

There was no posture-dependent difference in FVDm [in
cm: 0.95 (SD 0.13) in supine posture and 0.99 (SD 0.13) in
upright one] or BVDm [in cm: 0.42 (SD 0.03) and 0.43 (SD
0.03), respectively]. Application of LBPP reduced FVDm (\( P <
0.05 \)) in supine subjects. In upright subjects, LBPP25 had no
effect on FVDm, but LBPP50 elicited a slight reduction (\( P <
0.05 \)). BVDm was unaffected by LBPP, irrespective of the
subject’s posture.

Application of LBPP elicited increases in LVP when the
subjects were supine [in mmHg: 6.5 (SD 3.1) at B1, 9.7 (SD
3.6) during LBPP25, and 16.1 (SD 0.6) during LBPP50] or
upright (in mmHg: 32.6 (SD 5.5) at B3, 36.4 (SD 5.6) during
LBPP25, and 42.8 (SD 7.3) during LBPP50). It similarly
elicited a slight increase in FVP in both supine [in mmHg: 7.6
(SD 1.1) at B1, 10.1 (SD 1.5) during LBPP25, and 11.7 (SD
3.2) during LBPP50] and upright [in mmHg: 5.3 (SD 2.8) at
B3, 6.0 (SD 2.8) during LBPP25, and 6.7 (SD 2.6) during
LBPP50] subjects and also elicited increases in CVP in both
supine [in mmHg: 6.5 (SD 3.1) at B1, 9.7 (SD 3.6) during
LBPP25, and 16.1 (SD 0.6) during LBPP50] and upright [in
mmHg: 1.6 (SD 5.5) at B3, 5.4 (SD 5.6) during LBPP25, and
11.8 (SD 7.2) during LBPP50] subjects.

DISCUSSION

The major finding of this study is that the vascular response
in the leg to application of LBPP is dependent on the posture
of the subject and is different from the response in the arm

Fig. 3. Effects of LBPP on leg blood flow (LBF; top) and forearm blood flow
(FBF; bottom) in subjects assuming a supine or upright posture. Values are
means (and SD); \( n = 11 \) subjects. \( *P < 0.05 \) vs. the initial value in the supine posture; \( †P < 0.05 \) vs. the initial value in the upright posture.

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when the subject was upright. More specifically, application of LBPP markedly reduced LVC when subjects were supine but significantly increased LVC when they were upright. On the other hand, FVC declined on application of LBPP to supine subjects but was unchanged when the subjects were upright. The different peripheral vascular responses of the upper and lower limbs would contribute to the different systemic cardiovascular responses seen between the supine and upright postures during application of LBPP.

Some earlier studies reported that application of LBPP to supine subjects elicits an increase in CO (5, 20, 28), whereas others reported that CO was unaffected (2, 27) or even tended to decline (7, 8). The effect of LBPP on SV in supine subjects was similarly variable, with SV reportedly increased (5, 28), unchanged (2, 20), or tending to decline (7, 8). In the present study, application of LBPP25 to supine subjects had no effect on CO or SV, but both were significantly reduced by LBPP50. Given that HR was unchanged during LBPP50 in supine subjects, the reduction in CO is attributable to the concomitant reduction in SV. Shi et al. (28) reported that CVP increases significantly from control when 5 mmHg LBPP is applied to subjects in a supine position and that a gradual increase in CVP is seen with application of up to 40 mmHg LBPP. Consistent with that report, we found that CVP was increased by 10 mmHg during LBPP50 when subjects were supine. Because MAP also increases with increasing LBPP in the supine posture, the change in SV elicited by LBPP would be affected by both the increase in preload (i.e., increase in CVP) and the increase in afterload (i.e., increase in MAP).

TVC is reduced when LBPP is applied to supine subjects. This reduction is mainly due to mechanical compression of the vasculature in the lower part of the body and to the action of the peripheral reflexes, stimulated via the muscle mechanoreflex in the lower body (18, 19, 29, 31). Reneman et al. (25) demonstrated that changes in pressure around a limb were readily transmitted from the skin to the muscles. We therefore presume that each 25 mmHg change in LBPP caused a similar change in the lower body transmural pressure. Consistent with that idea, Nielsen (19) elicited proportional reductions in calf blood flow in response to application of external pressures while the calf was in a supine posture. This study suggested that the reductions could have been induced by increases in the area of the low-pressure vascular beds (e.g., postcapillary vessels) that partially collapsed under the pressure. That is, when the LBPP exceeds the luminal pressure in the postcapillary vessels and veins, which are collapsible, the transmural pressure in those vessels would become zero, and the vessels would collapse. Because flow in the collapsed veins obeys the basic laws of fluid dynamics, and transmural pressures at or near zero markedly reduce the CSA of the tube, there is a marked increase in viscous resistance to flow within the postcapillary vessels and veins under these conditions (13). We therefore postulate that this mechanical effect on vascular resistance is the main cause of the observed reduction in TVC in supine subjects. We found that both LVC and FVC declined during application of LBPP to supine subjects. However, although LVC declined in proportion to the increase in LBPP, there was no further reduction in FVC when LBPP was increased from 25 to 50 mmHg. Moreover, the percent change from baseline during LBPP50 was much greater for LVC than for FVC (71 vs. 21%; \( P < 0.05 \)). Thus, when LBPP is applied to supine subjects, the effects of activation of peripheral reflexes would contribute to the reduction in local vascular conductance in both the upper and lower limbs, whereas the effects of mechanical compression would exert an additive effect in the lower limbs, further reducing LVC but not FVC.

Although the increase in MAP was proportional to the increase in LBPP in both postures, the change from each baseline was much less when subjects were upright than when they were supine. Moreover, although CO, SV, TVC, and LVC declined when LBPP was applied to supine subjects, they increased when the subjects were upright. The increase in CO elicited by application of LBPP to upright subjects is consistent with earlier observations (20). In an upright posture, hydrostatic pressure causes a pooling of \( \sim 600 \) ml of blood in the lower part of the body (10). This leads to several compensatory reactions (e.g., an increase in HR and a decrease in TVC) that tend to restore blood pressure and blood volume in the central part of the body, mainly via the high- and low-pressure baroreflexes (26). The increase in SV that we see on application of LBPP to upright subjects suggests that LBPP causes a substantial translocation of blood from the lower to the central body. This restoration of the central blood volume could load the high- and low-pressure baroreceptors, leading to vasodilation in the peripheral circulation. If so, the reduction in HR elicited by applying LBPP to upright subjects likely would be due to loading of the high blood pressure baroreceptors.
baroreceptor activity, which would inhibit sympathetic nerve activity and override the muscle mechanoreflex-mediated sympathoexcitation, would in turn lead to the vasodilatation seen in the lower limbs. In addition, because when one assumes an upright posture the higher hydrostatic pressure in the lower body increases the pressure in the veins and arteries there (LVP averaged 32.6 mmHg in upright subjects but only 6.5 mmHg in supine ones), the collapse of the postcapillary vessels and veins that would likely occur when one is supine might not occur when one is standing upright. Thus, with application of LBPP to upright subjects, the ability of the postcapillary vessels and veins to remain open, combined with the effects of loading the baroreceptors, could in part explain the smaller rise in MAP, compared with supine subjects, and the increases in TVC and LVC. Alternatively, the greater rise in MAP seen in supine subjects could be attributable in part to reduced baroreflex buffering of the rise in MAP. Because the HR is already quite low when one is supine, vs. when one is upright, it is not reduced further in response to the rise in MAP, most likely because there is little sympathetic activity to withdraw, and vagal activity is already quite high. Similarly, sympathetic vasoconstrictor tone is likely to be low in this setting, so that again there would be little activity for the baroreceptors to withdraw. The same would not be true when one is standing upright. In addition, because the LBPP-induced reduction in the transmural venous pressure in the lower legs of upright subjects would reduce venous blood pooling, the venoarterial reflex also may act to dilate the small arteries, thereby increasing TVC and LVC. In addition, myogenic responses could also contribute to posture-related differences in responses to LBPP. For example, the rise in MAP induced by LBPP in supine subjects would be expected to elicit myogenic vasoconstriction in the arm and elsewhere in the body, leading the reductions in FVC, LVC, and TVC. On the other hand, in an upright posture, LBPP could reduce arteriolar transmural pressure leading to myogenic relaxation, thereby contributing to the rise in LVC.

Application of LBPP to upright subjects elicited increases in LVC, but FVC was unchanged, suggesting that the aforementioned reflex-induced vasodilatation did not occur in the upper arms. Although it has been reported that muscle sympathetic nerve activity is similar in the upper arm and lower leg during lower body negative pressure or HUT (15, 24), the findings of other studies suggest sympathetic regulation may differ in the upper and lower limbs. For instance, different responses are seen in the upper and lower limbs during mental stress (1), and the effectiveness of $\alpha$- and $\beta$-receptors is greater in the legs than in the arms (22), suggesting that a LBPP-induced reduction in sympathetic activity in upright subjects affects the upper and lower limbs differently.

Limitations

We estimated CVP and LVP based on the venous pressure in the inferior vena cava. The reason we used the inferior vena cava instead of the femoral vein is that the catheter tip is more stable there during LBPP and HUT. However, because the location of the catheter tip was slightly outside the LBPP chamber, in supine subjects, the actual LVP might have been higher than the one estimated here (4). On the other hand, in upright subjects, the magnitude of the LBPP (50 mmHg) was below the considerable venous pressure in the legs, so that blood flow remained elevated during LBPP. This suggests that the hydrostatic column in the veins was uninterrupted between the legs and the heart. In that case, our estimate of LVP from downstream (upper part of the column) is likely accurate. We also estimated the changes in CVP from the inferior vena cava pressure because the inferior vena cava is a relatively large vein and is directly connected to the heart. In calculating the vascular conductance during LBPP and HUT for each of the three subjects participating in this experiment, we used the mean venous pressures. In fact, even if each venous pressure were varied to the extent of the standard deviation, the arterial-venous pressure difference changed by only a few percent, indicating that the effect of changes in venous pressure on changes in conductance is likely small. Thus, although it is more accurate to measure each venous pressure simultaneously with measurements of flow in each subject, the main findings would not be affected.

In summary, femoral vascular conductance (LVC) is markedly reduced on application of LBPP to subjects in a supine position but is significantly increased when subjects are positioned upright. At the same time, FVC is reduced in supine subjects but is unchanged in upright ones. Together, these findings indicate that the vascular response in the leg to application of LBPP is posture dependent and is different in the lower and upper limbs when subjects assume an upright posture. These differences in the peripheral vascular responses of the upper and lower limbs would be expected to contribute to the difference in the systemic cardiovascular responses to LBPP seen in supine and upright subjects.

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