Gender affects calf venous compliance at rest and during baroreceptor unloading in humans

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Monahan, Kevin D., and Chester A. Ray. Gender affects calf venous compliance at rest and during baroreceptor unloading in humans. Am J Physiol Heart Circ Physiol 286: H895–H901, 2004. First published November 6, 2003; 10.1152/ajpheart.00719.2003.—Leg venous compliance is a determinant of peripheral venous pooling during orthostatic stress such that high venous compliance could contribute to reduced orthostatic tolerance. We tested the hypotheses that 1) calf venous compliance is reduced during baroreceptor unloading, and 2) calf venous compliance is greater in women than men. Twelve men (27 ± 2 yr) and 12 women (25 ± 2 yr) were studied in the supine posture. Calf venous compliance was determined by inflating a thigh venous collecting cuff to 60 mmHg for 8 min and then decreasing cuff pressure at a rate of 1 mmHg/s to 0 mmHg. The slope of the pressure-compliance relation (compliance = β1 + 2β2; cuff pressure), which is the first derivative of the quadratic pressure-volume relation ([Δlimb volume] = β0 + β1×(cuff pressure) + β2×(cuff pressure)²) during the reduction in collecting cuff pressure, was used to assess venous compliance at baseline and during one-legged lower body negative pressure (LBNP: −50 mmHg). At baseline, calf venous compliance was 48% lower (P < 0.001) in women than men and decreased in men (Δ−25 ± 8%; P < 0.05) but not women (Δ1 ± 11%) during LBNP. Rhythmic ischemic handgrip (Δ6 ± 9%) and cold pressor testing (Δ−9 ± 7%) did not alter calf venous compliance in a subgroup of men (n = 6). These data indicate gender-dependent effects on calf venous compliance under conditions associated with low sympathetic outflow (i.e., rest) and high sympathetic outflow (i.e., LBNP). However, they cannot explain gender-associated differences in orthostatic tolerance.

veins; orthostasis; autonomic nervous system; baroreflex; blood pressure

INTERESTINGLY, cardiovascular system responses to orthostasis are nearly abolished if the inferior fluid shift of thoracic blood volume into the legs is prevented (14). These data indicate that the ability of the lower limb vasculature to accept orthostasis-induced fluid shifts is a critical determinant of the hemodynamic stress incurred during orthostasis. A physiological determinant of this inferior fluid shift has long been presumed to involve the compliance of the leg veins. Specifically, high venous compliance in the legs may promote greater venous pooling of blood in the leg and contribute to reduced orthostatic tolerance (21). Furthermore, because veins appear to be richly innervated with sympathetic nerve endings (1), it is believed that reflexive changes in sympathetic nerve activity may reduce venous compliance (26) and assist in arterial blood pressure regulation by reducing peripheral blood pooling.

In the present study, we used a noninvasive method of determining limb venous compliance (15) to test the hypothesis that baroreceptor unloading (i.e., sympathetic activation) reduces calf venous compliance in vivo in humans. Moreover, due to the association between high venous compliance and low orthostatic tolerance (26), we further tested the hypothesis that calf venous compliance is greater in women than men. If supported experimentally, this latter finding could provide insight into a potential mechanism contributing to reduced orthostatic tolerance in women (7, 13, 29, 36). To test these hypotheses, measures of calf venous compliance were obtained under conditions associated with basal sympathetic and heightened sympathetic outflow.

MATERIALS AND METHODS

Subjects
Twenty-four healthy subjects (12 men and 12 women) were studied. Subjects were healthy on the basis of medical history and physical examination, resting arterial blood pressure <140/90 mmHg, non-smoking status, body mass index <27 kg/m², not taking any medications with known cardiovascular or autonomic nervous system actions, and no history or symptoms of venous insufficiency. Written informed consent was obtained from all subjects on a Pennsylvania State University College of Medicine Institutional Review Board approved form.

Experimental Design
Subjects were studied supine and refrained from caffeine ingestion for 12 h and food consumption for 4 h before being tested. Approximately one-half of the men (7 of 12) and women (6 of 12) were...
studied in the morning with the remaining subjects studied in the afternoon.

Protocol 1. The purpose of this protocol was to determine whether 1) calf venous compliance is greater in women than men and 2) baroreceptor unloading reduces calf venous compliance in men and women. Subjects were enclosed in a one-legged lower body negative pressure (LBNP) chamber up to the level of the umbilicus 20 min before data acquisition. This LBNP chamber allowed for application of negative pressure only to the left leg and the entire pelvis. The right leg from the level of the upper thigh down was positioned outside the chamber and exposed only to atmospheric pressure (17). This chamber allowed the effect of sympathetic activation per se on calf venous compliance to be determined without the confounding effects of changes in atmospheric pressure. Subjects were instrumented for simultaneous measurement of calf volume (strain-gauge plethysmography) and venous collecting cuff pressure. The right leg, in which venous compliance was determined, was positioned above the heart level to promote venous drainage. Calf venous compliance was determined by using the method of Halliwill et al. (15). After instrumentation and a period of preceding rest (20 min), venous collecting cuff pressure was applied at 60 mmHg for 8 min. After this 8-min period, collecting cuff pressure was reduced at a rate of 1 mmHg/s to 0 mmHg (baseline condition) (Fig. 1). In a second trial, LBNP began (~50 mmHg) 2 min before collecting cuff pressure was applied at 60 mmHg (8 min) and then reduced at a rate of 1 mmHg/s to 0 mmHg (LBNP condition). LBNP was applied throughout the entire period of cuff inflation (8 min) and deflation (1 min). These two trials (baseline and LBNP) were separated by 20 min of preceding rest and were randomized to avoid an order effect.

Protocol 2. The purpose of this protocol was to determine whether the reduction in calf venous compliance observed during LBNP in men was specific to baroreflex-induced sympathoexcitation. Calf venous compliance was determined in an identical manner as in protocol 1. Three trials were performed (baseline, rhythmic ischemic handgrip, and cold pressor stimulus). After instrumentation and a period of preceding rest (20 min), venous collecting cuff pressure was applied at 60 mmHg for 8 min to the right leg. After this 8-min period, the collecting cuff pressure was reduced at a rate of 1 mmHg/s to 0 mmHg (baseline condition). In a second trial, collecting cuff pressure was applied at 60 mmHg (8 min) and then reduced at a rate of 1 mmHg/s to 0 mmHg (baseline condition). In a third trial, collecting cuff pressure was applied at 60 mmHg (8 min) and then reduced at a rate of 1 mmHg/s to 0 mmHg. In the final 2 min of this period and during the final minute period in which pressure was reduced to 0 mmHg, the subject performed rhythmic ischemic handgrip to fatigue (30% of their individual maximal voluntary contraction at a rate of 30 contractions/ min). Ischemia was obtained by inflating a blood pressure cuff positioned around the upper arm of the exercising limb to 220 mmHg. In a third trial, collecting cuff pressure was applied at 60 mmHg (8 min) and then reduced at a rate of 1 mmHg/s to 0 mmHg. In the final minute of this 8-min period and during the 1-min period in which pressure was reduced to 0 mmHg, the subject submerged a hand in a bucket of ice and water (cold pressor test). Both ischemic handgrip and cold pressor testing elicit prompt robust (~2-fold) increases in muscle sympathetic nerve activity in humans within 2 min (22, 35). On the basis of this fact, as well as the discomfort and inability to perform these tasks for extended periods of time, the duration of the experimental interventions was briefer in protocol 2 than in protocol 1. These three trials were separated by 20 min and were randomized.

Measurements

Venous compliance plethysmography. Changes in calf volume were measured noninvasively by using strain-gauge plethysmography (model EC4; D. E. Hokanson, Bellevue, WA) at the maximal calf circumference. A venous collecting cuff was placed around the thigh and was connected to an external air source that allowed pressure to be precisely and rapidly modulated within the cuff. Venous collecting cuff pressure was measured directly with a pressure transducer (Xcaliber; Spectramed, Oxnard, CA) positioned in-line with the venous collecting cuff and air source.

Data Analysis

All data were recorded to a Macintosh computer (MacLab 8e; ADInstruments) for later analyses.

Collecting cuff pressure was used as a surrogate for intravenous pressure (15). Pressure-volume relations were generated during the 1-min period in which venous collecting cuff pressure was reduced from 60 to 0 mmHg and averaged over 2-mmHg pressure increments, as described previously (15, 24). Pressures <10 mmHg were excluded because they may violate the assumption that collecting cuff pressure is equal to intravenous pressure (15). The resulting pressure-volume curves during this stepdown in pressure are nonlinear and well described by the quadratic regression equation \[\text{[\text{change in venous pressure}]} = \beta_0 + \beta_1 \times \text{[cuff pressure]} + \beta_2 \times \text{[cuff pressure]}^2\]. \(\beta_0\) (i.e., y-intercept) is a complex parameter that represents several dynamically interacting factors. Factors represented by this variable include unstrained volume, hysteresis present in the pressure-volume relation, and the difference between resting venous pressure (~6 mmHg) and a venous pressure of zero (15). On the basis of this complex interaction, interpretation of changes in \(\beta_0\) must be done conservatively, because a change in any or all of these previously mentioned factors might contribute to changes in \(\beta_0\). Furthermore, because of the derived nonlinear pressure-volume curves, a single number cannot characterize the scope of this relation, because compliance becomes a function of a specific pressure (i.e., compliance is distinctly different at each pressure level). Accordingly, to simplify data presentation, the first derivative of the pressure-volume curve [compliance \(= \beta_1 + 2 \times \beta_2 \times \text{[cuff pressure]}\)] was calculated by using the regression parameters \(\beta_1\) and \(\beta_2\) (i.e., slope components) from the quadratic regression equation.
equation. The first derivative yields a linear pressure-compliance relation that can be evaluated graphically (15). The slope of this pressure-volume curve and the pressure-compliance lines are ~48% less steep in women compared with men indicating lower levels of calf venous compliance in women.

Calf venous capacitance was estimated during each trial by visually identifying the point at which the pressure-volume relation appeared to shift from a rapid filling response (capacitance response) to a slower, less-pronounced increase in volume after application of venous collecting cuff pressure indicative of calf vein creep or transcapillary filtration (19). These measures were made by the same investigator blinded to the gender and trial condition and are reported as the relative (%) change in calf volume from the point before collecting cuff pressure application.

Differences in subject characteristics were determined by an unpaired t-test, and repeated-measures ANOVA was used to determine the effects of sympathetic activation on calf venous compliance. Specific contrasts were made by using Newman-Keuls post hoc tests. Univariate correlations were used to assess the strength of relations among variables of interest. Statistical significance was set at \( P < 0.05 \). All data are presented as means \( \pm \) SE.

**RESULTS**

**Subject Characteristics**

Men and women did not differ in respect to age (27 \( \pm \) 2 vs. 25 \( \pm \) 2 yr for men and women, respectively). However, the men were taller (178 \( \pm \) 2 vs. 164 \( \pm \) 3 cm; \( P < 0.05 \)) and weighed more (77 \( \pm \) 3 vs. 57 \( \pm \) 2 kg; \( P < 0.05 \)) than the women.

**Effect of Gender and LBNP on Calf Venous Compliance**

At baseline, the pressure-volume curves were less steep (Fig. 2 and Table 1) and calf venous compliance, assessed as the slope \( (10^{-3}) \) of the pressure-compliance curve (Fig. 2), was 48% lower in women \( (-0.91 \pm 0.14) \) compared with men \( (-1.74 \pm 0.15; \ P < 0.001) \). Baroreceptor unloading reduced calf venous compliance (slope of the pressure-compliance relation) in men \( (\Delta -25 \pm 8\% ; \ P < 0.05) \) but not women \( (\Delta 1 \pm 11\% ; \text{ANOVA interaction term } P < 0.05) \) (Figs. 3 and 4). Similar baseline and LBNP effects were observed when the regression parameters \( \beta_1 \) and \( \beta_2 \) were used to assess group and condition effects (Table 1). Calf venous capacitance was greater in men than women \( (3.7 \pm 0.2 \) vs. \( 3.0 \pm 0.2\% ; \ P < 0.05 \) during the baseline trial (Fig. 5). LBNP reduced the calf venous capacitance response in both men \( (\Delta -15 \pm 6\% ) \) and women \( (\Delta -19 \pm 5\% ) \) (Fig. 5).

**Effect of Rhythmic Ischemic Handgrip and Cold Pressor on Calf Venous Compliance in Men**

Rhythmic ischemic handgrip and cold pressor testing did not alter the slope of the pressure-volume or pressure-compliance curves in the subgroup of men \( (n = 6) \) tested (Table 2 and Fig. 6). Moreover, the venous capacitance response did not differ among baseline \( (4.5 \pm 0.4\% ) \), rhythmic ischemic handgrip \( (4.3 \pm 0.4\% ) \), or cold pressor \( (4.1 \pm 0.5\% ) \) trials \( (\text{all } P > 0.05) \). These data indicate that sympathoexcitation mediated by baroreceptor unloading, but not muscle reflex activation or cold stress, reduced calf venous compliance in men. Similar effects were observed when the regression parameters \( \beta_1 \) and \( \beta_2 \) were assessed (Table 2).

**Physiological Correlates**

Calf venous compliance at baseline correlated significantly with height \( (r = -0.74) \), weight \( (r = -0.69) \), body mass index \( (r = -0.46) \), and calf venous capacitance \( (r = -0.61) \) when all subjects (men and women) were considered together. When men and women were considered separately, only height in the men \( (r = -0.60) \) and calf venous capacitance \( (r = -0.61) \) in women remained significantly correlated with calf venous compliance measured at baseline.

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**Table 1. Pressure-volume regression parameters (protocol 1)**

<table>
<thead>
<tr>
<th>Baseline</th>
<th>( \Delta ) limb volume = 1.164 ( \pm ) 0.241 + 0.098 ( \pm ) 0.008 ( \times ) (cuff pressure) (- 0.00087 \pm 0.00008 \times ) (cuff pressure)(^2)</th>
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<tr>
<td>Men</td>
<td>( \Delta ) limb volume = 1.653 ( \pm ) 0.177 + 0.054 ( \pm ) 0.007(^*) ( \times ) (cuff pressure) (- 0.00045 \pm 0.00008* \times ) (cuff pressure)(^2)</td>
</tr>
<tr>
<td>Women</td>
<td>( \Delta ) limb volume = 1.107 ( \pm ) 0.235 + 0.080 ( \pm ) 0.008(\dagger) ( \times ) (cuff pressure) (- 0.00064 \pm 0.00008\dagger \times ) (cuff pressure)(^2)</td>
</tr>
<tr>
<td>Lower body negative pressure</td>
<td>( \Delta ) limb volume = 1.151 ( \pm ) 0.249 + 0.053 ( \pm ) 0.009(\dagger) ( \times ) (cuff pressure) (- 0.00046 \pm 0.00007 \times ) (cuff pressure)(^2)</td>
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\( \Delta \) Limb volume \( = \beta_0 + \beta_1 \times (\text{cuff pressure}) + \beta_2 \times (\text{cuff pressure})^2 \). \( *P < 0.05 \) vs. men; \( \dagger P < 0.05 \) vs. baseline.
DISCUSSION

The primary findings from the present study are that 1) calf venous compliance is lower in women than men at rest, 2) LBNP (i.e., baroreceptor unloading) reduces calf venous compliance in men but not women, 3) reductions in calf venous compliance during sympathoexcitation appear to be specific to baroreceptor unloading and not muscle reflex engagement or cold stress in men, and 4) calf venous capacitance is lower in women than men at rest, but is equally reduced in men and women during baroreceptor unloading. Collectively, these findings suggest that calf venous compliance and its modulation by sympathoexcitation are unlikely to contribute mechanistically to decreased orthostatic tolerance in women (7, 13, 29, 36).

We demonstrate lower calf venous compliance at baseline in women than in men. To the best of our knowledge, this is the first demonstration of this gender-associated effect. Previously, calf venous compliance was shown not to differ statistically in men and women, despite being ~20% lower in women (7, 8). We believe that our ability to demonstrate such a gender effect is related to our method of assessing venous compliance that is less dependent on physiological assumptions inherent in other methods used to assess venous compliance in vivo (15, 24), such as assuming that resting venous pressure is equal to zero, and to our larger sample size. The lower level of calf venous compliance we observed in women is consistent with reduced level of peripheral venous pooling in the lower leg during orthostatic stress (7, 12, 25) and reduced venous capacitance response (present study). Mechanisms underlying this gender effect are unknown, but may involve differences in the structural components of the venous wall (e.g., collagen and elastin content) (5) or in local modulators of venous tone (16). However, we are unaware of any data examining these issues in the peripheral venous system of men and women. Additionally, the finding that calf venous compliance is lower, not greater, in women than men suggests that venous compliance is unlikely to contribute to reduced orthostatic tolerance in women (7, 13, 29, 36).

Fig. 4. Venous compliance derived from the slope of the pressure-compliance relation in men and women at baseline and during LBNP (ANOVA interaction term; \( P < 0.05 \)). Calf venous compliance is reduced in men, but not women, during baroreceptor unloading. \( ^\dagger P < 0.05 \) from baseline; \( ^* P < 0.05 \) vs. men at same time point.

Fig. 5. Calf venous capacitance (%change in calf volume) was determined at the transition between the steep filling phase and slower plateau phase of changes in calf volume during application of collecting cuff pressure at 60 mmHg during the compliance trials. Calf venous capacitance is greater in men than women in both the baseline and LBNP trials. LBNP reduced calf venous capacitance in both men and women. \( ^* P < 0.05 \) vs. men at same time point; \( ^\dagger P < 0.05 \) from baseline.
The second major finding of the present study was that in men, but not women, sympathoexcitation is associated with a reduction in calf venous compliance. This statement is supported by the 25% decrease in calf venous compliance in men during baroreceptor unloading. In women, no such change in venous compliance was observed during LBNP. It is unlikely that this lack of reduction in calf venous compliance during LBNP contributes to reduced orthostatic tolerance in women (7, 13, 29, 36). The primary support for this statement comes from the observations that 1) baseline levels of calf venous compliance and venous capacitance are lower, not greater, in women, which should aid in orthostatic blood pressure regulation and reduce the impact that sympathomodulation of venous compliance could exert due to a baseline effect; 2) venous capacitance, unlike venous compliance, is reduced during one-legged LBNP similarly in men (Δ−15 ± 6%) and women (Δ−19 ± 5%); and 3) this reduction in calf venous capacitance during LBNP occurs independent of changes in calf venous compliance. Collectively, these findings indicate that baseline levels of calf venous compliance and not its responses during LBNP are likely to be of greater importance in determining the hemodynamic stress (i.e., reduction in thoracic blood volume and the magnitude of peripheral venous pooling) of a physiological challenge such as orthostasis. Thus other mechanisms such as lower cardiovagal baroreflex sensitivity (2), lower blood volume (7), and blunted increase in muscle sympathetic nerve activity in response to head-up tilting (29), as well as other potential factors (7), are likely to be primary factors contributing to lower orthostatic tolerance in women.

The mechanism(s) underlying the differential gender-related effects of sympathoexcitation on calf venous compliance (i.e., no reduction in venous compliance during LBNP in women, but a reduction in men) are unclear. It appears that sympathetic fibers innervate the peripheral venous system (1, 20, 32) and that intravenous administration of norepinephrine increases venous tone in individuals with intact autonomic function (32). Thus sympathoexcitation may exert an influence of the peripheral venous vessels through either direct (neural innervation) or indirect actions (circulating norepinephrine). These data suggest that responses to either endogenous norepinephrine release and stimulation of abluminal adrenergic receptors or those effects exerted by norepinephrine when present in the general circulation may differ qualitatively in men and women. Prior data obtained in humans from the arterial circulation of the forearm are consistent with this suggestion (18). We do not have direct recordings of sympathetic nerve traffic directed toward the peripheral veins or of plasma norepinephrine levels in the present study. Therefore, we cannot determine the relative contribution of each of these mechanisms to the findings of the present study.

Two earlier studies (11, 15) utilizing the same technique of assessing venous compliance were unable to demonstrate an effect of sympathoexcitation on venous compliance. It is likely that at least two factors contributed to this lack of effect of sympathoexcitation on venous compliance. First, the size and/or composition of the subject groups may have contributed to the previous negative findings (11, 15). Specifically, these previous studies did not statistically test for a gender-associated effect on calf venous compliance, and the study by Freeman et al. (11) included a disproportionately larger number of women subjects. Thus consideration of men and women collectively in the analyses or the larger number of female subjects in the study group may have obscured the ability to demonstrate a reduction in limb venous compliance during sympathoexcitation. Second, both of the previous studies used fatiguing ischemic handgrip to elicit increases in sympathetic outflow as opposed to baroreceptor unloading used in the present study. Ischemic handgrip to fatigue is a complex physiological stressor that elicits increases in sympathetic nervous system outflow primarily via activation of the muscle reflex and also increases circulating epinephrine (33). Thus it is possible that the stimuli to the peripheral veins differ between muscle reflex and baroreflex activation. Consistent with these prior studies, we confirmed that ischemic handgrip does not reduce calf venous compliance in men. Moreover, we demonstrate that cold stress does not reduce calf venous compliance in men. Collectively, these data indicate specificity for reductions in calf venous compliance during sympathoexcitation in men that occurs during baroreceptor unloading but not muscle reflex activation or cold stress.

One other study (31) has attempted to address whether sympathetic activation modulates limb venous compliance. In this study, various levels of upright tilt did not result in a reduction in limb venous compliance. However, it is important to emphasize that this study: 1) examined a disproportionately higher percentage of females than male subjects; 2) tested...
exclusively adolescents (13–19 yr old); 3) made venous compliance measures shortly after making blood flow measurements, which may have modified the ability of sympathetic outflow to influence venous compliance; and 4) made measurements in partially filled leg veins because the leg was below heart levels for several data points, which reduces the range of pressures examined. Thus it is likely that one or more of these factors contributed to the failure to demonstrate an effect of sympathetic activation on limb venous compliance.

Despite the differential effects of gender on calf venous compliance both at rest (i.e., lower in women) and during LBNP (i.e., reduced by LBNP in men but not women) the venous capacitance responses were shifted downward in women at baseline but was similarly reduced in both men and women during LBNP. These data indicate that a reduction in calf venous compliance is not necessary to observe a reduced venous capacitance response. In men, the capacitance response was reduced during LBNP and likely occurred due to a reduction in the slope of the pressure-volume relation, because no shift was seen in the y-intercept ($\beta_0$). In women, the slope of the pressure-volume relation was unchanged by LBNP. This finding suggests that the pressure-volume relation must be shifted downward in order for a reduction in venous capacitance to be observed in women during LBNP (Fig. 3B, top). Consistent with this suggestion, the y-intercept ($\beta_0$) was lower during LBNP in women. This downward shift in the pressure-volume relation may be due to a reduction in the unstressed volume of the leg (10, 34). It is unclear why women but not men showed a downward shift in $\beta_0$. However, men consistently demonstrated no downward shift in the y-intercept ($\beta_0$) during three distinct sympathoexcitatory maneuvers (LBNP, rhythmic ischemic handgrip, and cold stress).

Several limitations deserve mention. First, collecting cuff pressure was used as a surrogate for intravenous pressure. As previously described (24), we believe that this assumption is valid (15). In the present study, when LBNP was applied and calf blood flow was presumably reduced, it is possible that venous filling and subsequently, the time required for venous pressure to rise to the levels of the collecting cuff pressure was increased. To account for such an effect, we increased the venous collecting cuff pressure application time from 4 to 8 min (24). Importantly, this increased period of cuff application does not alter the ability of collecting cuff pressure to act as a surrogate for intravenous pressure (15). Second, we assessed venous compliance only in the lower leg. Therefore, it is possible that different results may be obtained if venous circulations in other areas of the body are studied, such as in the pelvic region in which women tend to pool more blood than men (37). However, we believe that the leg is a physiologically relevant area to examine on the basis of its critical role in adapting to orthostatic stress. Third, we cannot determine which skeletal muscle and/or skin veins contributed to our findings. The magnitude of sympathetic innervation of veins in skeletal muscle appears to decrease as a function of the depth of the veins such that deep veins, which are critical in the volume changes during venous compliance measures (6), are thought to be almost devoid of sympathetic innervation (9, 27, 28). On the basis of these data, it is possible that the reductions in venous compliance during LBNP in men occurred in some of the veins of the calf and not others. Finally, the menstrual phase of the women was not controlled for. It is acknowledged that this factor may influence the results in women (23). However, this issue does not limit the applicability of the present data and is likely to be representative of a general response.

In conclusion, these data provide experimental support for the concept that leg venous compliance is lower in women than men and that sympathoexcitation during baroreceptor unloading reduces calf venous compliance in men but not women. This reduction in calf venous compliance in men during LBNP appears to be specific to baroreceptor unloading. Moreover, calf venous capacitance is lower in women than men and is similarly reduced in both genders by LBNP. Collectively, these findings suggest that baseline calf venous compliance and not its modulation during sympathoexcitation is likely to be a better surrogate measure for the hemodynamic challenge incurred during orthostasis. Lastly, the present findings suggest that mechanisms other than calf venous compliance and its modulation by sympathoexcitation explain reduced orthostatic tolerance in women.

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