Age- and fitness-related differences in limb venous compliance do not affect tolerance to maximal lower body negative pressure in men and women

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Hernandez, J. P., and W. D. Franke. Age- and fitness-related differences in limb venous compliance do not affect tolerance to maximal lower body negative pressure in men and women. J Appl Physiol 97: 925–929, 2004. First published April 30, 2004; 10.1152/japplphysiol.01328.2003.—Aging and chronic exercise training influence leg venous compliance. Venous compliance affects responses to an orthostatic stress; its effect on tolerance to maximal lower body negative pressure (LBNP) in the elderly is unknown. The purpose of this study was to determine the influence of age and fitness, a surrogate measure of exercise training, on calf venous compliance and tolerance to maximal LBNP in men and women. Forty participants, 10 young fit (YF; age = 22.6 ± 0.5 yr, peak oxygen uptake = 57.1 ± 2.0 ml·kg⁻¹·min⁻¹), 10 young unfit (YU; 23.1 ± 1.0 yr, 41.1 ± 2.0 ml·kg⁻¹·min⁻¹), 10 older fit (OF; 73.9 ± 2.0 yr, 39.0 ± 2.0 ml·kg⁻¹·min⁻¹), and 10 older unfit (OU; 70.9 ± 1.6 yr, 27.1 ± 2.0 ml·kg⁻¹·min⁻¹), underwent graded LBNP to presyncope or 4 min at −100 mmHg. By utilizing venous occlusion plethysmography, calf venous compliance was determined by using the first derivative of the pressure-volume relation during cuff pressure reduction. We found that the more fit groups had greater venous compliance than their unfit peers (P < 0.05) as did the young groups compared with their older peers (P < 0.05) such that OU < YU = OF < YF. LBNP tolerance did not differ between groups. In conclusion, these data suggest that aging reduces, and chronic exercise increases, venous compliance. However, these data do not support a significant influence of venous compliance on LBNP tolerance.

METHODS

Participants. Forty participants, free of any diagnosed cardiovascular disease and not on any cardiac medications, were recruited from the collegiate and surrounding communities for this investigation. All participants reported no tobacco use. The participants were parsed into four groups on the basis of age and fitness: 20 young participants (<30 yr, 10 men and 10 women) and 20 older participants (>60 yr, 10 men and 10 women) were subsequently divided into fit and unfit groups (n = 10 each; 5 men and 5 women) according to their fitness level. All participants underwent a maximal graded exercise test (Bruce protocol for younger participants and modified Bruce protocol for the older) to determine their fitness status. Peak oxygen uptake (VO₂peak) estimates were obtained for all the participants by using the time to termination of the stress test as the criterion. The participants were grouped into fit and unfit by using age- and sex-based norms (12). All the young women were tested during the follicular phase (days 3–10) after the onset of the menstrual cycle) of their menstrual cycle, and the older women were all postmenopausal (18). Participant characteristics are summarized in Table 1.

General experimental design. Participants reported to the laboratory on four separate occasions. The first meeting was to assess anthropometric status and determine VO₂peak. The second visit served to orient the participants to the testing apparatus and protocol. The third visit was for the LBNP tolerance test, and the final visit was for determination of limb venous compliance. Before data collection, all participants were verbally informed of the risks and benefits of this study and provided written informed consent. All participants re-
frained from any exercise, alcohol, or caffeine ingestion for 12 h and food intake for 3 h before their LBNP and venous compliance tests. The Institutional Review Board of Iowa State University approved this investigation; the results reported here are part of an ongoing investigation in our laboratory.

LBNP testing. Each participant reported to the laboratory no earlier than 48 h after the \( V_{O_2 \text{ peak}} \) test and after instrumentation assumed a supine posture inside the LBNP testing chamber. Once inside, they straddled a padded bicycle seat with their feet well clear of the base of the chamber and were sealed at the level of the iliac crest. After 12 min of rest at ambient barometric pressure, negative pressure was induced by using a commercially available vacuum and quantified with a pressure transducer (model PS309, Validyne, Northridge, CA). Graded LBNP was invoked with 10-mmHg increases in negative pressure every 4 min. The LBNP test was terminated when the participant either completed 4 min at \(-100\) mmHg, at the onset of presyncopal signs, or by participant request concurrent with presyncopal symptoms. Signs and symptoms of impending presyncope included dizziness, nausea, profuse sweating, or a rapid change in blood pressure defined as either a decrease in systolic blood pressure by 25 mmHg or a decrease in diastolic blood pressure by 15 mmHg within 1 min.

Venous compliance. Participants reported to the laboratory for the venous compliance test within 1 wk of the LBNP test. The test used was a modified version of that reported elsewhere (14, 20). Briefly, participants were placed in the supine position with the right leg elevated above heart level and supported at the ankle and thigh. By using the formula \( \Delta V = \Delta P \cdot L \), calf volume was calculated from the mean of four girth measurements obtained equidistantly between the medial malleolus and the tibial plateau (r) and from one calf segment length, the distance between the medial malleolus and the tibial plateau (L). Changes in limb volume relative to baseline were measured noninvasively using strain gauge plethysmography at the maximal calf circumference. A venous collecting cuff was placed \(-5\) cm proximal to the knee on the right leg and inflated to 60 mmHg for 8 min and then reduced at a rate of 5 mmHg/s (over 1 min) to 0 mmHg.

Analysis. LBNP tolerance was quantified as the LBNP tolerance index (LTI). This index was calculated as the sum of the products of the knee on the right leg and in the OU group. Their data were included in the statistical analysis.

Regression models were calculated by using the general linear model procedure (SPSS), including between-participant classification for age and training status. The pressure-volume relation is not linear; therefore, a single number is not sufficient to characterize the slope of the pressure-volume curve. Thus the group-averaged regression parameters \( \beta_1 \) and \( \beta_2 \), determined by the pressure-volume curves for each participant in the relevant groups, were used together as an estimate of compliance, such that compliance = \( \beta_1 + \beta_2 \cdot (\text{cuff pressure}) \) or the derivative of the pressure-volume curve (14, 19). The coefficient of variation of this method has been reported to be 4.9% (14).

The anthropometric, \( V_{O_2 \text{ peak}} \), and LTI data were compared by using two-way ANOVA (age \& fitness). Post hoc comparisons were made by using the Tukey procedure. Because of the pressure-dependent aspect of the venous compliance measurement, Pearson’s \( R \) correlations were calculated for LTI and \( V_{O_2 \text{ peak}} \) vs. individual compliance at a pressure of 20 mmHg. Statistical significance was set at \( P < 0.05 \) with data reported as means \( \pm SE \).

RESULTS

Table 1 summarizes the anthropometric characteristics of all participants (n = 20 women and 20 men) in the study. The groups did not differ significantly in either height or body surface area. As desired, the groups differed significantly with respect to age and training fitness \((P < 0.05)\). The only exception was that older group (OF) and young untrained (UF) groups did not differ in their fitness. The older untrained (OU) and YU groups were fatter than their fit peers \((P < 0.05)\). The young fit (YF) group was leaner than the other three groups \((P < 0.05)\). The YU group had significantly greater calf volume than the YF \((P < 0.05)\) (Table 1).

In both age groups, the fit participants had steeper slopes of the pressure-volume curves than did their unfit counterparts \((P < 0.05)\). Furthermore, the fit groups for each age group had \(-50\% \) greater (average percent difference from 20 to 50 mmHg) compliance than the unfit groups (Fig. 1, Table 2). The OF group had a steeper pressure-volume slope than did both the YU and OU groups \((P < 0.05)\) (Fig. 1, Table 2). The difference in compliance between the OF and YU groups was \(-35\%\). The YU group had steeper pressure-volume slopes than did the OU group \((P < 0.05)\) (Fig. 1, Table 2).

There was no difference in tolerance to maximal LBNP between any of the groups: YU = 264 \pm 18, OU = 304 \pm 19, YF = 291 \pm 17, YU = 282 \pm 34 mmHg-min (Fig. 2). All participants terminated the protocol because of signs or symptoms of impending presyncope except for three participants who finished the entire protocol. One was in YF and two were in the OU group. Their data were included in the statistical analyses.

Table 1. Anthropometric data for all participants

<table>
<thead>
<tr>
<th>Variable</th>
<th>Young Unfit</th>
<th>Old Unfit</th>
<th>Young Fit</th>
<th>Old Fit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>23.1 ± 1</td>
<td>70.9 ± 1*‡</td>
<td>22.6 ± 0.5</td>
<td>73.9 ± 2*‡</td>
</tr>
<tr>
<td>Height, cm</td>
<td>171.7 ± 3.0</td>
<td>167.7 ± 3.0</td>
<td>173.6 ± 2.0</td>
<td>170.4 ± 4.0</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>88.8 ± 5.0‡</td>
<td>84.6 ± 5.0‡</td>
<td>67.5 ± 3.0</td>
<td>75.2 ± 4.0‡</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>27.2 ± 3.0</td>
<td>28.5 ± 2.0‡</td>
<td>16.4 ± 2.0</td>
<td>34.6 ± 2.0‡</td>
</tr>
<tr>
<td>BMI</td>
<td>30.3 ± 1.0</td>
<td>25.7 ± 1.0</td>
<td>22.3 ± 2.0*†</td>
<td>29.8 ± 0.5*‡</td>
</tr>
<tr>
<td>BSA, m2</td>
<td>2.01 ± 0.01</td>
<td>1.86 ± 0.01</td>
<td>1.98 ± 0.01</td>
<td>2.13 ± 0.01</td>
</tr>
<tr>
<td>( V_{O_2 \text{ peak}}, \text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1} )</td>
<td>27.1 ± 2.0‡</td>
<td>57.1 ± 2.0‡</td>
<td>39.0 ± 2.0</td>
<td>12.0 ± 2.0</td>
</tr>
<tr>
<td>Calf volume, ml</td>
<td>3,782.2 ± 259‡</td>
<td>3,249.3 ± 247</td>
<td>2,753.7 ± 144</td>
<td>3,066.9 ± 220</td>
</tr>
</tbody>
</table>

Values are means \( \pm SE \) for 40 subjects. BMI, body mass index; BSA, body surface area; \( V_{O_2 \text{ peak}} \), peak oxygen uptake. *\( P < 0.05 \) vs. young unfit. †\( P < 0.05 \) vs. old unfit.
Similarly, there was no relationship between compliance at 20 mmHg and LTI \((r = -0.125, P = 0.444; \text{Fig. 3})\). There was a tendency toward a positive relationship between compliance at 20 mmHg and \(\dot{V}O_2\) peak \((r = 0.297, P = 0.063)\) (Fig. 3).

**DISCUSSION**

The purpose of this investigation was to determine the effects of differences in venous compliance associated with aging and fitness level on tolerance to maximal LBNP. We found an increased venous compliance with fitness in both young and older participants and a decreased venous compliance with age in both fitness categories. Surprisingly, there was no significant difference in the pressure-volume slopes between the YU and the OF groups. However, the primary findings of this investigation were that, despite differences in compliance with age and fitness, there were no differences in tolerance to the simulated maximal orthostatic stress of LBNP and no relationship between differences in venous compliance and tolerance.

The present results concerning the effects of age (19, 21, 22, 28) and fitness (5, 19, 23, 28) on venous compliance are largely consistent with previous findings. Collectively, these studies provide strong evidence indicating a profound effect of chronic exercise training on venous compliance in the older population. Thus endurance training can attenuate the reductions in compliance that are associated with aging. However, it remains to be determined how quickly these venous adaptations occur in response to endurance exercise training. Parenthetically, the present results are similar to those of Monahan and colleagues (19) and further support the utility of this method as opposed to more traditional assessments of the slope of the pressure-volume relationship.

Preventing the shift of fluid into the lower extremities with antishock trousers can reduce the reflex increases in heart rate and stroke volume seen in response to LBNP (13). A reduction in the compliance of the venous system may improve tolerance via the same means. However, in young participants, reductions in venous compliance consequent to 18 days of head-down bed rest did not affect orthostatic tolerance (1). In comparing young and older “physically active” participants, Tsutsui and colleagues (29) found that leg compliance was significantly lower in the older participants. The older participants also had higher orthostatic tolerance, which was attributed to an attenuated reduction in venous return due to the reduced compliance. Several issues affect comparisons between their results and those found here. Only 13 of their 37 participants actually became presyncopal. There are likely

**Table 2. Pressure-volume regression equations**

<table>
<thead>
<tr>
<th>Group</th>
<th>Equation</th>
</tr>
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<tbody>
<tr>
<td>Young unfit</td>
<td>(\Delta\text{Limb volume} = 0.988 \pm 0.256 + 0.101 \pm 0.015\times (\text{cuff pressure}) - 0.00090 \pm 0.00012 \times (\text{cuff pressure})^2)</td>
</tr>
<tr>
<td>Older unfit*</td>
<td>(\Delta\text{Limb volume} = 0.897 \pm 0.088 + 0.059 \pm 0.014\times (\text{cuff pressure}) - 0.000456 \pm 0.000146 \times (\text{cuff pressure})^2)</td>
</tr>
<tr>
<td>Young fit†</td>
<td>(\Delta\text{Limb volume} = 1.334 \pm 0.316 + 0.161 \pm 0.096\times (\text{cuff pressure}) - 0.001397 \pm 0.000197 \times (\text{cuff pressure})^2)</td>
</tr>
<tr>
<td>Older fit‡</td>
<td>(\Delta\text{Limb volume} = 0.962 \pm 0.264 + 0.131 \pm 0.013\times (\text{cuff pressure}) - 0.00108 \pm 0.000118 \times (\text{cuff pressure})^2)</td>
</tr>
</tbody>
</table>

Values are means ± SE. \(\Delta\), Change. *\(P < 0.05\) vs. young of same fitness category. †\(P < 0.05\) vs. age-matched unfit.
differences in participant characteristics because neither fitness nor exercise habits were characterized by Tsutsui and coworkers. In the present study, all the participants included in the analysis became presyncope, and all the fit participants had been exercising regularly for at least 1 yr. The OF participants had been training at least three times weekly in a structured exercise program. Moreover, Tsutsui and colleagues assessed leg compliance while the participants were undergoing LBNP, whereas the participants of the present study were assessed at rest. Increases in leg muscle sympathetic nerve activity and subsequent alterations in leg blood flow due to the LBNP likely confound interpretation of their results.

Other studies have indicated that attenuation of causal displacement of blood volume by mild muscle tension (26) or antishock trousers (13) can affect the cardiovascular responses to an orthostatic stress. Although not the focus of the present study, we recently found younger fit people, or those with the greatest compliance, to have an earlier increase in heart rate (−40 mmHg vs. the last stage stage of LBNP completed before presyncope) than young unfit, older unfit, and older fit individuals (15). This group also showed an earlier decline in stroke volume (−20 vs. −40 mmHg) than the unfit and older groups. All groups showed significantly lower stroke volume, cardiac output, and mean arterial pressure at presyncope than rest, whereas only the young fit and unfit groups had significantly higher heart rates at presyncope (15). Collectively, these studies suggest that differences in compliance do not affect tolerance but do affect the cardiovascular responses to an orthostatic stress.

Our participant pool consisted of equal numbers of men and women, and differences in compliance with age and fitness were similar to those observed by Monahan et al. (19), whose participants were men. This suggests that the findings of Monahan et al. might be extended to women. However, Monahan and Ray (20) compared the compliance of men and women and found that the women had a 48% lower resting calf venous compliance than the men. Additionally, they found that calf venous compliance was reduced with LBNP in men but not in women (20). We found that women in the YU group had a 40% lower resting compliance than the men in the same group. This difference was not seen between YF women and men or in older participants. Although the fitness status of their participants was not reported (20), it might be that these gender differences are not seen in more fit or older individuals. Regardless, as shown here, these differences do not appear to affect LBNP tolerance.

It has been suggested that endurance training can decrease orthostatic tolerance (2, 24) with one of the mechanisms for this reduction being an increased venous compliance. If this were correct, then endurance training might be contraindicated for an older population already at a greater risk of falls. Our findings of no difference in orthostatic tolerance with training in either the young or older groups are not consistent with this notion. Our findings imply that exercise training in both age groups, sufficient enough to increase VO$_2$ peak and compliance, does not negatively affect tolerance to a maximal orthostatic stress.

Several limitations need to be considered when reading the present investigation. First, although LBNP causes central hypovolemia, it is not a pure orthostatic stressor because the participants remain in the supine position. Nevertheless, LBNP is a widely utilized technique in the investigation of orthostatic stress. Several advantages of LBNP include the fact that it is noninvasive, is relatively comfortable for participants, and can be discontinued quickly. Participants remain at rest in the supine position during LBNP, facilitating physiological measurements and minimizing the likelihood of confounding skeletal muscle activity (3). Second, besides the use of LBNP, the fact that our participants were clinically healthy needs to be considered when interpreting the present findings and extrapolating them to clinical populations. Third, the use of venous occlusion plethysmography to measure compliance is a measure of whole limb compliance, which varies with age (7). This method assumes that venous collecting cuff pressure is equal to venous pressure. We believe that the use of the 8-min collecting period accounted for possible differences in whole limb blood flow (14, 19). Finally, given that the present study was cross-sectional in nature with the attendant limitations of this design, longitudinal investigations to determine the effects of lower limb exercise training on compliance and orthostatic tolerance in an older population are warranted.

In conclusion, venous compliance was reduced with age and increased with improved fitness. Neither age nor fitness was associated with differences in tolerance to maximal LBNP in men and women. Thus age-associated reductions in venous compliance were similar in both young and older groups.
compliance can be offset by endurance training without compromising tolerance to a simulated maximal orthostatic stress.

ACKNOWLEDGMENTS

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REFERENCES