Changes in ventricular twist and untwisting with orthostatic stress: endurance athletes versus normally active individuals

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Esch BT, Scott JM, Haykowsky MJ, Paterson I, Warburton DE, Cheng-Baron J, Chow K, Thompson RB. Changes in ventricular twist and untwisting with orthostatic stress: endurance athletes versus normally active individuals. J Appl Physiol 108: 1259–1266, 2010. First published March 4, 2010; doi:10.1152/japplphysiol.01186.2009.—Endurance-trained individuals exhibit larger reductions in left ventricular (LV) end-diastolic volume in response to lower body negative pressure (LBNP) compared with normally active individuals. However, the relationship between LV torsion and untwisting and the LV volume response to LBNP in endurance athletes is unknown. Eight endurance-trained athletes [maximal oxygen consumption (Vo2max): 66.4 ± 7.2 ml·kg⁻¹·min⁻¹] and eight normally active individuals (Vo2max: 41.9 ± 9.0 ml·kg⁻¹·min⁻¹) underwent two cardiac magnetic resonance imaging (MRI) assessments, the first during supine rest and the second during –30 mmHg LBNP. Right ventricular (RV) and LV volumes were assessed, myocardial tagging was applied in order to quantify LV peak torsion and peak untwisting rate, and filling rates were measured with phase-contrast MRI. In response to LBNP, endurance-trained individuals had greater reductions in RV and LV end-diastolic volume and stroke volume (P < 0.05). Endurance athletes had reduced untwisting rates (20.3 ± 8.7°/s), while normally active individuals had increased untwisting rates (–16.2 ± 32.1°/s) in response to LBNP (P < 0.05). Changes in peak untwisting rate were significantly correlated with change in peak torsion (R = 0.87, P < 0.05), with the change in early filling rate and VO2max, but not with changes in end-diastolic or end-systolic volume (P > 0.05). We conclude that increased untwisting rates in normally active subjects may mitigate the drop in early filling rate with LBNP and thus may be a compensatory mechanism for the reduction in stroke volume with volume unloading. The opposite response in athletes, who showed a decreased untwisting rate, may contribute to their larger reductions in LV end-diastolic and stroke volumes with volume unloading and their orthostatic intolerance.

orthostatic tolerance; ventricular torsion; exercise; magnetic resonance imaging

ENDURANCE-TRAINED ATHLETES are less tolerant of orthostatic stressors such as standing upright or lower body negative pressure (LBNP) (15). In response to orthostatic stress, endurance athletes exhibit greater reductions in left ventricular (LV) end-diastolic volume (EDV) and stroke volume compared with normally active or sedentary individuals (10, 16). These large reductions in LV volumes are related to enhanced LV compliance and reduced ventricular interactions (1, 10, 16). It is possible that other mechanisms, such as reductions in LV twist function, may contribute to the reduced LV filling seen in endurance athletes during orthostatic stress.

Counterclockwise apical rotation and clockwise basal rotation combine to create LV torsion (3, 25), which aids the efficient ejection of blood by creating high pressures with less myocardial shortening (2). Beginning early in diastole, LV recoil drives ventricular untwisting, which is ~40% complete before mitral valve opening, while radial and long-axis relaxation occur later, predominantly during filling (17). The early nature of LV untwisting makes it an important contributor to low LV pressure generation and the associated transmitial pressure gradient that drives early filling (4, 13). Therefore, alterations in LV untwisting will likely have significant consequences for LV filling.

The relationship between LV untwisting and the large reductions in LV volumes exhibited during orthostatic stress in endurance-trained individuals remains unknown. The purpose of this investigation was to examine the effects of a moderate orthostatic challenge on LV torsion and untwisting in endurance-trained and normally active individuals with cardiac magnetic resonance imaging (MRI). We hypothesized that the larger reduction of preload in endurance athletes may be amplified by the associated larger impairment in systolic function and thus untwisting. A secondary aim was to assess changes in right ventricular (RV) volumes during LBNP, as well as group differences between endurance-trained and normally active individuals.

METHODS

Participants. We recruited 16 men between the ages of 19 and 44 to participate in this investigation. Participants included eight endurance-trained athletes (2 cyclists, 5 triathletes, 1 biathlete) who trained in excess of 10 h/wk and had done so for >5 yr. The remaining eight participants were normally active individuals who did not partake in regimented aerobic exercise training. A subset of these participants have completed a separate investigation, and their aerobic fitness assessment [maximal oxygen consumption (VO2max)] results have been included in the present investigation. Institutional ethics approvals were obtained from the University of Alberta Health Research Ethics Board, and all participants provided written informed consent before participation.

General protocol. Upon arrival at the Alberta Cardiovascular and Stroke Research Centre (ABACUS) at the Mazankowski Alberta Heart Institute, participants’ height and mass were measured. Each individual underwent an incremental exercise test on a cycle ergometer in order to assess maximal aerobic power (VO2max). Individuals cycled on an electronically braked ergometer (Ergometrics er800s; Ergoline, Bitz, Germany), where the workload increased 20–30 W every 2 min until anaerobic threshold (29) and then increased 20–30 W every minute until exhaustion. Expired gas analysis was completed with a calibrated metabolic cart (Parvomedics, Salt Lake City, UT).

On a separate day, participants underwent a comprehensive cardiac volumetric and functional assessment with a 1.5-T MRI scanner.
Cardiac magnetic resonance imaging acquisition. Short-axis cines covering the length of the RV and LV were acquired in order to assess volumes and ejection fraction. Image acquisition parameters were as follows: repetition time (TR) = 3.0 ms; echo time (TE) = 1.5 ms; flip angle = 60°; slice thickness = 8 mm; 10–12 slices; matrix = 256 × 160; field of view = 300–380 mm; and temporal resolution = 30 phases. Short-axis phase-contrast cines acquired at the level of the mitral annulus were used to measure early (E) and atrial (A) filling blood velocities. Additionally, summation of the through-plane velocities across the area of the mitral valve allowed for calculation of peak early and atrial transmitral filling rates (ml/s). Peak early diastolic annular velocities (E′) in the RV and LV free walls were assessed from four-chamber steady-state free precession (SSFP) cines by tracking the tissue motion. Typical MR image acquisition parameters for tissue tagging were as follows: TE = 2.2 ms; TR = 4.0 ms; flip angle = 12°; slice thickness = 8 mm with an 8-mm gap between slices; 5 short axis slices; matrix = 192 × 128; field of view = 300–380 mm; and 5 views per segment for a 20-ms temporal resolution. Tags were applied 250 ms after the R wave in order to minimize tag fading up to the time of early diastole when peak untwisting rates occur. Myocardial tissue tagging was used to measure basal and apical rotation curves, which were subtracted to yield torsion curves, from which peak torsion and peak untwisting rate were calculated. The basal slice was taken at the level of the mitral valve, and the apical slice was as apical as possible while maintaining a portion of the ventricular chamber within the image throughout the cardiac cycle. Circumferential strain and diastolic strain rates were measured with the average strains of the five short-axis tagging slices. The total degrees of rotation, as well as circumferential shortening (strain), were referenced to diastasis (9). The acquisition of all data was cardiac gated based on the electrocardiogram and acquired during end-expiratory breath holds. Images were acquired in the order listed above. LV and RV volume acquisition was completed within the first 5 min of the imaging protocol.

Lower body negative pressure. Participants were scanned while supine in a custom-built, MRI-compatible LBNP chamber. The chamber contained the subject’s lower body up to the level of the iliac crest. The LBNP chamber dimensions were customized to fit into the magnet bore with a wooden skeleton (half-cylinder shape) covered in a synthetic, airtight material to ensure MRI compatibility. The chamber was attached to a vacuum system that was controlled by a variable transformer, allowing modifiable pressure outputs. Pressure inside the chamber was monitored continuously with a calibrated differential pressure manometer and was held constant throughout the LBNP challenge (~30 mmHg).

After participants entered the chamber and were inserted into the magnet, a complete resting baseline cardiac MRI scan was completed (~20 min). After baseline assessment of ventricular function, the pressure in the chamber was reduced to 30 mmHg below atmospheric pressure. Five minutes of cardiovascular acclimatization at ~30 mmHg was allowed before the onset of image acquisition, which consisted of an identical cardiac MRI evaluation (~15 min). Before the second cardiac scan began, a four-chamber scouting image was reacquired to ensure identical slice location as at baseline, while the positioning of the images was confirmed with anatomic landmarks. Heart rate (electrocardiogram) and blood pressure (automated sphygmomanometer) were also monitored and recorded throughout baseline and LBNP.

Data analysis. Assessment of RV and LV volumes was performed by manual endocardial tracing of short-axis cine images at end diastole and end systole, and volumes were calculated by a true method of disks (22) (Argus; Siemens Medical Systems). Stroke volume and ejection fraction were calculated with the measures of EDV and end-systolic volume (ESV). Papillary muscles were included as part of the ventricular cavity volume and were excluded for calculation of LV mass (14). LV mass was calculated by using the endocardial trace coupled with an epicardial trace in order to determine myocardial area at each short-axis slice level in end diastole. Internal LV length was considered to be the length from the apex to the mitral annulus.

LV cavity diameter and wall thickness of a midventricular (papillary muscles) short-axis slice in systole and diastole were utilized to determine LV end-diastolic internal diameter as well as calculated end-systolic wall stress (23). End-systolic wall stress was used as an index of afterload.

Custom-designed image morphing software was applied to the myocardial tagging images to determine the spatial deformation field for the myocardium for each slice as a function of cardiac phase (http://elastix.isi.uu.nl). The tag-endocardium intersection points were identified manually and digitized. Torsion was calculated as the instantaneous difference between the rotation at the base and the apex. Peak untwisting rate was calculated separately for the apex and the base as well as being combined as the maximal difference between apical and basal untwisting rates. Total peripheral resistance was calculated as follows: (systolic blood pressure + diastolic blood pressure)/cardiac output. All MRI assessments were completed in a blinded fashion.

Statistics. At rest, group differences were compared with the two-sample Kolmogorov-Smirnov nonparametric test. To compare group responses to LBNP, the same statistical test was applied to the absolute change in a given variable for both groups. Linear regressions were conducted to identify significantly related relationships between two variables. Statistical analysis was performed with Statistica 6.0 and SPSS software, and significance was set at \( P < 0.05 \). The study size of eight subjects per group was based on a minimum expected 13-ml difference in the drop in stroke volume between normally active and endurance-trained groups (standard deviation of 8 ml), which has been observed at 20 mmHg of LBNP (10), yielding a power of 0.8 with a \( P \) value < 0.05.

RESULTS

Group characteristics. Participant characteristics are listed in Table 1. The groups were matched for age, height, and mass. By design, endurance-trained athletes had significantly higher absolute and relative \( \text{VO}_{2\text{max}} \). Endurance athletes also had a larger LV mass and diameter compared with the normally active group (\( P < 0.05 \)).

Resting cardiac volumes and function. Resting cardiac volumes and function are shown in Table 2. The groups did not differ at rest with respect to systolic or diastolic blood pressure, LV ejection fraction, or cardiac output. Endurance athletes had significantly higher resting LVEDV and LV stroke volume.

Table 1. Participant physical characteristics and training history

<table>
<thead>
<tr>
<th></th>
<th>ET (n = 8)</th>
<th>NA (n = 8)</th>
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<tbody>
<tr>
<td>Age, yr</td>
<td>31.0 ± 9.7</td>
<td>33.0 ± 7.3</td>
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<tr>
<td>Height, cm</td>
<td>179.1 ± 11.2</td>
<td>177.3 ± 7.3</td>
</tr>
<tr>
<td>Mass, kg</td>
<td>74.4 ± 12.0</td>
<td>79.4 ± 7.5</td>
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<tr>
<td>Years training</td>
<td>11.1 ± 4.5</td>
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<tr>
<td>Hours of training/week</td>
<td>11.5 ± 3.1</td>
<td></td>
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<tr>
<td>( \text{VO}_{2\text{max}}, \text{ml·kg}^{-1}·\text{min}^{-1} )</td>
<td>66.4 ± 7.2</td>
<td>41.9 ± 9.0</td>
</tr>
<tr>
<td>( \text{VO}_{2\text{max}}, \text{l/min} )</td>
<td>5.0 ± 0.7*</td>
<td>3.6 ± 0.6</td>
</tr>
<tr>
<td>LV mass, g</td>
<td>176.8 ± 20.3</td>
<td>146.1 ± 23.1</td>
</tr>
<tr>
<td>LV internal diameter, mm</td>
<td>60.0 ± 3.6*</td>
<td>53.9 ± 4.2</td>
</tr>
<tr>
<td>LV length, cm</td>
<td>6.6 ± 0.6</td>
<td>5.8 ± 1.2</td>
</tr>
</tbody>
</table>

Values are means ± SD. ET, endurance trained; NA, normally active; LV, left ventricle. *Significantly different from normally active (\( P < 0.05 \)).
Table 2. Cardiac volumes and function

<table>
<thead>
<tr>
<th></th>
<th>Rest ET</th>
<th>NA</th>
<th>Change with LBNP ET</th>
<th>NA</th>
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</thead>
<tbody>
<tr>
<td>Heart rate, beats/min</td>
<td>57.3 ± 6.2</td>
<td>68.4 ± 15.3</td>
<td>1.7 ± 4.0</td>
<td>−2.6 ± 6.9</td>
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<tr>
<td>Systolic BP, mmHg</td>
<td>123.5 ± 4.9</td>
<td>120.7 ± 7.5</td>
<td>−3.0 ± 5.8</td>
<td>−2.1 ± 3.5</td>
</tr>
<tr>
<td>Diastolic BP, mmHg</td>
<td>71.1 ± 6.2</td>
<td>73.7 ± 9.4</td>
<td>1.0 ± 6.9</td>
<td>2.0 ± 4.8</td>
</tr>
<tr>
<td>LV EDV, ml</td>
<td>211.9 ± 31.3*</td>
<td>168.8 ± 38.5</td>
<td>−26.6 ± 8.7*</td>
<td>17.3 ± 6.6</td>
</tr>
<tr>
<td>LV ESV, ml</td>
<td>83.9 ± 17.8</td>
<td>66.2 ± 16.7</td>
<td>−8.0 ± 7.6</td>
<td>−4.0 ± 5.1</td>
</tr>
<tr>
<td>LV SV, ml</td>
<td>128.0 ± 16.2*</td>
<td>103.2 ± 22.1</td>
<td>−26.0 ± 7.3*</td>
<td>−14.0 ± 9.1</td>
</tr>
<tr>
<td>LV EF, %</td>
<td>60.5 ± 3.7</td>
<td>61.6 ± 2.5</td>
<td>−5.4 ± 3.4</td>
<td>−2.3 ± 3.7</td>
</tr>
<tr>
<td>Cardiac output, l/min</td>
<td>7.3 ± 1.1</td>
<td>6.8 ± 1.1</td>
<td>−1.3 ± 0.6</td>
<td>−1.1 ± 0.8</td>
</tr>
<tr>
<td>E, m/s</td>
<td>0.65 ± 0.11</td>
<td>0.63 ± 0.07</td>
<td>−0.13 ± 0.06</td>
<td>−0.13 ± 0.06</td>
</tr>
<tr>
<td>A, m/s</td>
<td>0.32 ± 0.04</td>
<td>0.35 ± 0.07</td>
<td>−0.04 ± 0.03</td>
<td>−0.03 ± 0.03</td>
</tr>
<tr>
<td>E/A</td>
<td>2.06 ± 0.47</td>
<td>1.87 ± 0.41</td>
<td>−0.21 ± 0.30</td>
<td>−0.27 ± 0.28</td>
</tr>
<tr>
<td>E filling rate, ml/s</td>
<td>674.7 ± 108.2*</td>
<td>515.4 ± 80.7</td>
<td>−227.3 ± 69.9*</td>
<td>−126.0 ± 52.5</td>
</tr>
<tr>
<td>A filling rate, ml/s</td>
<td>293.2 ± 34.5</td>
<td>255.2 ± 61.6</td>
<td>−69.5 ± 23.5*</td>
<td>−26.5 ± 39.0</td>
</tr>
<tr>
<td>E/A (filling rate)</td>
<td>2.34 ± 0.54</td>
<td>2.08 ± 0.41</td>
<td>−0.31 ± 0.21</td>
<td>−0.30 ± 0.33</td>
</tr>
<tr>
<td>LV E’, m/s</td>
<td>0.16 ± 0.04</td>
<td>0.13 ± 0.03</td>
<td>−0.06 ± 0.02</td>
<td>−0.03 ± 0.01</td>
</tr>
<tr>
<td>TPR, mmHg·1−1·min</td>
<td>12.8 ± 2.9</td>
<td>12.6 ± 2.4</td>
<td>2.9 ± 2.0</td>
<td>3.2 ± 2.0</td>
</tr>
<tr>
<td>Wall stress, 102 dyn/cm²</td>
<td>84.4 ± 11.2</td>
<td>79.3 ± 15.5</td>
<td>−0.3 ± 17.2</td>
<td>1.0 ± 19.7</td>
</tr>
<tr>
<td>RV EDV, ml</td>
<td>233.5 ± 35.8*</td>
<td>182.2 ± 45.5</td>
<td>−38.0 ± 18.4*</td>
<td>−21.6 ± 8.3</td>
</tr>
<tr>
<td>RV ESV, ml</td>
<td>103.9 ± 25.2*</td>
<td>77.8 ± 22.2</td>
<td>−61.1 ± 11.1</td>
<td>−5.8 ± 6.9</td>
</tr>
<tr>
<td>RV SV, ml</td>
<td>129.9 ± 17.6*</td>
<td>104.3 ± 28.0</td>
<td>−32.1 ± 15.2*</td>
<td>−15.8 ± 9.7</td>
</tr>
<tr>
<td>RV EF, %</td>
<td>55.9 ± 5.8</td>
<td>57.4 ± 5.9</td>
<td>−5.7 ± 4.5</td>
<td>−2.5 ± 4.7</td>
</tr>
<tr>
<td>RV E’, m/s</td>
<td>0.15 ± 0.04</td>
<td>0.14 ± 0.03</td>
<td>−0.04 ± 0.03</td>
<td>−0.03 ± 0.03</td>
</tr>
</tbody>
</table>

Values are means ± SD. LBNP, lower body negative pressure; BP, blood pressure; EDV, end-diastolic volume; ESV, end-systolic volume; SV, stroke volume; EF, ejection fraction; E, early peak mitral blood velocity; A, atrial peak mitral blood velocity; E’, early diastolic myocardial annular velocity; TPR, total peripheral resistance; RV, right ventricle. *Significantly different from normally active (P < 0.05).

Resting RVEDV, RVESV, and RV stroke volume were significantly higher in the endurance athletes (P < 0.05). There were no group differences in resting RV ejection fraction. End-systolic wall stress and total peripheral resistance were not different between groups at baseline.

The groups did not differ at rest in E- or A-wave velocities or E/A, but the corresponding early filling volumetric flow rates were significantly larger in the endurance-trained group (P < 0.05) (Table 2). Neither RV nor LV E’ was significantly different between groups at baseline (Table 2). Resting LV torsion or apical and basal rotations were not different between groups (Table 3). Peak untwisting rate, peak basal untwisting rate, and peak apical untwisting rate were not different between groups at rest (Table 3). Baseline peak circumferential strain also was significantly different between groups (Table 3).

Table 3. LV rotations and strain

<table>
<thead>
<tr>
<th></th>
<th>Rest ET</th>
<th>NA</th>
<th>Change with LBNP ET</th>
<th>NA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic valve closure, ms</td>
<td>330.4 ± 16.7</td>
<td>312.1 ± 36.6</td>
<td>−1.12 ± 12.4*</td>
<td>−13.3 ± 12.4</td>
</tr>
<tr>
<td>Mitral valve opening, ms</td>
<td>388.5 ± 17.7</td>
<td>362.4 ± 43.6</td>
<td>3.3 ± 23.9</td>
<td>2.8 ± 14.1</td>
</tr>
<tr>
<td>IVRT, ms</td>
<td>57.1 ± 6.6</td>
<td>53.0 ± 10.6</td>
<td>8.2 ± 8.7</td>
<td>13.2 ± 11.1</td>
</tr>
<tr>
<td>Peak torsion, °</td>
<td>170.0 ± 3.4</td>
<td>180.0 ± 3.7</td>
<td>−1.2 ± 2.9</td>
<td>0.9 ± 3.1</td>
</tr>
<tr>
<td>Time of peak, ms</td>
<td>335.2 ± 19.6</td>
<td>325.7 ± 19.6</td>
<td>−0.05 ± 12.5</td>
<td>−9.2 ± 13.5</td>
</tr>
<tr>
<td>% Untwisting during IVRT</td>
<td>102 ± 8</td>
<td>106 ± 5</td>
<td>2.6 ± 14.5</td>
<td>16.3 ± 14.7</td>
</tr>
<tr>
<td>Peak torsion/length, °/cm</td>
<td>1.7 ± 0.5</td>
<td>1.8 ± 0.6</td>
<td>−0.2 ± 0.4</td>
<td>0.2 ± 0.5</td>
</tr>
<tr>
<td>Peak untwisting rate, °/s</td>
<td>−135.4 ± 39.7</td>
<td>−121.2 ± 29.9</td>
<td>20.3 ± 8.7*</td>
<td>−16.2 ± 32.1</td>
</tr>
<tr>
<td>Time of peak, ms</td>
<td>418.2 ± 17.4</td>
<td>395.5 ± 45.4</td>
<td>−17.8 ± 17.5</td>
<td>−7.2 ± 18.4</td>
</tr>
<tr>
<td>Peak torsion, °/s</td>
<td>127.9 ± 9</td>
<td>128.10</td>
<td>−5 ± 11</td>
<td>−10 ± 11</td>
</tr>
<tr>
<td>Peak untwisting rate/length, °/s·cm·1·s⁻¹</td>
<td>−20.5 ± 6.0</td>
<td>−20.9 ± 5.2</td>
<td>3.6 ± 5.8*</td>
<td>−3.2 ± 5.6</td>
</tr>
<tr>
<td>Basal untwisting rate, °/s</td>
<td>46.7 ± 26.8</td>
<td>27.7 ± 15.6</td>
<td>−11.5 ± 19.0*</td>
<td>18.6 ± 25.4</td>
</tr>
<tr>
<td>Time of peak, ms</td>
<td>426.9 ± 17.1</td>
<td>416.8 ± 37.5</td>
<td>−9.5 ± 17.9</td>
<td>−7.6 ± 30.0</td>
</tr>
<tr>
<td>Peak of systole, °/s</td>
<td>130 ± 9</td>
<td>135 ± 6</td>
<td>−3 ± 11</td>
<td>−7 ± 9</td>
</tr>
<tr>
<td>Apical untwisting rate, °/s</td>
<td>−106.2 ± 36.7</td>
<td>−109.0 ± 32.5</td>
<td>18.5 ± 17.2</td>
<td>4.0 ± 29.6</td>
</tr>
<tr>
<td>Time of peak, ms</td>
<td>399.1 ± 31.9</td>
<td>389.7 ± 47.5</td>
<td>−15.6 ± 18.6</td>
<td>−19.6 ± 15.5</td>
</tr>
<tr>
<td>Peak of systole, °/s</td>
<td>120 ± 10</td>
<td>126 ± 12</td>
<td>−1 ± 9*</td>
<td>−13 ± 10</td>
</tr>
<tr>
<td>Circ. strain, °/s</td>
<td>−16.6 ± 2.7</td>
<td>−14.9 ± 1.3</td>
<td>3.2 ± 3.7</td>
<td>0.4 ± 2.3</td>
</tr>
<tr>
<td>Time of peak, ms</td>
<td>344.0 ± 13.7</td>
<td>322.7 ± 37.7</td>
<td>−10.9 ± 13.0</td>
<td>−8.0 ± 12.1</td>
</tr>
<tr>
<td>Peak of systole, °/s</td>
<td>104 ± 6</td>
<td>104 ± 7</td>
<td>−3 ± 6</td>
<td>−8 ± 8</td>
</tr>
<tr>
<td>Circ. strain, °/s</td>
<td>139.9 ± 18.4</td>
<td>134.6 ± 20.7</td>
<td>−35.6 ± 15.0*</td>
<td>−26.0 ± 12.6</td>
</tr>
<tr>
<td>Time of peak, ms</td>
<td>494.3 ± 15.7</td>
<td>471.6 ± 40.3</td>
<td>−0.5 ± 23.0</td>
<td>7.7 ± 15.9</td>
</tr>
<tr>
<td>Peak of systole, °/s</td>
<td>150 ± 10</td>
<td>153 ± 8</td>
<td>0 ± 12</td>
<td>−8 ± 12</td>
</tr>
</tbody>
</table>

Values are means ± SD. IVRT, isovolumic relaxation time; Circ. strain, circumferential strain. *Significantly different from normally active (P < 0.05).
was not different between groups (Table 3). All timing parameters were similar between groups at baseline (Table 3).

Cardiovascular responses to LBNP. Figure 1 shows a representative time course of LV twist and untwisting rates and circumferential strain and strain rates from a normally active individual. Sample short-axis tagging images from this subject, from the base and apex both at baseline and with LBNP, highlight the consistency of the slice prescriptions between conditions.

![Fig. 1. A: sample short-axis MRI tagging images at the apex and base in a normally active subject, both at baseline and with lower body negative pressure (LBNP). B–E: sample torsion, untwisting rate, circumferential strain, and diastolic strain rate time courses, respectively, from this subject both at baseline (solid line) and with LBNP (dashed line). F–I: similar data for an endurance trained athlete, respectively, exemplifying the opposite direction of changes in twist and untwisting rates in normally active and endurance-trained subjects with LBNP.](image-url)
The change in response to −30 mmHg LBNP did not differ for heart rate, systolic blood pressure, diastolic blood pressure, or cardiac output between groups (Table 2). Endurance athletes had a significantly larger absolute reduction in both LV EDV and LV stroke volume compared with the normally active group; however, change in ESV did not differ between groups (Table 2). LV ejection fraction fell to a greater extent in endurance athletes, although group differences were not statistically significant. Furthermore, change in total peripheral resistance and wall stress from baseline to −30 mmHg did not differ between groups. Similar to the LV, RV EDV and stroke volume were reduced with LBNP to a greater extent in endurance athletes (P < 0.05), yet the change in ESV was not different between groups.

The change in peak E- and A-wave volumetric filling rates (ml/s) were significantly different between groups, again with a larger reduction in endurance athletes (P < 0.05, Table 2), but the corresponding peak E- and A-wave velocities were similarly reduced in both groups. There were no group differences for the change in E-to-A wave ratios with LBNP.

Change in peak torsion from rest to −30 mmHg was not significantly different between groups; however, there was a trend for the normally active group to increase peak torsion and for the endurance-trained individuals to reduce peak torsion in response to LBNP (Table 3). This is reflected in Fig. 2, where the opposing twist and untwisting rate responses to LBNP for the normally active and endurance-trained athletes are apparent. There were significant group differences in response to LBNP for peak untwisting rate, whereby the normally active group increased untwisting rate and the endurance athletes reduced their peak rate of untwist (Table 3, P < 0.05). Seven of eight normally active participants increased their peak rate of untwist, whereas seven of eight endurance athletes had a slower peak rate of untwist in response to LBNP (Figs. 3 and 4). Change in peak torsion was significantly correlated to the change in peak untwisting rate (R = −0.87, P < 0.05, Fig. 2). The change in peak basal untwisting rate was significantly different between groups (P < 0.05, Table 3), while the change in peak apical untwisting rate was not different (Table 3). Circumferential strain was not altered statistically between groups; however, there was a trend toward a greater reduction in circumferential strain following LBNP in endurance athletes (Table 3, P = 0.09). The reductions in early diastolic circumferential strain rates with LBNP were significantly larger for the endurance athletes (Table 3, P < 0.05). The timing of aortic valve closure (ms) and the timing of peak apical rotation velocity (% of systole) occurred earlier with LBNP in normally active subjects than in endurance-trained subjects (Table 3, P < 0.05).

\( VO_{2\text{max}} \) (indexed to body mass) was significantly correlated with change in peak torsion (R = −0.57) and change in peak untwisting rate (R = 0.70), whereby the higher \( VO_{2\text{max}} \) an individual had, the greater the reduction in peak torsion and peak untwisting rate in response to LBNP (Fig. 5, A and B). Absolute \( VO_{2\text{max}} \) was related to change in EDV with LBNP (R = −0.61, P < 0.05), suggesting that those with the highest \( VO_{2\text{max}} \) had the largest reductions in EDV. Change in circumferential strain was significantly related to change in EDV (R = 0.60). Change in peak untwisting rate was not related to change in EDV or change in ESV (Fig. 5, C and D) or change in wall stress (P > 0.05). However, the change in untwisting rate was correlated with the absolute LVEDV with LBNP (Fig. 5E, P < 0.05). Finally, the change in the early filling rate correlated with the change in peak torsion (R = −0.48, P < 0.05) and the change in untwisting rate (R = 0.60, P < 0.05, Fig. 5F).

**DISCUSSION**

The major new findings of this investigation are that 1) the changes in peak torsion and peak untwisting rate with LBNP were not correlated with changes in LVESV or LVEDV (Fig. 5, C and D); however, they were significantly correlated with the absolute LVEDV with LBNP (Fig. 5E) and with the change in early filling rate (Fig. 5F); 2) the change in peak torsion and peak untwisting rate were significantly related to \( VO_{2\text{max}} \) where increased fitness levels were associated with a drop in peak torsion and untwisting rates with LBNP but with the opposite trend for sedentary individuals (Fig. 5, A and B); and
3) endurance athletes demonstrated greater reductions in RVEDV and RV stroke volume with LBNP.

**Untwisting rate and diastolic filling.** The early transmitral pressure gradient is responsible for early diastolic filling (4, 13). Therefore, alteration of either left atrial or LV pressure will have consequences for early LV filling. By reducing RV stroke volume with LBNP in the present investigation, left atrial pressure would be reduced (1, 16) resulting in a lower transmitral filling gradient in both groups. A reduced transmitral filling gradient during LBNP is suggested by the observed reduction in peak early filling rate (Table 2) and corresponding reductions in early diastolic circumferential strain rates (Table 3).

In addition to reduced left atrial pressure, alterations to early LV diastolic pressure decay may also have had a significant impact on the transmitral filling gradient and peak early filling rate in this investigation. From previous studies, and confirmed in the present study, ~40% of LV untwisting occurs before mitral valve opening, making peak untwisting rate important for LV diastolic pressure decay (8, 18). Previous investigations have shown reductions in minimum LV pressure following acute preload reduction (4, 6). This compensatory reduction in LV minimum pressure may be partially related to an increase in peak untwisting rate. Normally active individuals demonstrated an increased peak untwisting rate in response to LBNP, whereas endurance athletes did not. As shown in Fig. 5F, all subjects had reduced filling rates with LBNP, the extent of the reduction is significantly correlated with the change in the LV untwisting rate. This response may help normally active individuals maintain peak early filling rate and LVEDV to a greater extent than endurance athletes during orthostatic stress.

**Describing group disparities in untwisting rate during LBNP.** It is well established that endurance-trained athletes have a significantly larger reduction in LVEDV with volume unloading compared with normally active individuals (with matched LBNP pressures) (10, 16), which give rise to a correspondingly larger reduction in stroke volume in athletes, via the Frank-Starling relationship. Indeed, it was shown in the present study that the athletes dropped LVEDV by 26.6 ± 7.3 ml and 14.0 ± 9.1 ml, respectively. Alterations in systolic function are strongly linked to LV untwisting, particularly with exercise (18, 28), but in the present study the changes in LV twist and untwisting rates with LBNP do not have significant correlations with the changes in LVEDV, LVESV or LV stroke volume, as exemplified in Fig. 5, C and D. Thus, while increased torsion is shown to be strongly associated with increased untwisting rates (R = −0.84, P < 0.001, Fig. 4A), the central blood volume dependence of twist function is disassociated from both preload and end-systolic volumes,

![Fig. 4. Peak untwisting rate in endurance-trained athletes. Data are for each individual and group mean at baseline and during −30 mmHg LBNP.](image)

![Fig. 5. A and B: relationship between maximal oxygen consumption (Vo2) and changes in peak torsion (A) and peak untwisting rate (B). C and D: relationship between change in peak untwisting rate and change in both left ventricular end-diastolic volume (LVEDV; C) and end-systolic volume (LVESV; D). E: relationship between change in peak untwisting rate and absolute LVEDV with LBNP. F: dependence of change in the early filling rate on change in untwisting rate.](image)
although the changes in twist function are significantly corre-
related with the absolute LVEDV during LBNP, as shown in Fig.
5E. It is likely that the correlation between $V_{O_{2\max}}$ and changes 
in twist function with LBNP, shown in Fig. 5, A and B, is 
related to their correlation with absolute LVEDV, given the 
strong relationship between cardiovascular performance and 
increased LVEDV (5). Finally, the correlation of the changes 
in untwisting rates with the change in the early filling rate (Fig.
5F), independent of the change in preload, suggests that the 
athletes have reduced LV suction with LBNP, while normally 
active subjects have increased suction. A previous dog study 
showed, similar to the endurance-trained athletes in the present 
study, that twist function is reduced with a reduction in preload 
(7), which might be expected given the nature of the Frank-
Starling mechanism. Specifically, all other factors being held 
constant, a reduction in preload would be expected to be 
associated with a reduction in peak torsion. The different 
response in the normally active subjects may thus be related to 
their lower tolerance for reductions in function associated with 
their smaller absolute LV volumes and stroke volumes. In-
creased twist and untwisting rates may thus reflect a compen-
satory mechanism to offset the reduction in preload with 
reduction in central blood volume.

A second possible mechanism that may explain the group 
differences in peak untwisting rate may be the effects on 
sympathetic nervous output in response to carotid baroreceptor 
stimulation. Recent investigations have shown that peripheral 
baroreceptors are indeed active during low levels of LBNP (11, 
20). In addition, Sarnoff et al. (24) demonstrated in 1960 that 
carotid sinus hypotension results in increased contractility and 
an increased rate of early relaxation. The findings of Sarnoff 
and colleagues are similar to the increased peak torsion and 
twisting rate observed with LBNP in normally active indi-
viduals in our investigation. The contractile influence of the 
carotid sinus is withdrawn when sympathetic outflow is inhib-
ited (24), which may be the case in endurance athletes. Symp-
athetic activity from the carotid baroreceptors may also be 
inhibited by the predominance of parasympathetic activation 
observed in endurance athletes (26).

Right ventricular function. The majority of previous inves-
tigations examining cardiac responses to orthostatic stress have 
either ignored the RV or simply measured ventricular diame-
ters or areas (1, 10, 12, 16, 21). Our findings of larger RV 
volume reductions in endurance athletes during LBNP are 
suggestive of either a more compliant RV or greater vascular 
capacitance (27). Some investigations suggest RV adaptations 
to endurance training (19), but to our knowledge an assessment 
of RV compliance in athletes has not been completed. Overall, 
greater reductions in RV volume in endurance athletes may 
contribute to their reduced orthostatic tolerance.

Limitations. The results of this investigation should be 
interpreted with several limitations in mind. Given the small 
study sample, some relationships, such as the change in LVEDV 
and untwisting rate, may have been significant with a larger num-
ber of subjects. The completed imaging studies at baseline or 
with unloading were 15–20 min in duration. While 5 min of 
acclimatization was included to allow the majority of volume 
changes to take place, it is possible that volumes continued to 
change during the study. Also, MRI tissue tagging studies did 
not provide full coverage of motion over the cardiac cycle. 
Because of the decay of the MRI tissue tagging preparation 
over the cardiac cycle, tissue tagging was applied after the 
early systolic phases to ensure tag persistence to the end of diastole; thus the rate of systolic twist could not be reported. 
The tissue tagging preparation was delayed by 200 ms after the 
electrocardiogram trigger, and thus all tissue deformations, 
including twist and circumferential strain, were referenced to 
diastasis (9) as opposed to the more conventional end-diastole 
cardiac phase. While this alternate reference phase will not 
affect the calculation of untwisting rates or circumferential 
strain rates, it will yield different peak twist and peak circum-
ferential strain values compared with data referenced to end 
diastole. The difference between the diastasis reference used in 
this study and the end-diastolic reference is the change in twist 
or strain associated with atrial contraction. It is thus likely that 
the magnitude of peak twist is underestimated compared with 
the conventional end-diastolic referenced calculations, although, 
as shown in Fig. 2, there is a significant correlation between the 
change in twist and untwisting rates with LBNP calculated with 
the diastasis-referenced approach used in this study. The inter-
pretation of the findings in this study is also limited by the lack 
of invasive measures of left atrial or LV pressures and can 
therefore only infer the effects of LBNP on the filling pressures 
or the transmitral gradient based on hemodynamic events. 
However, previous investigations have demonstrated the ef-
effects of preload reduction on the transmitral filling gradient (4, 
13). Additionally, no measures of baroreceptor function or 
nervous activity were made, and so we can only speculate about their impact on our results. Finally, we assessed LV 
rotation under moderate LBNP. Examining untwisting rates as 
individuals approach presyncope may provide further insights 
into how this mechanism ultimately affects orthostatic intoler-
ance in athletes.

Conclusions. Using cardiac MRI, this investigation demon-
strated a differential LV rotation response to reduced central 
blood volume between endurance-trained athletes and nor-
mally active individuals. Athletes with higher cardiovascular 
performance trended toward reduced twist and untwisting rates 
with volume unloading, while normally active subjects showed 
an opposite response. In all subjects, the change in twist function 
was uncoupled from the change in LVEDV or LVESV, but the 
changes in twist and untwisting rates were correlated with 
the change in early filling rates. Increased twist function in nor-
mally active subjects with a drop in central blood volume may 
reflect a compensatory mechanism to offset the reduction in 
systolic function associated with the drop in LVEDV. The 
opposite response in athletes may contribute to their larger 
changes in LVEDV and stroke volume with volume unloading 
and their orthostatic intolerance.

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