Left ventricular mechanical limitations to stroke volume in healthy humans during incremental exercise

Eric J. Stöhr, José González-Alonso, and Rob Shave

Centre for Sports Medicine and Human Performance, Brunel University, Uxbridge; and Cardiff School of Sport, University of Wales Institute Cardiff, Cardiff, United Kingdom

Submitted 29 March 2011; accepted in final form 9 May 2011

Stöhr EJ, González-Alonso J, Shave R. Left ventricular mechanical limitations to stroke volume in healthy humans during incremental exercise. Am J Physiol Heart Circ Physiol 301: H478–H487, 2011. First published May 13, 2011; doi:10.1152/ajpheart.00314.2011.—During incremental exercise, stroke volume (SV) plateaus at 40–50% of maximal exercise capacity. In healthy individuals, left ventricular (LV) twist and untwisting (“LV twist mechanics”) contribute to the generation of SV at rest, but whether the plateau in SV during incremental exercise is related to a blunting in LV twist mechanics remains unknown. To test this hypothesis, nine healthy young males performed continuous and discontinuous incremental supine cycling exercise up to 90% peak power in a randomized order. During both exercise protocols, end-diastolic volume (EDV), end-systolic volume (ESV), and SV reached a plateau at submaximal exercise intensities while heart rate increased continuously. Similar to LV volumes, two-dimensional speckle tracking-derived LV twist and untwisting velocity increased gradually from rest (all \( P < 0.001 \)) and then leveled off at submaximal intensities. During continuous exercise, LV twist mechanics were linearly related to ESV, SV, heart rate, and cardiac output (all \( P < 0.01 \)) while the relationship in SV was exponential. In diastole, the increase in apical untwisting was significantly larger than that of basal untwisting (\( P < 0.01 \)), emphasizing the importance of dynamic apical function. In conclusion, during incremental exercise, the plateau in LV twist mechanics and their close relationship with SV and cardiac output indicate a mechanical limitation in maximizing LV output during high exercise intensities. However, LV twist mechanics do not appear to be the sole factor limiting LV output, since EDV reaches its maximum before the plateau in LV twist mechanics, suggesting additional limitations in diastolic filling to the heart.

In healthy individuals, the increase in cardiac output from rest to exercise is achieved by a combination of both enhanced heart rate (HR) and stroke volume (SV) (18, 21, 25). Although some investigators have contested a plateau in SV during incremental exercise (14, 38), a considerable number of studies have shown that SV levels off at \( \sim 40–50\% \) of the maximal exercise capacity (18, 21, 22, 25, 26). This leveling off of SV is the result of a plateau in both end-diastolic volume (EDV) and end-systolic volume (ESV) (25). Maintained EDV and ESV suggest that LV filling and ejection do not increase further above moderate exercise intensities. However, this is surprising considering that central venous pressure and inotropic state appear to increase continuously to the point of task failure (12, 22). Thus the plateau in SV may be related to cardiac mechanical constraints in accommodating a greater EDV or further decreasing ESV.

Previous studies have shown that left ventricular (LV) twist and untwisting (“LV twist mechanics”) play an important role in normal systolic and diastolic function at rest, contributing to LV ejection and filling (6, 13, 27, 28, 31). Two recent studies have further demonstrated that systolic and diastolic LV twist mechanics are significantly enhanced in healthy individuals performing low- to moderate-intensity exercise (9, 23), whereas twist and untwisting are unaltered in patients with hypertrophic cardiomyopathy during mild effort (23). Although these findings underline the importance of dynamic twist mechanics for LV function in individuals without any known cardiac disease, the normal response of LV mechanics to exercise at intensities exceeding 40% peak power has never been assessed. It is possible that the previously observed plateau in EDV and ESV despite progressive increases in central venous pressure and contractility may be reflective of an underlying limit in cardiac twist mechanics.

The aim of the present study was to examine the relationships between LV twist mechanics and SV, HR, cardiac output, ESV, and EDV to gain insight into the factors underlying the plateau in SV. To determine whether the relationships would be directly caused by the exercise performed, healthy individuals were assessed during both continuous and discontinuous incremental exercise. We hypothesized that a limit in twist mechanics at submaximal exercise intensities is an important factor underlying the leveling off in SV during incremental exercise in healthy individuals.

METHODS

Study Population

Following ethical approval from the Brunel University Research Ethics Committee, nine healthy recreationally active males (age 26 ± 4 yr, height 175.1 ± 4.9 cm, peak power 249 ± 31 W, peak HR 173 ± 14 beats/min) provided verbal and written informed consent to take part in the study. To ensure optimal echocardiographic images, participants were examined for quality of images before enrolment. This study conforms to the code of ethics of the World Medical Association (Declaration of Helsinki).

Familiarization and Exercise Testing

Participants attended the laboratory a total of four times with visits separated by 48–72 h. On days 1 and 2, participants were familiarized with supine cycling (Lode, Angio 2003, Groningen, Netherlands) in the left lateral position tilted at a 45° angle [see...
On day 3, each participant performed a continuous incremental exercise test to volitional fatigue from which individual peak power (Lode, Angio 2003) and peak HR (Vivid 7; GE Medical, Horton, Norway) were determined. On the experimental day, following 10 min of rest on the supine cycle ergometer, each participant performed incremental exercise to volitional fatigue. To have confidence that our results were reproducible and that the observation would be directly related to the exercise performed, each participant completed both a continuous and discontinuous exercise protocol in a randomized order separated by 1 h of rest. Exercise during the continuous and discontinuous trials was performed for 4 min at 25 ± 3, 75 ± 9, 125 ± 15, 174 ± 22, and 224 ± 28 W, which equated to 10, 30, 50, 70, and 90% of the individual peak power attained during the initial continuous incremental exercise to fatigue. In addition to counterbalancing the two trials, the order of exercise stages within the discontinuous trial was also randomized. Following completion of each stage during the discontinuous trial, participants were given up to 10 min recovery in the supine position to allow HR to return to baseline. To avoid changes in hydration status between the continuous and discontinuous exercise test, participants were provided with a 4.5% glucose solution to drink ad libitum after their first trial.

Throughout both exercise trials, mean arterial blood pressure (MAP) was assessed using a beat-by-beat arterial blood pressure monitoring system (FinometerPRO, FMS; Finapres Measurement Systems, Arnhem, Netherlands) and recorded continuously for off-line analysis (PowerLab; ADInstruments, Chalgrove, UK). MAP was calculated as the average blood pressure obtained from the beat-by-beat pressure waveforms during the last 2 min of each exercise stage (Chart Version 5.5.6; ADInstruments). HR was recorded continuously via the ECG inherent to the ultrasound (Vivid 7; GE Medical).

Fig. 1. Systemic cardiovascular and global left ventricular (LV) function during continuous and discontinuous incremental exercise. Mean arterial pressure, heart rate (HR), and cardiac output increased continuously while end-diastolic volume (EDV), end-systolic volume (ESV), and stroke volume (SV) reached a plateau at submaximal exercise intensities. Filled and open squares represent continuous and discontinuous exercise, respectively. W, workload. Data are means ± SE. *P < 0.01 between continuous and discontinuous trials (n = 9).
LV mechanics and stroke volume during exercise

Cardiovascular responses to incremental exercise of the high HR during later stages of incremental exercise, we used LV parasternal short-axis images on the level of the papillary muscles recorded at end-expiration, and three consecutive cardiac cycles were saved for offline analysis. Because of increasing HRs with incremental exercise, the time that participants had to perform end-expiratory breath-hold to acquire three cardiac cycles was progressively reduced.

Isovolumic relaxation time (IVRT) was assessed using pulsed-wave Doppler of the septal mitral annulus as previously described (3). LV speckle tracking twist mechanics. LV systolic and diastolic rotation were assessed from parasternal short-axis images recorded at the LV base on the level of the mitral valve and at the apex as close to the point of end-systolic luminal obliteration as possible (37), which was achieved by moving the transducer one to two intercostal spaces lower than the basal image. To ensure reproducibility of images at all stages of exercise, the position of the ultrasound transducer during baseline assessment was marked on the participant’s chest. This enabled rapid identification of a similar apical imaging window, allowing the sonographer to then visually adjust and acquire comparable cross-sectional views. Furthermore, frame rate was kept constant between all subjects and all conditions at 97 frames/s; imaging depth for both LV basal and apical short-axis views was also standardized within participants (33). A single focal point was positioned in the center of the ventricular cavity for all short-axis images. Images were analyzed off-line for two-dimensional (2-D) speckle tracking-derived basal and apical rotation and rotational velocities (EchoPAC, Version 7.0.0; GE Medical). 2-D speckle tracking was successful at low and high exercise intensities up to near maximal effort (see Supplemental Video 2). To adjust for inter- and intraindividual variability of HR, raw data were exported to a spreadsheet (Microsoft, Seattle, WA) and normalized to the percentage of systolic and diastolic heart rate, respectively (7). Normalization was achieved by cubic spline interpolation of systolic and diastolic data to 300 points, respectively (GraphPad Prism 5.00 for Windows, San Diego, CA). LV twist, untwisting, and the respective velocities were obtained by subtraction of basal rotation/rotation velocity data from apical rotation/rotation velocity data. Peak untwisting velocity was determined as the greatest negative deflection following peak twisting velocity. In addition to peak values, the absolute time it took for LV twist indexes to reach their peak was determined from the frame-by-frame speckle tracking analysis and expressed in milliseconds. Comparison between temporal occurrence of mitral valve opening and peak diastolic untwisting velocity was performed to assess whether peak diastolic twist indexes occurred before, simultaneously with, or following mitral valve opening.

**Statistical Analysis**

Data are presented as means ± SD unless otherwise stated. The change in blood pressure and LV function indexes during the continuous and discontinuous protocol was analyzed using repeated-measures ANOVA. Paired-samples t-test was used post hoc to detect differences between conditions; Bonferroni correction was applied to account for multiple comparisons. Between the responses during the continuous and discontinuous trial was performed using two-way repeated-measures ANOVA. Relationships between variables were assessed using Pearson’s product moment correlation. Alpha was set a priori to 0.05. All statistical analyses were performed using STATISTICA (version 6; StatSoft, Tulsa, OK).

### Table 1. Cardiovascular responses to incremental exercise

<table>
<thead>
<tr>
<th>Heart rate, beats/min</th>
<th>Workload, % peak power output</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
</tr>
<tr>
<td>Cont</td>
<td>62 ± 1</td>
</tr>
<tr>
<td>Discont</td>
<td>63 ± 7</td>
</tr>
<tr>
<td>EDV, ml</td>
<td>135 ± 6</td>
</tr>
<tr>
<td>Cont</td>
<td>128 ± 10</td>
</tr>
<tr>
<td>Discont</td>
<td>46 ± 4</td>
</tr>
<tr>
<td>ESV, ml</td>
<td>44 ± 6</td>
</tr>
<tr>
<td>Cont</td>
<td>89 ± 8</td>
</tr>
<tr>
<td>Discont</td>
<td>84 ± 5</td>
</tr>
<tr>
<td>Q, l/min</td>
<td>5.5 ± 0.8</td>
</tr>
<tr>
<td>Cont</td>
<td>5.2 ± 0.6</td>
</tr>
<tr>
<td>Discont</td>
<td>79 ± 9</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>84 ± 9</td>
</tr>
<tr>
<td>IVRT, ms</td>
<td>75 ± 10</td>
</tr>
<tr>
<td>Cont</td>
<td>75 ± 16</td>
</tr>
</tbody>
</table>

Values are means ± SD. Cont, continuous incremental exercise; Discont, discontinuous incremental exercise; IVRT, isovolumic relaxation time; Q, cardiac output; EDV, end-diastolic volume; ESV, end-systolic volume; SV, stroke volume; MAP, mean arterial pressure. *P < 0.01 compared with rest. †P < 0.01 compared with 10%. ‡P < 0.01 compared with 30%. •P < 0.01 compared with 50% exercise. &P < 0.01 compared with 70%. NS, not significant.
RESULTS

**LV Volumes and Arterial Blood Pressure**

During the initial stages of both continuous and discontinuous incremental exercise, EDV and SV significantly increased while ESV significantly decreased compared with rest (all $P < 0.01$; Fig. 1). Following this initial response, EDV reached a plateau at ~30% peak power while ESV and SV leveled off at ~50% peak power (Table 1). As a result of the progressive rise in HR, cardiac output increased continuously up to 70% peak power and then also plateaued (all $P < 0.01$). Because of a significantly higher HR during the later stages of the continuous trial, the increase in cardiac output was also larger during the continuous protocol (both $P < 0.01$). In contrast, the increase in MAP was significantly lower during the later stages of the continuous trial ($P < 0.01$). Because of a significantly higher HR during the later stages of the continuous trial, the increase in cardiac output was also larger during the continuous protocol (both $P < 0.01$). In contrast, the increase in MAP was significantly lower during the later stages of the continuous trial ($P < 0.01$). During both continuous and discontinuous exercises, IVRT declined continuously and was not significantly different between trials ($P < 0.01$). Body mass was unaltered before and following both protocols (precontinuous: 70.5 ± 8.3 kg; postcontinuous: 70.4 ± 8.4 kg; prediscontinuous: 70.5 ± 8.3 kg; postdiscontinuous: 70.2 ± 8.4 kg; all $P > 0.05$).

**LV Twist Mechanics**

Peak LV systolic and diastolic basal rotation, apical rotation, twist, and the respective velocities increased significantly from rest to exercise (all $P < 0.01$, Fig. 2). Similar to the SV response, the increase in LV twist, twist velocity, and untwisting velocity reached a plateau at ~50% peak power and remained at this level for all subsequent exercise stages (Table 2). Compared with the discontinuous trial, twist and twisting velocity were significantly higher at 70% peak power during continuous incremental exercise ($P = 0.01$); however, all other twist indexes did not differ between the two protocols ($P > 0.05$). In both trials, the increase in diastolic apical rotation velocity from rest to 90% maximal exercise capacity was significantly higher than the increase in basal rotation velocity ($P < 0.01$, Fig. 3). In addition to the significant change in peak values, temporal analysis showed that peak diastolic apical rotation and peak untwisting velocity reached their peak at the same time as mitral valve opening at all exercise stages ($P < 0.01$) while peak LV diastolic basal rotation velocity occurred significantly after mitral valve opening at 70 and 90% maximal exercise capacity (all $P < 0.01$, Fig. 4).

As shown in Figs. 5 and 6, during continuous exercise LV, twist mechanics correlated linearly with SV, HR, cardiac output, and ESV ($P < 0.01$), whereas the relationships between LV mechanics and EDV appeared to have an exponential pattern. Furthermore, during both trials, LV twist and untwisting velocity were strongly related ($P = 0.01$, Fig. 7).

**DISCUSSION**

This is the first study to examine whether the plateau in SV at submaximal exercise intensities is underpinned by...
constraints in LV twist and untwisting in healthy individuals. There were five novel findings. 1) Similar to the previously observed plateau in SV, LV systolic and diastolic twist mechanics also reached an upper limit at moderate exercise intensities and remained at this level thereafter. 2) The change in LV twist mechanics during incremental exercise correlated with ESV, SV, HR, and cardiac output. 3) At all exercise intensities, enhanced peak LV untwisting velocity was

### Table 2. Peak systolic and diastolic LV twist indexes at rest and during incremental exercise

<table>
<thead>
<tr>
<th>Workload, % peak power output</th>
<th>Control</th>
<th>10%</th>
<th>30%</th>
<th>50%</th>
<th>70%</th>
<th>90%</th>
<th>Cont vs. discont</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Twist, degrees</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cont</td>
<td>13.9 ± 3.9</td>
<td>15.4 ± 2.4</td>
<td>19.8 ± 5.1*</td>
<td>23.8 ± 6.0*†</td>
<td>26.8 ± 4.2**‡</td>
<td>24.7 ± 6.9**‡</td>
<td>P = 0.01</td>
</tr>
<tr>
<td>Discont</td>
<td>11.0 ± 4.2</td>
<td>17.2 ± 3.9</td>
<td>20.1 ± 6.3*</td>
<td>25.3 ± 7.0*</td>
<td>21.2 ± 3.6*</td>
<td>22.4 ± 3.1*</td>
<td></td>
</tr>
<tr>
<td><strong>Apical rotation, degrees</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cont</td>
<td>10.0 ± 2.7</td>
<td>11.7 ± 2.2</td>
<td>15.4 ± 4.7</td>
<td>18.3 ± 5.6*†</td>
<td>19.5 ± 3.1**‡</td>
<td>18.5 ± 5.2**‡</td>
<td>NS</td>
</tr>
<tr>
<td>Discont</td>
<td>8.0 ± 3.4</td>
<td>14.3 ± 3.4*</td>
<td>16.5 ± 4.3*</td>
<td>19.1 ± 5.4*</td>
<td>16.8 ± 3.3*</td>
<td>15.8 ± 2.8*</td>
<td></td>
</tr>
<tr>
<td><strong>Basal rotation, degrees</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cont</td>
<td>−4.4 ± 2.3</td>
<td>−4.2 ± 2.0</td>
<td>−6.2 ± 2.3*†</td>
<td>−6.5 ± 2.6†</td>
<td>−8.0 ± 2.5†</td>
<td>−7.8 ± 3.3</td>
<td>NS</td>
</tr>
<tr>
<td>Discont</td>
<td>−3.6 ± 2.3</td>
<td>−4.2 ± 2.1</td>
<td>−4.3 ± 2.8*†</td>
<td>−7.2 ± 3.7†</td>
<td>−5.6 ± 2.2†</td>
<td>−7.1 ± 2.5</td>
<td></td>
</tr>
<tr>
<td><strong>Twist vel, degree/s</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cont</td>
<td>103 ± 21</td>
<td>105 ± 18</td>
<td>150 ± 31*†</td>
<td>200 ± 49**‡</td>
<td>232 ± 35**†</td>
<td>216 ± 42**†</td>
<td>P = 0.01</td>
</tr>
<tr>
<td>Discont</td>
<td>91 ± 22</td>
<td>130 ± 36</td>
<td>147 ± 42*</td>
<td>208 ± 43**‡</td>
<td>193 ± 38*</td>
<td>206 ± 53*</td>
<td></td>
</tr>
<tr>
<td><strong>Basal rot vel, degree/s</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cont</td>
<td>−63 ± 15</td>
<td>−73 ± 19</td>
<td>−95 ± 30*</td>
<td>−114 ± 42*</td>
<td>−141 ± 32**‡</td>
<td>−142 ± 36**‡</td>
<td>NS</td>
</tr>
<tr>
<td>Discont</td>
<td>−57 ± 24</td>
<td>−71 ± 29</td>
<td>−74 ± 29</td>
<td>−113 ± 43*†</td>
<td>−106 ± 32*</td>
<td>−113 ± 36*†</td>
<td></td>
</tr>
<tr>
<td><strong>Apical rot vel, degree/s</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cont</td>
<td>89 ± 22</td>
<td>107 ± 32*</td>
<td>149 ± 37*†</td>
<td>183 ± 43*†</td>
<td>199 ± 45*†</td>
<td>192 ± 44*†</td>
<td>NS</td>
</tr>
<tr>
<td>Discont</td>
<td>75 ± 36</td>
<td>131 ± 28*</td>
<td>150 ± 30*</td>
<td>177 ± 48*</td>
<td>178 ± 53*</td>
<td>163 ± 52*</td>
<td></td>
</tr>
<tr>
<td><strong>Untwisting vel, degree/s</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cont</td>
<td>−116 ± 38</td>
<td>−157 ± 59</td>
<td>−218 ± 96*</td>
<td>−264 ± 113*</td>
<td>−278 ± 93*†</td>
<td>−284 ± 94*†</td>
<td></td>
</tr>
<tr>
<td>Discont</td>
<td>−101 ± 38</td>
<td>−157 ± 59</td>
<td>−218 ± 96*</td>
<td>−264 ± 113*</td>
<td>−278 ± 93*†</td>
<td>−284 ± 94*†</td>
<td></td>
</tr>
</tbody>
</table>

Values are means ± SD. Rot, rotation; vel, velocity. *P < 0.01 compared with rest. †P < 0.01 compared with 10%. ‡P < 0.01 compared with 30%. NS, not significant.

Fig. 3. Peak diastolic rotation velocities at rest and during continuous (A) and discontinuous (B) incremental exercise. Peak diastolic apical rotation velocity was significantly higher at all exercise intensities compared with peak diastolic basal rotation velocity. Consequently, the increase in LV untwisting velocity was almost solely mediated by enhanced apical untwisting. Data are means ± SE. For clarity, all data are expressed as positive values. *P < 0.01 compared with apical diastolic velocity (n = 9).
Continuous and discontinuous incremental exercise were similar in LV twist mechanics and SV, further suggesting that the ability to maximize LV systolic and diastolic twist velocities also reach their peak at moderate exercise intensities.

In previous studies, central venous pressure has been shown to increase continuously during incremental exercise up to maximal oxygen consumption. Thus, the presently observed plateau in EDV may, therefore, have been related to an inability of the LV to further improve diastolic filling above moderate exercise intensities. During continuous incremental exercise, this does not, however, appear to be related to diastolic untwisting, since diastolic untwisting increased further when maximal EDV had been attained. The mechanisms for the linear increase in EDV during discontinuous exercise and the plateau in EDV during continuous exercise in this study are not clear. Previous studies have shown conflicting EDV responses to incremental exercise, possibly related to differences in training status or posture.

LV Twist Mechanics and SV

In the present study, the changes in EDV, ESV, and SV during continuous and discontinuous incremental exercise were similar to those reported by previous studies, showing an initial increase followed by a plateau at moderate exercise intensities. The present data further support the concept of a limit in cardiac function at submaximal exercise intensities by showing that, during both continuous and discontinuous incremental exercise, LV systolic and diastolic twist velocities also reach their peak at moderate exercise intensities.

In previous studies, central venous pressure has been shown to increase continuously during incremental exercise up to maximal oxygen consumption. Thus, the presently observed plateau in EDV may, therefore, have been related to an inability of the LV to further improve diastolic filling above moderate exercise intensities. During continuous incremental exercise, this does not, however, appear to be related to diastolic untwisting, since diastolic untwisting increased further when maximal EDV had been attained. The mechanisms for the linear increase in EDV during discontinuous exercise and the plateau in EDV during continuous exercise in this study are not clear. Previous studies have shown conflicting EDV responses to incremental exercise, possibly related to differences in training status or posture.

LV Twist Mechanics and SV

In the present study, the changes in EDV, ESV, and SV during continuous and discontinuous incremental exercise were similar to those reported by previous studies, showing an initial increase followed by a plateau at moderate exercise intensities. The present data further support the concept of a limit in cardiac function at submaximal exercise intensities by showing that, during both continuous and discontinuous incremental exercise, LV systolic and diastolic twist velocities also reach their peak at moderate exercise intensities.

In previous studies, central venous pressure has been shown to increase continuously during incremental exercise up to maximal oxygen consumption. Thus, the presently observed plateau in EDV may, therefore, have been related to an inability of the LV to further improve diastolic filling above moderate exercise intensities. During continuous incremental exercise, this does not, however, appear to be related to diastolic untwisting, since diastolic untwisting increased further when maximal EDV had been attained. The mechanisms for the linear increase in EDV during discontinuous exercise and the plateau in EDV during continuous exercise in this study are not clear. Previous studies have shown conflicting EDV responses to incremental exercise, possibly related to differences in training status or posture.

LV Twist Mechanics and SV

In the present study, the changes in EDV, ESV, and SV during continuous and discontinuous incremental exercise were similar to those reported by previous studies, showing an initial increase followed by a plateau at moderate exercise intensities. The present data further support the concept of a limit in cardiac function at submaximal exercise intensities by showing that, during both continuous and discontinuous incremental exercise, LV systolic and diastolic twist velocities also reach their peak at moderate exercise intensities.

In previous studies, central venous pressure has been shown to increase continuously during incremental exercise up to maximal oxygen consumption. Thus, the presently observed plateau in EDV may, therefore, have been related to an inability of the LV to further improve diastolic filling above moderate exercise intensities. During continuous incremental exercise, this does not, however, appear to be related to diastolic untwisting, since diastolic untwisting increased further when maximal EDV had been attained. The mechanisms for the linear increase in EDV during discontinuous exercise and the plateau in EDV during continuous exercise in this study are not clear. Previous studies have shown conflicting EDV responses to incremental exercise, possibly related to differences in training status or posture.
although absolute differences were small, MAP was significantly higher during the discontinuous protocol compared with the continuous trial. Conversely, LV twist was significantly lower during the discontinuous protocol. These data are in accordance with earlier findings showing that increased afterload reduces peak LV systolic twist (8). Thus enhanced arterial blood pressure may offset the positive inotropic effect caused by augmented sympathetic activity during exercise intensities exceeding 50% maximal capacity and thereby limit the increase in LV twist. Because the energy required for active diastolic untwisting is stored during systole (15, 17), the increase in arterial blood pressure may also indirectly attenuate the increase in LV untwisting velocity. This would explain the strong relationship between systolic twist and diastolic untwisting velocity observed in the present investigation.

Fig. 5. Relationships between LV twist mechanics and SV, HR, and cardiac output during continuous (●) and discontinuous (○) incremental exercise (n = 9). The increase in LV twist mechanics correlated significantly with the change in SV, HR, and cardiac output during both continuous and discontinuous incremental exercise. The y-axes for untwisting velocity are inversed to reflect the increase in untwisting velocity. Data are means ± SE.

Fig. 6. Relationships between LV twist mechanics and EDV and ESV during continuous (●) and discontinuous (○) incremental exercise (n = 9). Although the relationships with ESV were clearly linear, the relationships between LV twist mechanics and EDV during continuous incremental exercise were not significant and appeared more exponential, suggesting that the early plateau in SV is the result of reduced filling that may not be related to cardiac systolic or diastolic mechanics. The y-axes for untwisting velocity are inversed to reflect the increase in untwisting velocity. Data are means ± SE.
In addition, Takeuchi and Lang (35) have reported a reduced peak LV untwisting velocity in arterial hypertension at rest, further suggesting an impact of elevated arterial blood pressure on LV twist mechanics. However, in contrast to the present data, Takeuchi and Lang (35) also reported a delay in peak LV untwisting. Our study shows that, during exercise in healthy individuals, despite extensive shortening of the cardiac cycle, peak LV untwisting occurs simultaneously with mitral valve opening at all exercise intensities. Therefore, a delay in peak LV untwisting velocity beyond mitral valve opening during exercise is likely indicative of cardiac dysfunction.

**Uncoupling of Basal and Apical Twist Mechanics During Incremental Exercise**

To establish an intraventricular pressure gradient that maximizes LV suction for diastolic filling, pressure at the LV apex must be lower than at the base. Accordingly, during exercise, greater apical untwisting compared with basal untwisting is beneficial for LV filling. Indeed, Doucende et al. (9) showed that the increase in apical untwisting during incremental exercise up to \(~40\%\) maximal exercise capacity was significantly higher than the increase in basal untwisting. Our data extend these findings by showing that this uncoupling increases more as exercise intensity increases to near maximal levels. This finding underlines the importance of an apical untwisting reserve to meet an enhanced cardiovascular demand in healthy individuals, which may be absent in cardiac disease (23). Furthermore, the previous and present data indicate that, during exercise, a differential response in LV rotation at the base and the apex is normal. Similarly, Akagawa et al. (2) observed a greater increase in apical subendocardial rotation than basal subendocardial rotation following dobutamine infusion in healthy individuals at rest. Some authors have proposed that this response may be caused by region-specific adrenoreceptor sensitivity (24). In this regard, data are available showing that electrical activation at the apex persists longer than at the base (29), which may result in an enhanced \(Ca^{2+}\) release and a faster reuptake in apical myocytes. Moreover, we have previously shown that basal rotation predominates over apical rotation during heat stress, a condition that is characterized by a reduction in EDV (34). In contrast, the greater apical rotation during incremental exercise in the present study is likely related to the increase in EDV, as has recently been shown using saline infusion (39). Thus enhanced venous return from the exercising muscles and the resultant increased EDV may have contributed to a change in myofiber alignment and increased LV twist and untwisting in a mechanically more efficient manner (1). Collectively, the present data suggest that the LV apex, in contrast to the base, has a greater “reserve” to respond to exercise. By implication, it follows that the lower potential of the LV base to respond may represent a key factor in the limitation of overall LV twist mechanics to increase beyond moderate exercise intensities.

Similar to the observed difference in peak basal and apical rotation, the time taken for diastolic rotation velocities to reach their peak also differed between the base and the apex at higher exercise intensities. Figure 4 shows that, during continuous incremental exercise at 70% and 90% of peak power, peak LV diastolic basal rotation velocity occurred after mitral valve opening, whereas peak apical untwisting still occurred before or simultaneously with the start of early LV filling. Because both peak apical and basal diastolic untwisting plateau at these exercise intensities, it is possible that the higher peak basal untwisting later in diastole is reflective of an enhanced atrial contribution to filling action rather than a reduction in basal function. This agrees with the previous observation of a relationship between peak diastolic basal rotation velocity and early filling velocity during moderate-intensity exercise (9). The functional significance of this association during exercise and other conditions of altered hemodynamics and inotropic state is, however, currently not clear and requires further study.

**Implications for Pathological and Physiological Adaptations**

In recent years, the number of clinical trials examining LV twist mechanics in acute and chronic pathology has risen steadily (13, 30, 32), yet the normal response of LV twist mechanics to stress in healthy individuals is still poorly understood. In the clinical and athletic environment, exercise tests are frequently used to expose cardiovascular abnormalities and establish physiological performance. The present study provides insight into the normal response of LV twist mechanics during incremental exercise to near maximal exercise capacity. Failure of LV twist mechanics to progressively increase up to moderate relative exercise intensities, peak LV untwisting velocity occurring markedly following mitral valve opening, and apical mechanics not increasing to a greater extent than basal rotation during the course of a diagnostic exercise test may all reflect underlying pathology. Equally, highly trained individuals that have a higher SV at rest and during exercise may display a different response in LV twist mechanics reflecting chronic myocardial adaptations to exercise training. Despite some small differences between trials, the present investigation also demonstrates that LV twist and untwisting are very similar whether incremental exercise is performed continuously or discontinuously. The option to employ a discontinuous protocol, which drastically reduces the time that individuals are exposed to acute cardiovascular stress, may be an important advantage in some populations and conditions.

**Technical Considerations and Limitations**

At present, the assessment of LV twist mechanics with 2-D speckle tracking ultrasound entails some inherent methodological...
limitations, mostly pertaining to image quality and through-plane motion of myocardial tissue. While through-plane motion cannot be avoided, it appears to have relatively little impact on tracking of myocardial tissue during incremental exercise, since tracking in the present study was successful in >90% of myocardial segments, indicated by the tracking score provided by the software and confirmed by visual inspection. This successful tracking was likely related to the assessment of echocardiographic image quality in participants before enrolment and the standardization of image acquisition. To ensure accuracy and comparability of data, image acquisition must take into account frame rates (16), imaging depth (33), and the level of the apical short-axis view (37). In this study, a constant frame rate of 97 frames/s between all participants and all conditions was applied. Furthermore, imaging depth within the basal and apical short-axis views was also standardized, and the apical short-axis level was chosen as caudal as possible to estimate the largest “true” LV twist. Despite pronounced differences in myocardial velocities, the pattern of response in apical rotation (high rotational velocity) and basal rotation (low rotational velocity) was very similar in systole and diastole during both trials, which suggests that the observed change during exercise is physiological in nature. Despite the stringent standardization, speckle tracking values may be slightly underestimated because of elevated HRs at higher exercise intensities, although this error was probably minimized by applying cubic spline interpolation and averaging data over three cardiac cycles. The much lower temporal resolution inherent to magnetic resonance imaging and three-dimensional ultrasound modalities would likely result in a greater error in the assessment of LV twist indexes, whereas the present study demonstrates that the assessment of LV twist mechanics with 2-D speckle tracking echocardiography during incremental exercise up to high exercise intensities is feasible.

The authors acknowledge that the assessment of LV volumes using the linear Teichholz method is not the current gold standard in echocardiography. However, the Teichholz method was chosen because of the limited amount of time available for image acquisition during each stage of exercise. Moreover, the Teichholz method has been shown to provide accurate estimation of LV volumes in individuals without wall motion abnormalities (19).

In conclusion, during incremental exercise, the plateau in LV twist mechanics and their close relationship with SV and cardiac output indicate a mechanical limitation in maximizing LV output during high exercise intensities. However, LV twist mechanics do not appear to be the sole factor responsible for the plateau in SV, since EDV reaches its maximum before the plateau in LV twist mechanics.

ACKNOWLEDGMENTS

We thank all participants for their commitment throughout the study. We also thank Emilie Timlin for excellent assistance during data collection.

DISCLOSURES

None.

REFERENCES


