The impact of endurance exercise training on left ventricular systolic mechanics

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Baggish AL, Yared K, Wang F, Weiner RB, Hutter AM Jr, Picard MH, Wood MJ. The impact of endurance exercise training on left ventricular systolic mechanics. Am J Physiol Heart Circ Physiol 295: H1109–H1116, 2008. First published July 11, 2008; doi:10.1152/ajpheart.00395.2008.—Although exercise training-induced changes in left ventricular (LV) structure are well characterized, adaptive functional changes are incompletely understood. Detailed echocardiographic assessment of LV systolic function was performed on 20 competitive rowers (10 males and 10 females) before and after endurance exercise training (EET; 90 days, 10.7 ± 1.1 h/wk). Structural changes included LV dilation (end-diastolic volume = 128 ± 25 vs. 144 ± 28 ml, P < 0.001), right ventricular (RV) dilation (end-diastolic area = 2,850 ± 550 vs. 3,260 ± 530 mm2, P < 0.001), and LV hypertrophy (mass = 227 ± 51 vs. 256 ± 56 g, P < 0.001). Although LV ejection fraction was unchanged (62 ± 3% vs. 60 ± 3%, P = not significant), all direct measures of LV systolic function were altered. Peak systolic tissue velocities increased significantly (basal lateral SΔ = 0.9 ± 0.6 cm/s, P = 0.004; and basal septal SΔ = 0.8 ± 0.4 cm/s, P = 0.008). Radial strain increased similarly in all segments, whereas longitudinal strain increased with a base-to-apex gradient. In contrast, circumferential strain (CS) increased in the LV free wall but decreased in regions adjacent to the RV. Reductions in septal CS correlated strongly with changes in RV structure (∆RV end-diastolic area vs. ∆LV septal CS; r² = 0.898, P < 0.001) and function (∆peak RV systolic velocity vs. ∆LV septal CS, r² = 0.697, P < 0.001). EET leads to significant changes in LV systolic function with regional heterogeneity that may be secondary to concomitant RV adaptation. These changes are not detected by conventional measurements such as ejection fraction.

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were repeated after the 90-day period of organized team training activity.

All potential subjects were questioned confidentially about anabolic steroid use and were excluded if a history of use was elicited. Individuals were excluded from the final data analysis if they undertook any breaks in training of ≥3 days during the study period.

**Echocardiography.** Echocardiography was performed using a commercially available system (Vivid-I, GE Healthcare, Milwaukee, WI) with a 1.9–3.8-MHz phased-array transducer. Images were obtained after 20 min of quiet rest between 2:00 PM and 5:00 PM and were separated from the previous training session by ≥24 h. Two-dimensional, pulsed-Doppler, and color tissue-Doppler imaging from standard parasternal and apical transducer positions were performed. The two-dimensional frame rate was 25–75 frames/s, and the tissue Doppler frame rate was >100 frames/s for all images. Echocardiography was performed by two trained sonographers, and each sonographer performed both baseline and poststudy imaging on the same individuals. All data were stored digitally, and the poststudy data analysis (EchoPac, version 6.5, GE Healthcare) was performed by two cardiologists (A. L. Baggish and M. J. Wood) blinded to study time point.

Two-dimensional measurements were made in accordance with routine clinical standards (21). LV ejection fraction, end-diastolic volume, and end-systolic volume were calculated using the modified Simpson’s biplane technique. Right ventricular (RV) fractional area change, a validated index of RV function, was calculated by outlining the endocardial borders of the RV in diastole and systole in the apical four chamber view and calculating the difference between the two areas expressed as a percentage of end-diastolic RV area (1). LV mass was calculated using the area-length method. Longitudinal tissue velocities were measured off-line from two-dimensional color-coded tissue-Doppler images and reported as the average of three consecutive cardiac cycles. The E-to-E’ ratio was calculated by dividing the peak transmitral E wave velocity by the peak basal lateral wall E’ velocity. Strain measurements were made using commercially available speckle-tracking analysis software (EchoPac, Version 6.5, GE Healthcare). Short-axis strain values were obtained at the mid-LV level as designated by maximal papillary muscle circumference. Longitudinal values were obtained from the apical four-chamber view and thus reflect septal and lateral wall territory. In accordance with accepted convention, baseline systolic strain values in the longitudinal and circumferential vectors are presented as negative values (segment shortening), whereas baseline radial strain values are presented as positive values (segment lengthening). Strain changes from baseline to posttraining are reported as positive values in cases of increased strain or negative values in case of decreased strain. Resting heart rates were obtained from the final loop of each study. Cardiac output was determined by calculating the product of LV stroke volume and heart rate.

**Statistical analysis.** Measurements are presented as means ± SD. The paired t-test and the Wilcoxon matched pair test were used to assess the significance of interval measures. Comparison of baseline strain measurements in each principal vector was performed with analysis of variance with Bonferroni correction for multiple comparisons. Correlation analysis was performed using the Spearman and Pearson method as appropriate for data distribution. A P value of <0.05 was considered significant.

**RESULTS**

**Study group demographics and historical parameters.** Twenty individuals completed the study training period and had echocardiographic images that were suitable for comprehensive strain and strain rate analysis. The final cohort is comprised of an equal number of males (n = 10) and females (n = 10) with a mean age of 19.9 ± 0.9 yr. No individuals had a personal history of hypertension, but 5 out of 20 (25%) had a family history of hypertension. Medication use, limited to oral contraceptives and topical antiacne agents, was reported in 5 out of 20 (25%) individuals.

Past competitive experience and study period training regimens. Prior participation in organized competitive rowing was 4.5 ± 2.3 yr (range = 2–8 yr), whereas prior university level competitive experience was 1.8 ± 0.6 yr (range = 1–3 yr). During the 8 wk before enrollment, individuals performed 5.2 ± 1.2 h/wk of unsupervised training, which was comprised of 4.9 ± 1.6 h/wk of aerobic training and 0.5 ± 0.3 h/wk of strength training. During the 90-day study period, individuals engaged in 11.6 ± 2.4 h/wk of organized team training that was exclusively dedicated to endurance activity (aerobic = 10.7 ± 1.1 h/wk; and strength = 0.9 ± 1.1 h/wk). All subjects engaged in organized training sessions ≥5 days/wk though the entire study period.

**Clinical and cardiac parameters at baseline.** Baseline clinical and cardiac parameters are shown in Table 1. Baseline values of LV strain and strain rate are shown in Tables 2, 3, and 4. There were no significant differences in radial strain among the six LV wall segments, although a trend existed toward higher radial strain in the inferior, lateral, and posterior walls. Radial strain rate was similar in all regions [P = not significant (NS), Table 2]. In contrast, significant regional heterogeneity existed in the other two principal vectors of peak systolic strain. At baseline, significantly

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**Table 1. Clinical and cardiac parameters at baseline and after 90 days of endurance exercise training**

<table>
<thead>
<tr>
<th>Clinical parameter</th>
<th>Baseline</th>
<th>Posttraining</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>19.0±0.9</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Height, cm</td>
<td>179±9</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Body mass, kg</td>
<td>75.9±11.5</td>
<td>75.8±10.6</td>
<td>NS</td>
</tr>
<tr>
<td>Body surface area</td>
<td>1.94±0.19</td>
<td>1.94±0.18</td>
<td>NS</td>
</tr>
<tr>
<td>Body mass index</td>
<td>23.5±2.0</td>
<td>23.5±1.8</td>
<td>NS</td>
</tr>
<tr>
<td>Pulse, beats/min</td>
<td>60±8</td>
<td>49±7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>110±11</td>
<td>109±9</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>58±6</td>
<td>49±6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RV area change, %</td>
<td>2.2±0.6</td>
<td>2.2±0.6</td>
<td>NS</td>
</tr>
<tr>
<td>LVIDd, mm</td>
<td>48±5</td>
<td>51±6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVEDV, ml</td>
<td>128±25</td>
<td>144±28</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LVIDs, mm</td>
<td>34±4</td>
<td>36±4</td>
<td>0.001</td>
</tr>
<tr>
<td>LVESV, ml</td>
<td>49±10</td>
<td>59±13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV posterior wall, mm</td>
<td>10.0±0.8</td>
<td>10.8±0.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV mass, g</td>
<td>227±51</td>
<td>256±56</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV mass/BSA, g/m²</td>
<td>116±18</td>
<td>131±21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RVAd, mm²</td>
<td>43±5</td>
<td>46±6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RVAs, mm²</td>
<td>2.85±0.50</td>
<td>3.260±530</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RVAs, mm²</td>
<td>1.868±0.320</td>
<td>1.640±0.200</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Values are means ± SD. LVIDd, left ventricular (LV) end-diastolic major dimension; LVEDV, LV end-diastolic volume; LVIDs, LV end-systolic major dimension; LVESV, LV end-systolic volume; BSA, body surface area; RVAd, RV end-diastolic volume; RVAs, RV systolic area; LVEF, LV ejection fraction; S’; systolic tissue-Doppler velocity; E/E’; peak transmitral-pulsed Doppler velocity/peak basal lateral LV early-diastolic tissue velocity; N/A, not applicable; NS, not significant.
higher values of circumferential strain and strain rate were observed in the septal and anteroseptal portions of the LV when compared with the remaining four regions of interest \((P < 0.05\), Table 3). Longitudinal strain increased from LV base to apex (basal lateral LV = \(-18.4 \pm 3.1\%\) vs. apical lateral LV = \(-24.0 \pm 3.3\%, P < 0.05\); basal septal LV = \(-18.1 \pm 2.0\%\) vs. apical septal LV = \(-24.1 \pm 3.7\%, P < 0.05\)) with intermediate values observed in the midventricle \((P < 0.05\), Table 4). A similar increasing gradient from base to apex was observed with longitudinal strain rate; however, this observation was not significant.

**Clinical and cardiac parameters following endurance training.** Resting heart rate \((60 \pm 8\) vs. \(49 \pm 7\) beats/min, \(P < 0.001\)) and diastolic blood pressure \((58 \pm 6\) vs. \(49 \pm 6\) mmHg, \(P < 0.001\)) were reduced after 90 days of EET. In contrast, systolic blood pressure \((110 \pm 11\) vs. \(109 \pm 9\) mmHg, \(P = \text{NS}\)) and body mass \((76.0 \pm 11.6\) vs. \(75.8 \pm 10.6\) kg, \(P = \text{NS}\)) were unchanged (Table 1).

Baseline and posttraining LV structural measurements are shown in Table 1. LV end-diastolic major dimension \((\Delta = 2.8 \pm 1.2\) mm, \(P < 0.001\)) and end-systolic major dimension \((\Delta = 2.2 \pm 1.6\) mm, \(P = 0.001\)) were increased significantly after training. In similar fashion, LV end-diastolic volume \((\Delta = 15.6 \pm 8.6\) ml; \(P < 0.001\)), end-systolic volume \((\Delta = 10.2 \pm 6.0\) ml; \(P < 0.001\)), stroke volume \((\Delta = 6.5 \pm 4.9\) ml; \(P = 0.002\)), and mass \((\Delta = 29 \pm 7\) g; \(P < 0.001\)) were larger at the conclusion of the study period. Despite the increase in stroke volume, the greater increases in end-systolic volume \((\Delta = 21 \pm 12\%\) and end-diastolic volume \((\Delta = 12 \pm 6\%\) relative to their respective baseline values resulted in a trend toward reduced overall LV ejection fraction \((62.0 \pm 3.0\%\) vs. \(60.2 \pm 3.0\%, P = \text{NS}\)) and a reduction in resting cardiac output by \(13 \pm 9\%\) \((4.7 \pm 1.3\) vs. \(4.1 \pm 0.9\) l/min, \(P = 0.003\)) due to the decrease in resting heart rate.

Peak systolic LV tissue velocity increased in both the basal septum \((\Delta = 0.8 \pm 0.4\) cm/s; \(P = 0.008\)) and the basal lateral LV wall \((\Delta = 0.9 \pm 0.6\) cm/s; \(P = 0.004;\) Table 1). Changes in LV strain over the course of the study period are depicted in Fig. 1, A–C. Radial strain increased significantly and by a similar magnitude in all mid-LV segments (Fig. 1A). Circumferential strain increased similarly in 4 out of 6 segments (anterior \(\Delta = 3.4 \pm 2.2\), lateral \(\Delta = 3.3 \pm 2.4\), posterior \(\Delta = 3.2 \pm 2.5\), and inferior \(\Delta = 3.0 \pm 3.6\%, P = \text{NS}\)) but decreased significantly in the remaining 2 out of 6 segments (septal \(\Delta = -3.6 \pm 1.7\), and anteroseptal \(\Delta = -3.3 \pm 2.7\%, P = \text{NS}\), \(P\) value compared with 4 alternative segments was <0.05; Fig. 1B). Longitudinal strain increased at all levels within the LV, although a base-to-apex gradient with the highest increases in longitudinal strain occurring in the apex (Fig. 1C). Strain rate was not significantly different in any LV segment after the exercise training period. Given the potential contribution of increased LV end-diastolic volume to the observed changes in LV strain, the correlation between LV strain change in each measured region and overall LV end-diastolic volume change was assessed. These analyses detected no significant correlations.

**Heterogeneity of LV strain change with exercise training: the impact of RV dilation.** After the 90-day study period, RV dilation was observed with increases in RV internal major dimension \((\Delta = 3.4 \pm 1.6\) mm, \(P < 0.001\)) and end-diastolic dimension \((\Delta = 400 \pm 170\) mm\(^2\), \(P < 0.001\)). This was accompanied by enhanced RV systolic function \((\Delta RV\) fractional area change = \(16 \pm 8\%\), \(P < 0.001\); and \(\Delta RV\) peak \(S' = 1.3 \pm 0.6\) cm/s, \(P < 0.001\)). Further examination of the pattern of circumferential LV strain change led to the hypothesis that RV adaptation may be contributing to the observed heterogeneity. Specifically, we hypothesized that changes in RV structure and function were responsible for the isolated reduction in LV circumferential strain observed in the septal and anteroseptal myocardium.

To address this hypothesis, a series of correlation analyses was performed. First, we examined the correlation between change in RV internal diameter, the simplest index of RV size, and change in LV septal circumferential strain. We observed a significant inverse correlation between change in RV internal diameter and a decrease in LV septal circumferential strain \((r^2 = 0.659, P < 0.001\)). A similar, yet stronger correlation was observed between the change in LV end-diastolic area and the change in LV septal circumferential strain \((r^2 = 0.898, P < 0.001;\) Fig. 2A). Finally, we examined the relationships between RV systolic functional parameters and LV septal circumferential strain change. Strong inverse relationships between LV septal circumferential strain change and RV fractional area change \((r^2 = 0.452, P = 0.00)\) and peak RV systolic tissue velocity \((r^2 = 0.697, P < 0.001;\) Fig. 2B) were observed. In contrast, no correlations between LV free wall circumferential strain changes and RV measurement changes were detected. Furthermore, changes in radial and longitudinal LV strain did not correlate with any changes in RV structure or function.

### Table 2. Baseline regional LV radial strain values

<table>
<thead>
<tr>
<th></th>
<th>Anterior</th>
<th>Lateral</th>
<th>Posterior</th>
<th>Inferior</th>
<th>Septal</th>
<th>Antero Septal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strain, %</td>
<td>48.1±9.7</td>
<td>51.5±14.0</td>
<td>51.7±10.7</td>
<td>51.3±11.0</td>
<td>47.4±11.9</td>
<td>50.0±9.2</td>
</tr>
<tr>
<td>Strain rate, s(^{-1})</td>
<td>1.9±0.5</td>
<td>2.1±0.5</td>
<td>2.1±0.6</td>
<td>2.0±0.5</td>
<td>1.8±0.4</td>
<td>1.8±0.4</td>
</tr>
</tbody>
</table>

Values are means ± SD. *\(P < 0.05\) compared to anterior region as reference.

### Table 3. Baseline regional LV circumferential strain values

<table>
<thead>
<tr>
<th></th>
<th>Anterior</th>
<th>Lateral</th>
<th>Posterior</th>
<th>Inferior</th>
<th>Septal</th>
<th>Antero Septal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strain, %</td>
<td>-20.4±4.1</td>
<td>-18.7±5.3</td>
<td>-17.5±5.8</td>
<td>-18.2±5.2</td>
<td>-24.1±3.7*</td>
<td>-23.4±3.5*</td>
</tr>
<tr>
<td>Strain rate, s(^{-1})</td>
<td>-1.5±0.4</td>
<td>-1.4±0.4</td>
<td>-1.3±0.5</td>
<td>-1.3±0.4</td>
<td>-1.5±0.3</td>
<td>-1.7±0.4</td>
</tr>
</tbody>
</table>

Values are means ± SD. *\(P < 0.05\) compared to anterior region as reference.
myocardial contractility and its determinants include preload, afterload, heart rate, and intrinsic cellular contractility (4). The interpretation of serial strain measurements must account for these potential contributing factors. Individuals in the present study had a marked reduction in resting heart rate, suggesting that a true physiological training effect occurred. The relationship between systolic strain and heart rate is biphasic with strain values paralleling increases in heart rate until a threshold at which strain begins to decline with further heart rate increases (45). Since this threshold is far above the heart rate range observed in this study, it is unlikely that the EET-induced decline in heart rate contributed to the observed increases in strain. Increases in ventricular preload, due to increases in either end-diastolic LV pressure or volume, may lead to enhanced systolic function as explained by the Starling principle (43). The E-to-E\(^{-1}\) ratio, a validated index of mean left atrial pressure and thus mean LV end-diastolic pressure, was unchanged after training. We did, however, observe significant increases in LV end-diastolic volume following EET. In absence of an explanatory rise in left atrial pressure, this increase is most likely due to the eccentric LV hypertrophy with an enhancement of diastolic function, which accompanies EET as previously reported (3, 23, 46). EET enhancement of diastolic function with resultant increases in LV end-diastolic volume has the potential to increase LV preload and thus affect LV systolic function. However, an examination of the relationships between the change in LV end-diastolic volume and regional changes in systolic LV strain showed no significant correlations between these parameters. Thus we conclude that neither the pressure nor the volume components of resting LV preload contributed to the observed increase in systolic function (30, 36). Finally, similar baseline and posttraining systolic blood pressures suggest that resting LV afterload was not an important factor in our observations. Given the above rationale that changes in heart rate, preload, and afterload do not appear to explain changes in LV strain, we conclude that EET-induced increases in LV strain reflect the enhancement of intrinsic LV contractility. We do, however, acknowledge that echocardiographic and clinical indexes of cardiac loading conditions may be less precise than invasive techniques, and thus we cannot fully exclude the fact that small but potentially significant changes in LV preload or afterload occurred with EET. As such, further work comparing EET-induced LV strain changes with previously established load-independent indexes of contractility is warranted.

The mechanisms by which EET leads to increased LV contractility remain speculative. It is most likely that an EET-induced systolic enhancement results from a complex cascade initiated by hemodynamic stress and followed by cellular responses. Participation in an EET requires sustained four- to fivefold increases in cardiac output with accompanying increases in systemic systolic blood pressure. A study by Karjalainen et al. (20) showed that LV mass is associated with

### DISCUSSION

We present novel, longitudinal data defining the impact of endurance exercise training (EET) on LV systolic mechanics. In this study, a 90-day period of training led to LV hypertrophy and dilatation with a significant enhancement of systolic function. Although LV ejection fraction was unchanged, more direct indexes of LV contractility including strain and peak systolic tissue velocity increased significantly. Specifically, LV radial strain, longitudinal strain, and peak systolic velocity increased in all measured myocardial segments. In contrast, circumferential strain responded variably with increased values in the LV free wall but decreased values in regions of the LV adjacent to the RV. In aggregate, these data suggest that sustained EET leads to global enhancement of LV systolic function with distinct regional heterogeneity that may result from concomitant RV adaptation.

Several prior studies have examined the impact of exercise training on LV systolic function. A meta-analysis of cross-sectional data showed no difference in LV ejection fraction or LV fractional area change among trained athletes compared with sedentary controls (39). An assessment of LV characteristics among elite distance runners demonstrated a high prevalence of reduced LV ejection fraction but concluded that this was a secondary effect of LV dilation (22). duManoir et al. (9) examined resting LV fractional area change before and after 10 wk of rowing training and demonstrated no significant change. In summary, these works suggest that EET has no significant effect on LV function.

Consistent with the data summarized above, individuals in this study experienced a trend toward reduced LV ejection fraction. Taken in isolation, this finding may be interpreted as further evidence that exercise training either reduces or has no effect on LV systolic function. However, a concomitant consideration of LV ejection fraction and more direct measurements of systolic function suggest that LV ejection fraction has inherent limitations for the serial assessment of systolic function. This is due to the fact that ejection fraction is not able to account for geometric changes and thus lacks sensitivity to track LV function in the presence of significant changes in chamber architecture.

Strain and tissue velocity data from this study show that a significant increase in systolic function does occur despite a static LV ejection fraction among individuals engaging in EET. Recent advances in the ability to measure LV strain have afforded the opportunity to characterize myocardial contractility in a wide range of experimental and clinical settings (6, 10, 11, 25, 35, 37, 44). Normal values and measurement variability data for this imaging modality have recently been published (18, 42). Several recent studies have characterized resting LV strain and the impact of a single exercise session on LV strain in trained athletes (32–34).

Systolic strain, the measure of change in myocardial length during the contractile portion of the cardiac cycle, reflects myocardial contractility and its determinants include preload, afterload, heart rate, and intrinsic cellular contractility (4). The interpretation of serial strain measurements must account for these potential contributing factors. Individuals in the present study had a marked reduction in resting heart rate, suggesting that a true physiological training effect occurred. The relationship between systolic strain and heart rate is biphasic with strain values paralleling increases in heart rate until a threshold at which strain begins to decline with further heart rate increases (45). Since this threshold is far above the heart rate range observed in this study, it is unlikely that the EET-induced decline in heart rate contributed to the observed increases in strain. Increases in ventricular preload, due to increases in either end-diastolic LV pressure or volume, may lead to enhanced systolic function as explained by the Starling principle (43). The E-to-E\(^{-1}\) ratio, a validated index of mean left atrial pressure and thus mean LV end-diastolic pressure, was unchanged after training. We did, however, observe significant increases in LV end-diastolic volume following EET. In absence of an explanatory rise in left atrial pressure, this increase is most likely due to the eccentric LV hypertrophy with an enhancement of diastolic function, which accompanies EET as previously reported (3, 23, 46). EET enhancement of diastolic function with resultant increases in LV end-diastolic volume has the potential to increase LV preload and thus affect LV systolic function. However, an examination of the relationships between the change in LV end-diastolic volume and regional changes in systolic LV strain showed no significant correlations between these parameters. Thus we conclude that neither the pressure nor the volume components of resting LV preload contributed to the observed increase in systolic function (30, 36). Finally, similar baseline and posttraining systolic blood pressures suggest that resting LV afterload was not an important factor in our observations. Given the above rationale that changes in heart rate, preload, and afterload do not appear to explain changes in LV strain, we conclude that EET-induced increases in LV strain reflect the enhancement of intrinsic LV contractility. We do, however, acknowledge that echocardiographic and clinical indexes of cardiac loading conditions may be less precise than invasive techniques, and thus we cannot fully exclude the fact that small but potentially significant changes in LV preload or afterload occurred with EET. As such, further work comparing EET-induced LV strain changes with previously established load-independent indexes of contractility is warranted.

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peak blood pressure during heavy dynamic exercise in trained individuals (20). Although it is logical to conclude that EET-related pressure/volume challenge, which results in LV hypertrophy, also leads to enhanced resting LV systolic function, this speculation deserves further attention. The cellular response to such stimuli is an area of active interest, and the roles of gene polymorphism and growth factor activation in pathological and EET-induced cardiac hypertrophy have been recently shown.

Fig. 1. Regional changes in radial (A), circumferential (B), and longitudinal (C) left ventricular strain following 90-days of endurance exercise training. Values and grayscale reflect strain (in %) change from baseline values. S, septal; AS, anteroseptal; A, anterior; L, lateral; P, posterior; I, inferior; BS, basal septal; MS, midseptal; AL, anterolateral; ML, midlateral; BL, base lateral. *P < 0.05 vs. baseline; †P < 0.001 vs. baseline.
that we performed strain analysis at the mid-LV level where circumferential vector is uncertain but may be due to the fact that the RV appears to impact septal strain only in the RV dilation and enhanced systolic function may reflect a link between septal circumferential strain reduction and both changes in RV size and function. The strong inverse relationship between septal circumferential strain reduction is significantly associated with analyses that demonstrate the magnitude of interventricular myocardium such as those reported in this cohort may there-fore constitute a significant portion of this model. Distinct layers of myocardium, a subepicardial layer with circumferentially oriented fibers and a subendocardial layer with longitudinally coursing fibers, comprise the RV (17). “Cross-over” fibers from both RV layers, predominantly those with circumferential orientation, traverse into the interventricular septum where they constitute a significant portion of this structure (12). Structural or functional changes in the RV myocardium such as those reported in this cohort may therefore impact interventricular septal function. Our correlation analyses demonstrate that the magnitude of interventricular circumferential strain reduction is significantly associated with changes in RV size and function. The strong inverse relationship between septal circumferential strain reduction and both RV dilation and enhanced systolic function may reflect a tethering effect of RV cross-over fibers on the intervening septum. Why the RV appears to impact septal strain only in the circumferential vector is uncertain but may be due to the fact that we performed strain analysis at the mid-LV level where the majority of fibers are oriented along the circumferential plane (5). The importance of this potential ventricular interdependence on exercise capacity and on long-term cardiac function is uncertain.

Data presented here further clarify our understanding of how the LV responds to EET and have several important implications. First, we have demonstrated that LV strain and tissue velocity are more sensitive and discriminate indicators of systolic adaptation to EET than conventional indexes like LV ejection fraction. As such, these direct measures of systolic function should be used in the assessment of the LV response to EET either in conjunction with or in place of conventional indexes. Second, although EET is a well-recognized primary disease prevention strategy and a therapy for a growing number of cardiovascular diseases, the mechanisms behind its effectiveness remain elusive. Detailed characterization of EET-induced myocardial adaptation in healthy individuals is an essential step in understanding how EET prevents and ameliorates intrinsic heart disease. Finally, LV strain appears to be a sensitive and quantifiable index of a physiological training effect. As such, it may be a robust method to assess both the response to training regimens and the degree of deconditioning that occur with training cessation. This potential application may be useful in assessing the cardiac impact of therapeutic exercise regimens and competitive athletic training. Further work to clarify the relationship between cardiac strain and exercise capacity is needed.

Several limitations and areas for future work are noteworthy. We performed a serial assessment of clinical parameters and resting cardiac function and thus cannot comment on how our observations relate to myocardial function during exercise. Further work is being done to examine these relationships. Second, the exercise regimen used in this study consisted exclusively of moderate intensity, long-distance running. The hemodynamic stressors of rowing are complex with both an isometric and isotonic component, and thus care must be taken when extrapolating these data to other forms of EET. Additionally, although EET was the dominant form of exercise training in this study, a the small but significant amount of dedicated strength training may have contributed to our observations. Furthermore, the individuals in this study were athletes with significant prior exercise experience. Although they were enrolled at a time point of relative deconditioning, we cannot exclude the fact either baseline or interval changes reflect exercise experience before the time of enrollment. As such, the relevance of our results to truly sedentary individuals newly engaging in EET deserves further study. We next used correlation analyses to examine the role of the RV in the development of the observed heterogeneous LV strain change pattern. Although the relationships between reduced septal circumferential strain and RV adaptation were impressive, the correlation does not imply causality, and these findings must be considered as strongly hypothesis-generating. Finally, we observed a reduction in resting cardiac output following EET due to reduction in resting heart rate despite modest increases in stroke volume. To our knowledge, this has not been previously reported. We suspect this reduction in cardiac output may reflect more efficient peripheral skeletal muscle substrate utilization and thus the need for less delivery. Although EET was the dominant training modality in this study, the comparatively small but significant amount of strength training performed...
may have contributed to these proposed changes in skeletal muscle function. Confirmation of this finding and study of the proposed link between training-induced skeletal muscle adaptation and resting cardiac output reduction are warranted.

In conclusion we have characterized the impact of EET on LV systolic function. Ninety days of EET lead to concomitant LV dilation and hypertrophy with the enhancement in LV systolic function as reflected by increased strain and tissue velocities. Furthermore, ETT-associated changes in LV systolic mechanics occur with a distinct pattern of heterogeneity that may due to simultaneous adaptation of the RV. Strain imaging appears to be a sensitive and robust indicator of the cardiovascular response to aerobic exercise training with a number of potential future applications.

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REFERENCES


