Morphological and Functional Adaptation of Left and Right Atria Induced by Training in Highly Trained Female Athletes

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Background—Exercise is able to induce atrial remodeling in top-level athletes. However, evidence is mainly limited to men and based on cross-sectional studies. The aim of this prospective, longitudinal study was to investigate whether exercise is able to influence left and right atrial morphology and function also in female athletes.

Methods and Results—Two-dimensional echocardiography was performed before season and after 16 weeks of intensive training in 24 top-level female athletes. Left and right atrial myocardial deformation was assessed by two-dimensional speckle-tracking echocardiography. Left atrial volume index (24.0±3.6 versus 26.7±6.9 mL/m²; P<0.001) and right atrial volume index (15.66±3.09 versus 20.47±4.82 mL/m²; P<0.001) significantly increased after training in female athletes. Left atrial global peak atrial longitudinal strain and peak atrial contraction strain significantly decreased after training in female athletes (43.9±9.5% versus 39.8±6.5%; P<0.05 and 15.5±4.0% versus 13.9±4.0%; P<0.05, respectively). Right atrial peak atrial longitudinal strain and peak atrial contraction strain showed a similar, although non-significant decrease (42.8±10.6% versus 39.3±8.3%; 15.6±5.6% versus 13.1±6.1%, respectively). Neither biventricular E/e’ ratio nor biatrial stiffness changed after training, suggesting that biatrial remodeling occurs in a model of volume rather than pressure overload.

Conclusions—Exercise is able to induce biatrial morphological and functional changes in female athletes. Biatral enlargement, with normal filling pressures and low atrial stiffness, is a typical feature of the heart of female athletes. These findings should be interpreted as physiological adaptations to exercise and should be considered in the differential diagnosis with cardiomyopathies. (Circ Cardiovasc Imaging. 2014;7:222-229.)

Key Words: athlete’s heart syndrome ■ atrial function ■ atrial remodeling ■ echocardiography ■ speckle tracking ■ women

The hemodynamic adaptations associated with exercise conditioning in competitive athletes have been extensively reported and previous studies have demonstrated that they vary according to the type and intensity of exercise.1-4 Cardiac changes consist of interrelated morphological and functional modifications, involving not only the left ventricle (LV) but also the left atrium (LA).5-7 Furthermore, similar hemodynamic and physiological influences affect both the right and left heart of highly trained athletes, determining a symmetrical cardiac enlargement induced by exercise conditioning.8,9

Clinical Perspective on p 229

Although several echocardiographic studies have investigated the effects of training on cardiac geometry and function, most are restricted to male athletes or are not specifically focused on the heart of female athletes.10-14 A previous study has demonstrated that highly trained female athletes exhibit LV dimensional changes as an adaptation to physical training in comparison with sedentary controls.15 However, most of these studies have a cross-sectional design and longitudinal assessment of training-specific cardiac changes has been rarely performed in elite athletes, particularly in women.16-17 Furthermore, only a few studies have investigated the adaptation of LA and right atria (RA) to intensive training;8,16 even if the investigation of atrial adaptation in the athletic population is of particular interest, considering the existing controversies on the relationship between exercise-induced atrial remodeling and the incidence of atrial fibrillation among competitive athletes.18-20 The majority of previous studies focused on pure endurance or resistance sports. Instead, the most popular team-based sport activities, such as volleyball for women or basketball and soccer for men, incorporate a...
combination of endurance (dynamic), strength/resistance (static), and celerity training.21

The aim of this study was to investigate prospectively whether an intensive combined training program can significantly influence LA and RA morphology and function in competitive female volleyball players and whether this adaptation is associated with an improvement or a worsening of atrial function.

Methods

Study Population

Twenty-six female volleyball players, members of 2 elite sports teams, were enrolled in this study. Pretraining echocardiographic examination was collected after 3 months of detraining. Detraining was defined as the partial or complete loss of anatomic, physiological, and performance adaptations induced by training, as a consequence of usual training regime suspension;22 during this period, none of the athletes practiced ≥3 hours/wk of exercise. Post-training examination was performed after 16 weeks of supervised intensive training, consisting of 16 hours/wk, distributed in 8 sessions/wk. Training sessions were comparable between the 2 teams in aerobic–anaerobic components, kind of exercise, and hours of training per week.

Athletes were excluded from the study if they withdrew from the training program ≥10 days for musculoskeletal injuries. For this reason, 2 athletes were excluded, and the final population of this study consisted of 24 athletes.

Twenty-four age- and sex-matched healthy sedentary subjects were enrolled and used as controls. The same design of data collection was performed in a group of 12 male, basketball athletes, playing in a top team and practicing a high-volume training program to provide a reference group of men undergoing similar training regimens. A detailed analysis, including the evaluation of echocardiographic predictors of biatrial remodeling, was not performed in the athletic group of men because of the small sample size of this group and according to the fact that the present study aimed to investigate the training-induced adaptation of both atria primarily in female athletes.

Participants were asymptomatic and showed a negative family history of cardiac disease or sudden cardiac death. None of the athletes had cardiovascular structural or functional abnormalities, hypertension, and type I diabetes mellitus. Participants underwent complete physical examination, ECG, standard echocardiography, and treadmill ECG test. After the rationale and the study protocol were explained, the participants gave informed consent. The investigational protocol was approved by the local ethical committee.

Echocardiographic Measurements

Echocardiographic examination was performed by 1 cardiologist using a high-quality echocardiograph (Vivid 7; GE Healthcare, Milwaukee, WI), equipped with an M4S 1.5-MHz to 4.0-MHz transducer, and a 1-lead ECG was continuously displayed. Subjects were studied in the steep left-lateral decubitus position. Offline data analysis, from 3 stored cycles, was performed by an experienced reader, blinded to the study time point, using a dedicated software (EchoPac; GE Healthcare). Heart rate (HR) was measured from the superimposed ECG obtained during the echocardiographic examination.

Size Quantification of Left and Right Heart Chamber

LA and RA dimensions were measured at the end of LV systole, when these chambers get to their maximum size during cardiac cycle, as recommended.23,24 RA and LA area and volume were calculated by biplane method of disks (modified Simpson rule) in the apical 4-chamber view for the former and both 4- and 2-chamber views for the latter, obtaining an average value. LA size was assessed excluding the pulmonary veins and LA appendage from LA tracing. The plane of mitral annulus was used as inferior border.23 A mild enlargement of LA was defined as LA volume ≥29 mL/m², a moderate as ≥34 mL/m², and a severe as ≥40 mL/m².21 RA dimension was measured excluding the area between the leaflets and the annulus, after the RA endocardium, excluding the inferior and superior vena cava and RA appendage.24 RA enlargement was defined as an RA end-systolic area ≥18 cm².23 Biatrial volumes were indexed to body surface area (BSA), calculated using the Dubois and Dubois formula.22 Right ventricular (RV) end-diastolic chamber size was assessed using the measurement of basal and midcavity diameters from the apical 4-chamber view at end diastole.25

To identify potential predictors of atrial remodeling associated with training, LV volumes, LV mass (LVM), and LVM index were obtained as recommended.21

Standard and Tissue Doppler Imaging

Pulsed-wave and tissue Doppler imaging analyses were performed to determine LV and RV diastolic function, according to the current recommendations (Data Supplement).24,26 The mitral and tricuspid E/e’ ratio was calculated and considered as a reliable index of LA and RA filling pressures.24,26–28

Speckle-Tracking Echocardiography of RA and LA

Two-dimensional (2D) speckle-tracking echocardiography was obtained and recorded using conventional 2D gray-scale echocardiography during breath holding with stable electrocardiographic tracing, as described previously for LA and RA.9,29–30 Offline analysis was performed using a commercially available semiautomated 2D strain software (EchoPac PC, version 112, rev. 1.1; GE Healthcare), obtaining peak atrial longitudinal strain (PALS) and peak atrial contraction strain (PACS), measures of atrial reservoir and atrial active conduit, respectively.

Time-to-peak longitudinal strain and time-to-peak contraction strain were also obtained for both the LA and RA and indexed to relative risk interval (ms). The E/e’ ratio was used in conjunction with PALS to derive a noninvasive dimensionless parameter of LA and RA stiffness, as previously reported (Data Supplement).9,31,32

Statistical Analysis

Normal distribution of all continuous variables was examined using the Shapiro–Wilk test, and data are presented as mean±SD or median and interquartile range, as appropriate. Categorical variables are expressed as percentages. The unpaired t test and the Mann–Whitney U test were used according to data distribution to assess between-groups significance. The paired t test and the Wilcoxon matched-pair test were used to assess the within-subjects significance of pretraining and post-training measurements, as appropriate for data distribution. A P value ≤0.05 was considered significant. Correlation analysis was performed to find association between continuous variables using the Spearman and Pearson methods, as appropriate for data distribution. Univariate linear regression analysis was performed to identify predictors of atrial remodeling. Statistics were performed using SPSS version 14.0 software for Windows (Statistical Package for the Social Sciences Inc, Chicago, IL).

Results

The demographic characteristics of female athletes and female controls are reported in Table 1. The mean age of the female athletic population was 24.9±4.1 years. As expected, female athletes significantly increased their weight and BSA (P<0.05), whereas the resting HR significantly decreased (P<0.05) after training. The mean age of the reference group of male athletes was 26.0±4.2 years, BSA was 2.3±0.1 m², and resting HR was 54.2±4.8 bpm. During the study period, none of the male and female athletes experienced palpitations or symptoms, requiring further investigations.

LA Adaptation

Differences in left heart measurements between pretraining data collected in female athletes and data measured in controls and between pretraining and post-training data obtained in female
athletes are reported in Table 2. Although E/e' ratio did not differ between pretraining measurements obtained in female athletes and data collected in controls, female athletes had a higher pretraining LA volume index when compared with sedentary subjects (P=0.008). Furthermore, female athletes showed differences in pretraining LV volumes and pretraining LA strain, even if the PALS/PACS ratio was comparable between female athletes and controls. Pretraining LV end-diastolic volume (LVEDV) index was higher in female athletes when compared with that in controls (52.1±8.7 versus 45.3±6.9 mL/m², respectively; P=0.012); conversely, pretraining LVM index was comparable between female athletes and controls (66.2±11.3 versus 61.0±15.9 g/m², respectively; P=0.80).

LA morphology and function did change after 16 weeks of intensive training in female athletes: LA volume and LA volume index increased significantly when compared with pretraining measurements obtained in female athletes and data collected in controls on RA morphology and function (Figure 1). Before training, 95% of female athletes showed a normal LA volume index and 5% a mild LA enlargement. After training, 45% of female athletes showed a LA volume index ≥29 mL/m², with 30% presenting a mild LA enlargement and 15% a moderate enlargement. None of the female athletes experienced a severe LA enlargement during the study.

Although LA size increased in female athletes, E/e' ratio did not vary during the study (P=0.96). Although s' peak did not change (10.6±1.1 versus 10.6±1.6 cm/s; P=0.47), e' peak increased (16.4±1.8 versus 17.6±2.4 cm/s; P=0.025) and a' decreased (8.6±1.4 versus 7.7±1.7 cm/s; P=0.015) after training in female athletes. The morphological remodeling was accompanied in female athletes by a significant reduction in LA global PALS and LA global PACS (P<0.05; Figure 1). Neither the PALS/PACS ratio nor LA stiffness index significantly varied with training in women.

In competitive male athletes, LA volume (65.9±21.2 versus 73.8±30.8 mL; P=0.17) and LA volume index (28.3±7.7 versus 31.4±11.7 mL/m²; P=0.20) tended to increase during the observation period, although no statistically significant differences were found between pretraining and post-training data. E/e' ratio (5.4±1.1 versus 4.8±0.4; P=0.068) and LA global PACS (36.2±4.0% versus 37.5±4.1%; P=0.51) increased significantly after training (11.5±2.2% versus 12.2±2.1%; P=0.42), and PALS/PACS ratio (3.2±0.6 versus 3.1±0.5; P=0.72) did not vary significantly, whereas LVM index increased significantly after training (100.0±15.7 versus 157.3±26.8 g/m²; P<0.001).

RA Adaptation

As reported in Table 3, no significant differences were observed between pretraining data collected in female athletes and data measured in controls on RA morphology and function. Differences in pretraining and post-training data were assessed by paired t-tests. "Pretraining" refers to the mean of the data collected in female athletes and sedentary controls at baseline. "Post-Training" refers to the mean of the data collected in female athletes and sedentary controls, respectively, after 16 weeks of training.

Table 2. Differences in Left Heart Measurements Between Female Athletes and Female Sedentary Controls and Between Pretraining and Post-Training Data Collected in Female Competitive Athletes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls (n=24)</th>
<th>Female Competitive Athletes (n=24)</th>
<th>Pretraining</th>
<th>Post-Training</th>
<th>P Value Athletes vs Controls</th>
<th>P Value Pretraining vs Post-Training</th>
<th>Mean Change (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA area, cm²</td>
<td>14.2±1.9</td>
<td>16.4±1.6</td>
<td>17.3±2.6</td>
<td>0.000</td>
<td>0.010</td>
<td>0.8 (−0.1, 1.7)</td>
<td></td>
</tr>
<tr>
<td>LA volume, mL</td>
<td>34.3±8.8</td>
<td>46.0±7.2</td>
<td>52.9±12.1</td>
<td>0.000</td>
<td>0.001</td>
<td>7.0 (3.6, 10.4)</td>
<td></td>
</tr>
<tr>
<td>LA volume index, mL/m²</td>
<td>20.5±4.9</td>
<td>24.6±3.0</td>
<td>28.1±5.5</td>
<td>0.003</td>
<td>0.001</td>
<td>3.5 (1.8, 5.2)</td>
<td></td>
</tr>
<tr>
<td>E/A ratio</td>
<td>1.7±0.4</td>
<td>1.8±0.4</td>
<td>1.8±0.3</td>
<td>0.068</td>
<td>0.33</td>
<td>0.1 (−0.1, 0.2)</td>
<td></td>
</tr>
<tr>
<td>e'/a' ratio</td>
<td>2.2±0.4</td>
<td>2.0±0.4</td>
<td>2.4±0.6</td>
<td>0.063</td>
<td>0.001</td>
<td>0.4 (0.2, 0.7)</td>
<td></td>
</tr>
<tr>
<td>E/e' ratio</td>
<td>5.0±0.8</td>
<td>5.0±1.0</td>
<td>5.0±0.9</td>
<td>0.99</td>
<td>0.96</td>
<td>−0.01 (−0.5, 0.5)</td>
<td></td>
</tr>
<tr>
<td>LA global PALS, %</td>
<td>39.4±10.0</td>
<td>43.9±9.5</td>
<td>39.8±6.5</td>
<td>0.18</td>
<td>0.037</td>
<td>−4.2 (−8.3, −0.1)</td>
<td></td>
</tr>
<tr>
<td>LA global PACS, %</td>
<td>13.9±3.0</td>
<td>15.5±4.0</td>
<td>13.9±4.0</td>
<td>0.19</td>
<td>0.033</td>
<td>−1.8 (−3.4, −0.2)</td>
<td></td>
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<tr>
<td>LA stiffness index</td>
<td>0.15±0.05</td>
<td>0.12±0.04</td>
<td>0.13±0.04</td>
<td>0.031</td>
<td>0.306</td>
<td>0.01 (0.2, 0.7)</td>
<td></td>
</tr>
<tr>
<td>LA PALS/PACS ratio</td>
<td>3.0±1.3</td>
<td>2.9±0.4</td>
<td>3.0±0.7</td>
<td>0.56</td>
<td>0.23</td>
<td>0.2 (−0.1, 0.4)</td>
<td></td>
</tr>
<tr>
<td>LA TPLS, ms</td>
<td>351.4±72.5</td>
<td>374.1±40.9</td>
<td>390.1±34.3</td>
<td>0.23</td>
<td>0.13</td>
<td>12.1 (−8.3, 32.4)</td>
<td></td>
</tr>
<tr>
<td>LA TPCS, ms</td>
<td>588.0±159.1</td>
<td>755.8±160.9</td>
<td>809.5±164.2</td>
<td>0.002</td>
<td>0.055</td>
<td>54.4 (−3.7, 112.6)</td>
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<tr>
<td>LA TPLS/RR ratio</td>
<td>0.45±0.11</td>
<td>0.41±0.05</td>
<td>0.41±0.05</td>
<td>0.25</td>
<td>0.81</td>
<td>−0.01 (−0.04, 0.02)</td>
<td></td>
</tr>
<tr>
<td>LA TPCS/RR ratio</td>
<td>0.75±0.19</td>
<td>0.82±0.06</td>
<td>0.84±0.07</td>
<td>0.071</td>
<td>0.42</td>
<td>−0.01 (−0.03, 0.06)</td>
<td></td>
</tr>
</tbody>
</table>

CI indicates confidence interval; LA, left atrial; PACS, peak atrial contraction strain; PALS, peak atrial longitudinal strain; RR, relative risk; TPCS, time-to-peak contraction strain; and TPLS, time-to-peak longitudinal strain.
function, with the exception of a higher RA PALS value in the control group. Conversely, both pretraining RV midcavity and basal end-diastolic diameter (EDD) were higher in female athletes when compared with those in sedentary subjects (28.8±4.1 versus 22.5±2.2 mm; P<0.001; 36.0±4.5 versus 30.1±3.2 mm; P<0.005, respectively).

After 16 weeks of intensive training, a significant increase in RA area, RA volume, and RA volume index was observed in female athletes (P<0.001; Table 3; Figure 2). Although none of the athletic women had an RA enlargement before training, 10% of female athletes exhibited a mild RA enlargement after 16 weeks of training. None of the athletes experienced a moderate or severe RA enlargement after training.

Although a trend toward decrease was observed after 16 weeks of training, no significant differences were found between pretraining and post-training measurements in RA PALS and RA PACS in female athletes (Table 3; Figure 2). As was observed for the LA, neither RA PALS/PACS nor RA stiffness index varied significantly after training. % peak (13.6±1.9 versus 13.6±2.1 cm/s; P=0.10), $e$ peak (15.6±3.2 versus 15.9±3.0 cm/s; $P=0.86$), and $a$ peak (10.1±2.2 versus 10.6±2.8 cm/s; $P=0.66$) did not change with training in female athletes.

In competitive male athletes, RA area (19.7±3.9 versus 21.1±3.3 cm²; $P<0.05$), RA volume index (24.9±8.0 versus 27.7±7.2 mL/m²; $P<0.05$), and RV basal EDD (39.7±6.3 mm; $P<0.05$) increased significantly after training. Conversely, neither RA PALS (39.8±8.0% versus 40.9±4.4%; $P=0.73$) nor RA PACS (12.1±2.5% versus 12.7±2.7%; $P=0.64$) changed in male athletes, with PALS/PACS ratio remaining stable after training (3.3±0.7 versus 3.3±0.8; $P=0.99$).

See Table I in the Data Supplement for biventricular changes in morphology and myocardial deformation observed in female athletes before and after training.

**Predictors of Biatrial Volumes in Female Athletes**

**Left Atrium**

Univariate predictors of pretraining LA volume included BSA ($\beta=0.75$; adjusted $R^2=0.54$; $P<0.001$), LV EDV ($\beta=0.57$; adjusted $R^2=0.28$; $P=0.009$), RV midcavity EDD ($\beta=0.53$; adjusted $R^2=0.24$; $P=0.015$), resting HR ($\beta=0.53$; adjusted $R^2=0.24$; $P=0.017$), inferior vena cava diameter ($\beta=0.51$; adjusted $R^2=0.21$; $P=0.26$), and RR interval ($\beta=0.47$; adjusted $R^2=0.18$; $P=0.036$). Univariate predictors of post-training LA volume included LV EDV ($\beta=0.66$; adjusted $R^2=0.41$; $P=0.001$), BSA ($\beta=0.62$; adjusted $R^2=0.35$; $P=0.004$), LV systolic volume ($\beta=0.50$; adjusted $R^2=0.21$; $P=0.025$), and RR interval ($\beta=0.44$; adjusted $R^2=0.15$; $P=0.048$).

Neither E/e' ratio nor LA stiffness were identified as predictors of pretraining and post-training LA volumes. Furthermore, no significant correlations were observed among...
ΔLA volume (post-training versus pretraining) and the other echocardiographic parameters expressed as Δ.

**Right Atrium**

Univariate predictors of pretraining RA volume included transtricuspid E wave (β=-0.61; adjusted $R^2=0.33$; $P=0.015$), RV midcavity EDD (β=0.60; adjusted $R^2=0.33$; $P=0.005$), and RV basal EDD (β=0.57; adjusted $R^2=0.29$; $P=0.008$). Univariate predictors of post-training RA volume included LVM (β=0.51; adjusted $R^2=0.26$; $P=0.027$) and RV basal EDD (β=0.49; adjusted $R^2=0.24$; $P=0.035$).

Neither $E/e'$ ratio nor RA stiffness were identified as predictors of pretraining or post-training RA volumes. No significant correlations were observed between RA strains and resting HR and between ΔRA volume (post-training versus pretraining) and the other echocardiographic parameters, expressed as Δ.

We additionally performed correlations between LV and RV dimensional parameters. A significant correlation was found between baseline RV basal EDD and LVEDV ($R=0.67$; $P<0.005$) and LV stroke volume index ($R=0.54$; $P<0.05$), whereas baseline RV midcavity EDD correlated with LVM ($R=0.49$; $P<0.05$) and with LVEDV ($R=0.46$; $P<0.05$).

**Discussion**

**Exercise Training and Biatral Morphological Adaptation**

Previous cross-sectional echocardiographic studies have observed that women demonstrate a significant cardiovascular remodeling in response to physical training. Although cross-sectional studies provide useful information to differentiate the echocardiographic features of athletes and nonathletes, they cannot be taken as definitive proof of a cause-effect relationship between training and an adaptive cardiac remodeling. Longitudinal training studies with repeated measures within individuals may, at least in part, overcome these drawbacks. Nonetheless, even if prospective studies have analyzed the longitudinal adaptations of the LV to exercise conditioning, few longitudinal investigations have been conducted on LA dimensional and functional changes occurring during the training program, and no prospective, longitudinal data on RA changes are available, particularly in female athletes. The present study provides longitudinal data demonstrating significant training-induced changes in biatrial size after a 16-week sport-specific training program in competitive female volleyball players. We observed an exercise-induced biatrial remodeling with a significant increase in atrial size for both the LA and RA, which correlated with biventricular dimensions. Interestingly, although a relevant percentage of the study population experienced a mild atrial enlargement, only a few athletes exhibited a moderate LA enlargement, and none of the participants experienced a severe biatrial dilatation.

**Exercise Training and Biatral Functional Adaptation**

In this study, a 16-week intensive training program was able to induce in female athletes morphological as well as functional adaptations on both left and right heart. Two-dimensional speckle-tracking echocardiography allowed us to find that both left and right PALS and PACS decreased after training. A peculiar pattern of myocardial deformation dynamics has been observed in athletes in comparison with that in sedentary subjects with reduction of LA and RA atrial strain values; furthermore, this typical pattern has been confirmed in a longitudinal study investigating the effects of an 8-month training program on LA, demonstrating that an exercise-induced reduction of LA strain values can be observed in competitive adolescent soccer players. In this study, we confirmed these previous findings in female athletes as well. Even if a reduction of PALS and PACS values can be observed in comparison with

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls (n=24)</th>
<th>Pretraining</th>
<th>Post-Training</th>
<th>$P$ Value Athletes vs Controls</th>
<th>$P$ Value Pretraining vs Post-Training</th>
<th>Mean Change (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA area, cm$^2$</td>
<td>12.8±1.6</td>
<td>12.4±1.5</td>
<td>14.5±2.0</td>
<td>0.35</td>
<td>0.001</td>
<td>2.8 (1.8, 3.8)</td>
</tr>
<tr>
<td>RA volume, mL</td>
<td>31.5±6.2</td>
<td>29.0±5.8</td>
<td>38.5±9.4</td>
<td>0.18</td>
<td>0.001</td>
<td>10.4 (5.1, 15.8)</td>
</tr>
<tr>
<td>RA volume index, mL/m$^2$</td>
<td>18.4±4.4</td>
<td>15.6±3.1</td>
<td>20.6±4.9</td>
<td>0.05</td>
<td>0.001</td>
<td>5.4 (2.6, 8.3)</td>
</tr>
<tr>
<td>$E/A$ ratio</td>
<td>1.9±0.4</td>
<td>1.7±0.3</td>
<td>2.1±0.7</td>
<td>0.10</td>
<td>0.20</td>
<td>0.3 (−0.1, 0.8)</td>
</tr>
<tr>
<td>$E'/e'$ ratio</td>
<td>4.0±0.8</td>
<td>4.0±1.4</td>
<td>3.7±1.0</td>
<td>0.81</td>
<td>0.39</td>
<td>−0.01 (−0.74, 0.71)</td>
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<tr>
<td>RA PALS, %</td>
<td>50.9±10.7</td>
<td>42.8±10.6</td>
<td>39.3±8.3</td>
<td>0.022</td>
<td>0.22</td>
<td>−2.5 (−9.2, 4.2)</td>
</tr>
<tr>
<td>RA PACS, %</td>
<td>17.1±5.4</td>
<td>15.6±6.6</td>
<td>13.1±6.1</td>
<td>0.41</td>
<td>0.083</td>
<td>−2.8 (−7.1, 1.6)</td>
</tr>
<tr>
<td>RA stiffness index</td>
<td>0.09±0.02</td>
<td>0.09±0.04</td>
<td>0.10±0.03</td>
<td>0.60</td>
<td>0.81</td>
<td>−0.01 (−0.04, 0.03)</td>
</tr>
<tr>
<td>RA PALS/PACS ratio</td>
<td>3.2±1.0</td>
<td>3.0±0.9</td>
<td>3.9±3.2</td>
<td>0.55</td>
<td>0.16</td>
<td>0.8 (−0.3, 1.9)</td>
</tr>
<tr>
<td>RA TPSL, ms</td>
<td>367.1±37.8</td>
<td>363.7±53.0</td>
<td>386.7±63.4</td>
<td>0.82</td>
<td>0.24</td>
<td>8.4 (−31.2, 48.2)</td>
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<tr>
<td>RA TPS, ms</td>
<td>638.1±84.6</td>
<td>752.9±190.2</td>
<td>784.6±199.9</td>
<td>0.024</td>
<td>0.52</td>
<td>14.5 (−67.9, 97.0)</td>
</tr>
<tr>
<td>RA TPSL/RR ratio</td>
<td>0.46±0.06</td>
<td>0.40±0.07</td>
<td>0.41±0.10</td>
<td>0.010</td>
<td>0.76</td>
<td>−0.01 (−0.06, 0.03)</td>
</tr>
<tr>
<td>RA TPS/R ratio</td>
<td>0.81±0.08</td>
<td>0.82±0.12</td>
<td>0.81±0.16</td>
<td>0.84</td>
<td>0.96</td>
<td>−0.02 (−0.09, 0.05)</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; PACS, peak atrial contraction strain; PALS, peak atrial longitudinal strain; RA, right atrial; RR, relative risk; TPCS, time-to-peak contraction strain; and TPLS, time-to-peak longitudinal strain.
control subjects, none of the athletes showed pathological values of LA/RA myocardial deformation. Indeed, the observed value of LA PALS was significantly higher when compared with data reported in patients with early hypertension or pulmonary hypertension.35,36 Even if a direct comparison between athletes and patients with paroxysmal atrial fibrillation has not been performed in this study, recent research by Yoon et al37 reported that global LA strain in subjects having paroxysmal atrial fibrillation was 27.3±7.2%, with LA stiffness being 0.41±0.24. Conversely, athletes in this study exhibit a clearly high value of global LA strain and a markedly lower value of LA stiffness, even lower when compared with controls by Yoon et al,37 being 0.29±0.10. Furthermore, even if biatrial size increased after training, LA and RA stiffness did not vary, and the PALS/PACS ratio remained constant after 16 weeks of intensive training because of a balanced reduction of both PALS and PACS. Of note, a slight improvement of left and right diastolic function has been observed during the study, particularly at tissue Doppler imaging analysis, with LV filling pressures, estimated by E/e' ratio, being stable and within the range of normality. Taken together, these findings indicate that the reduction of atrial myocardial deformation should be regarded as an adaptive phenomenon physiologically induced by training, and the correlation between resting HR and time-to-peak longitudinal and contraction atrial strain seems to suggest a resting atrial functional reserve, indicative of an economized heart function at rest, which likely can be recruited during the effort, similarly to the training-related modulation of the HR.

Heart of Athletes and Training Stimulus: Female Versus Male

Uncertainties persist about the ability of the female heart to adapt in response to exercise conditioning. Rubal et al38 demonstrated that sedentary college women exhibit significant changes in LV wall thickness, LVM, and LV end-diastolic dimension after a 10-week endurance conditioning period, whereas Haykowsky et al39 reported that 10 weeks of combined endurance/strength training are an insufficient stimulus to elicit alterations in active but not in well-trained female volunteers. In a study primarily investigating biventricular adaptation induced by a 90-day training program in university athletes, Baggish et al17 documented a significant increase in LA and RA dimensions in a mixed population of male and female rowers. In this study, we demonstrated that changes in biatrial size can be observed after 16 weeks of intensive training in highly trained female athletes with previous training experience, suggesting that atrial remodeling can be observed not only in men but also in women practicing sports at a high level. A recent study by Mosén and Steding-Ehrenborg,40 aiming to compare atrial volumes obtained in male and female athletes directly, reported that atrial adjustment to training is more modest in women. Our study aimed to investigate the training-induced biatrial remodeling in women primarily, and a direct
comparison between male and female athletes was beyond the scope of the present study. However, we observed in a longitudinal study a significant exercise-induced morphological remodeling of both RA and LA in female athletes, and, albeit not significantly different in men, the variation in LA and RA volumes after training was similar between female and male athletes, being greater for RA volume in women (LA volume, Δ=8 mL in men and Δ=7 mL in women; RA volume, Δ=7 mL in men and Δ=10 mL in women). Although sex differences in the cardiac adaptation between male and female athletes have been primarily attributed to the effect of androgenic hormones on cardiac protein synthesis, other determinants might play central roles in sex differences in cardiac adaptation, such as muscle mass, training volume, and blood volume expansion, all variables conditioned by sex as well as by the discipline the athletes were engaged in. Whether these determinants might influence the in-seasonal cardiovascular changes more than sex remains a challenge for future investigations.

Global Exercise-Induced Cardiac Remodeling

In this study, the training-induced increase in LA and RA dimensions parallels LV and RV enlargement, respectively, as demonstrated by the significant correlation among LA, LVEDV, and LV stroke volume and among RA, RV basal, and midcavity diameters, confirming the interactive and dynamic relationship between atria and ventricles. Furthermore, a correlation was found among LV and RV dimensional parameters, supporting the concept that cardiac remodeling in athletes is a balanced, biventricular phenomenon, with an interdependence between right and LV cavities, which is well known to be increased particularly in the case of volume overload.

Even if exercise conditioning is able to induce an adaptation of all cardiac chambers, the increase in biventricular volumes occurred in our study population with a greater extent when compared with the increase in biventricular dimensions, with a 15.0% and 32.7% post-training increase in LA and RA size, respectively, and a 7.5% and 13.5% increase in LV and RV dimensions, respectively. These findings should be explained by the anatomic features of the ventricles and by the thin wall structure of the atria, able to respond to a greater extent to the hemodynamic adaptations induced by exercise conditioning.

Because RV filling is primarily affected by the increased venous return, we demonstrated a significant training-induced increase of the inferior vena cava diameter, supporting the hypothesis that in female athletes volleyball training induces a myocardial remodeling in the form of exercise-induced hemodynamic overload, which likely plays a relevant role in the mechanistic cascade for RV adaptation.

Limitations

The small sample size is the main limitation of this study. However, we studied a selected cohort of athletes, and pooling data from additional teams to extend the sample size could result in uncontrollable differences across subjects in factors such as athletic skill, coaching practices, or competitive setting, and it may well have presented greater threats to validity. Furthermore, the population of men athletes is composed of basketball players, and although metabolic and cardiovascular similarities exist between volleyball and basketball, this represents a limitation of the study. Finally, even if a good reproducibility has been demonstrated for echocardiographic measurements of the right heart, a RV-focused apical 4-chamber view has to show the maximum diameter of the RV without foreshortening and making sure that the crux and apex of the heart are viewed, as recommended. However, repeated-measures studies stress the difficulty to image the RV in the same angle in the same subject.

Conclusions

In female athletes, a 16-week intensive training program is able to induce a physiological adaptation of the heart, which is associated with a regular and harmonious remodeling of the 4 chambers. Biatrial enlargement, with normal filling pressures, low biatrial stiffness, and normal biatrial longitudinal strains, is a typical feature of the heart of female athletes. These findings may contribute to the differential diagnosis with cardiomyopathies and should be interpreted as a physiological adaptation to intensive training.

Acknowledgments

We thank Chairmen of Santa Croce Volleyball Club, San Mariano Volleyball Club, and Mens Sana Basket Siena, all members of medical and coaching staff, athletes, and managers for their support in the study.

Disclosures

None.

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7. D’Ascenzi F, Cameli M, Zacà V, Lisi M, Santoro A, Causarano A, Mondillo S. Supernormal diastolic function and role of left atrial myocardi- 
Although several echocardiographic studies have investigated the effects of training on cardiac geometry and function, most are restricted to male athletes or are not specifically focused on the heart of female athletes. Particularly, the investigation of left atrial morphological and functional adaptation to exercise conditioning is crucial, considering the existing controversies on the relationship between training-induced atrial remodeling and the incidence of atrial fibrillation among competitive athletes. In this prospective and longitudinal study, we investigated the adaptation of both the right and left atrium in competitive female athletes, demonstrating that 16 weeks of intensive training are able to induce significant biatrial morphological changes, with greater biatrial volumes after training when compared with pretraining data. Conversely, intracavity filling pressures were normal in competitive athletes and did not vary after training, supporting the hypothesis that the increase in biatrial size occurs in athletes in a model of volume rather than pressure overload. Furthermore, a regular and harmonious remodeling of the 4 cardiac chambers was demonstrated, with the biatrial adaptation that parallels the balanced, biventricular remodeling. Thus, biatrial enlargement, with normal filling pressures, low biatrial stiffness, and normal biatrial longitudinal strains, is a typical feature of the heart of female athletes. These findings may contribute to the differential diagnosis of cardiomyopathies and should be interpreted as a physiological adaptation to intensive training.
Morphological and Functional Adaptation of Left and Right Atria Induced by Training in Highly Trained Female Athletes

Flavio D'Ascenzi, Antonio Pelliccia, Benedetta Maria Natali, Valerio Zacà, Matteo Cameli, Federico Alvino, Angela Malandrino, Paola Palmitesta, Alessandro Zorzi, Domenico Corrado, Marco Bonifazi and Sergio Mondillo

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SUPPLEMENTAL MATERIAL

SUPPLEMENTAL METHODS

Standard and Tissue Doppler Imaging

PW Doppler analysis was performed in the apical 4-chamber view to obtain mitral and tricuspid inflow velocities to assess LV and RV inflow. For LV a 1-mm to 3-mm sample volume was placed between mitral leaflet tips during diastole, as recommended (25). For the RV the sample volume was placed at the tips of the tricuspid leaflets (23). Care was taken to measure at held end-expiration taking an average of 3 consecutive beats. Early filling (E-wave), late diastolic filling (A-wave) velocities and their ratio E/A were obtained for the LV and the RV.

To perform TDI analysis, an apical 4-chamber view was used. For the left ventricle, the sample volume was positioned at or 1 cm within the septal and the lateral insertion sites of mitral leaflets to cover the longitudinal excursion of the mitral annulus in both systole and diastole (25). For the RV, to perform TDI analysis of the right side, an apical 4-chamber view was used with a tissue Doppler mode region of interest highlighting the RV free wall (23). The pulsed Doppler sample volume was placed in either the tricuspid annulus or the middle of the basal segment of the RV free wall. Peak systolic (s’), early diastolic (e’), and late diastolic (a’) annular velocities were obtained. s’ was considered as a relatively load-independent index of LV longitudinal systolic function and basal RV longitudinal function. e’ and the derived e’/a’ ratio were used as load-independent markers of ventricular diastolic relaxation.

Speckle tracking echocardiography
Care was taken to obtain true apical images using standard anatomic landmarks in each view and not foreshorten the left and right atria, allowing a more reliable delineation of the atrial endocardial border. The optimal frame rate for the 2-dimensional image acquisition was set between 60 and 80 frames per second. Off-line analysis was performed by one experienced and independent operator who was not directly involved in the image acquisition and was blinded to the study period, using a commercially available semi-automated 2-dimensional strain software (EchoPac, GE, USA).

Endocardial surfaces were manually traced in both 4- and 2-chamber views for the left atrium and only in 4-chamber view for the right atrium, by a point-and-click approach in order to create a region of interest (ROI) with the automatic adjustment of the system. All measurements were taken from the onset of QRS complex, as previously described for left and right atria (9,28,29). After a manual adjustment of the tracked area, the software divides the ROI into 6 segments, and the resulting tracking quality for each segment was automatically scored as either acceptable or non-acceptable, with the possibility of further manual correction. Segments with no adequate image quality have been excluded and the final value was obtained with the remaining atrial sections.

PALS and PACS were obtained for both LA and RA, calculating the average of all segments and the average values obtained from 4-chamber and 2-chamber view for the left atrium (LA global PALS and global PACS). LA and RA PALS were used to estimate LA and RA reservoir function, while LA and RA PACS were used to measure the phase of LA and RA active conduit in late diastole during atrial contraction.

Inter-observer and intra-observer variability was assessed in previous studies by our research group for both left and right atria (7,29). In this study, the software was able to correctly track 97%
of the segments analyzed for the left atrium and in the 92% of the segments for the right atrium, with the basal lateral segment being the more complicated segment to trace.

LV and RV longitudinal strain were determined as recommended (29). For the right ventricle, both free wall and septal longitudinal strain were determined.
**SUPPLEMENTAL TABLE**

**Supplemental table 1.** Changes in biventricular dimensions and longitudinal deformation observed pre-training and after 16 weeks of intensive supervised training program in competitive female athletes.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-training</th>
<th>Post-training</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV mass index, g/m²</td>
<td>65.9 ± 11.2</td>
<td>74.7 ± 14.4</td>
<td>.004</td>
</tr>
<tr>
<td>LV EDV index, mL/m²</td>
<td>52.1 ± 8.7</td>
<td>55.7 ± 9.5</td>
<td>.14</td>
</tr>
<tr>
<td>LV mass/LV EDV ratio</td>
<td>1.32 ± 0.33</td>
<td>1.36 ± 0.39</td>
<td>.53</td>
</tr>
<tr>
<td>Global LV longitudinal strain, %</td>
<td>-19.7 ± 1.8</td>
<td>-20.5 ± 2.1</td>
<td>.25</td>
</tr>
<tr>
<td>RV EDD basal, mm</td>
<td>36.0 ± 4.6</td>
<td>38.2 ± 4.4</td>
<td>.038</td>
</tr>
<tr>
<td>RV EDD mid cavity, mm</td>
<td>28.7 ± 4.2</td>
<td>32.6 ± 3.7</td>
<td>.001</td>
</tr>
<tr>
<td>RV free wall longitudinal strain, %</td>
<td>-24.2 ± 6.3</td>
<td>-27.9 ± 5.8</td>
<td>.026</td>
</tr>
<tr>
<td>Global RV longitudinal strain (including interventricular septum), %</td>
<td>-22.0 ± 4.0</td>
<td>-23.9 ± 4.1</td>
<td>.079</td>
</tr>
<tr>
<td>IVC diameter, mm</td>
<td>17.0 ± 3.3</td>
<td>20.8 ± 4.6</td>
<td>.004</td>
</tr>
</tbody>
</table>

LV, left ventricular; EDV, end-diastolic volume; RV, right ventricular; EDD, end-diastolic diameter; IVC, inferior vena cava.