Remodeling of Left Ventricular Hypertrophy in Elite Athletes After Long-Term Deconditioning

Antonio Pelliccia, MD; Barry J. Maron, MD; Rosanna De Luca, MD; Fernando M. Di Paolo, MD; Antonio Spataro, MD; Franco Culasso, PhD

Background—The clinical significance and long-term consequences of left ventricular (LV) hypertrophy associated with intensive athletic conditioning remain unresolved.

Methods and Results—We prospectively evaluated 40 elite male athletes who had shown marked LV cavity enlargement of ≥60 mm, wall thickness of ≥13 mm, or both in a longitudinal fashion with serial echocardiograms, initially at peak training (age 24±4 years) and subsequently after a long-term deconditioning period (1 to 13 years; mean, 5.6±3.8). After detraining, LV cavity dimension decreased by 7% (61.2±2.9 to 57.2±3.1 mm; P<0.001), maximum wall thickness by 15% (12.0±1.3 to 10.1±0.8 mm; P<0.001), and mass normalized to height by 28% (194±25 to 140±21 g/m; P<0.001). However, individual subject analysis showed persistent substantial cavity dilatation (≥60 mm) in 9 athletes (22%); in contrast, wall thickness returned to normal in each athlete. Multiple regression analysis demonstrated that approximately 50% of the incomplete reduction in cavity dimension was explained by increased body weight and recreational physical activity performed during the follow-up period. No athlete had developed cardiac symptoms, impaired exercise performance, or evidence of LV dysfunction.

Conclusions—LV remodeling was evident after long-term detraining, with significant reduction in cavity size and normalization of wall thickness. Resolution of cavity enlargement was, however, incomplete in most cases, and substantial chamber dilatation persisted in >20% of athletes. The possibility that this residual LV hypertrophy, apparently part of the athlete’s heart syndrome, may have future long-term clinical implications in some individuals cannot be excluded with certainty. (Circulation. 2002;105:944-949.)

Key Words: athlete ■ hypertrophy ■ remodeling ■ ventricles ■ deconditioning

Long-term athletic training is associated with cardiac morphological changes, including increased left ventricular (LV) cavity dimension, wall thickness, and mass, described as athlete’s heart.1–3 The extent to which absolute LV dimensions increase with training is usually mild2 but may be substantial in elite athletes5,6 and suggestive of structural heart diseases, such as cardiomyopathies.7 Indeed, hypertrophic cardiomyopathy (HCM) and, less frequently, idiopathic dilated cardiomyopathy (DCM) represent underlying pathologic substrates responsible for sudden, unexpected death in young athletes.8,9 Therefore, extreme alterations in LV morphology observed in highly trained athletes unavoidably raise several critical issues, including the clinical significance and long-term consequences of the hypertrophy induced by training and the likelihood of complete reversibility after deconditioning.10

To address these important questions, which potentially impact large populations of athletes, we have studied the natural history of LV hypertrophy in elite athletes by assessing in a longitudinal fashion the extent to which marked LV morphological alterations (believed to be physiological adaptations to systematic athletic conditioning) were reversible after cessation of training and competition.

Methods

Selection of Study Population

Among the athletes examined at the Institute of Sports Science (Rome) in the period of 1985 to 1994 with a medical program that routinely included echocardiography,11 we found 280 subjects with evidence of substantial LV hypertrophy, defined here in clinical terms as end-diastolic cavity dimension ≥60 mm, maximum wall thickness ≥13 mm, or both.5,6 Because the primary intent of our study was to assess the long-term clinical implications of the athlete’s heart and differentiation from cardiomyopathies, we used the arbitrary cutoff value of 13 mm for wall thickness, which is above accepted upper normal limits12,13 and compatible with diagnosis of HCM,14 and 60 mm for cavity dimension, which exceeds the 95% prediction interval in healthy individuals independent of height, body weight, age, and sex.12,13 is associated with an increased incidence of cardiovascular events in a large study population,15 and instinctively suggests the diagnosis of DCM.16

At the time of the present investigation, 160 of the 280 athletes (57%) were still engaged in systematic training and competition. Of the remaining 120 athletes, we were able to contact by telephone 88
who had discontinued systematic training for at least 1 year and represented potential candidates for our study. Of these, 40 consented to be reevaluated and represent our study population.

Characterization of Study Population
The 40 subjects had been formerly engaged in rowing (n=29), canoeing (n=5), cycling (n=4), and tennis and middle-distance running (n=1 each). All were elite competitors, including 21 finalists or medalists at Olympic Games or World Championships. Ages were 24±4 years (range, 18 to 34) when examined at peak training and 33±5 years (range, 22 to 46) when examined again after cessation of competition.

All subjects were judged to be free of cardiovascular disease on the basis of medical history, physical examination (with blood pressure consistently <140/90 mm Hg), and echocardiography. Specifically, HCM was excluded in athletes with LV wall thickness ≥13 mm on the basis of symmetrically distributed hypertrophy, enlarged cavity size, and normal diastolic filling pattern.14 DCM was excluded in athletes with LV cavity dimension ≥60 mm on the basis of normal systolic function, absence of wall motion abnormalities, and normal diastolic filling pattern.7,14

The period from cessation of systematic training and competition to the final evaluation was 5.6±3.8 years (range, 1 to 13). Fifteen of the 40 former athletes had completely eliminated any physical activity, whereas the other 25 had been engaged in light recreational exercise programs, such as cycling, running, or circuit weight training, with a median caloric expenditure of 1590 kcal/wk.

Electrocardiography
Standard 12-lead ECGs were recorded at rest on the same day of the echocardiographic study and at least 24 hours after the last athletic activity. Electrocardiographic criteria for LV hypertrophy were assessed by the Sokolow-Lyon index (SV1 + RV5 or RV6 ≥35 mm) and Romhilt-Estes point score (≥4 points). ECG and blood pressure were also recorded during fatigue-limited, incremental exercise testing performed at final evaluation with bicycle-ergometer Cardio-line SDS 3D.

Echocardiography
Echocardiographic studies were performed using Hewlett-Packard 77020 AC at first evaluation and Sonos 5500 at last evaluation. Images of the heart were obtained in multiple cross-sectional planes using standard transducer positions. LV cavity dimensions and anterior ventricular septal and posterior free wall thickness were obtained from M-mode ECGs in accordance with previous recommendations.17 To enhance the accuracy of LV wall thickness measurements, these dimensions were also verified from two-dimensional images.3 Measurements of LV dimensions were made with a hand-held caliper by one experienced investigator (A.P.) who was blinded to the identity of the subject and level of conditioning.

LV mass was calculated by the formula of Devereux18 and normalized to height.19 Relative wall thickness (h/r) was the ratio of the average of ventricular septal and posterior free wall thicknesses to the cavity radius. LV ejection fraction was calculated from end-diastolic and end-systolic volumes in the apical 4-chamber view. Parameters of LV filling were obtained with pulsed Doppler echocardiography. Because this technique was first implemented at our institution in 1987, these data were not available in all athletes at peak training.

Reproducibility
Interobserver variability was assessed by two observers (A.P. and B.J.M.), independently and without knowledge of the identity of the subjects, in a subset of 30 echocardiographic tracings randomly selected from the 80 studies that constitute the overall analysis. Intraobserver variability was tested from blinded measurements made on the same tracings, 6 months apart, by one observer (A.P.).

Statistical Analyses
Data were expressed as mean±SD. Differences between means were assessed using the paired Student’s t test and Wilcoxon test. A 2-tailed P value <0.05 was considered evidence of statistical significance. Multiple regression and stepwise regression analyses were used to assess the influence of selected variables (age, weight, height, body surface area, blood pressure, heart rate, duration of deconditioning, and persistent physical activity) on LV dimensional changes.20 Concordance of echocardiographic measurements between observers was assessed using paired Student’s t test and intraclass correlation.20

Results
Changes in LV Dimensions With Long-Term Detraining

Cavity Size
Over the follow-up period, LV end-diastolic cavity dimension decreased by 7%, from 61.2±2.09 mm at peak training to 57.2±3.1 mm after detraining (P<0.001). Individual subject analysis showed most of these athletes (37; or 92%) had reduction in cavity dimension of ≥2 mm (including 17 with decrease of ≥5 mm), whereas the remaining 3 subjects showed little or no change (0 to 1 mm); no athlete showed an increase in cavity size with detraining (Figure 1). Nevertheless, absolute cavity dimensions remained enlarged (ie, ≥55 mm12) in most of the deconditioned athletes (34 [85%]), including 9 (22%) with more substantial dilatation of ≥60 mm, consistent in absolute dimensional terms with dilated cardiomyopathy.16 No differences in cavity dimensions were found between the 15 completely deconditioned athletes.
athletes and the 25 who participated in some recreational physical activities after cessation of their athletic career (57.2±3.3 versus 57.2±3.0 mm).

**Wall Thickness**
Maximum LV wall thickness (in the anterior ventricular septum of each athlete) decreased by 15% from 12.0±1.3 at peak training to 10.1±0.8 mm (P<0.001) after detraining. Individual subject analysis showed that most athletes (25 [62%]) had a decrease of ≥2 mm, including 11 with more marked reduction of 3 to 5 mm. Fifteen athletes (38%) had little or no change (0 or 1 mm), but no athlete showed an increase in wall thickness with detraining (Figure 2). Absolute wall thickness was ≥13 mm in 13 of the 40 athletes at peak training but was within normal limits (≥12 mm) in each athlete after detraining (Figure 3).

**Mass**
LV mass normalized to height decreased by 28%, from 194±25 at peak training to 140±21 g/m (P<0.001) after detraining; mass exceeded normal limits (≥143 g/m²) in all athletes at peak training and returned within normal in 22 (or 55%) after detraining. No significant changes were evident in left atrium and aortic root dimensions between peak training and long-term detraining (Table 1).

**Determinants of LV Dimensional Changes**
Multiple regression analysis showed that the extent of decrease in LV cavity dimension was significantly associated only with increased body weight and persistent physical activity over the follow-up period (r=0.472; P<0.001 and r=0.351; P<0.001, respectively). Multiple R² derived from the model that included these two variables was 0.45, indicating that 45% of the variability in LV cavity dimension observed between peak training and detraining could be explained by increased body weight and recreational physical activity performed during that period of time. Increase in resting heart rate after the long-term detraining showed no significant impact on decrease in LV cavity dimension. Changes in LV wall thickness and mass were not significantly associated with any of the examined variables.

**Left Ventricular Function**
LV ejection fraction was within normal limits in all athletes at the end of the follow-up period and did not differ significantly between peak conditioning and deconditioning (61±6% versus 59±7%, NS). No athlete developed systolic dysfunction (ie, ejection fraction <50%) or segmental wall motion abnormalities.

Paired assessments of LV diastolic filling by pulsed Doppler-echocardiography were available in 26 athletes both at peak training and after long-term detraining. Early diastolic peak-flow velocity showed no differences (69.5±13.7 versus 65.0±10.9 cm/s; NS); however, late diastolic peak-flow velocity (associated with atrial contraction) increased (29.6±7.8 to 46.0±12.0 cm/s; P<0.001). Consequently, the ratio of early-to-late diastolic peak-flow velocities decreased after detraining (2.6±0.9 to 1.5±0.5; P<0.001). LV filling pattern was normal in each athlete at peak training and in 25 of the 26 athletes after detraining.

**Electrocardiograms**
Comparative assessment of electrocardiographic pattern at peak training and after detraining was possible in 32 athletes. Resting heart rate, PR and QTc intervals, and R- and S-wave voltages in precordial leads showed significant reduction.
after detraining. Also, the proportion of athletes with electrocardiographic evidence of LV hypertrophy decreased significantly after detraining (Table 2).

**Clinical Findings With Long-Term Detraining**

Over the long-term follow-up period, none of the 40 detrained athletes had adverse cardiovascular events or developed clinical evidence of LV systolic or diastolic dysfunction. At the most recent evaluation, each athlete performed maximal exercise testing (>85% of maximum heart rate), achieving high-intensity workload (mean, 305±50 watt) without symptoms or ST-T wave changes.

During follow-up, body weight increased from 86.4±8 to 92.7±13 kg (P<0.001). Systolic blood pressure showed no change (128±10 versus 126±12 mm Hg; NS), but diastolic blood pressure increased mildly (78±7 to 83±10 mm Hg; P<0.01). Heart rate also increased significantly, from 51±10 to 58±10 bpm (P<0.001).

**Reproducibility**

**Interobserver**

LV cavity dimension measured by one observer was 59.5±3.8 mm (range, 53 to 68) and by the second observer was 59.1±3.7 mm (53 to 68). Mean interobserver difference was 1.5±1.5 mm (range, −5 to +5), and measurements by the 2 observers did not differ in statistically significant terms (P=0.31; NS). Concordance of the measurements of the 2 observers, as evaluated by intraclass correlation, was 84%, and Spearman’s correlation r was 0.82 (P<0.0001).

Maximum LV wall thickness measured by one observer was 11.6±1.1 mm (range, 8 to 14) and by the second observer was 11.4±1.2 mm (9 to 13). Mean interobserver difference was 0.7±0.8 mm (range, −3 to +2), and measurements by the 2 observers did not differ in statistically significant terms (P=0.39; NS). Concordance of the measurements of the 2 observers, as evaluated by intraclass correlation, was 60%; Spearman’s correlation r was 0.51 (P=0.004).

**Intraobserver**

LV cavity dimension, as measured by the same observer, was 59.1±3.6 mm (range, 52 to 67) at first assessment and

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**TABLE 1. Morphological and Functional Findings in 40 Athletes at Peak Training and After Long-Term Detraining**

<table>
<thead>
<tr>
<th></th>
<th>Peak Training</th>
<th>Long-Term Detraining</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>24±4</td>
<td>33±5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(18–34)</td>
<td>(22–46)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV mass, g/m</td>
<td>194±25</td>
<td>140±21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(158–263)</td>
<td>(81–193)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LA, mm</td>
<td>39.7±3.2</td>
<td>39.3±3.9</td>
<td>NS</td>
</tr>
<tr>
<td>(32–45)</td>
<td>(32–47)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ao, mm</td>
<td>34.3±2.2</td>
<td>34.7±2.3</td>
<td>NS</td>
</tr>
<tr>
<td>(30–38)</td>
<td>(30–40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EF, %</td>
<td>60.8±6.0</td>
<td>59.0±6.8</td>
<td>NS</td>
</tr>
<tr>
<td>(50–77)</td>
<td>(50–72)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E-max, cm/s</td>
<td>69±14</td>
<td>65±11</td>
<td>NS</td>
</tr>
<tr>
<td>(36–94)</td>
<td>(46–78)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A-max, cm/s</td>
<td>29±8</td>
<td>46±12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(21–45)</td>
<td>(28–67)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EF slope, cm²/s²</td>
<td>492±137</td>
<td>340±93</td>
<td>0.003</td>
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<tr>
<td>(262–648)</td>
<td>(150–455)</td>
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<td></td>
</tr>
<tr>
<td>E/A</td>
<td>2.6±0.9</td>
<td>1.5±0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(1.2–4)</td>
<td>(0.7–3.2)</td>
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</tbody>
</table>

**TABLE 2. Electrocardiographic Findings in 32 Elite Athletes at Peak Training and After Long-Term Detraining**

<table>
<thead>
<tr>
<th></th>
<th>Peak Training</th>
<th>Long-Term Detraining</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR, bpm</td>
<td>51±10</td>
<td>58±10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(40–75)</td>
<td>(44–77)</td>
<td></td>
<td></td>
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<tr>
<td>PR interval, s</td>
<td>0.17±0.03</td>
<td>0.16±0.02</td>
<td>0.003</td>
</tr>
<tr>
<td>(0.13–0.24)</td>
<td>(0.12–0.21)</td>
<td></td>
<td></td>
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<tr>
<td>QTc interval, s</td>
<td>0.40±0.04</td>
<td>0.39±0.03</td>
<td>0.03</td>
</tr>
<tr>
<td>(0.33–0.47)</td>
<td>(0.35–0.44)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SV₁, mV</td>
<td>10.3±3.7</td>
<td>8.2±3.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(4–19)</td>
<td>(4–15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SV₂, mV</td>
<td>16.4±7.3</td>
<td>13.4±4.8</td>
<td>0.007</td>
</tr>
<tr>
<td>(5–37)</td>
<td>(5–25)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV₆, mV</td>
<td>23.4±5.6</td>
<td>19.0±6.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(11–36)</td>
<td>(10–37)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sokolow-Lyon, n (%)</td>
<td>14 (44)</td>
<td>4 (12)</td>
<td>0.01</td>
</tr>
<tr>
<td>Romhilt-Estes, n (%)</td>
<td>10 (31)</td>
<td>2 (6)</td>
<td>0.02</td>
</tr>
<tr>
<td>Incomplete RBBB, n (%)</td>
<td>19 (59)</td>
<td>14 (44)</td>
<td>NS</td>
</tr>
<tr>
<td>Early repolarization pattern, n (%)</td>
<td>11 (34)</td>
<td>8 (25)</td>
<td>NS</td>
</tr>
<tr>
<td>Inverted/flattened T waves, n (%)</td>
<td>7 (22)</td>
<td>4 (12)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean±SD (range) unless otherwise indicated. HR indicates heart rate; RBBB, right bundle branch block; and Sokolow-Lyon, Romhilt-Estes, subjects with positive criteria for LV hypertrophy according to Sokolow-Lyon or Romhilt-Estes point score, respectively.
59.3±3.4 mm (55 to 67) at second evaluation; mean difference was 1±1 mm (range, −2 to +4) (P=0.40, NS). Maximum LV wall thickness was 11.7±1.3 mm (range, 10 to 15) at first assessment and 11.9±1.5 (10 to 16) at second evaluation; mean difference was 0.5±0.5 mm (range, −1 to +1) (P=0.3, NS).

### Discussion

Morphological cardiac alterations in athletes, commonly known as athlete’s heart, have been widely described in several cross-sectional echocardiographic studies1–6 that have supported the view that LV remodeling in athletes is a benign phenomenon, representing a physiological adaptation to systematic exercise conditioning. However, the dimensional LV changes observed in some elite athletes may be substantial in absolute terms and unavoidably raise a clinical dilemma and differential diagnosis between athlete’s heart and structural cardiac diseases, such as HCM or DCM.5,6 These are important medical considerations in that the latter pathologic conditions are frequently responsible for sudden death in young athletes.8,9 Presently, however, there are insufficient data to resolve the uncertainty of whether or not such marked alterations in LV chamber dimensions have potential long-term clinical significance and represent evidence of an incipient pathologic condition.10

In the present study, we have examined this issue by evaluating in a longitudinal fashion a unique population of highly trained athletes with marked LV hypertrophy, initially at peak conditioning and then once again after cessation of their competitive athletic career. To this purpose, we relied largely on absolute LV dimensions (rather than dimensions normalized to indexes such as body surface area) to place our data in the context of clinical cardiovascular diagnosis and methodology used in customary practice.

On the basis of this analysis, we have made potentially important observations regarding the natural history of LV hypertrophy in athletes. We found that substantial LV cavity dilatation (ie, end-diastolic dimension of ≥60 mm) in the dimensional range of DCM16 was only partially reversible after long periods of deconditioning. Although reduction in cavity dimensions occurred in >90% of our former athletes, the final dimensions remained markedly enlarged (≥60 mm) in >20%. Similarly, LV mass remained increased in the about half of our former athletes. Therefore, because our athletes had been exposed to particularly intense and prolonged athletic training at an elite level, we cannot exclude the possibility that the incomplete LV remodeling may represent a long-term, irreversible consequence of extreme athletic conditioning.

However, persistent cavity enlargement in our former athletes could be partially explained by several factors. Multiple regression analysis showed that this incomplete remodeling was associated with an increase in body weight after deconditioning (in 70% of the former athletes) and persistent, recreational physical activity (in 60% of the former athletes). Both these factors represent stimuli for increased LV cavity size (and mass)1,2,3 and may have mitigated the reduction in LV dilatation with detraining.

Indeed, anatomic changes induced by the long-term hemodynamic load associated with exercise training, such as the remodeling with expansion of the interstitial (matrix) collagen compartment11 or chronic stretching of the pericardium,22 may have precluded a more substantial reduction in cavity size during detraining. Also, we cannot exclude the possibility that our subjects represent a selected subset of the athlete population, who have inherited (or are genetically predisposed to have) LV cavity enlargement as a determinant of athletic achievement in endurance sports.23 Therefore, persistently enlarged cavity sizes in detrained athletes may in fact represent the usual or normal dimensions in some athletes rather than a residual training effect.

Presently, we cannot be certain of the clinical significance attributable to the incomplete LV remodeling described here. We found no clinical or echocardiographic evidence of systolic or diastolic LV dysfunction, cardiac symptoms, or impaired physical performance in our former athletes, but we cannot exclude the possibility that this marked residual chamber enlargement may represent a subtle cardiomyopathic process that could ultimately lead to clinical consequences later in life.24 These considerations are of particular relevance, given the youthful age (mean, 33 years) of our athletes. Eventually, understanding the significance of residual LV dilatation in deconditioned athletes will require longitudinal follow-up over longer time periods.

Remodeling observed in this study with respect to LV wall thickness contrasted with that of cavity enlargement. Each of those athletes with absolute LV wall thickness of ≥13 mm, compatible with the diagnosis of HCM,5 showed complete normalization with detraining (Figure 3). This finding is consistent with previous experiences.25,26 In a small group of elite rowers and canoeists, we observed that markedly increased LV wall thicknesses (13 to 16 mm) returned to normal within an average deconditioning period of 13 weeks in the absence of significant LV cavity changes.26 Therefore, marked LV wall thickening in athletes resembling HCM proved to be a completely physiological phenomenon, which is evident only when intensive training in endurance sport disciplines is maintained.

In conclusion, our findings are most consistent with the benign and physiological nature of LV hypertrophy in elite athletes. However, the long-term clinical significance of incomplete resolution of marked LV cavity enlargement remains unresolved.

### Acknowledgments

This study was supported in part by grants from the Minneapolis Heart Institute Foundation and the Paul G. Allen Foundations (to Dr Maron).

### References


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*Circulation*. 2002;105:944-949; originally published online February 4, 2002;
doi: 10.1161/hc0802.104534
*Circulation* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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