

Relationship between Cardiac Remodeling and Exercise Capacity in Elite Athletes: Incremental Value of Left Atrial Morphology and Function Assessed by Three-Dimensional Echocardiography



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Background: Data are scarce regarding left atrial (LA) adaptation to regular physical exercise. The aim of this study was to examine left ventricular (LV) and also LA morphologic and functional remodeling in elite athletes using three-dimensional (3D) echocardiography.

Methods: In this retrospective analysis, the study group consisted of 138 elite athletes (mean age, 20 ± 4 years; 62% men) and 50 sedentary control subjects. Electrocardiographically gated full-volume 3D data sets were obtained for offline analysis using dedicated software for 3D LA and LV measurements. Body surface area-indexed LA maximal volume (LAVmax) and LV end-diastolic volume were determined. LA total emptying fraction, LA passive and LA active emptying fraction, and LV global longitudinal strain were also calculated. Athletes also underwent cardiopulmonary exercise testing to determine peak oxygen uptake.

Results: Athletes demonstrated higher 3D LAVmax (32 ± 6 vs 26 ± 8 mL/m²) and indexed LV end-diastolic volume (85 ± 12 vs 62 ± 10 mL/m²) compared with control subjects ($P < .001$ for both). Functional measures of the left ventricle and left atrium, such as the absolute value of 3D LV global longitudinal strain ($19 \pm 2\%$ vs $22 \pm 2\%$), LA total emptying fraction ($58 \pm 6\%$ vs $64 \pm 6\%$), and active emptying fraction ($24 \pm 10\%$ vs $32 \pm 10\%$) were lower in athletes ($P < .001$ for all). Male athletes had higher indexed LV end-diastolic volume compared with female athletes (89 ± 13 vs 80 ± 8 mL/m², $P < .001$), but LAVmax did not differ between genders (32 ± 6 vs 33 ± 5 mL/m², $P = .18$). Besides heart rate, gender, and body surface area, 3D LAVmax, LV global longitudinal strain, and LA passive emptying fraction were independent predictors of peak oxygen uptake.

Conclusions: Regular physical exercise results in marked LA and LV remodeling with considerable gender differences as explored by 3D echocardiography. In contrast with various cardiovascular diseases, more pronounced LA dilation and lower resting functional measures are associated with better exercise performance. (J Am Soc Echocardiogr 2020;33:101-9.)

Keywords: Athlete's heart, 3D echocardiography, Left atrium, Exercise capacity

Intense exercise training is associated with significant hemodynamic demands and subsequent cardiac remodeling, also referred to as athlete's heart. The sport discipline, frequency and intensity of training, gender, and age may all influence the nature of cardiac adaptation.

The most pronounced structural changes have been observed in elite, competitive athletes; typically, biatrial and biventricular enlargement and/or hypertrophy are observed.¹⁻³ Functional measurements often result in low-normal values at rest.^{1,4} Despite the pronounced

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Abbreviations

2D = Two-dimensional
3D = Three-dimensional
BSA = Body surface area
CPET = Cardiopulmonary exercise testing
EF = Emptying fraction
FWLS = Free wall longitudinal strain
GCS = Global circumferential strain
GLS = Global longitudinal strain
HR = Heart rate
LA = Left atrium/atrial
LAVmax = Left atrial maximal volume
LAVmin = Left atrial minimal volume
LAPreAV = Left atrial pre-A-wave volume
LV = Left ventricle/ventricular
LVEDVi = Indexed left ventricular end-diastolic volume
LVEF = Left ventricular ejection fraction
LVMi = Indexed left ventricular mass
RV = Right ventricular
RVEDVi = Indexed right ventricular end-diastolic volume
RVEF = Right ventricular ejection fraction
Vo₂/kg = Peak oxygen uptake

cardiac remodeling in athletes, it is still a matter of debate whether exercise capacity can be predicted by cardiac size or by resting functional measurements.⁵⁻⁷

Traditionally, the left ventricle (LV) is the main focus of physiologic and clinical cardiovascular research, but the importance of left atrial (LA) structure and mechanics should not be underestimated. Detailed assessment of LA morphology and function provides additive data in various cardiovascular diseases.^{8,9} LA remodeling may have a strong impact on exercise performance in athletes and also on exercise-induced atrial fibrillation.¹⁰

The majority of studies regarding LA volumes and function in athletes are based on two-dimensional (2D) echocardiographic assessment, but 2D methods rely strongly on precise angulation, which could be complicated in the case of the LA. Three-dimensional (3D) echocardiography-based analysis of the LA may overcome all limitations of conventional echocardiography, providing data free of angulation issues and also geometric assumptions about LA shape¹¹ (Figure 1). Moreover, speckle-tracking-based approaches offer an objective and quantitative evaluation of myocardial function. Accurate assessment of structural and functional cardiac remodeling in athletes competing in sport disciplines of combined exercise nature may aid in understanding the physiologic degree of adaptation to high dynamic and static training and its relation to exercise capacity.

Accordingly, our aim was to examine LA and left ventricular

morphology and function in elite athletes with mixed exercise regimens and their relation to exercise capacity using 3D echocardiography.

METHODS

Between March 2017 and May 2018, we consecutively examined elite athletes enrolled through our center's complex sports cardiology

screening program (approved by the Medical Research Council; ETT-TUKEB No. 13687-0/2011-EKU). The participants gave written informed consent to every procedure of our study. In this retrospective study, inclusion criteria were elite athletes, defined as being a member of the national team in the corresponding age group and with a mixed-type exercise regimen ($n = 154$). All of the examinations were performed during in-competition phase and ≥ 24 hours following the last athletic training. Detailed medical history and training regimen were obtained along with routine physical examination and 12-lead electrocardiogram. Echocardiographic studies took place before cardiopulmonary exercise testing (CPET). Subjects with uncommon echocardiographic and/or electrocardiographic changes¹² or suboptimal echocardiographic image quality for 3D analysis and athletes who suspended regular training in the preceding 6 months were not included. One hundred thirty-eight athletes were included in the present analysis. Fifty healthy, sedentary volunteers from our existing database (no previous participation in intensive training, < 3 hours of exercise/wk) with no relevant medical history, no signs or symptoms of cardiovascular disease, and normal results on electrocardiography and echocardiography served as the control group, with similar age and gender distribution. Body surface area (BSA) was calculated using the Mosteller formula.¹³

Echocardiography

Conventional Echocardiographic Measurements. Echocardiographic acquisitions were obtained using a Vivid E95 ultrasound system equipped with a 4V-D phased-array transducer (GE Vingmed Ultrasound, Horten, Norway). Chamber dimensions were quantified according to current guidelines.¹⁴ LV wall thicknesses and diameters were evaluated in the parasternal long-axis view at the level of mitral valve coaptation. LA anteroposterior diameter was measured in the parasternal long-axis view perpendicular to the aortic root at the level of sinuses. LA and right atrial areas were calculated by contouring atrial endocardial borders in the apical four-chamber view, and LA and right atrial volumes were estimated using the Simpson method indexed to BSA. LV inflow by pulsed-wave Doppler at the level of the mitral valve coaptation was obtained to determine early (E) and late diastolic (A) peak velocities, their ratio, and E-wave deceleration time. Pulsed-wave Doppler tissue imaging was used to measure systolic (s'), early (e'), and late diastolic (a') velocities at the mitral lateral and medial annulus. The ratio of E-wave velocity to averaged e' velocities of the mitral medial and lateral annulus was calculated as an estimate of LV filling pressures.

Three-Dimensional Echocardiographic Measurements.

Beyond routine echocardiographic protocol, electrocardiographically gated full-volume 3D data sets reconstructed from four or six cardiac cycles optimized for the LV, LA, and right ventricle were obtained from apical view with a minimum volume rate of 25 volumes/sec for offline analysis. Image quality was verified bedside to avoid "stitching" and "dropout" artifacts of the 3D data. Further measurements were performed on a separate workstation using dedicated software (4D LALV Function and 4D RV Function 2; TomTec Imaging, Unterschleissheim, Germany). Concerning the LV and LA, the software detects endocardial surfaces of the chambers, and following manual correction it traces its motion throughout the cardiac cycle. In the case of the LV, we determined indexed LV end-diastolic volume (LVEDVi), indexed LV end-systolic volume, indexed LV stroke volume, and indexed LV mass (LVMi), and to characterize global LV function, LV ejection fraction (LVEF) and deformation parameters such as

HIGHLIGHTS

- LA morphology and function are significantly altered in the athlete's heart.
- Considerable gender differences in LA adaptation to exercise are also present.
- Several LA parameters correlate with exercise capacity.
- LA morphology and function are independent predictors of exercise capacity.

global longitudinal strain (GLS) and global circumferential strain (GCS) were also assessed.

To examine LA 3D morphology and function, the timing of late diastolic atrial contraction was confirmed by mitral annular motion to measure LA maximal volume (LAVmax), LA minimal volume (LAVmin), and LA pre-A-wave volume (LAPreAV) indexed to BSA. Total emptying volume was defined as LAVmax – LAVmin. Using these volumetric data, we calculated LA total emptying fraction (EF) as $100 \times (\text{LAVmax} - \text{LAVmin}) / \text{LAVmax}$, LA passive EF as $100 \times (\text{LAVmax} - \text{LAPreAV}) / \text{LAVmax}$, and LA active EF as $100 \times (\text{LAPreAV} - \text{LAVmin}) / \text{LAPreAV}$, as parameters of LA reservoir, conduit, and contractile function, respectively (Figure 2). We also quantified true conduit volume as indexed LV stroke volume – (LAVmax – LAVmin). The software also automatically calculates 3D LA GLS.

We have also determined indexed right ventricular end-diastolic volume (RVEDVi) and indexed right ventricular (RV) end-systolic volume to quantify RV 3D morphology, and for the assessment of RV function we measured indexed RV stroke volume, RV ejection fraction (RVEF), and RV free wall longitudinal strain (FWLS).

Cardiopulmonary Exercise Testing

CPET for peak oxygen uptake (VO_2/kg) quantification was performed on a treadmill using an incremental protocol commencing at a 2-min 6 km/h flat race followed by 8 km/h uphill running with an increasing slope of 1.5% every minute until exhaustion. The volume and composition of the exhaled gases were analyzed breath by breath using an automated cardiopulmonary exercise system (Respiratory Ergostik; Geratherm, Bad Kissingen, Germany). Subjects were encouraged to achieve maximal effort, which was confirmed by respiratory exchange ratio, lactate curves by regular fingertip lactate measurements every 2 min during the test, and by reaching the predicted maximal heart rate (HR) and a plateau in oxygen uptake.

Statistical Analysis

Statistical analysis was performed using dedicated software (Statistica version 12; Statsoft, Tulsa, OK). The Shapiro-Wilk test was used to test normality of distribution. Data are presented as mean $\pm$ SD. Gender-based matching of the two study groups was confirmed using a χ^2 test. The unpaired Student's *t* test was used to compare groups, and the Pearson test was performed for correlation analysis as appropriate. Multiple linear regression analysis was applied to find independent predictors that determine VO_2/kg . To avoid multicollinearity issues, tolerance was set as >0.5 . *P* values $< .05$ were considered to indicate statistical significance. Intra- and interobserver variability were evaluated using Lin's concordance correlation and also using the coefficient of variation. To assess the intraobserver reproducibility of the most relevant parameters, the operator of the offline measurements repeated the 3D analysis in a randomly chosen subset of 10 athletes and five control subjects blinded to previous results (Supplemental Table 1). Interobserver variability was determined by 3D analysis of the same 15 subjects by a second experienced operator in a blinded fashion (Supplemental Table 1).

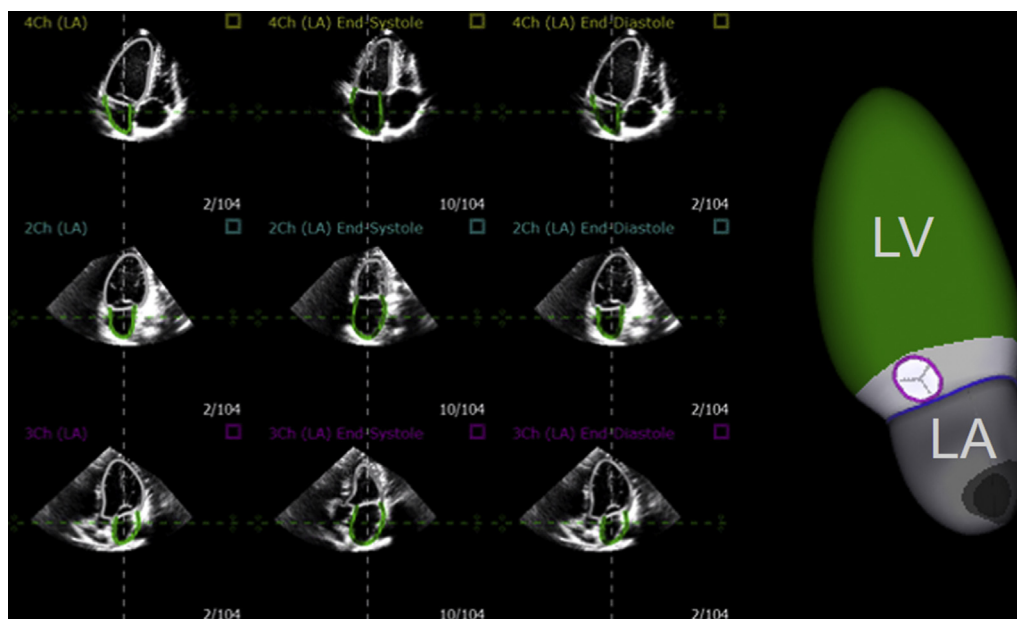


Figure 1 Three-dimensional echocardiographic analysis of the LA. Following correction of the left atrial long axis, the algorithm detects the left atrial endocardial border and traces its motion throughout the cardiac cycle in multiple planes, also allowing manual editing if needed. Therefore, a 3D model of the LA is generated, and changes in left atrial volume and GLS can be calculated. 2ch, Two-chamber view; 3ch, three-chamber view; 4ch, four-chamber view.

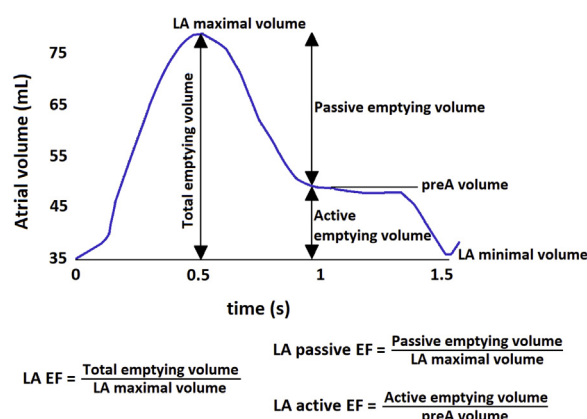


Figure 2 LA volume-time curve with the phasic volumes and the calculation of LA functional indices. LA EF = LA total EF.

Table 2 Conventional echocardiographic parameters of athlete and control groups

Variable	Athlete (n = 138)	Control (n = 50)	P
LVIDd, mm	51.9 ± 4.2	46.7 ± 4.2	<.001
IVSd, mm	10.3 ± 1.6	8.7 ± 1.2	<.001
PWd, mm	9.2 ± 1.2	7.6 ± 1.2	<.001
RWT, %	0.38 ± 0.05	0.35 ± 0.05	<.001
LA diameter, mm	37.2 ± 4.4	31.5 ± 4.5	<.001
LA area, cm ²	19.3 ± 4.0	14.9 ± 3.4	<.001
LAVi, mL/m ²	29.4 ± 8.6	23.0 ± 9.3	<.001
RA area, cm ²	18.1 ± 3.8	14.2 ± 3.5	<.001
RAVi, mL/m ²	27.9 ± 7.6	21.5 ± 8.1	<.001
Transmitral E wave, cm/sec	82.5 ± 15.5	92.8 ± 20.1	<.001
Transmitral A wave, cm/sec	51.7 ± 12.6	64.7 ± 14.9	<.001
E/A ratio	1.67 ± 0.47	1.51 ± 0.45	<.05
DT, msec	179.6 ± 42.4	163.9 ± 29.7	<.05
E/e' average	5.70 ± 1.20	5.61 ± 1.57	.98
Mitral lateral s', cm/sec	11.2 ± 2.3	11.8 ± 2.1	<.05
Mitral lateral e', cm/sec	17.2 ± 3.1	18.6 ± 3.5	<.01
Mitral lateral a', cm/sec	6.7 ± 2.1	7.6 ± 1.7	<.01
Mitral medial s', cm/sec	8.9 ± 1.3	9.1 ± 1.3	.34
Mitral medial e', cm/sec	12.5 ± 2.2	14.2 ± 2.4	<.001
Mitral medial a', cm/sec	6.9 ± 1.6	7.3 ± 1.6	<.05

DT, Deceleration time; IVSd, interventricular septal thickness; LAVi, LA volume index; LVIDd, LV end-diastolic diameter; PWd, posterior wall thickness; RA, right atrial; RAVi, right atrial volume index; RWT, relative wall thickness.

Data are expressed as mean ± SD.

letes. Similarly to the morphologic changes of the LV, LA dilation was seen in athletes, with significantly higher 3D LAVmax, LAVmin, LAPreAV, total emptying volume index, and true conduit volume. LA total EF and LA active EF were significantly lower in the athlete group. LA passive EF did not differ between groups, but it showed a tendency toward lower values in athletes (Figure 3). Athletes demonstrated lower 3D LA GLS as well. Similarly to the LV, 3D RV volumes were significantly higher in athletes along with lower RVEFs, but RV FWLS was comparable between the athletes and control subjects (Table 3).

Comparison of 3D echocardiographic data in female and male athletes is shown in Table 4. Male athletes had significantly higher 3D LV volume indices and LVMI. On the other hand, LVEF was significantly lower in male athletes, and LV GLS and GCS were also lower compared with female athletes. In contrast with the LV volumetric adaptation, 3D LAVmax and LAVmin did not differ between genders. Interestingly, however, LA functional differences were present, with significantly higher 3D LA total EF and LA GLS in women, resulting in higher total emptying volume index as well. Male athletes demonstrated significantly higher RV volumes along with lower RVEFs compared with women, while RV FWLS did not differ between genders (Table 4).

Table 1 Baseline characteristics of athlete and control groups

Variable	Athlete (n = 138)	Control (n = 50)	P
Age, y	19.6 ± 4.3	19.9 ± 2.8	.66
Gender, female	53	20	.84
BSA, m ²	2.00 ± 0.20	1.78 ± 0.24	<.001
SBP, mm Hg	136.1 ± 16.7	128.4 ± 13.7	.29
DBP, mm Hg	73.5 ± 10.1	79.6 ± 12.4	<.001
HR, beats/min	68.0 ± 11.7	83.2 ± 16.2	<.001
VO ₂ /kg, mL/kg/min	52.2 ± 6.7		

DBP, Diastolic blood pressure; SBP, systolic blood pressure. Data are expressed as mean ± SD or as number.

RESULTS

Basic demographic and morphometric data of the two study groups are shown in Table 1. The mean age of our athletes was 20 years. They had been participating in competitive sports for 11 ± 5 years, with a current average training duration of 18 ± 7 hours per week. Athletes had significantly higher BSAs and lower resting diastolic blood pressures and resting HRs compared with control subjects (Table 1).

Basic 2D echocardiographic parameters are shown in Table 2. LV end-diastolic diameter, wall thicknesses, and relative wall thickness were significantly higher in athletes compared with control subjects. Conventional measures of LA morphology, such as anteroposterior diameter, LA area, and 2D LA volume index, were significantly higher in athletes, and similar changes were observed in right atrial area and volume index as well. Twenty-five percent of our athletes exceeded the upper limit of 2D LAVmax (>34 mL/m²) suggested in most recent guidelines. Athletes demonstrated lower transmitral E- and A-wave velocities along with significantly higher E/A ratios and also longer deceleration times. The control group demonstrated significantly higher Doppler tissue imaging–derived mitral lateral and also medial e' and a' velocities, but E/e' ratio did not differ between the two groups (Table 2).

Three-dimensional echocardiographic data are summarized in Table 3. Athletes demonstrated significantly higher 3D LV volumes and LVMI compared with control subjects. Functional measures of the LV, such as LVEF, GLS, and GCS, were significantly lower in ath-

Table 3 Three-dimensional echocardiographic data of athlete and control groups

Variable	Athlete (n = 138)	Control (n = 50)	P
LVEDVi, mL/m ²	85.4 ± 12.4	62.0 ± 10.3	<.001
LVESVi, mL/m ²	37.3 ± 6.9	23.9 ± 5.3	<.001
LVSVi, mL/m ²	48.0 ± 7.3	38.1 ± 6.3	<.001
LVMi, g/m ²	94.9 ± 14.4	68.9 ± 11.7	<.001
LVEF, %	56.3 ± 4.2	61.6 ± 4.3	<.001
LV GLS, %	−18.8 ± 1.9	−21.5 ± 1.6	<.001
LV GCS, %	−27.4 ± 2.9	−29.9 ± 9.0	<.01
LAVmax, mL/m ²	32.0 ± 5.8	26.3 ± 7.7	<.001
LAVmin, mL/m ²	13.5 ± 3.2	9.6 ± 3.6	<.001
LA total emptying volume index, mL/m ²	18.6 ± 3.7	16.8 ± 4.9	<.05
LAPreAV, mL/m ²	17.8 ± 4.3	14.0 ± 4.9	<.001
LA total EF, %	58.1 ± 6.2	64.2 ± 5.7	<.001
LA active EF, %	24.1 ± 9.5	32.0 ± 9.6	<.001
LA passive EF, %	44.6 ± 7.6	46.9 ± 8.0	.07
LA true conduit volume, mL/m ²	29.4 ± 6.3	21.3 ± 8.7	<.01
LA GLS, %	32.2 ± 7.3	38.5 ± 7.4	<.001
RVEDVi, mL/m ²	88.2 ± 13.8	63.5 ± 11.9	<.001
RVESVi, mL/m ²	40.6 ± 9.1	26.1 ± 6.4	<.001
RVSVi, mL/m ²	47.7 ± 6.4	37.7 ± 6.9	<.001
RVEF, %	54.3 ± 4.8	56.2 ± 6.9	<.001
RV FWLS, %	−29.1 ± 7.4	−30.6 ± 4.6	.22

LVESVi, Indexed LV end-systolic volume; LVSVi, indexed LV stroke volume; RVESVi, indexed RV end-systolic volume; RVSVi, indexed RV stroke volume.

Data are expressed as mean ± SD.

Univariate correlations between 3D echocardiography-derived parameters and $\dot{V}O_2/\text{kg}$ in athletes are summarized in Table 5. Three-dimensional LAVmax showed a weak but significant positive correlation with age, LVEDVi, LVMi, and RVEDVi. Higher LA total EF and LA active EF were weakly associated with higher LV GLS (better deformation), higher RVEF, and higher RV FWLS (better deformation), while LA active EF showed a weak relationship with LVEF. LA passive EF showed a weak inverse correlation with age. Although 2D LA measurements did not show any relationship with $\dot{V}O_2/\text{kg}$, several 3D LA, LV, and RV parameters had weak but significant correlations with exercise performance: higher LVEDVi, LVMi, LAVmax, and RVEDVi were associated with better $\dot{V}O_2/\text{kg}$, as were lower resting functional parameters, such as LVEF, LV GLS, LA total EF, LA passive EF, and RVEF (Table 5). We found no correlation between LA size and LA functional parameters in athletes.

Multiple linear regression models were built to identify independent predictors of $\dot{V}O_2/\text{kg}$ in the athlete group. In the first model (Table 6), 3D LV and LA morphologic and functional parameters, such as LAVmax, LA total EF, LA active EF, LA passive EF, LVEDVi, LVMi, LVEF, LV GLS, and LV GCS along with basic demographic and morphometric data (age, gender, and BSA) and HR, were included in the analysis. According to our results, gender, LAVmax, LA passive EF, LV GLS, HR, and BSA were independent predictors of exercise capacity, with a cumulative R value of 0.722 ($P < .0001$). Male gender was associated with better exercise

performance. In the second model, 3D RV parameters (RVEDVi, RV FWLS) replaced two nonsignificant predictors from the previous analysis (Table 7). In this case, gender, LAVmax, LA passive EF, LV GLS, HR, and BSA, as well as RVEDVi and RV FWLS, were independent predictors of $\dot{V}O_2/\text{kg}$, with further improvement of the model (cumulative R value of 0.792, $P < .0001$).

Intra- and interobserver variability of the key 3D LA parameters demonstrated high reproducibility of 3D LA analysis (Supplemental Table 1).

DISCUSSION

Detailed understanding of physiologic (and pathophysiologic) alterations of the LA is lacking in the contemporary literature concerning athlete's heart. We aimed to characterize LA morphology and function using 3D echocardiography in elite athletes. We found prominent LA enlargement with lower resting atrial function, with considerable differences between genders. Three-dimensional LA and LV morphology and function showed correlation with $\dot{V}O_2/\text{kg}$; moreover, using multivariate linear regression, LAVmax and LA passive EF were independent predictors of peak exercise capacity.

Atrial remodeling in athletes represents a dynamic adaptation to the hemodynamic load associated with exercise training. Beyond volume overload, increased cardiac output during exercise is also associated with increased LV filling pressures; therefore the LA is also a subject of pressure overload.^{15,16} In response to these significant hemodynamic demands, marked changes in LA morphology and function are expected. The nature of these changes is also influenced by other factors, such as age, gender, ethnicity, type of sport, cumulative years of training, and degree of conditioning.^{4,17-20} To the best of our knowledge, our study is the first to correlate LA morphology and function assessed by 3D echocardiography with CPET in a relatively large set of elite athletes. The atrial enlargement and low-normal function found in our population do not represent dysfunction but a physiologic aspect of the "athlete's heart": less contraction in a higher volume chamber can achieve the same stroke volume as a smaller one with more pronounced shortening.^{4,21}

The same applies to the LA as well; moreover, resting bradycardia in athletes shifts the diastolic filling of the LV even more toward the early period.^{22,23} All these changes refer to a more effective LA-LV diastolic coupling based mainly on passive hemodynamics instead of active contraction. During exercise, however, this functional reserve capacity will be able to actively support adequate LV filling and systemic forward flow when HR increases.²⁴

A recent meta-analysis confirmed a significant increase in LAVmax compared with sedentary control subjects.²⁵ However, conflicting results have been reported regarding the influence of gender on atrial size. In contrast to our results, D'Andrea *et al.*²⁶ demonstrated that LA size was greater in male compared with female athletes. Nevertheless, the aforementioned meta-analysis using 2D echocardiography concluded that gender does not influence LA volumes, which is in line with our 3D data. Badano *et al.*¹¹ suggested reference values for 3D LA volumes and phasic functional indices measuring 276 healthy Italian volunteers using the same software applied in our study. Comparing our control subjects with their reference values of the same age range, we found similar LA volumes, while the athletes demonstrated clear LA enlargement. They found that LA volumes indexed to BSA were similar in men and women and increasing across age categories.

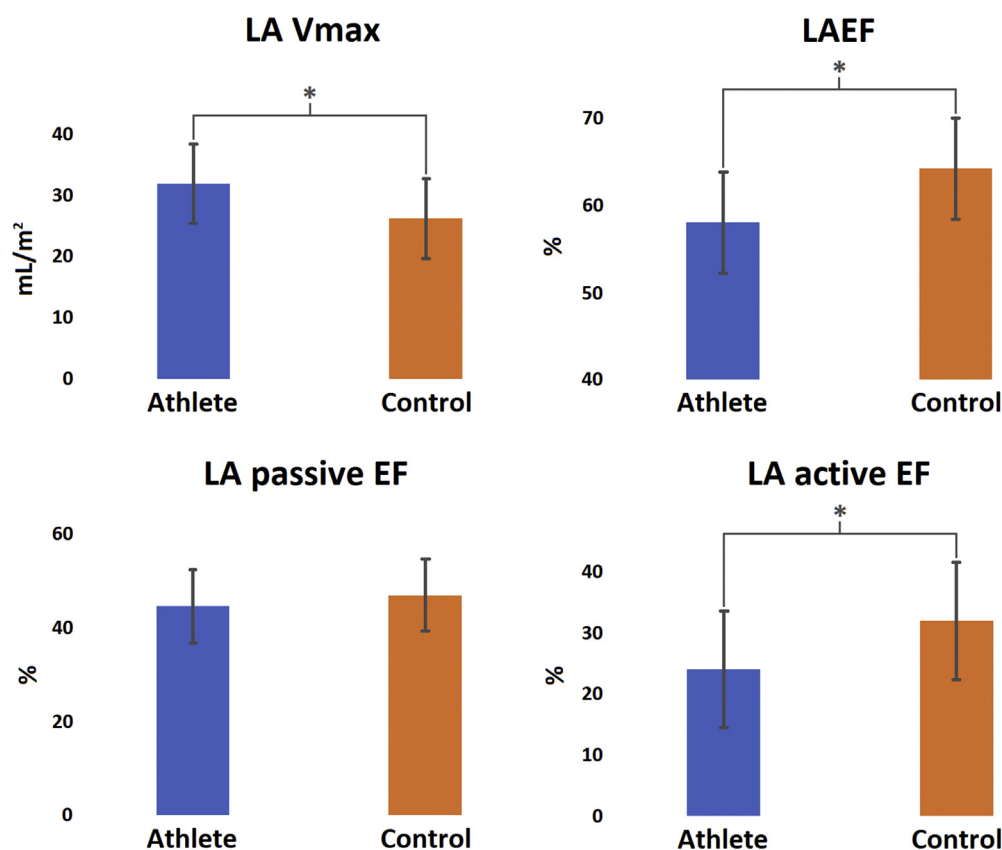


Figure 3 Comparison of LA morphology and function in athletes and control subjects. * $P < .05$. LAEF = LA total EF.

Along with LA morphology, LA functional parameters also demonstrate dynamic changes in athletes. Most of the studies using 2D volumetric or speckle-tracking echocardiography approach demonstrated normal LA reservoir function and reduced contractile function along with maintained passive emptying properties compared with sedentary control subjects.^{27,28} Although reservoir function in athletes was reported to be preserved in several studies, there is evidence of decreased resting reservoir function at midseason compared with the preseason period, suggesting that LA adaptation to exercise may also involve lower resting reservoir function of the chamber.^{28,29} Moreover, a recent meta-analysis found that both LA reservoir and contractile functions are lower in athletes.³⁰ In line with these data, in our study, 3D LA total EF and LA GLS, markers of LA reservoir function, were significantly lower in athletes compared with nontrained control subjects. In contrast to other LA phasic functional parameters, LA passive EF was found to be comparable between the study groups, which may be attributable to the supernormal LV early diastolic function in athletes, facilitating LA emptying in the conduit phase.^{23,31} These findings are consistent with those of a previous study also applying 3D echocardiography.³² Data are scarce regarding gender differences in LA functional adaptation: according to previous data using 2D speckle-tracking echocardiography in runners, women exhibit similar LA functional changes, with significantly higher LA contractile function compared with men.³³ According to our results, female athletes have significantly higher LA total EF and LA GLS but similar LA passive emptying and contractile properties compared with male athletes.

Besides gender, HR, and morphometric parameters such as BSA, in our multivariate linear regression model, 3D- but not 2D-derived LAVmax was an independent predictor of VO_2/kg . Interestingly, 3D LVEDVi was not a predictor of exercise performance, suggesting that the assessment of LA morphologic adaptation using 3D echocardiography may provide incremental value in the characterization of athlete's heart. Moreover, cardiac functional parameters such as LV GLS and LA passive EF were also independent predictors of fitness. LV GLS was proved to be a strong marker of LV functional status,^{34,35} and LA passive EF may be perceived as a composite marker of LV diastolic function, LA stiffness, and filling pressures, which may explain their predictive value.^{36,37} Previous studies using cardiac magnetic resonance examinations in athletes observed strong correlations between cardiac size and cardiopulmonary fitness.^{5,38} In parallel with our results, more pronounced LV and LA morphologic remodeling was found to be associated with better exercise capacity in echocardiographic studies as well.^{5,39} Interestingly, fewer data are available about the relationship between cardiac function and exercise capacity. La Gerche *et al.*⁵ demonstrated an inverse correlation between LVEF and VO_2/kg , but they did not find a relationship between LV deformation parameters and exercise performance. Another study enrolling older soccer referees found a direct relationship between LV longitudinal deformation and VO_2/kg .⁶ Our findings suggest that LV and LA morphology correlate directly, while resting functional parameters have inverse relationships with peak exercise capacity in mixed trained athletes. Our second multivariate linear regression model revealed that RV

Table 4 Comparison of 3D echocardiographic data in female and male athletes

Variable	Male athlete (n = 85)	Female athlete (n = 53)	P
LVEDVi, mL/m ²	89.0 ± 13.1	79.7 ± 8.3	<.001
LVESVi, mL/m ²	39.7 ± 6.8	33.6 ± 5.3	<.001
LVSVi, mL/m ²	49.3 ± 7.8	46.1 ± 5.9	<.05
LVMi, g/m ²	98.7 ± 15.6	88.9 ± 9.5	<.001
LVEF, %	55.4 ± 3.5	57.9 ± 4.7	<.01
LV GLS, %	−18.3 ± 1.8	−19.4 ± 1.9	<.001
LV GCS, %	−26.9 ± 2.4	−28.1 ± 3.4	<.05
LAVmax, mL/m ²	31.5 ± 5.9	32.9 ± 5.4	.18
LAVmin, mL/m ²	13.5 ± 3.3	13.3 ± 3.2	.73
LA total emptying volume index, mL/m ²	18.0 ± 3.6	19.5 ± 3.7	<.05
LAPreAV, mL/m ²	17.8 ± 4.6	17.8 ± 3.8	.91
LA total EF, %	57.2 ± 5.7	59.5 ± 6.7	<.05
LA active EF, %	23.2 ± 9.9	25.4 ± 8.7	.20
LA true conduit volume, mL/m ²	31.2 ± 6.3	26.6 ± 5.4	<.001
LA passive EF, %	44.0 ± 7.4	45.6 ± 7.8	.24
LA GLS, %	31.0 ± 6.6	34.3 ± 7.8	<.01
RVEDVi, mL/m ²	92.9 ± 13.7	80.8 ± 10.2	<.001
RVESVi, mL/m ²	43.8 ± 9.0	35.5 ± 6.8	<.001
RVSVi, mL/m ²	49.1 ± 6.6	45.5 ± 5.6	<.01
RVEF, %	53.1 ± 4.2	56.3 ± 5.0	<.001
RV FWLS, %	−28.1 ± 6.9	−30.6 ± 4.0	.07

LVEDVi, Indexed LV end-systolic volume; LVSVi, indexed LV stroke volume; RVESVi, indexed RV end-systolic volume; RVSVi, indexed RV stroke volume.

Data are expressed as mean ± SD.

morphology and function (i.e., RVEDVi, RV FWLS) are also independent predictors of VO_2/kg besides the parameters that were revealed in our first model. Interestingly, better exercise performance is associated with lower LV longitudinal deformation but with higher RV longitudinal deformation. This finding is consistent with our previous study.²

Limitations

Examining mixed training type athletes may represent a limitation of our study, as the potentially different effect of only dynamic or only static exercise to LA and LV remodeling could not be investigated. Moreover, the cross-sectional study design did not enable examination of longitudinal changes of LA morphology and function, and we cannot conclude that the features identified are due strictly to the effects of training. Nonetheless, our population of highly trained elite athletes may effectively represent the typical athlete's heart. Athletes were examined only at rest, but changes during exercise testing may be of high interest as well. A further limitation might be that the majority of data regarding LA function were derived from 2D speckle-tracking echocardiographic analysis; therefore, although we quantified similar functional properties of the LA, our 3D results are not directly comparable with previous observations using 2D speckle-tracking echocardiography. On the other hand, 3D analysis of the LA may over-

Table 5 Univariate correlation analysis in athletes

Variable	LAVmax	LA total EF	LA active EF	LA passive EF	VO_2/kg
Age	$r = 0.25$ $P < .01$	$r = -0.13$ $P = .12$	$r = 0.06$ $P = .49$	$r = -0.22$ $P < .01$	$r = -0.02$ $P = .85$
LVEDVi	$r = 0.51$ $P < .001$	$r = -0.06$ $P = .48$	$r = 0.02$ $P = .79$	$r = -0.07$ $P = .43$	$r = 0.33$ $P < .001$
LVMi	$r = 0.39$ $P < .001$	$r = -0.08$ $P = .31$	$r = -0.04$ $P = .61$	$r = -0.06$ $P = .50$	$r = 0.23$ $P < .01$
LVEF	$r = 0.07$ $P = .41$	$r = 0.31$ $P < .001$	$r = 0.23$ $P < .01$	$r = 0.13$ $P = .12$	$r = -0.24$ $P < .01$
LV GLS	$r = -0.02$ $P = .78$	$r = -0.29$ $P < .001$	$r = -0.23$ $P < .01$	$r = -0.13$ $P = .13$	$r = 0.30$ $P < .001$
RVEDVi	$r = 0.35$ $P < .001$	$r = -0.04$ $P = .64$	$r = 0.05$ $P = .56$	$r = -0.09$ $P = .31$	$r = 0.38$ $P < .001$
RVEF	$r = 0.067$ $P = .45$	$r = 0.27$ $P < .01$	$r = 0.14$ $P = .13$	$r = 0.20$ $P < .05$	$r = -0.24$ $P < .01$
RV FWLS	$r = -0.12$ $P = .22$	$r = -0.23$ $P < .05$	$r = -0.07$ $r = 0.48$	$r = -0.21$ $P < .05$	$r = 0.03$ $P = .98$
VO_2/kg	$r = 0.25$ $P < .01$	$r = -0.23$ $P < .01$	$r = 0.01$ $P = .99$	$r = -0.24$ $P < .01$	

Table 6 Multivariate linear regression analysis: independent predictors of VO_2/kg

Covariate	β	P
Age	−0.002	.979
Gender	−0.741	<.001
LAVmax	0.364	<.001
LA total EF	0.012	.880
LA true EF	0.034	.621
LA passive EF	−0.170	.03
LVEDVi	−0.047	.569
LVEF	0.027	.758
LVMi	−0.054	.480
LV GLS	0.212	.001
LV GCS	−0.018	.809
BSA	−0.453	<.001
HR	0.157	.04
Cumulative R	0.722	
Standard error	4.72%	
Cumulative P	<.0000001	

come several shortcomings of 2D echocardiography, such as angulation issues or geometric assumptions.

CONCLUSION

Athlete's heart has distinct features and unique properties that have some overlap with pathologic phenotypes. Athletes' atrial

Table 7 Multivariate linear regression analysis: independent predictors of Vo_2/kg

Covariate	β	P
Age	0.096	.162
Gender	-0.828	<.001
LAVmax	0.222	<.01
LA true EF	0.128	.058
LA passive EF	-0.190	<.01
LVEDVi	0.115	.431
LVMi	-0.054	.611
LV GLS	0.389	<.001
LV GCS	0.055	.42
RVEDVi	0.272	<.01
RV FWLS	-0.133	<.05
BSA	-0.671	<.001
HR	0.268	<.001
Cumulative R	0.792	
Standard error	4.25%	
Cumulative P	<.0000001	

enlargement in our study may not be an expression of dysfunction. Given the lower LV volumes in female athletes compared with male athletes, LA volumes are comparable between genders. Three-dimensional LAVmax and LA passive EF in line with 3D LV GLS are better indicators of exercise capacity than the more commonly used 3D LVEDVi, suggesting that LA remodeling might be an important evaluating step in sports cardiology. Furthermore, we must keep in mind the fact that excellent exercise capacity does not preclude significant pathology. Using advanced echocardiographic techniques in sports cardiology may help elucidate more profound details of exercise physiology and pathophysiology.

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SUPPLEMENTARY DATA

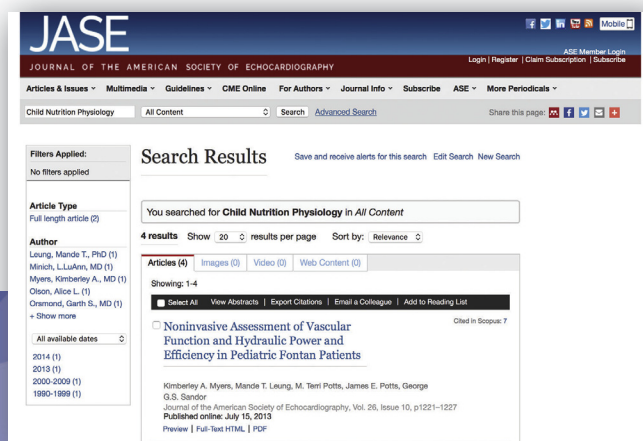
Supplementary data to this article can be found online at <https://doi.org/10.1016/j.echo.2019.07.017>.

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APPENDIX**Supplemental Table 1** Intra- and interobserver variability of key 3D LA parameters

Variable	Intraobserver variability, ICC (95% CI)	Intraobserver variability, CV	Interobserver variability, ICC (95% CI)	Interobserver variability, CV
LAVmax	0.970 (0.920–0.988)	1.6%	0.961 (0.897–0.986)	2.5%
LAVmin	0.974 (0.932–0.990)	3.3%	0.976 (0.940–0.991)	2.6%
LAPreAV	0.974 (0.944–0.988)	3.2%	0.882 (0.744–0.947)	6.1%

CV, Coefficient of variation; ICC, intraclass correlation coefficient.