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Female athlete's heart: Systolic and diastolic function related to circulatory dimensions

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There are relatively few studies on female athletes examining cardiac size and function and how these measures relate to maximal oxygen uptake (VO_{2max}). When determining sports eligibility, it is important to know what physiological adaptations and characteristics may be expected in female athletes, taking body and cardiac size into account. The purposes of this study were (a) to compare right and left heart dimensions and function in female endurance athletes (ATH) and in non-athletic female controls of similar age (CON); and (b) to explore how these measures related to VO_{2max}. Forty-six ATH and 48 CON underwent a maximal bicycle exercise test and an echocardiographic examination at rest, including standard and color tissue Doppler investigation. All heart dimensions indexed for body size were larger in ATH (all $P < 0.01$). The diastolic mitral E/A ratio was 27% higher in ATH ($P < 0.001$) while systolic left and right atrioventricular longitudinal displacement was 7% ($P = 0.002$) and 15% ($P < 0.001$) larger in ATH, respectively. Half (50.3%) of the variability in VO_{2max} could be explained by left ventricular end-diastolic volume. Our results could be useful in evaluating female endurance athletes with suspected cardiac disease and contribute to understanding differences between female athletes and non-athletes.

Echocardiography is one of the tools available for preparticipation screening and in determining sports eligibility (Corrado et al., 2005). This includes measures of cardiac dimensions and, especially in indeterminate cases, cardiac function. As pointed out in a recent meta-analysis upon male athletes (Utomi et al., 2013), the knowledge is limited regarding functional adaptations of the heart in female endurance athletes. This is in part due to the fact that there are relatively few studies in exclusively female athletes including a non-athletic control group.

There is unequivocal evidence of larger left ventricular (LV) dimensions and mass in both male (Pelliccia et al., 1996; Naylor et al., 2008) and female (Pelliccia et al., 1996; Whyte et al., 2004) endurance athletes compared with untrained individuals. However, we know less about adaptations of the right ventricle (RV) and atria (Henriksen et al., 1999; D'Andrea et al., 2013), especially in female athletes. While there are a few previously published studies presenting limited measures of cardiac function in female athletes (George et al., 1999; Henriksen et al., 1999; Guazzi et al., 2001; Whyte et al., 2004), studies utilizing novel echocardiographic modalities such as tissue Doppler imaging in female athletes are lacking.

Endurance sports impose high aerobic demands and female endurance athletes generally have a substantially greater maximal aerobic capacity (VO_{2max}) compared with non-athletic women of similar age (Rubal et al., 1981; Saito & Matushita, 2004). The higher $VO2_{max}$ is to a large extent brought about by cardiac adaptations resulting in larger maximal stroke volume (Bassett & Howley, 2000). The higher maximum stroke volume could theoretically be accomplished by increases in cardiac dimensions, systolic and/or diastolic function, or a combination of these factors. Previous studies have found a relationship between cardiac dimension and VO_{2max} in young men (Osborne et al., 1992) and in female rowers (Saito & Matushita, 2004). How VO_{2max} is related to cardiac systolic and diastolic function in women with different degrees of aerobic fitness is yet to be elucidated. In respect of sports eligibility, the relation of VO_{2max} to cardiac dimension is of importance, as enlarged cavity dimensions paralleled by high aerobic capacity may be seen as a physiological rather than a pathological phenomenon.

The aims of this study were: (a) to determine and compare right and left cardiac dimensions and function in a group of female endurance athletes and in a group of non-athletic women of similar age; and (b) to explore how cardiac dimensions and function relate to VO_{2max} in the same women.

Methods

Subjects

Female athletes (ATH) competing on a national or regional level in a variety of endurance sports were recruited in 2008 to 2009 through contact with their clubs. To be included, athletes needed to be under 26 years of age, had been training for at least five years, and had started dedicated training before the age of 15. Female students not engaged in regular endurance or resistance training and of similar age as ATH were recruited as controls (CON). All subjects had to be healthy, nicotine-free, and non-pregnant. Using the Åstrand classification of aerobic fitness (Åstrand, 1960), we excluded ATH presenting with an aerobic capacity categorized as "average" or lower (i.e., $VO_{2max} < 44$ mL/kg/min), and CON presenting with "high" aerobic fitness according to the same classification (i.e., ≥ 49 mL/kg/min).

In accordance with inclusion and exclusion criteria, the final sample included 46 ATH and 48 CON. Orienteering was the most frequent sport exerted by the athletes ($n = 17$, 37%), followed by mid- and long-distance running ($n = 6$), triathlon ($n = 5$), canoeing ($n = 5$), biathlon ($n = 4$), cycling ($n = 3$), swimming ($n = 3$) and handball ($n = 3$). Athletes trained 13 ± 5 h/week on average and had been competing for 6 ± 2 years. A majority of ATH were among the top athletes in their sport, and six ATH had won medals in world- or European championships, 13 had won medals in national championships, and 11 had medals from junior national championships.

Informed consent was obtained from all subjects and the study was approved by the regional ethical review board in Linköping, Sweden.

Cardiopulmonary exercise testing

Subjects were instructed to refrain from heavy exercise 24 h before examination and keep at least 12 h of alcohol and caffeine abstinence. All participants underwent a maximal upright bicycle cardiopulmonary exercise test including a 6-min steady state workload of 100 W followed by a continuous increment in workload of 10 W each minute until exhaustion, using an electrically braked bicycle ergometer (eBike Basic, GE Medical Systems, GmbH, Freiburg, Germany) with continuous electrocardiographic monitoring (Marquette CASE 8000, GE Medical Systems, Milwaukee, WI, USA). Exhaled air was analyzed on a breath-by-breath basis for O_2 and CO_2 content and presented as 15-s averages (Jaeger Oxycon Pro, Viasys Healthcare, Hoechberg, Germany or MedGraphics CardiO2 and CPX/D Systems, Spiropharma, Denmark). Maximal oxygen consumption (VO_{2max}) was determined as the average of the two highest consecutive measurements. Standard criteria for termination of exercise were used, aiming at VO_2 leveling off and a respiratory exchange ratio > 1.1.

Echocardiographic examination

Echocardiographic examination (utilizing Vivid 7 or Vivid E9, GE Healthcare, Horten, Norway) was carried out just before, or on another day than the exercise test. Subjects were examined at rest in the lateral decubitus position. All data were stored digitally (EchoPAC version BT 11, GE Healthcare, Horten, Norway) enabling offline analysis.

M-mode was utilized for measurements of LV posterior and septal wall thickness in diastole (PWT and SWT, respectively) and LV internal diameter in end-diastole and end-systole (LVIDd and LVIDs, respectively), from which LV fractional shortening (LV-FS) was calculated. LV mass (LVM) and relative wall thickness (RWT) were calculated as: $LVM = 0.8\{1.04[(LVIDd + PWT + SWT)^3 - LVIDd^3] + 0.6\}$ and $RWT = (2\ PWT)LVIDd^{-1}$ (Lang et al., 2006).

Systolic displacements of the mitral and tricuspid annular planes (LV-AVD, RV-AVD, respectively) were measured with M-mode echocardiography at four sites for each annular plane. The apical four-chamber view was used for measuring anterior and posterior parts of the RV-AVD, as well as for the lateral and septal parts of RV-AVD and LV-AVD, while the apical two-chamber view was used for measuring anterior and posterior parts of LV-AVD.

Two-dimensional echocardiography was used for measuring basal diastolic right ventricular (RV) dimension (RVD1) and RV proximal outflow tract diameter (RVOT-Prox) (Rudski et al., 2010), LV length in diastole (LVILd) and left and right atrial areas in systole (LAAs and RAAs). The modified Simpson biplane technique was used for calculating diastolic and systolic LV volumes (LVEDV and LVESV) and LV ejection fraction (LV-EF).

Pulsed-wave Doppler with a sample volume of 5 mm placed at the tip of the mitral leaflets was utilized in the four-chamber view to measure transmitral blood flow. Early diastolic (E) and late diastolic (A) filling velocities were recorded and E/A ratio was calculated. Blood flow velocity was also recorded 5–10 mm into the right pulmonary vein in systole (P_S) and diastole (P_D) and the P_S/P_D ratio was determined.

Color tissue Doppler imaging (TDI) was utilized in offline analysis to measure myocardial peak velocities in systole (s′), early (e′) and late (a′) diastole in the basal LV and RV. Measurements were averaged over two or three cardiac cycles, with markers of aortic valve opening and closure superimposed on color-TDI images, ensuring measurements from ejection and filling phase only. Basal RV velocity was determined by averaging measurements from the RV free wall and septum, while basal LV velocity was calculated by taking the average velocities of basal measurements from septal, anteroseptal, lateral, anterior, posterior, and posterolateral LV wall. The E/e′ ratio was calculated using an average of septal and lateral e′ (Nagueh et al., 2009).

Body surface area (BSA) was used for indexing cardiac morphological measurements, adopting the approach of transferring BSA into the same dimension as the variable being scaled (Batterham & George, 1998). One-dimensional measures (wall thickness, internal dimensions) were indexed by $BSA^{1/2}$ (root BSA), two-dimensional measures (atrial areas) were indexed by BSA and three-dimensional measures (LVM, LVEDV) were scaled by $BSA^{3/2}$ (cubed root BSA). Myocardial peak velocities and systolic displacement were indexed by LVILd, as it has previously been shown that these may be length-dependent because of the basal longitudinal function parameters representing a summation effect of the longitudinal contraction (Batterham et al., 2008).

Statistical analysis

Data are presented as mean ± standard deviation, and range for anthropometric and dimensional variables. Differences in means between ATH and CON were tested with Student's *t*-test, and a *P*-value ≤ 0.05 was considered a statistically significant difference. IBM SPSS Statistics 21 was used for all data analysis (IBM Software, 2012, Armonk, New York, USA).

Correlation analysis was performed to explore relationships between VO_{2max} and dimensional and functional cardiac variables. The strongest correlations were further explored by simple and multiple hierarchical linear regression. Correlation and regression analysis was further used for investigating the influence of heart rate upon diastolic measures and LV length upon systolic longitudinal cardiac function.

Reproducibility

Inter-observer variability was tested against a second, experienced echocardiographist and was together with intra-observer variability explored in 16 randomly selected subjects by using the S-method first proposed by Dahlberg (1948): $S_{\text{method}} = \sqrt{\left(\sum d_i^2/2n\right)}$, where d_i is the difference between the i:th paired measurement and n is the number of differences. The covariance (in percent) was then calculated as the coefficient of variation (%COV) by dividing S_{method} by overall means. Inter-observer COV: LV length (average of systolic and diastolic length) 4.8%, LVEDV 7.6%, LV-EF 5.6%, RV dimension (average of RVOT-prox and RVD1) 7.2% and TDI-variables (average of S′, E′ and A′ measurements in four myocardial regions) 9.4%. Intra-observer COV: LV length 5.5%, LVEDV 10.7%, LV-EF 4.7%, RV dimension 8.4% and TDI-variables 10.7%.

Furthermore, the single measure intra-class correlation coefficient (ICC) was calculated for inter- and intra-observer variability in an absolute agreement two-way mixed model. Inter-observer ICC: LV length 0.70, LVEDV 0.91, LV-EF 0.59, RV dimension 0.72 and TDI-variables 0.85. Intra-observer ICC: LV length 0.71, LVEDV 0.82, LV-EF 0.71, RV dimension 0.64 and TDI-variables 0.78.

Results

Subject characteristics and data from exercise testing are presented in Table 1.

Echocardiographic data

Athletes presented with biventricular and bi-atrial enlargement compared with CON, with and without indexing by the appropriate power of BSA (Table 2). After indexing, one-dimensional variables were 5–13% larger in ATH compared with CON, while two- and three-dimensional variables were 25–35% larger in ATH. Relative wall thickness was similar between groups (0.33 ± 0.05 in both ATH and CON, $P = 0.998$) while eccentric hypertrophy (i.e., LVM/BSA > 95 g/m^2 and RWT ≤ 0.42) (Lang et al., 2006) was apparent in 19 (41%) of the ATH and in two (4%) of the CON.

M-mode derived measures of LV and RV longitudinal function were 7% and 15% higher in ATH than in CON, respectively (Table 3), while systolic myocardial peak velocity in the basal RV was 9% higher in ATH. Significant correlations were seen between LV length (LVILd) and LV-AVD ($r = 0.379$, $P < 0.001$), LV-s′ ($r = 0.359$, $P = 0.001$) and RV-AVD ($r = 0.412$, $P < 0.001$), but not with RV-s′. Regression models are presented in Fig. 1. Indexing longitudinal displacement and peak myocardial velocities by LVILd modified the statistically significant differences, as seen in Table 3.

LV mitral inflow velocities at rest were different between groups (Table 4). The 27% higher E/A ratio in ATH was the result of statistically significant higher E-wave (+8%) and lower A-wave (−13%) velocities in ATH. LV-E/e′ ratio was similar in ATH and CON. Significant correlations were seen between HR and A ($r = 0.534$, $P < 0.001$), E/A ($r = -0.477$, $P < 0.001$), LV-a′ ($r = 0.404$, $P < 0.001$) and LV-e′/a′ ($r = -0.400$, $P < 0.001$). Regression models are presented in Fig. 2. The E-wave, LV-e′ and RV diastolic measures were found to be independent of HR, both in the whole group and in ATH and CON groups separately.

Aerobic capacity related to echocardiographic parameters

VO_{2max} correlated to a higher extent with dimensional variables than any systolic or diastolic functional measurement, and relationships remained moderately strong when correlating VO_{2max} with LVEDV and LVM indexed by cubed root BSA (Table 5). After indexing measures of longitudinal function by LV length, only RV-AVD remained statistically significant when correlated with VO_{2max} ($r = 0.357$, $P = 0.001$).

The univariate regression model for LVEDV as single determinant of VO_{2max} (mL) was 742 + (20 × LVEDV), with R^2 0.503 ($P < 0.001$). Entering the most highly correlated dimensional, systolic and diastolic variable into a stepwise multiple regression resulted in a model with an adjusted R^2 of 0.547 ($P < 0.001$) with the following equation: VO_{2max} (mL) = −130 + (15 × LVEDV) + (53

Table 1. Subject characteristics and data from cardiopulmonary exercise testing

	Athletes ($n = 46$)	Controls ($n = 48$)	P
Age (years)	21 ± 2 (17–26)	21 ± 2 (17–26)	0.743
Weight (kg)	61 ± 6 (45–77)	58 ± 6 (41–75)	**0.009**
Height (m)	1.68 ± 0.06 (1.55–1.79)	1.66 ± 0.05 (1.50–1.78)	**0.028**
BSA (m^2)	1.69 ± 0.10 (1.42–1.88)	1.63 ± 0.09 (1.39–1.86)	**0.008**
SBP (mm Hg)	112 ± 11 (90–140)	111 ± 9 (95–140)	0.804
DBP (mm Hg)	65 ± 6 (50–80)	68 ± 8 (60–85)	0.065
HR_{REST} (beats/min)	54 ± 8 (38–71)	71 ± 10 (54–91)	**<0.001**
VO_{2max} (L/min)	3.2 ± 0.3 (2.5–4.2)	2.3 ± 0.4 (1.5–3.1)	**<0.001**
VO_{2max} (mL/kg/min)	52 ± 5 (44–64)	39 ± 5 (28–48)	**<0.001**

Data presented as mean ± standard deviation (range).

Bold styling denotes statistical significance.

BSA, body surface area; DBP, diastolic blood pressure; HR_{REST}, resting heart rate; SBP, systolic blood pressure; VO_{2max}, maximum oxygen uptake.

Table 2. Cardiac dimensions, LV volume and mass

	LAAs* (cm^2)	SWT† (mm)	PWT† (mm)	LVM‡ (g)	LVIDd† (mm)	LVILd† (mm)	LVEDV‡ (mL)	RAAs* (cm^2)	RVOT-Prox† (mm)	RVD1† (mm)
Absolute measurements										
Athletes (*n* = 46)§	18 ± 3 (12–23)	8.7 ± 1 (7–12)	8.4 ± 1 (6–10)	156 ± 25(102–220)	51 ± 3 (44–57)	85 ± 5 (75–96)	114 ± 19 (80–149)	16 ± 3 (10–23)	29 ± 3 (20–36)	35 ± 5 (23–42)
Controls (*n* = 48)	14 ± 3 (8–19)	7.8 ± 1 (4–10)	7.6 ± 1 (6–11)	114 ± 24 (61–175)	46 ± 3 (39–54)	79 ± 5 (70–92)	86 ± 13 (61–119)	11 ± 2 (6–15)	26 ± 4 (17–34)	31 ± 4 (24–42)
P	**<0.001**	**<0.001**	**0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.001**
Measurements indexed by the appropriate power of body surface area										
Athletes	10 ± 2	6.7 ± 1	6.5 ± 1	71 ± 11	40 ± 3	65 ± 4	52 ± 7	9 ± 2	23 ± 3	27 ± 3
Controls	8 ± 1	6.1 ± 1	6.0 ± 1	55 ± 11	36 ± 2	62 ± 4	41 ± 6	7 ± 1	20 ± 3	25 ± 3
P	**<0.001**	**0.001**	**0.004**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**<0.001**	**0.004**

*Indexed by BSA.

†Indexed by root BSA.

‡Indexed by cubed root BSA.

§Image quality did not permit data acquisition of RVOT-prox in 3 ATH and RVD1 in 1 CON.

Data presented as mean ± standard deviation and (range) for absolute measurements.

Bold styling denotes statistical significance.

LAAs, left atrial area in systole; LVEDV, left ventricular end-diastolic volume; LVIDd and LVILd, left ventricular internal diameter and internal length in diastole, respectively; LVM, left ventricular mass; PWT, posterior wall thickness; RAAs, right atrial area in systole; RVD1, right ventricular basal internal diameter in diastole; RVOT-Prox, proximal right ventricular outflow tract diameter in diastole; SWT, septal wall thickness.

Table 3. Measures of systolic function

	Athletes (*n* = 46)	Controls (*n* = 48)*	*P*
LV-EF (%)	59 ± 4	57 ± 4	**0.039**
LV-FS (%)	36 ± 4	34 ± 4	**0.024**
LV-AVD (mm)	15 ± 2	14 ± 1	**0.002**
$LV\text{-}AVD_{index}$	1.8 ± 0.2	1.8 ± 0.2	0.940
RV-AVD (mm)	21 ± 2	19 ± 2	**<0.001**
$RV\text{-}AVD_{index}$	2.5 ± 0.3	2.3 ± 0.3	**0.001**
LV-s'(cm/s)	6.7 ± 0.7	6.7 ± 0.8	0.761
$LV\text{-}s'_{index}$	0.79 ± 0.08	0.84 ± 0.10	**0.024**
RV-s'(cm/s)	8.9 ± 1.1	8.2 ± 0.9	**0.001**
$RV\text{-}s'_{index}$	1.06 ± 0.15	1.04 ± 0.12	0.551

*Image quality did not permit data acquisition of RV-AVD in 2 ATH and LV-s' in 5 CON.

Bold styling denotes statistical significance.

AVD, atrioventricular-plane displacement; EF, ejection fraction; FS, fractional shortening; $_{index}$, denotes indexing by diastolic LV length in cm; LV and RV, left and right ventricular; s', peak systolic myocardial velocity.

× RV-AVD) + (115 × E/A). Three univariate regression models are presented in Fig. 3, where RVOT-Prox and RVD1 were condensed into one variable and LAAs and RAAs into another.

Discussion

We found that endurance-trained female athletes presented with substantial bi-atrial and biventricular dimensional remodeling compared with non-athletes, as well as with differences in systolic and diastolic functional characteristics at rest.

Cardiac dimensions

Our sample of female endurance athletes showed classic features of "athletes's heart", including lower HR at rest and elevated LV dimensions, volume, and mass. In addition, we found a proportional enlargement of the RV and both atria, and all differences remained statistically significant when indexing by BSA, indicating that the athletes in this study were highly trained. Several variables were larger than published reference values for healthy women (Lang et al., 2006). No athlete exceeded a RWT of 0.42 while 12 (26%) had enlarged LVIDd (54–57 mm), 16 (35%) had a wall thickness above reference (10–12 mm) and 26 (57%) had a LVM above reference values (152–220 g). These findings corroborate a previous large-scale study in female endurance athletes (Pelliccia et al., 1996), and a meta-analysis suggested higher upper limits for LVIDd and wall thickness in female endurance athletes (Whyte et al., 2004).

Current guidelines for measurement of right heart dimensions and function only present upper reference limits for a healthy population of intermixed ages and sex (Rudski et al., 2010). The RV and RA in female athletes have rarely been studied. One of our athletes had a RVOT-Prox 1 mm above this 95% confidence limit reference value (>35 mm) and six (13%) athletes

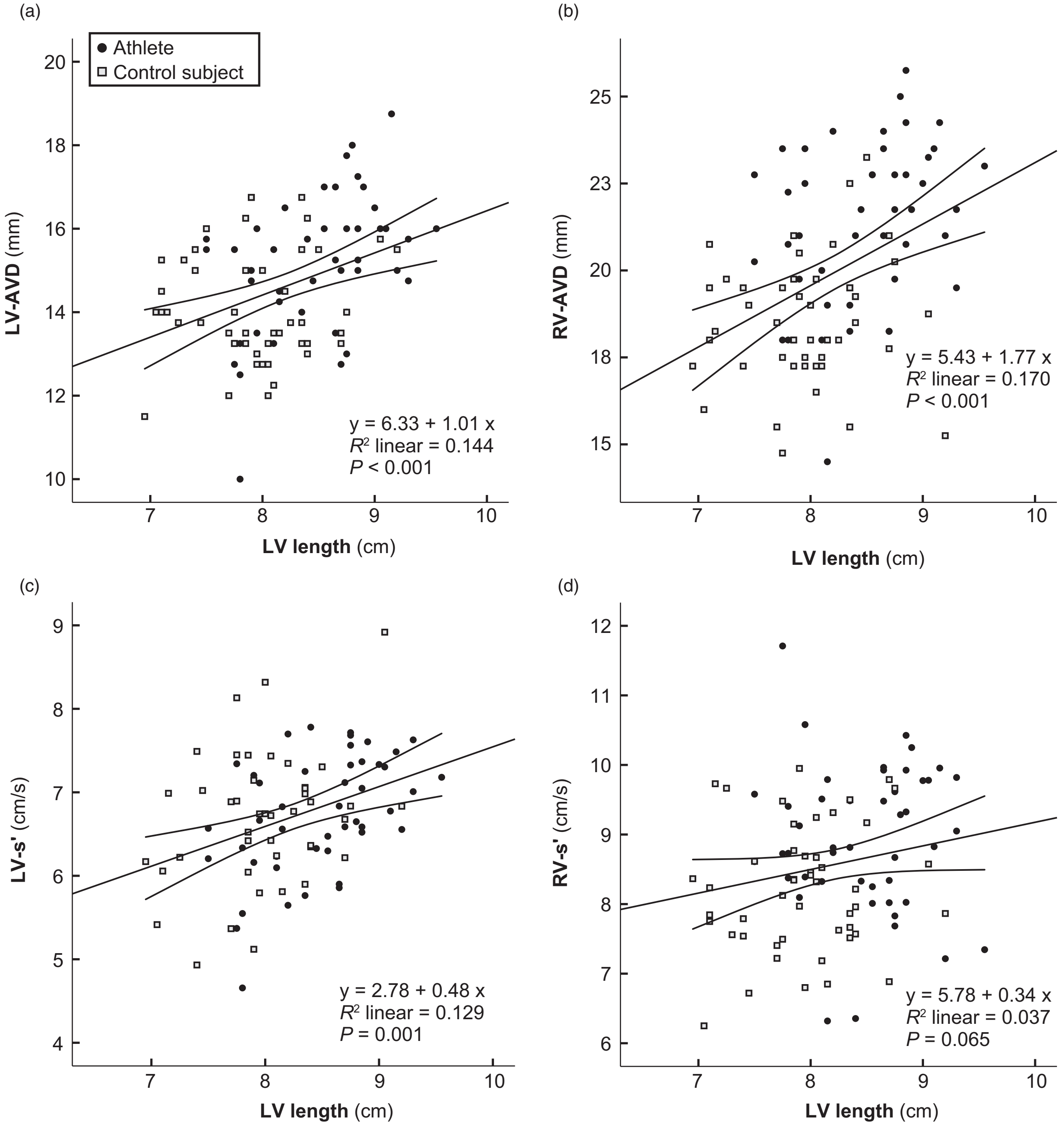

Fig. 1. Measures of systolic left and right ventricular longitudinal function as a function of left ventricular (LV) length. Panel 1a and 1b show dependency of left- and right atrio-ventricular displacement (LV-AVD, RV-AVD, respectively) on left ventricular length, measured in diastole. Systolic peak myocardial velocities (s′) in the basal left (panel 1c) but not basal right (panel 1d) ventricle could partially be explained by LV length. Fit-line for all subjects presented with 95% confidence limits of the mean.

exceeded the upper RAAs reference of > 18 mm^2 (19–23 mm^2), whereas none of the controls exceeded upper reference limits. It is noteworthy that the mean values of RV measurements found in ATH in the current study are almost identical to those found by Henriksen et al. (1999) in elite female orienteers, and a recent study in a mixed sample of men and women found differences between athletes and controls of similar magnitude as in the present study (D'Andrea et al., 2013).

Systolic function

Systolic displacement of the left and right atrio-ventricular planes was larger in ATH, paralleled by higher RV-s′ (but not LV-s′) in ATH, which could imply that at least the RV adapts to training with increases in longitudinal motion. Others have shown that about 60% of the LV stroke volume in both athletes and untrained subjects comes from displacement of the

Table 4. Measures of diastolic function

	Athletes (n = 46)*	Controls (n = 48)	P
E (m/s)	0.92 ± 0.17	0.86 ± 0.11	**0.029**
A (m/s)	0.34 ± 0.09	0.39 ± 0.09	**0.007**
E/A	2.9 ± 0.9	2.3 ± 0.7	**<0.001**
P_S (m/s)	0.49 ± 0.10	0.45 ± 0.10	0.080
P_D (m/s)	0.62 ± 0.11	0.58 ± 0.11	0.065
P_S/P_D	0.82 ± 0.21	0.82 ± 0.26	0.998
LV-e' (cm/s)	12.2 ± 1.5	11.8 ± 1.2	0.156
RV-e' (cm/s)	12.0 ± 1.6	11.6 ± 1.6	0.274
LV-a' (cm/s)	3.2 ± 0.8	3.4 ± 0.9	0.197
RV-a' (cm/s)	5.3 ± 1.4	5.1 ± 1.5	0.584
LV-e'/a'	4.0 ± 1.2	3.6 ± 0.9	0.063
RV-e'/a'	2.4 ± 0.7	2.5 ± 0.9	0.728
LV-E/e'	7.8 ± 2.0	7.4 ± 1.1	0.318

*Image quality did not permit data acquisition of E in 1 ATH; LV-e' in 6 CON; LV-a' in 5 CON and RV-a' in 3 CON.
Bold styling denotes statistical significance.
E and A, early and late diastolic inflow velocities into the LV; LV and RV, left and right ventricular; e' and a', early and late diastolic myocardial peak velocities, respectively; P_S and P_D, systolic and diastolic blood velocities in the pulmonary vein, respectively.

atrio-ventricular plane (Carlsson et al., 2007). It is noteworthy and of importance that the differences in longitudinal cardiac function were altered after indexing by cardiac length, with eradication of statistically significant larger LV-AVD and RV-s′ in ATH, and introduction of a statistically significant higher LV-s′ in CON.

Previous results are conflicting regarding left and right ventricular adaptation in longitudinal systolic function following endurance training. In studies upon predominantly male subjects, higher LV-AVD (Carlhall et al., 2001) and LV-s′ (Caso et al., 2002; Koc et al., 2007) have been shown in ATH, while other report similar LV-AVD (Wisloff et al., 2001) and LV-s′ (Pela et al., 2004; Poh et al., 2008) in ATH and CON. RV-s′ is consistently reported higher in athletes (Caso et al., 2002; Pela et al., 2004; Koc et al., 2007; Poh et al., 2008) while one study (Carlhall et al., 2001) report higher RV-AVD in male ATH than in CON.

Although Batterham et al. (2008) previously pointed out that LV elongation in athletes is important as this may influence longitudinal function, all but one (Pela et al., 2004) of previous studies comparing athletes with control subjects have refrained from indexing by LVILd. The basal displacement and velocities in the heart may be seen as total longitudinal myocyte contraction along the LV and RV walls, and both LV-AVD and myocardial velocities have been shown to increase from the apex toward the base (Carlsson et al., 2007; Krieg et al., 2007). As LVILd is measured from the base to the apex, it may be seen to represent total cardiac length and may be used for indexing RV as well as LV length. We concur with previous authors (Pela et al., 2004; Krieg et al., 2007; Batterham et al., 2008) suggesting that the results of studies presenting differences in non-indexed longitudinal velocities should be interpreted cautiously.

Diastolic function

We found enhanced measures of diastolic LV function at rest in ATH, which could reflect more efficient LV relaxation. Our finding of higher E-wave velocity in ATH compared with CON is of special interest, as the E-wave, in contrast to the A-wave and E/A ratio, was found to be independent of heart rate. As the A-wave is thought to decrease with lower HR, as atrial contraction becomes less important with longer LV filling time, bradycardia in athletes with consequent decrease in A-wave velocity is suggested to account for the common finding of increased E/A ratios in athletes (Pelliccia et al., 1996; Whyte et al., 2004). The difference in E/A ratio in this study may thus partly be explained by a lower HR at rest in ATH, but the higher E indicates a true difference in LV relaxation, and thereby diastolic function at rest.

Enhanced E-wave velocity in female ATH has to our knowledge not been reported previously. Pelliccia et al. (1996) reported higher E/A ratio in female athletes, attributed to lower A in athletes, while others report similar E/A ratios in different populations of trained vs untrained women (George et al., 1999; Guazzi et al., 2001). However, there are studies that provide support for an enhanced mitral E-wave velocity in populations that include both male and female athletes (Palka et al., 1999; Zoncu et al., 2002; D’Andrea et al., 2013) and in male athlete groups (Karjalainen et al., 1997; Nottin et al., 2004; Baggish et al., 2010).

Diastolic RV function in female athlete vs control comparisons has been reported being similar (Guazzi et al., 2001), while one study in male athletes found higher RV-e′ in ATH (Popovic et al., 2011). This discrepancy could be due to different populations of athletes regarding type of sport, training dose or possibly on a sex-related difference in how the RV adapts to exercise. However, Baggish et al. (2008) report similar RV diastolic myocardial velocities in male and female rowers prior to 90 days of training.

Aerobic capacity related to cardiac dimensions and function

We found that LVEDV could explain 50% of the variability in VO_{2max}, while inclusion of RV-AVD and E/A into the model had little impact on the ability to predict VO_{2max}. Nevertheless, there were statistically significant correlations between measures of systolic and diastolic function and VO_{2max}, which may indicate that differences in diastolic and systolic function between ATH and CON may contribute to an ability of ATH to achieve higher VO_{2max}.

Previously, Saito and Matushita (2004) have found a strong correlation between LVM and VO_{2max} and athletic performance in 22 female rowers. A strong relationship between LVM and VO_{2max} was also found in studies utilizing cardiac magnetic resonance imaging in male and female subjects (Steding et al., 2010; La Gerche et al., 2012). However, there are authors reporting RV

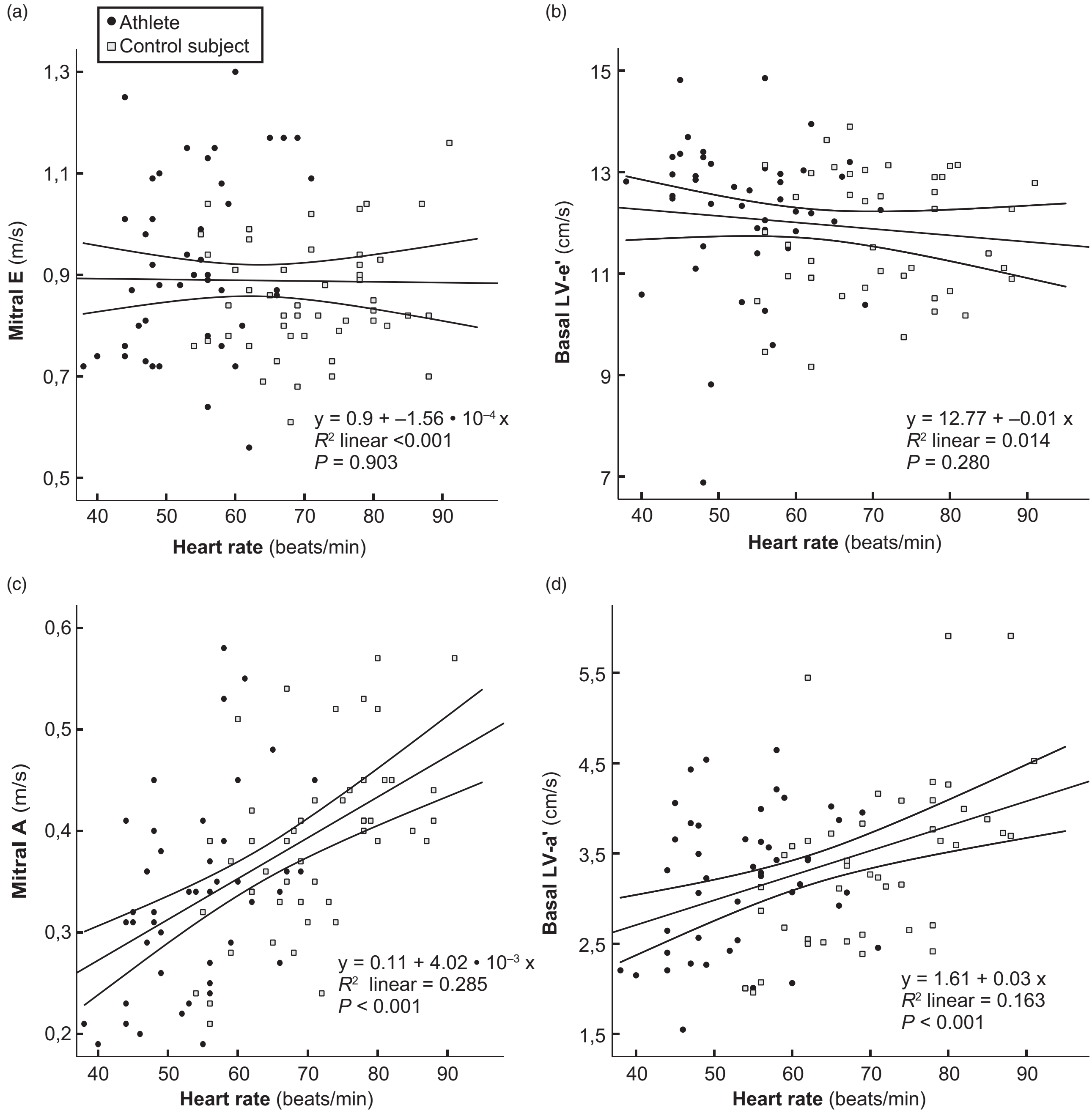

Fig. 2. Left ventricular (LV) diastolic measures and associations with heart rate at rest. Panels 2a and 2b present independency of early diastolic blood flow velocity over the mitral valve (E) and basal left ventricular myocardial peak velocities in early diastole (LV-e′) from heart rate at rest. Panels 2c and 2d show how late diastolic blood flow velocity over the mitral valve (A) and late diastolic myocardial velocities in the basal LV (LV-a′) were partially explained by heart rate at rest. Fit-line for all subjects presented with 95% confidence limits of the mean.

function rather than RV dimension (Popovic et al., 2011) and LV function rather than LV dimensions (Vanoverschelde et al., 1993) as predictors for VO_{2max}.

Comparisons between male and female athletes lie beyond the scope of this article. However, we believe several aspects of the current results are noteworthy regardless of sex, including the finding of a dependency of mitral A-wave and LV-a′ on heart rate and the need to take LV length into account when interpreting longitudinal systolic function. Furthermore, applying the approach of scaling cardiac dimensions by the appropriate power of BSA may aid in future comparisons between male and female athletes, as this may prevent over- and underestimating the influence of differences in body composition between sexes.

Limitations

The cross-sectional design has built-in limitations in determining causality, and thus, we cannot rule out the

Table 5. Correlations between maximal oxygen uptake (L/min) and dimensional and functional measurements in whole sample of females

Dimensional variables*	Absolute values	Indexed values†	Systolic variables		Diastolic variables	
LVEDV (mL)	$r = 0.709$ **$P < 0.001$**	$r = 0.562$ **$P < 0.001$**	RV-AVD (mm)	$r = 0.592$ **$P < 0.001$**	E/A	$r = 0.319$ **$P = 0.002$**
LVM (g)	$r = 0.692$ **$P < 0.001$**	$r = 0.534$ **$P < 0.001$**	RV-s' (cm/s)	$r = 0.396$ **$P < 0.001$**	LV-e' (cm/s)	$r = 0.254$ **$P = 0.017$**
RAAs (cm^2)	$r = 0.641$ **$P < 0.001$**	$r = 0.541$ **$P < 0.001$**	LV-EF (%)	$r = 0.351$ **$P = 0.001$**	E (m/s)	$r = 0.245$ **$P = 0.018$**
LVIDd (mm)	$r = 0.608$ **$P < 0.001$**	$r = 0.456$ **$P < 0.001$**	LV-AVD (mm)	$r = 0.320$ **$P = 0.002$**	A (m/s)	$r = -0.238$ **$P = 0.021$**
LAAs (cm^2)	$r = 0.604$ **$P < 0.001$**	$r = 0.503$ **$P < 0.001$**			P_D (m/s)	$r = 0.221$ **$P = 0.033$**

*Only the five strongest statistically significant correlations are presented for each set of variables.
†Dimensional variables indexed by different powers of body surface area, see Table 2 for details.
Bold styling denotes statistical significance.
For abbreviations, see Tables 2–4.

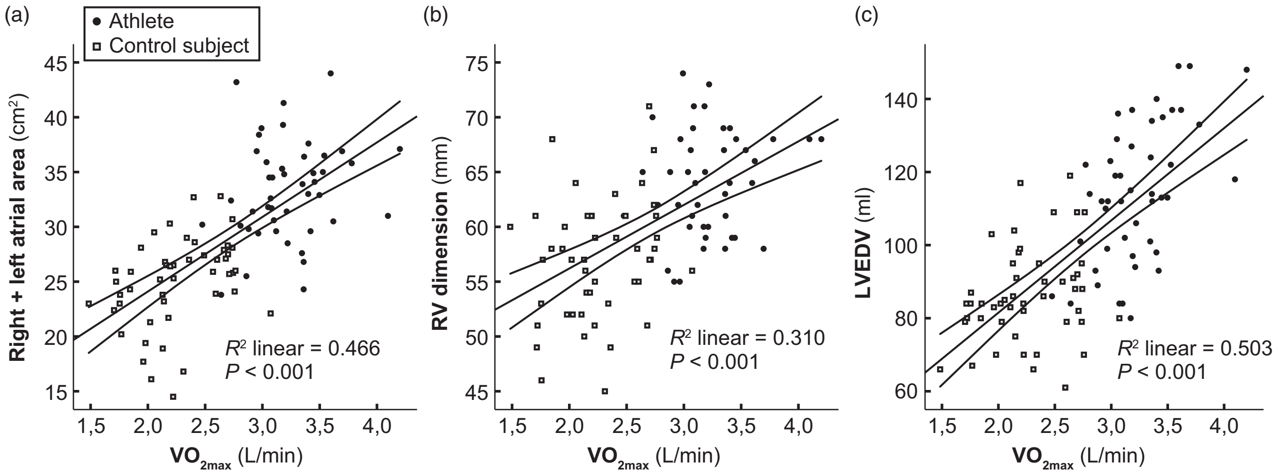

Fig. 3. Univariate regression models for predicting maximal oxygen uptake (VO_{2max}). Panels 3a-b show relationship between VO_{2max} and the sum of left and right atrial area (3a) and sum of right inflow (RVD1) and outflow tract (RVOT-Prox) dimensions (3b). Panel 3c shows relationship between left ventricular end-diastolic volume and VO_{2max}. Fit-line for all subjects presented with 95% confidence limits of the mean.

possibility that the differences between athletes and controls were due to constitutional factors. However, to reduce this risk we present cardiac dimensions indexed by body size and functional variables by heart size, and cardiac dimensions were still highly statistically different between groups. The present study was designed for echocardiographic measurements at rest only which leaves us without data during exercise, and how this relates to aerobic capacity.

Perspectives

For the physiologist interested in differences between cardiac function and dimensions in trained vs untrained women, this study adds knowledge by presenting exclusively female athletes and age-matched controls. Data regarding longitudinal function, as well as atrial and right ventricular measurements are scarce regarding female athletes, and our data may provide support in decisions on sports eligibility. We also provide data on the cardiac determinants of VO_{2max} in women, which may be helpful in understanding differences between athletes and controls.

Furthermore, our results imply that scaling measures of longitudinal heart function by cardiac length is important when comparing athletes with cardiac enlargement with controls, which is a practice not routinely applied. We have shown that some measurements of diastolic function are influenced by heart rate, which must be taken into account in interpreting differences between athletes and controls.

Key words: Echocardiography, sports cardiology, maximal oxygen uptake, endurance exercise, diastolic function.

References

Baggish AL, Wang F, Weiner RB, Elinoff JM, Tournoux F, Boland A, Picard MH, Hutter Jr AM, Wood MJ. Training-specific changes in cardiac structure and function: a prospective and longitudinal assessment of competitive athletes. J Appl Physiol 2008: 104 (4): 1121–1128.

Baggish AL, Yared K, Weiner RB, Wang F, Demes R, Picard MH, Hagerman F, Wood MJ. Differences in cardiac parameters among elite rowers and subelite rowers. Med Sci Sports Exerc 2010: 42 (6): 1215–1220.

Bassett DR Jr, Howley ET. Limiting factors for maximum oxygen uptake and determinants of endurance performance. Med Sci Sports Exerc 2000: 32 (1): 70–84.

Batterham A, Shave R, Oxborough D, Whyte G, George K. Longitudinal plane colour tissue-Doppler myocardial velocities and their association with left ventricular length, volume, and mass in humans. Eur J Echocardiogr 2008: 9 (4): 542–546.

Batterham AM, George KP. Modeling the influence of body size and composition on M-mode echocardiographic dimensions. Am J Physiol 1998: 274 (2 Pt 2): H701–H708.

Carlhall CJ, Lindstrom L, Wranne B, Nylander E. Atrioventricular plane displacement correlates closely to circulatory dimensions but not to ejection fraction in normal young subjects. Clin Physiol 2001: 21 (5): 621–628.

Carlsson M, Ugander M, Mosen H, Buhre T, Arheden H. Atrioventricular plane displacement is the major contributor to left ventricular pumping in healthy adults, athletes, and patients with dilated cardiomyopathy. Am J Physiol Heart Circ Physiol 2007: 292 (3): H1452–H1459.

Caso P, Galderisi M, Galderisi M, D'Andrea A, Di Maggio D, De Simone L, Martiniello AR, Mininni N, Calabro R, Sutherland GR. Analysis by pulsed Doppler tissue imaging of ventricular interaction in long-distance competitive swimmers. Am J Cardiol 2002: 90 (2): 193–197.

Corrado D, Pelliccia A, Bjornstad HH, Vanhees L, Biffi A, Borjesson M, Panhuyzen-Goedkoop N, Deligiannis A, Solberg E, Dugmore D, Mellwig KP, Assanelli D, Delise P, van-Buuren F, Anastasakis A, Heidbuchel H, Hoffmann E, Fagard R, Priori SG, Basso C, Arbustini E, Blomstrom-Lundqvist C, McKenna WJ, Thiene G. Cardiovascular pre-participation screening of young competitive athletes for prevention of sudden death: proposal for a common European protocol. Consensus Statement of the Study Group of Sport Cardiology of the Working Group of Cardiac Rehabilitation and Exercise Physiology and the Working Group of Myocardial and Pericardial Diseases of the European Society of Cardiology. Eur Heart J 2005: 26 (5): 516–524.

Dahlberg G. Errors of estimation. Statistical methods for medical and biological students. London; George Allen & Unwin Ltd, 1948: 122–132.

D'Andrea A, Riegler L, Golia E, Cocchia R, Scarafile R, Salerno G, Pezzullo E, Nunziata L, Citro R, Cuomo S, Caso P, Di Salvo G, Cittadini A, Russo MG, Calabro R, Bossone E. Range of right heart measurements in top-level athletes: the training impact. Int J Cardiol 2013: 164 (1): 48–57.

George KP, Gates PE, Whyte G, Fenoglio RA, Lea R. Echocardiographic examination of cardiac structure and function in elite cross trained male and female Alpine skiers. Br J Sports Med 1999: 33 (2): 93–98.

Guazzi M, Musante FC, Glassberg HL, Libonati JR. Detection of changes in diastolic function by pulmonary venous flow analysis in women athletes. Am Heart J 2001: 141 (1): 139–147.

Henriksen E, Landelius J, Kangro T, Jonason T, Hedberg P, Wesslen L, Rosander CN, Rolf C, Ringqvist I, Friman G. An echocardiographic study of right and left ventricular adaptation to physical exercise in elite female orienteers. Eur Heart J 1999: 20 (4): 309–316.

Karjalainen J, Mantysaari M, Viitasalo M, Kujala U. Left ventricular mass, geometry, and filling in endurance athletes: association with exercise blood pressure. J Appl Physiol 1997: 82 (2): 531–537.

Koc M, Bozkurt A, Akpinar O, Ergen N, Acarturk E. Right and left ventricular adaptation to training determined by conventional echocardiography and tissue Doppler imaging in young endurance athletes. Acta Cardiol 2007: 62 (1): 13–18.

Krieg A, Scharhag J, Kindermann W, Urhausen A. Cardiac tissue Doppler imaging in sports medicine. Sports Med 2007: 37 (1): 15–30.

La Gerche A, Burns AT, Taylor AJ, Macisaac AI, Heidbuchel H, Prior DL. Maximal oxygen consumption is best predicted by measures of cardiac size rather than function in healthy adults. Eur J Appl Physiol 2012: 112 (6): 2139–2147.

Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise J, Solomon S, Spencer KT, St John Sutton M, Stewart W. Recommendations for chamber quantification. Eur J Echocardiogr 2006: 7 (2): 79–108.

Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, Waggoner AD, Flachskampf FA, Pellikka PA, Evangelisa A. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. Eur J Echocardiogr 2009: 10 (2): 165–193.

Naylor LH, George K, O'Driscoll G, Green DJ. The athlete's heart: a contemporary appraisal of the 'Morganroth hypothesis'. Sports Med 2008: 38 (1): 69–90.

Nottin S, Nguyen LD, Terbah M, Obert P. Left ventricular function in endurance-trained children by tissue Doppler imaging. Med Sci Sports Exerc 2004: 36 (9): 1507–1513.

Osborne G, Wolfe LA, Burggraf, GW, Norman R. Relationships between cardiac dimensions, anthropometric characteristics and maximal aerobic power (VO2max) in young men. Int J Sports Med 1992: 13 (3): 219–224.

Palka P, Lange A, Nihoyannopoulos P. The effect of long-term training on age-related left ventricular changes by Doppler myocardial velocity gradient. Am J Cardiol 1999: 84 (9): 1061–1067.

Pela G, Bruschi G, Montagna L, Manara M, Manca C. Left and right ventricular adaptation assessed by Doppler tissue echocardiography in athletes. J Am Soc Echocardiogr 2004: 17 (3): 205–211.

Pelliccia A, Maron BJ, Culasso F, Spataro A, Caselli G. Athlete's heart in women. Echocardiographic characterization of highly trained elite female athletes. JAMA 1996: 276 (3): 211–215.

Poh KK, Ton-Nu TT, Neilan TG, Tournoux FB, Picard MH, Wood MJ. Myocardial adaptation and efficiency in response to intensive physical training in elite speedskaters. Int J Cardiol 2008: 126 (3): 346–351.

Popovic D, Damjanovic S, Markovic V, Vujisic-Tesic B, Petrovic M, Nedeljkovic, Arandjelovic A, Popovic B, Jakovljevic B, Stojiljkovic S, Ostojic SM. Systolic right ventricular adaptive changes in athletes as predictors of the maximal functional capacity: a pulsed tissue Doppler study. J Sports Med Phys Fitness 2011: 51 (3): 452–461.

Rubal BJ, Rosentswieg J, Hamerly B. Echocardiographic examination of

women collegiate softball champions. Med Sci Sports Exerc 1981: 13 (3): 176–179.
Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, Solomon SD, Louie EK, Schiller NB. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr 2010: 23 (7): 685–713, quiz 786–788.
Saito K, Matushita M. The contribution of left ventricular mass to maximal oxygen uptake in female college rowers. Int J Sports Med 2004: 25 (1): 27–31.
Steding K, Engblom H, Buhre T, Carlsson M, Mosen H, Wohlfart B, Arheden H. Relation between cardiac dimensions and peak oxygen uptake. J Cardiovasc Magn Reson 2010: 12 (1): 8.
Utomi V, Oxborough D, Whyte GP, Somauroo J, Sharma S, Shave R, Atkinson G, George K. Systematic review and meta-analysis of training mode, imaging modality and body size influences on the morphology and function of the male athlete's heart. Heart 2013: 99 (23): 1727–1733.
Vanoverschelde JJ, Essamri B, Vanbutsele R, d'Hondt A, Cosyns JR, Detry JR, Melin JA. Contribution of left ventricular diastolic function to exercise capacity in normal subjects. J Appl Physiol 1993: 74 (5): 2225–2233.
Whyte GP, George K, Nevill A, Shave R, Sharma S, McKenna WJ. Left ventricular morphology and function in female athletes: a meta-analysis. Int J Sports Med 2004: 25 (5): 380–383.
Wisloff U, Helgerud J, Stoylen A, Ellingsen O. Atrioventricular plane displacement in female endurance athletes. Med Sci Sports Exerc 2001: 33 (9): 1503–1510.
Zoncu S, Pelliccia A, Mercuro G. Assessment of regional systolic and diastolic wall motion velocities in highly trained athletes by pulsed wave Doppler tissue imaging. J Am Soc Echocardiogr 2002: 15 (9): 900–905.
Åstrand I. Aerobic work capacity in men and women with special reference to age. Acta Physiol Scand Suppl 1960: 49 (169): 1–92.