Sex Differences in Ventricular Remodeling and Function in College Athletes, Insights from Lean Body Mass Scaling and Deformation Imaging

Geneviève Giraldeau, MD [a,b], Yukari Kobayashi, MD [a,b], Gherardo Finocchiaro MD [a,b], Matthew Wheeler MD PhD [a,b], Marco Perez MD [a,b], Tatiana Kuznetsova MD PhD [b,c], Rachel Lord PhD [d], Keith P. George MD PhD [d], David Oxborough PhD [d], Ingela Schnittger MD [a,b], Victor Froelicher MD [a,b], David Liang, MD PhD [a,b], Euan Ashley MRCP, DPhil [a,b] *, and François Haddad, MD [a,b] *

a. Division of Cardiovascular Medicine, Stanford University School of Medicine, Stanford, CA

b. Stanford Cardiovascular Institute, Stanford, CA

c. Division of Epidemiology and Research, Leuven University, Belgium

d. Liverpool, John Moores University, United Kingdom

***** Both authors are equivalent last authors and equally mentored the project

Running title: Sex Differences in Athletic Remodeling

Address of correspondence: Please address correspondence to Francois Haddad, MD FAHA, Stanford Cardiovascular Institute, 300 Pasteur Drive, Palo Alto, CA, 94304; Telephone: (650) 723-8138, Fax: (650) 724-4034' Email: fhaddad@stanford.edu,

Grant support: The work was supported by the Stanford Cardiovascular Institute and the Pai Chan Lee Research Fund

ABSTRACT

Several studies suggest sex-differences in ventricular dimensions in athletes. Few studies have, however, made comparisons of data indexed for lean body mass (LBM) using allometry. Ninety Caucasian college athletes (mixed-sports) who were matched for age, ethnicity and sport total cardiovascular demands, underwent Dual Energy X-Ray Absorptiometry (DEXA) scan for quantification of LBM. Athletes underwent comprehensive assessment of left and right ventricular and atrial structure and function using 2D echocardiography as well as deformation imaging using the TOMTEC analysis system. The mean age of the study population was 18.9±1.9 years. Female athletes (n=45) had a higher fat free percentage (19.4±3.7%) compared to male athletes (11.5±3.7%). When scaled to body surface area (BSA), male had on average 19±3% (P< 0.001) higher LV mass; in contrast when scaled to LBM there was no significant difference in indexed LV mass -1.4 ± 3.0% (P=0.63). Similarly, when allometrically scaled to LBM, there was no significant sex-based difference in LV or left atrial volumes. Although female athletes had mildly higher LV ejection fraction (EF) and LV global longitudinal strain in absolute value, systolic strain rate and allometrically indexed stroke volume (SV) were not different between sexes (1.5±3.6% (P=0.63) and 0.0±3.7% (P=0.93) respectively). There were no differences in any of the functional atrial indices including strain or strain rate parameters. In conclusion, sex related differences in ventricular dimensions or function (stroke volume) appear less marked, if not absent, when indexing using LBM allometrically.

Key words: Athletics, Ventricular Remodeling and Function, Atrial remodeling, Lean body mass, Deformation imaging, echocardiography

Despite several years of investigation, the extent of sex differences in ventricular dimension and function in athletes remains a subject of debate.[1-11] Part of the controversy may be related to the fact that only few studies took into account body composition when scaling cardiac dimensions. In this study, we sought to determine, in college athletes, whether sex-related differences in ventricular dimensions persisted after adjustment for lean body mass (LBM). In second intention, we sought to compare sex associated differences in functional parameters including ventricular and atrial strain analysis.

Methods

In 2008, 315 Caucasian college athletes were included in the pre-season cardiac screening process at Stanford University using the AHA-12 point questionnaire, ECG and a screening echocardiogram. Of these participants, 124 volunteered to undergo Dual Energy X-Ray Absorptiometry (DEXA) for assessment of body composition. Of these subjects, we selected 90 (45 male, 45females) were matched according to age, ethnicity/race and total cardiovascular demand.[12] We excluded subjects who participated in sports in high dynamic and static component such as rowing, cycling and triathlon as these were asymmetrically distributed among sexes.[12] The sports disciplines included the following baseball, softball, La Crosse, short distance track running, wrestling, synchronous swimming, sailing and fencing. Height and weight were measured using standard techniques. Body surface area (BSA) was calculated with Dubois' formula. We present also data from 50 age, sex and race matched sedentary individuals for reference of the values in our laboratory. Body mass index (BMI) was calculated using standard formula weight divided height squared (kg/m2). Lean body mass (LBM) was estimated using DEXA scan (Norland XR 26 Mark II/HS, Norland Corporation, WIS).

All subjects underwent standard transthoracic two-dimensional (2D) and color Doppler echocardiography using the Philips IE33 system (Philips Medical Imaging, Eindhoven, the Netherlands) and a 3.5-MHz transducer. The echocardiograms were blindly interpreted by an experienced reader (GG) according to the American Society of Echocardiography guidelines.[13] Left ventricular (LV) wall thickness and diameters were measured from the long-axis views using 2D measurements at the upper papillary level to avoid any chordal attachments; septal bands were also excluded from the septal wall measurements. LV mass was calculated in diastole using estimating LV mass based on the area-length (*AL*) formula.[13] LV end-diastolic and end-systolic volumes (LVEDV and LVESV) were calculated using the 5/6 area length method as the 4 chamber end-diastolic volume often underestimate ventricular volumes; we used the 5/6 constant for the volume calculation to have the same constant as for the LV mass calculations. LV ejection fraction (LVEF) was obtained using the Simpson method in 4-chamber view. Stroke volume was derived using the difference between end-diastolic and end-systolic volumes using the area length method. Right ventricular (RV) end-diastolic area was measured in the apical 4 chamber view. Tricuspid annular plane systolic excursion (TAPSE) was measured using a 2D manual methodology. Atrial volumes were calculated using the apical 4 chamber views using the area-length method.[14]

Analysis of LV, RV and atrial (left and right) global longitudinal strain (GLS), were performed from apical 4-chamber (4C) views, using vendor independent software (TOMTEC Imaging System, Unterschleissheim, Germany) as shown in Figure 1. For LV GLS, the 6 segments in the apical 4 chamber view were averaged while the 3 lateral segments were averaged for RV GLS measures. For ventricular strain measurements, the beginning of the QRS was used as the point of reference. For the atrial GLS measurements, we used the beginning of the p-wave as the reference point to allow good discrimination of the atrial systole component, conduit function and reservoir function (Figure 1).[15]

Scaling of cardiac dimensions, volumetric and mass data to LBM was performed using allometric coefficients. The choices of coefficients were based on the literature especially the studies of George et al. and Bella et al.[16-18] We also verified that in our study population, the allometric coefficients used were body size independent (BSI); to be considered BSI, no relationship should be observed between the scaled parameter and the scaling parameter. For BSA or height, we used the allometric coefficients recommend by the ASE guidelines.[14]

Results are expressed as mean ± SD for normally distributed continuous variables or as number of cases and percentage for categorical variables. To determine the best allometric coefficient, we model the variable according to the following equation: $Y=aX^b$ where b is the allometric coefficient. Comparison of groups was performed using Student's t-test for continuous variables assuming equal or unequal variance as appropriate and Chi-square test or Fisher Exact Test, as appropriate for categorical variables. We also used multiple regression analysis to ensure that sex is not an independent determinant of indexed cardiac dimensions after accounting for other factors such as BMI, dynamic and resistive component of sports according to Mitchell classification according to total cardiovascular demand as high moderate or moderate.[12] Statistical analysis was performed using the PASW software (PASW 18.0 Inc, Chicago, IL). Inter-observer variability for LV mass measurements were measured using 15 athletes randomly selected (GG and YK). The absolute bias for the second reader was -6.4 g [-17.1, 4.4] and the relative bias was -4.5 % [-11.6, 2.6 %] with only one patient having a greater than 10% difference. The intra-class coefficient was 0.95 with a coefficient of variation of 3.7%.

Results

Forty-five male and forty five females were included in the study; 22% of female participated in high moderate sport activity compared to 20% of males with the remainder participating in low-moderate to moderate activity.[12] Compared to male athletes, female athletes had a smaller stature, lower body mass and had a higher percentage body fat (Table 1). Figure 2a shows the relationship between body fat percentage and BMI in males and females; the parallel lines suggest that the 2 groups are comparable across a wide range of BMI. Compared to females, males had on average 21% higher LBM/BSA ratio (Figure 2b and 2c).

Since female and male athletes differ with regards to their body size and composition, determining the appropriate scaling parameters is paramount. Table 2 summarizes allometric exponents for LBM and whether scaling outcomes are body size independent. Indexing to BSA did not yield body size independent scaling metrics for LV mass, LVEDV or ventricular dimensions (Table 1, Figure 3). Indexing EDV to LBM was best accomplished to the 0.7 power (Figure 3c and d). When scaling to LBM using allometric coefficients, no significant sex associated difference was observed for LV mass, LV volume or left atrial size. In contrast, indexing to BSA was associated with significant differences for all dimensions except LAV. These results are summarized in Tables 3 and 4 and Figure 4. Using multiple regression analysis and adjusting for co-factors such as cardiovascular demand category of Mitchell et al.[12] according to percentage maximal oxygen consumption of exercise active and maximal voluntary contraction, sex did not emerge as an independent correlate of LV mass or dimensions. For the purpose of presenting comparative values in sedentary subjects (less than 1 hour of active exercise a week), we recruited age, sex and race matched 50 individuals. Compared to the sedentary individuals, athletes in our cohort had greater LV mass index (71±11 vs. 62±11 g/m^2, $P<0.001$), average wall thickness (7.3± 0.9 vs. 6.7 ± 0.9, P=0.001), LA volume index (28± 7 vs. 25± 6, P=0.02); there was, however, no significant difference in average relative wall thickness (0.28±0.03 vs. 0.27±0.03, P=0.19).

Female athletes had on average a higher LVEF, LV GLS and early diastolic strain rate (Table 5). The strain in the lateral medial segment reached the most statistical difference (-21.6 ± 4.4 % vs. -19.4 ± 4.8%, P=0.03) while there was a trend for all the other segments. There was no sex-based difference in SV indexed for LBM, systolic strain rate, speckle derived early diastolic ventricular velocity (e’) or any of the functional atrial parameters (Table 5). With the exception of diastolic early strain rate, there were no significant differences for the other RV functional metrics. No difference was observed for any of the atrial strain components (Table 5). There were no significant relationships between indexed LV mass or volumes and any of the myocardial strain or strain rate metrics in our study population ($P > 0.5$ for all relationships).

Discussion

The main finding of our study is that when scaled for LBM, sex-related differences in ventricular or atrial dimensions decrease significantly or disappear. Moreover although small sex based differences in LVEF or LVGLS were observed in our study, these do not translate in differences in indexed stroke volume or ventricular strain rate, a potentially less load dependent metric of function.

Since female and male athletes differ in size and body composition, comparison between sexes requires the use of body size independent scaling metrics. Although in clinical practice, cardiac dimensions are usually scaled to BSA, this rarely leads to BSI as BSA is not linearly related to three dimensional or unidimensional cardiac parameters e.g. LV mass or wall thickness.[18,19] In contrast, as shown by our study as well as others, allometric scaling using LBM provides BSI metrics for all cardiac dimensions. The allometric coefficients that were found in our study were also very similar to the coefficients found in the MRI based study of George et al. on male army recruits, i.e. approximately 1 for LV mass, 0.70 for LV volumes, 0.33 for wall thickness and 0.66 for areas. Physiologically, LBM could yield stronger correlations than BSA in with cardiac dimensions in athletes as it represents the most metabolically active mass of the body.[17,20]

As our study highlights sex related differences in LV mass appears to be in great proportion related to differences in body composition. In fact, when indexing to BSA the relative difference in LV mass correspond to the difference in LBM to BSA ratio of approximately 20%. This is consistent with the sex associated difference in LV mass reported in the ASE guidelines (21% on average for linear dimensions) as well as by large population based studies such as The Multi-Ethnic *Study* of Atherosclerosis (21%), the Asklepios Study (21%) or the general population study of Devereux et al. (22%).[13,21,22] This consistent percentage suggests that if a population based study finds a significantly greater than 20% difference in LV mass indexed to BSA between sexes, one has to question whether a body size composition bias may have been introduced. Consistent with our finding, a recent study by Pressler et al. also observed no sex related differences in LV mass indexed to LBM in athletes participating in low to moderate intensity sports.[23] In their study however, female athletes participating in higher intensity sports had lower LV mass index compared to males.[23] Whether this difference is related to the method of estimating LBM in the study though skin folds or is due to differences in exercise intensity between groups will require further investigation.

Our study also addresses the question whether females have more eccentric ventricular remodeling than male athletes. Consistent with previous studies, we have also found that female have a lower mass to volume ratio suggesting more eccentric remodeling.[21] This however assumes that mass and volume should be scaled using the same allometric indexing. If we use the different allometric coefficient for volume found in our study and the study of George et al., the sex differences in remodeling pattern disappears or reverse between sexes. This somewhat more provocative concept will require further validation in larger studies. This would, however, be consistent with animal models demonstrating that females have higher LV hypertrophic response to exercise compare to males when compared for quantity of exercise.[24]

With regards to our secondary objectives, the small differences in LVEF or LVGLS did not translate in meaningful differences in stroke volume index or the more load independent metrics of ventricular function such as LV strain rate.[25] With regards to atrial function metrics, our study also suggests absence of meaningful sex related differences.

The main clinical implication of our study is that it highlights that in contrast to BSA, allometric LBM leads to body size independent scaling. This may be especially important to consider when screening a population with variable body size composition; for example in athletes with very small percentage of body fat and therefore higher LBM to BSA ratio; in these subjects scaling to BSA could overestimate the degree of chamber enlargement. Efforts to better define normative values of cardiac dimensions using LBM in athletes could therefore lead to narrower coefficient of variation and help better define "gray" zone athletes but this will require significantly large sample size and standardization of analysis protocols.

The main limitation of our study is its small sample size. Despite its small size, our study represents one of the largest studies in college pre-participation athletes. The groups were also well matched according to body composition (parallel BMI to fat percentage slopes) and total cardiovascular demands of sport discipline. In addition, we have considered the dynamic and resistive component of sport activity in our regression models for LV mass and volumes. Another limitation of our study, is that we recruited college athletes in a pre-participation clearance and our findings may not be generalizable to endurance or high resistance sports and longstanding athletes. More specifically, we do not have data examining whether these allometric coefficients after an intense period of training. Finally, it is important to note that our laboratory is more conservative when measuring ventricular mass, wall thickness and mass to volume ratio's with values closer to the recently published magnetic resonance based values.[26] This is important to consider if using our data in a different cohort.

Acknowledgement: We would like to acknowledge the support of Stanford Cardiovascular Institute, the Pai Chan Lee research fund as well as Montreal Heart Institute fellowship support for Genevieve Giraldeau.

Disclosures: None

1. 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;276:211-215.
2. Wilhelm M, Roten L, Tanner H, Wilhelm I, Schmid JP, Saner H. Gender differences of atrial and ventricular remodeling and autonomic tone in nonelite athletes. *Am J Cardiol* 2011;108:1489-1495.
3. Basavarajaiah S, Boraita A, Whyte G, Wilson M, Carby L, Shah A, Sharma S. Ethnic differences in left ventricular remodeling in highly-trained athletes relevance to differentiating physiologic left ventricular hypertrophy from hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2008;51:2256-2262.
4. Yilmaz DC, Buyukakilli B, Gurgul S, Rencuzogullari I. Adaptation of heart to training: a comparative study using echocardiography & impedance cardiography in male & female athletes. *Indian J Med Res* 2013;137:1111-1120.
5. Wernstedt P, Sjostedt C, Ekman I, Du H, Thuomas KA, Areskog NH, Nylander E. Adaptation of cardiac morphology and function to endurance and strength training. A comparative study using MR imaging and echocardiography in males and females. *Scand J Med Sci Sports* 2002;12:17-25.
6. Zemva A, Rogel P. Gender differences in athlete's heart: association with 24-h blood pressure. A study of pairs in sport dancing. *Int J Cardiol* 2001;77:49-54.
7. Pavlik G, Olexo Z, Banhegyi A, Sido Z, Frenkl R. Gender differences in the echocardiographic characteristics of the athletic heart. *Acta Physiol Hung* 1999;86:273-278.
8. Sharma S, Maron BJ, Whyte G, Firoozi S, Elliott PM, McKenna WJ. Physiologic limits of left ventricular hypertrophy in elite junior athletes: relevance to differential diagnosis of athlete's heart and hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2002;40:1431-1436.
9. Whyte GP, George K, Sharma S, Firoozi S, Stephens N, Senior R, McKenna WJ. The upper limit of physiological cardiac hypertrophy in elite male and female athletes: the British experience. *Eur J Appl Physiol* 2004;92:592-597.
10. Petersen SE, Hudsmith LE, Robson MD, Doll HA, Francis JM, Wiesmann F, Jung BA, Hennig J, Watkins H, Neubauer S. Sex-specific characteristics of cardiac function, geometry, and mass in young adult elite athletes. *J Magn Reson Imaging* 2006;24:297-303.
11. Spence AL, Naylor LH, Carter HH, Buck CL, Dembo L, Murray CP, Watson P, Oxborough D, George KP, Green DJ. A prospective randomised longitudinal MRI study of left ventricular adaptation to endurance and resistance exercise training in humans. *J Physiol* 2011;589:5443-5452.
12. Mitchell JH, Haskell W, Snell P, Van Camp SP. Task Force 8: classification of sports. *J Am Coll Cardiol* 2005;45:1364-1367.
13. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015;28:1-39 e14.
14. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton MS, Stewart WJ, Chamber Quantification Writing G, American Society of Echocardiography's G, Standards C, European Association of E. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. *J Am Soc Echocardiogr* 2005;18:1440-1463.
15. Mor-Avi V, Lang RM, Badano LP, Belohlavek M, Cardim NM, Derumeaux G, Galderisi M, Marwick T, Nagueh SF, Sengupta PP, Sicari R, Smiseth OA, Smulevitz B, Takeuchi M, Thomas JD, Vannan M, Voigt JU, Zamorano JL. Current and evolving echocardiographic techniques for the quantitative evaluation of cardiac mechanics: ASE/EAE consensus statement on methodology and indications endorsed by the Japanese Society of Echocardiography. *J Am Soc Echocardiogr* 2011;24:277-313.

16. Dewey FE, Rosenthal D, Murphy DJ, Jr., Froelicher VF, Ashley EA. Does size matter? Clinical applications of scaling cardiac size and function for body size. *Circulation* 2008;117:2279-2287.
17. Bella JN, Devereux RB, Roman MJ, O'Grady MJ, Welty TK, Lee ET, Fabsitz RR, Howard BV. Relations of left ventricular mass to fat-free and adipose body mass: the strong heart study. The Strong Heart Study Investigators. *Circulation* 1998;98:2538-2544.
18. George KP, Birch KM, Pennell DJ, Myerson SG. Magnetic-resonance-imaging-derived indices for the normalization of left ventricular morphology by body size. *Magn Reson Imaging* 2009;27:207-213.
19. Oxborough D, Sharma S, Shave R, Whyte G, Birch K, Artis N, Batterham AM, George K. The right ventricle of the endurance athlete: the relationship between morphology and deformation. *J Am Soc Echocardiogr* 2012;25:263-271.
20. Whalley GA, Doughty RN, Gamble GD, Oxenham HC, Walsh HJ, Reid IR, Baldi JC. Association of fat-free mass and training status with left ventricular size and mass in endurance-trained athletes. *J Am Coll Cardiol* 2004;44:892-896.
21. Natori S, Lai S, Finn JP, Gomes AS, Hundley WG, Jerosch-Herold M, Pearson G, Sinha S, Arai A, Lima JA, Bluemke DA. Cardiovascular function in multi-ethnic study of atherosclerosis: normal values by age, sex, and ethnicity. *AJR Am J Roentgenol* 2006;186:S357-365.
22. Chirinos JA, Segers P, De Buyzere ML, Kronmal RA, Raja MW, De Bacquer D, Claessens T, Gillebert TC, St John-Sutton M, Rietzschel ER. Left ventricular mass: allometric scaling, normative values, effect of obesity, and prognostic performance. *Hypertension* 2010;56:91-98.
23. Pressler A, Haller B, Scherr J, Heitkamp D, Esefeld K, Boscheri A, Wolfarth B, Halle M. Association of body composition and left ventricular dimensions in elite athletes. *Eur J Prev Cardiol* 2012;19:1194-1204.
24. Foryst-Ludwig A, Kreissl MC, Sprang C, Thalke B, Bohm C, Benz V, Gurgen D, Dragun D, Schubert C, Mai K, Stawowy P, Spranger J, Regitz-Zagrosek V, Unger T, Kintscher U. Sex differences in physiological cardiac hypertrophy are associated with exercise-mediated changes in energy substrate availability. *Am J Physiol Heart Circ Physiol* 2011;301:H115-122.
25. Voigt JU, Pedrizzetti G, Lysyansky P, Marwick TH, Houle H, Baumann R, Pedri S, Ito Y, Abe Y, Metz S, Song JH, Hamilton J, Sengupta PP, Kolias TJ, d'Hooge J, Aurigemma GP, Thomas JD, Badano LP. Definitions for a common standard for 2D speckle tracking echocardiography: consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging. *Eur Heart J Cardiovasc Imaging* 2015;16:1-11.
26. Kawel-Boehm N, Maceira A, Valsangiacomo-Buechel ER, Vogel-Claussen J, Turkbey EB, Williams R, Plein S, Tee M, Eng J, Bluemke DA. Normal values for cardiovascular magnetic resonance in adults and children. *J Cardiovasc Magn Reson* 2015;17:29.

Figure legends

Figure 1. Left ventricular and left atrial strain and strain rate measurements. After LV and LA myocardium is traced (the green contours), the software automatically tracks the ventricular or atrial wall on subsequent frames. Adequate tracking can be verified and corrected by adjusting the region of interest or the contour. Each curve shown in the middle and the right is the average curve of six segments. The curve starts from the beginning of the QRS in left ventricle (upper) and from the beginning of the p-wave in left atrium (lower). ε; strain, SR; strain rate, fx; function, LV; left ventricular, LA; left atrial

Figure 2 Anthropomorphic relationships between body mass index, body surface area, body fat, and lean body mass. The panel A shows the relationship between BMI and fat percentage and panel B shows the relationship between BSA and LBM. Red lines represent the approximate formula of the female and blue lines represent that of male subjects. The panel C shows the difference of LBM/BSA ratio between sexes. MBI; body mass index, BSA; body surface area, LBM; lean body mass

Figure 3. Relationship between indexed left ventricular mass and end-diastolic volume. LV mass indexed to body surface area has a significant linear relationship with BSA suggesting not body size independent metric (A), whereas LV mass indexed to lean body masshas no significant correlation with LBM (B). Indexed left ventricular end-diastolic volume has a significant linear correlation with LBM (C), whereas it has no significant correlation with allometric LBM (D). LV; left ventricular, BSA; body surface area, LBM; lean body mass, LVEDVI; left ventricular end-diastolic volume index.

Figure 4. Sex associated relative difference in structural indices using different scaling parameters. Allometric indexing to LBM significantly reduced differences between male and females. Data is presented for LV mass (panel A), LV end-diastolic volume (panel B), left atrial volume (panel C) and RV end-diastolic area (panel D).

Table 1. Anthropometric measures of the study population

Characteristic	Female (n=45)	Male (n=45)	P-value
Age (years)	18.6±0.8	19.2±1.3	0.01
Height (cm)	168±6	182±7	<0.001
Mass (kg)	63±9	83±11	<0.001
Body mass index (kg/m^2)	22.2±2.6	24.9±2.7	<0.001
Body surface area (m^2)	1.71±0.12	2.06±0.17	<0.001
Percentage fat (%)	19.5±3.6	11.6±3.8	<0.001
Lean body mass (kg)	50±5.6	72.5±8.4	<0.001
Lean body mass to body surface area ratio (kg/m^2)	29.2±1.6	35.2±2.0	<0.001
Sport Classification*			
High moderate (%)	10 (22)	9 (20)	1.0
Low moderate to moderate (%)	35 (78)	36 (80)	

* Sports classification is based on Task Force classification based on total cardiovascular demands. Because of the diversity of sports we combined low moderate and moderate sport classification. combined low

Table 2. Allometric and Ratiometric Scaling of Cardiovascular Parameters

$Y=aX^b$	LV mass	LVEDV	LVID	Wall Thickness	RVEDA	LAV	SV
LBM							
b	0.92± 0.07	0.76 ± 0.07	0.26 ±0.03	0.39 ±0.04	0.63 ± 0.07	0.65 ±0.12	0.62 ± 0.09
r^2	0.61	0.55	0.47	0.50	0.50	0.23	0.37
b selected	1	0.70	0.33	0.33	0.66	0.70	0.70
BSI	Yes	Yes	Yes	Yes	Yes	Yes	Yes
BSA							
b selected	1	1	1	1	1	1	1
BSI	**No**	**No**	**No**	**No**	Yes	Yes	Yes
Height							
b selected	2.7	2.7	1	1	2.7	2.7	2.7
BSI	Yes	Yes	Yes	Yes	**No**	Yes	**No**

Ratiometric scaling represents a coefficient of 1. The selected b for LBM is based on literature values and consistency in our cohort. Body size independent metric (BSI) refers to body size independent scaling considered for both sexes. For BSA and height, we used scaling indices based on ASE guidelines. LV indicates left ventricular, LVEDV; left ventricular end-diastolic volume, LVID; left ventricular internal dimension, RVEDA; right ventricular end-diastolic area, LAV; left atrial volume, SV; stroke volume. Wall thickness represents the average wall thickness.

Table 3. Comparison of left ventricular and atrial structural parameters

Characteristics	Female (n=45)	Male (n=45)	P-value
Left ventricular dimensions			
IVS (mm)	6.1 ± 1.0	7.1 ±0.1	< 0.001
PW (mm)	7.0 ± 1.1	8.2 ± 1.5	< 0.001
LVID (mm)	47.1 ± 4.2	52.2 ± 4.1	< 0.001
r-average SAX (mm)	6.8 ± 0.7	7.9 ± 1.5	< 0.001
r-average/LBM$^{0.33}$	1.9 ± 0.2	1.9 ± 0.2	0.24
LVID average/ LBM$^{0.33}$	1.33± 0.08	1.33 ±0.08	0.99
RWT	0.28 ± 0.06	0.30 ± 0.05	0.31
Left ventricular mass			
Absolute (g)	111 ± 20	159± 26	< 0.001
Indexed to BSA (g/m^2)	65 ± 9	77±10	< 0.001
Indexed to LBM	2.2 ± 0.3	2.2 ± 0.3	0.63
LV end-diastolic volume			
Absolute (ml)	142 ± 23	193 ± 33	< 0.001
Indexed to BSA (ml/m^2)	83 ± 12	94 ± 1	< 0.001
Indexed to LBM$^{0.7}$	9.2 ± 1.3	9.7± 1.5	0.17
LV Mass-to-Volume ratio	0.79 ± 0.09	0.83 ± 0.11	0.015
LV Mass- to-Volume ratio (Allometric correction)	0.24± 0.03	0.23±0.03	0.035
Left atrial volume			
Absolute (ml)	47.5 ± 11.7	59.1 ± 16.8	< 0.001
Indexed to BSA	27.7 ± 6.0	28.6 ± 7.5	0.54
Indexed to LBM$^{0.7}$	3.1 ± 0.7	2.9 ± 0.8	0.42

Table 4. Comparison of right ventricular and atrial structural parameters between sexes

Characteristics	Female (n=45)	Male (n=45)	P-value
Right ventricular dimensions (4 chamber view)			
Basal (cm)	3.7 ± 0.5	4.3 ± 0.5	< 0.001
Mid (cm)	2.9 ± 0.5	3.6 ± 0.5	< 0.001
Longitudinal (cm)	8.2 ± 0.7	9.1 ± 0.9	< 0.001
Basal/$LBM^{0.33}$	1.0 ± 0.1	10.5 ± 1.3	0.43
Mid/$LBM^{0.33}$	0.8 ± 0.1	0.9 ± 0.1	0.054
Longitudinal/$LBM^{0.33}$	2.3 ± 0.2	2.2 ± 0.2	0.39
Right ventricular area			
Absolute (cm^2)	22.8 ± 3.5	29.7 ± 3.9	< 0.0001
Indexed to BSA	13.4 ± 1.8	14.5 ± 1.8	< 0.01
Indexed to $LBM^{0.66}$	1.7 ± 0.2	1.8 ± 0.2	0.55
Right atrial volume			
Absolute (ml)	41.2 ± 10.9	56.1 ± 15.3	< 0.0001
Indexed to BSA	24.1 ± 5.7	27.2 ± 6.7	0.02
Indexed to $LBM^{0.7}$	2.7 ± 0.7	2.8 ± 0.7	0.37

Table 5. Comparison of functional parameters between sexes

Characteristic	Female (n=45)	Male (n=45)	P-value
Stroke volume			
Absolute (ml)	75 ± 12	98 ± 20	0.001
SV/ BSA (ml/m^2)	44 ± 7	48 ± 9	0.048
SV/ LBM$^{0.7}$ (ml/kg	4.9 ± 0.8	4.9 ±1.0	0.93
Left ventricular			
LVEF (%)	66 ± 4	63± 6	0.004
2D GLS manual strain (%)	-21.6 ± 1.9	-20.6 ± 2.0	0.02
GLS (%)	-22.0 ± 1.9	-20.6 ± 2.0	0.02
Systolic SR (%/s)	-1.08 ± 0.18	-1.06 ± 0.18	0.67
Diastolic early SR (%/s)	1.81 ± 0.40	1.56 ± 0.43	<0.01
Speckle derived e 'velocity (cm/s)	-11.0 ± 2.6	-10.5 ± 3.3	0.42
Right ventricular			
RVFAC (%)	41.8 ± 4.3	40.7 ± 4.3	0.26
Free-wall manual GLS (%)	-27.4 ± 2.5	-27.4 ± 2.9	0.94
Free-wall GLS (%)	-27.0 ± 3.0	-27.3 ± 3.3	0.65
GLS (%)	-24.9 ± 2.6	-24.7 ± 2.6	0.76
Systolic SR (%/s)	-1.5 ± 0.3	-1.5 ±0.3	0.58
Diastolic early SR (%/s)	2.02 ± 0.42	1.78 ± 0.60	0.043
Speckle derived e' velocity (cm/s)	-12.3 ± 3.0	-12.7 ± 3.4	0.62
Left atrial			
Longitudinal strain			
Atrial contraction (%)	-11.2 ± 4.4	-10.8 ± 3.8	0.65
Conduit phase (%)	35.8 ± 9.3	35.8 ± 9.1	0.97
Reservoir phase (%)	47.0 ± 9.3	46.6 ± 9.3	0.82
Right atrial			
Longitudinal strain			
Atrial contraction (%)	-13.2 ± 5.3	-15.2 ± 4.2	0.056
Conduit phase (%)	43.0 ± 12.4	42.6 ± 14.1	0.88
Reservoir phase (%)	56.2 ± 13.6	57.8 ± 15.1	0.61

LVEF; left ventricular ejection fraction, 2D; two-dimensional, GLS; global longitudinal strain, SR; strain rate, RVFAC; right ventricular fractional area change, SV; stroke volume, BSA; body surface area, LBM; lean body mass.