Athletic Remodeling in College Female Athletes, the "Morganroth Hypothesis" Revisited

Zoe Kooreman, MD[1,2], Geneviève Giraldeau, MD [1,2], Gherardo Finocchiaro, MD[1,2], Yukari Kobayashi, MD[1,2], Matthew Wheeler, MD[1,2], Marco Perez, MD[1,2], Kegan Moneghetti, MD, David Oxborough PhD[3], Keith P. George PhD[3], Jonathan Myers, PhD, Euan Ashley, MRCP DPhil[1,2]*, François Haddad, MD[1,2*]

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

2. Stanford Cardiovascular Institute, Stanford, CA

3. Liverpool, John Moores University, United Kingdom

***** Both authors are equivalent co-senior author of the study

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Address of correspondence: Please address correspondence to Francois Haddad, MD FAHA, Stanford Cardiovascular Institute, Palo Alto, CA, 94304. Email: fhaddad@stanford.edu.

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ABSTRACT

Background: There is limited data regarding ventricular remodeling in college female athletes, especially when appropriate scaling of cardiac dimensions to lean body mass (LBM) is considered. Moreover, it is not well established whether cardiac remodeling in female athletes is balanced process with proportional increase in left ventricular (LV) mass and volume or right and left ventricular size.

Methods: During the pre-participation competitive screening, seventy-two college female athletes volunteered to undergo Dual Energy X-Ray Absorptiometry (DEXA) scan for quantification of LBM and comprehensive 2D echocardiography including assessment of longitudinal myocardial strain. The athletes were divided in two groups according to the intensity of the dynamic and static components of their sport categories, i.e. a higher intensity dynamic and resistive group (n=37 participating in rowing, water polo and La Crosse) and a lower intensity group (n=35, participating in short distance running, sailing, synchronized swimming and softball). In addition, we recruited a group of 31 age matched non-athlete controls.

Results: The mean age of the study population was 18.7±1.0 years. When scaled to body surface area, the higher intensity group had 17.1 ± 3.6% (p <0.001) greater LV mass when compared to the lower intensity group and 21.7±4.0 % (P <0.001) greater LV mass than the control group. The differences persisted after scaling to LBM with 14.2 ± 3.2% (p <0.001) greater LV mass in the higher intensity group. In contrast, there was no difference in any of the relative remodeling indices including the LV mass to volume ratio, right to left ventricular area ratio or left atrial to LV volume ratio (p>0.50 for all). In addition, no significant difference was noted among the three groups in LVEF (p=0.22), LV global longitudinal strain (p=0.55), LV systolic strain rate (p=0.62) or RV global longitudinal strain (p=0.61).

Conclusion: Female collegiate athletes participating in higher intensity dynamic and resistive sports have higher indexed LV mass even when scaled to LBM. The remodeling process does however appear to be balanced process not only at the intraventricular level but also at the interventricular and atrio-ventricular levels.

Introduction

Pre-participation screening of competitive college athletes is adopted by the majority of College programs and usually involves a medical history and physical examination, an electrocardiogram and in selected cases a focused echocardiogram. The interpretation of echocardiograms in athletes may however be challenging as the pattern of cardiac remodeling in athletes may vary according to sport type as well as lean body mass.

Morganroth et al.[1] were the first to suggest that athletic remodeling varies according to the intensity of the dynamic or static components of the sport discipline. In their landmark study, Morganroth et al. observed that male endurance trained athletes (with higher dynamic component) had a greater left ventricular (LV) end-diastolic dimension with a normal wall thickness (eccentric remodeling) whereas wrestlers (with higher static component) had increased wall thickness but normal LV end-diastolic dimension, hence more concentric remodeling. Recently, the "Morgaroth" observation was challenged by recent studies suggesting that the increase in LV mass is proportional to the increase in LV volume (proportional remodeling) irrespective of the sport discipline.[1-7] Furthermore, difference in ventricular mass among sport discipline may be partially explained by differences in lean body mass (LBM) and not sport discipline.[8, 9]

In contrast to the many studies focusing on cardiac remodeling in male college athletes, few studies have focused on female college athletes especially when appropriate scaling of cardiac dimensions to lean body mass (LBM) is considered.[8, 9] For this study, we first hypothesized that college female athletes participating in higher intensity dynamic sports would have greater LV mass than lower intensity disciplines even after scaling to LBM. We further hypothesize that the cardiac remodeling in female athletes would be balanced irrespective of the intensity (dynamic) of the sport discipline, i.e. (1) LV mass would increase proportionally to ventricular volume, (2) right ventricular size proportionally to LV size, (3) atrial size proportionally to ventricular size and finally (4) right atria size proportionally left atria size. Finally, we hypothesize that ventricular function including longitudinal strain would be comparable among sport disciplines irrespective of sport intensity.

METHODS

As part of Stanford University athletic screening program, 75 college female athletes underwent pre-season cardiac screening using the American Heart Association (AHA)-12-point assessment, an electrocardiogram (ECG), a focused echocardiogram and a Dual Energy X-Ray Absorptiometry (DEXA)-based assessment of body composition. We excluded three African American athletes from analysis, as race is known to influence ventricular remodeling independent of sport category; none of athletes had an abnormal questionnaire, abnormal ECG or pathological echocardiographic findings leading to exclusion.[10, 11] We were able to divide participants into 2 groups according to dynamic or static component of their sport activity according to the classification of Mitchell et al.[12] (Figure 1), The first group included 37 subjects participating in higher intensity dynamic and static sport discipline including rowing, La Crosse or Water Polo (gray areas) while the second group included lower intensity dynamic sports including synchronized swimming, short distance track, softball, fencing and sailing. Although Water Polo is a sport discipline with moderate dynamic component, we chose to include it in the higher intensity group due to its higher static component and previous studies showing significant cardiac remodeling.[13, 14]

To further study the influence of physical activity on cardiac remodeling and function, we also recruited 32 healthy volunteers; one subject was subsequently excluded for mitral valve prolapse. The healthy volunteers had a normal AHA-12 points assessment, no family history of early cardiovascular disease and had to exercise less than 2 hours a week. Healthy volunteers did not, however undergo DEXA scans as this was only offered to athletes of the program.

Anthropometric measurements

Lean body mass (LBM) was estimated using DEXA scan (Norland XR 26 Mark II/HS, Norland Corporation, WIS). Body surface area (BSA) was calculated with Dubois' formula. Body mass index

(BMI) was calculated using standard formula weight divided height squared (kg/m2).

Standard echocardiographic measurements

All patients underwent standard transthoracic two-dimensional (2D) and color Doppler echocardiography using the Philips Sonos 7500 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 guidelines of the ASE.[15] LV mass was calculated in diastole using estimating LV mass based on the area-length (*AL*) formula (Figure 2).[16] LV end-diastolic and end-systolic volume (LVEDV and LVESV) were calculated using the 5/6 area length method to be consistent with the geometrical assumptions of the LV mass formula.[16] For quality control for measures of ventricular mass, we also measured ventricular mass in systole to verify that mass estimates were within 10% of each other; if not within 10%, a second reader (FH) read the studies and an average value of 2 readers was chosen (Figure 2). Atrial volumes were calculated using the apical 4 chamber views by the area-length method.[16]

Relative remodeling indices included: (1) LV mass to volume ratio (calculated using the 5/6 area length method), (2) relative LV wall thickness calculated using the average wall thickness and average ventricular diameter from the short axis view, (3) RV to LV end-diastolic area ratio and (4) relative atrial remodeling indices including LA volume to LV end-diastolic volume, RA to RV end-diastolic relative area and RA to LA relative area.

Measures of ventricular function included LV ejection fraction (LVEF) derived using the Simpson method in a 4 chamber view; stroke volume using the difference between end-diastolic and end-systolic volumes using the area-length methods; right ventricular (RV) fractional area change (RVFAC) and tricuspid annular plane systolic excursion (TAPSE) using 2D methodology. Analysis of LV and RV longitudinal strain (LS) were performed from the apical 4-chamber (4C) views, using vendor independent software (TOMTEC Imaging System, Unterschleissheim, Germany) as shown in Figure 2.[17] For LVLS, the 6 segments in the apical 4 chamber view were averaged while the 3 lateral segments were averaged for

RVLS measures. For the LV, strain rate parameters were also computed using the TOMTEC system. For ventricular strain measurements, the peak of the QRS was used as the reference point.

Scaling of cardiac dimensions

Scaling of cardiac dimensions or mass was based on BSA and LBM. For BSA, the allometric coefficient chosen was unity based on the recommendations of the American Society of Echocardiography[15]; we chose to scale wall thickness and ventricular dimension to height as this is more consistent with the dimension of the parameter being scaled and likely more body size independent. For LBM, we chose the ones suggested by the studies of George et al. and Bella et al.[8, 9, 18] For LV mass and volume scaling to LBM was done using unity as the allometric coefficient, linear dimensions to LBM with an exponent of 0.33 and areas with an exponent of 0.66.[8, 9, 18]

Statistical analysis

Results are expressed as mean ± SD for normally distributed continuous variables or as number of cases and percentage for categorical variables. 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. The inter-observer variability was tested using the absolute and relative difference as well as the intraclass coefficient and coefficient of variation. Statistical analysis was performed using the PASW software (PASW 22.0 Inc, Chicago, IL).

RESULTS

Population

The demographic and anthropomorphic characteristics of the study population are summarized in table 1. There was no significant different in age, BSA or BMI between the 3 groups. The percentage body fat were not statistically different between the higher intensity and lower intensity group. Athletes in the higher intensity group were, however taller and had a slightly higher values of LBM.

Differences in cardiac dimensions

As shown in table 2, the HIGH group had significantly greater LV mass, LV volume and atrial volume when scaled to BSA. Even after scaling to LBM (table 3), there was still a significant difference in cardiac dimensions between the HIGH and LOW group. Expressed as relative differences, the LV mass was 21.7±4.1 % and 17.1 ± 3.6% greater in the HIGH compared to the LOW and CON (Figure 3a). In contrast there was no significant difference between groups in any of the relative remodeling indices including mass to volume ratio (relative difference of 0.0 ± 2.7% and 3.0 ±2.7% and compared LOW and HIGHrespectively), average relative wall thickness, RV to LV area, LAV to LVEDV or RA to LA relative area.

When using as a threshold the 95th percentile of the LOW group (reference group), there was a greater percentage of elevated LV mass when scaled to BSA, compared to LBM or mass to volume ratio (Figure 3b). The low percentage of abnormal value using the mass to volume ratio could be explained by the strong linear relationship between the LV mass and LV volume (R^2= 0.71, P<0.001) across sports type. Similar findings were found with regards to relative differences in LAV (Figure 3d, e and f).

With regards to the specific sport categories in each group, no significant different in scaled ventricular mass was observed between rowing (2.46±0.36 g/kg (rowing), 2.54±0.36 g/kg (water polo), 2.39 ±0.22 (lacrosse), P=0.62) in the HIGH group; no other difference in indexed ventricular mass was noted in the LOW groups.

Assessment of body size independent scaling parameters

In our study, allometric scaling to LBM was associated with body size independent scaling in the HIGH and LOW groups. There was no significant relationship the LBM scaled dimension and LBM for LV mass: R^2= 0.008, P=0.60 (LOW) and R^2= 0.05, P=0.14 (HIGH); LVEDV, R^2= 0.08, P=0.15 (LOW) and R^2= 0.006, P=0.65 (HIGH) and LAV, R^2= 0.003, P=0.75(LOW) and R^2= 0.06, P=0.13(HIGH). In contrast, BSA did not yield body size independent scaling for LV mass in the high intensity athletes: R^2 = 0.14, P=0.02

for LV mass, $R^2 = 0.14$, P=0.02 for LVEDV or and $R^2 = 0.16$, P=0.01 for LAV.

Ventricular function and Sport discipline

Indexed stroke volume to BSA was 17.6±3.6 % and 19.6 ±4.4% and higher in the HIGH when compared to the LOW and CON groups respectively and 15.0 ± 3.6% higher in the HIGH group compared to the LOW group when scaled to LBM. There was no other significant difference in functional parameters in the HIGH group compared to the other groups (Table 5).

Inter-observer variability and quality control

Inter-observer variability for LV mass measurements were measured using 15 athletes randomly selected (GG and YK). The absolute difference for LV mass 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 intraclass coefficient was 0.95 and the coefficient of variation of 3.7%. For quality control, we compared values of ventricular mass between diastole and systole. The mean difference between measures in systole and diastole was -3.1 ± 5.4 % with only 12% of samples having differences more than 10% requiring averaging.

Discussion

Our study has two main findings. First, it confirms that difference in LV mass in female athletes participating in high intensity sports persist even after scaling to lean body mass. Second, in contrast to the original Morganroth observation in male athletes, our study supports the balanced nature of ventricular remodeling in female athletes with proportional increase in ventricular mass and volume irrespective of sport type. In addition, we observed that the remodeling process is also balanced at the interventricular, atrio-ventricular and inter-atrial level.

Few studies have focused on ventricular remodeling in female athletes the majority being cross-sectional studies. In one of the largest echocardiography based studies, Caselli et al. analyzed ventricular remodeling in 148 female Olympic athletes using 3D echocardiography and scaling to BSA.[2] They found that endurance (dynamic) and mixed (dynamic and static) sports had approximately 19% greater ventricular mass, and volume when compared to skilled (lower dynamic intensity) based sport categories.[2] Dressler et al. found slightly lower percentage increase in ventricular mass in the range of 11% in 276 female elite athletes [19] Five cross-sectional magnetic resonance (MRI) studies have compared ventricular remodeling in endurance female athletes compared to controls (n ranging from 20 to 59 athletes).[5, 20-23] These studies reported an increase in LV mass in the ranges from 19 to 26% when compared to on-athlete controls.[5, 20-23] Longitudinally, Howden et al. evaluated 5 female subjects who underwent endurance training, the change in ventricular remodeling that occur over 1 year in previously less active individuals and found that LV mass increased on average by 14%. Studies in male endurance using MRI find similar relative increase in LV mass. Prakken et al. and Luijkx et al. found that athletes participating in more dynamic sport activity have a 20 to 32% higher LV mass respectively.[20, 22] Echocardiography based studies in male athletes usually report greater differences in ventricular mass in the order of 39% likely due to an overestimation of wall thickness by echocardiography.[24, 25]

Our study represents the larger study scaling to LBM in college female athletes; as expected scaling to LBM reduces but does not eliminate the differences in LV mass or volume. Riley-Hagan et al. have previously shown in a smaller group of older female athletes participating in long distance running, cycling or cross-country skiing that endurance based disciplines had on average 17 to 19 % greater mass when compared to non-athletic controls.[23] The smaller difference of 14% observed in our study may be, in part, related to the pre-season timing of screening and by the fact that the athletes were not in the elite category.

One of the most important contribution of our study is the emphasis placed on the balance nature of cardiac remodeling in athletics. This challenges in part the Morganroth study observation that proposed that endurance based sports were associated with more eccentric remodeling.[26] In the study of Caselli et al. in Olympic based athletics, the mass to volume ratio appeared to be constant around one irrespective of the sport discipline.[2] These observation of balanced increase in LV mass and volume increase in athletes were confirmed by several cross-sectional and longitudinal based studies especially in male athletes.[1, 20, 22, [27, 28] Our study also highlights the balanced nature of the interventricular, atrio-ventricular and interatrial component of balanced remodeling. The balanced nature of ventricular remodeling does not appear to be limited to athletics. In fact, results from the Multi-Ethnic Study of Atherosclerosis (MESA) have previously shown that the mass to volume ratio is not influenced by level of activity although it is higher in older individuals, people of black race and in male subjects. As a reference, female subjects between 45 and 54 years in the MESA study had an average mass to volume ratio was 1.04. [6]

Functionally, sports with higher dynamic components have on avergae higher indexed stroke consistent with the higher cardiac output requirements often imposed by more aerobic-based physical activity. Consistent with the prior studies of Spence et al. and Andrea et al, no significant differences in LVEF or myocardial deformation indices were noted across sport discipline although the study was likely underpowered to show small differences. [1, 29] Moreover, and original to our study, no difference was observed for strain rate metrics among the different sport categories and controls.

Although not a major objective of our study, our study also highlights important methodological heterogeneity between the studies on ventricular remodeling. In fact, although the relative changes in mass or volume are consistent between the studies, the absolute values reported vary significantly. In our study, the measured values for both ventricular mass and mass to volume ratios in controls are comparable to the suggested reference cardiac MRI parameters of the study Kawel-Boehm et al.[30] but lower than previously reported echocardiographic studies.[25] In our study, measuring mass in both diastole and systole was associated with an excellent inter-reader reproducibility.

The clinical implications of the study are threefold. First, any future reference values for athletic screening should take into account sport category during screening. Second, the balanced nature of ventricular remodeling can be very useful when assessing for pathological remodeling in athletes. Building on this observation, Petersen et al. demonstrated that a maximal wall thickness to volume ratio of < 0.15 mm/ (mL/m^2) had a sensitivity of 80% and a specificity of 99% in differentiating pathological remodeling in athletics and pathological hypertrophy with an AUC of 0.99.[31] In their study however, athletes were younger than patients with LV hypertrophy which may have led stronger discrimination.[31] Finally, future studies, validating the best methods for reproducibility between laboratories will be needed prior to recommending reference value for athletic screening.

The main limitation of our study is its small sample size and different sports type. However, despite its small size, the current study represents one of the largest among college female athletes; we did not also observe differences related to sport type. Although the sport classification could lead itself to some criticism, we based our categorization on the Task Force recommendation of Mitchell et al. and previous studies in athletes participating Water-Polo.[12-14] Another limitation is that we did not use magnetic resonance imaging for quantification of cardiac structure. However; our measures were performed by Stanford Cardiovascular Institute Biomarker and Phenotypic Core Laboratory by experienced readers with results are consistent with magnetic resonance based studies. Finally, we did not have complete training history and maximal oxygen consumption of participants. In addition, patients were not screened using the The Physical Activity Readiness Questionnaire for Everyone or the AHA/ACSM Health/Fitness Facility Pre-participation Screening Questionnaire.

In conclusion, these data highlight sport specific differences in ventricular and atrial remodeling in female college athletes. Mass to volume ratio or relative wall thickness is emerging as a parameter independent of sport discipline and will likely emerge as very useful for screening pathological remodeling.

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Figure legends

Figure 1. Sport discipline classification based on oxygen uptake and maximal voluntary contraction (MVC). The gray shaded squares represent the group participating in higher dynamic-static component sports (HIGH) versus the lower dynamic-static component sports.

Figure 2. Representative measures for LV remodeling and myocardial deformation analysis. Panel A through C highlight the different components for measuring LV mass using the area length method; in our study, we measured mass in both diastole and systole integrating this for quality control method (conservation of mass principle). Panels D through F highlight the different longitudinal deformation metrics used in the study; E shows the average myocardial longitudinal strain curve and F the strain rate metrics. LS indicates longitudinal strain; SR, strain rate.

Figure 3. Relative difference in cardiac remodeling indices in the athletic and control groups. Panel A shows the difference in LV mass when scaled to BSA and LBM in the higher intensity sport group (HIGH) group compared to the control group (C) and the Lower intensity sport group (L) as well as for the mass to volume ratio (M/V). Panel B shows percentage of athletes presenting a value higher than the 95% of value in the lower intensity group; in our study the limit chosen for LVM indexed to BSA is consistent with the upper limit in the recent MRI study of Kawel-Boehm.[30] Panel C shows the strong linear relationship between LV mass and volume in the 3 groups. Panel D, E and F shows corresponding analysis for atrial remodeling.