

## TITLE PAGE

# **Influence of gender on right ventricle adaptation to endurance exercise: an ultrasound two-dimensional speckle-tracking stress study**

### **Short title**

## **Influence of gender on right ventricle adaptation to exercise**

### **First author's surname: Sanz-de la Garza**

Maria Sanz-de la Garza, MD<sup>1\*</sup>; Geneviève Giraldeau, MD<sup>2</sup>, Josefa Marin<sup>1</sup>, Gonzalo Grazioli, MD<sup>1</sup>, Montserrat Esteve<sup>1</sup>, Luigi Gabrielli, MD<sup>3</sup>, Carlos Brambila, MD<sup>4</sup>, Laura Sanchis, Bart BijnensPhD<sup>5</sup>, Marta Sitges, MD, PhD<sup>1</sup>

<sup>1</sup>Cardiology Department, IDIBAPS, Hospital Clínic, Barcelona, Spain

<sup>2</sup>Montreal Heart Institute, Montreal, Canada

<sup>3</sup>Catholic University of Chile, Santiago De Chile, Chile

<sup>4</sup>Angeles del Carmen Hospital, Guadalajara, Mexico

<sup>5</sup>ICREA, Universitat Pompeu Fabra, Barcelona, Spain.

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**Address for correspondence:** María Sanz-de la Garza

Cardiology Department; IDIBAPS, Hospital Clínic

Villarroel 136, 08036 Barcelona, Spain

**Phone #** 34- 93- 227 9305; **Fax #** 34- 93- 451 41 48 **E-mail:** [meriluprime@hotmail.com](mailto:meriluprime@hotmail.com)

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## **ABSTRACT:**

**Background:** Characteristic right ventricle (RV) remodelling is related to endurance exercise in male athletes (MAs), but data in female athletes (FAs) are scarce. Our aim was to evaluate sex-related influence on exercise-induced RV remodelling and on RV performance during exercise.

**Methods:** Forty endurance athletes (>10 training hours/week, 50% female) and 40 age-matched controls (<3 hours moderate exercise/week, 50% female) were included. Echocardiography was performed at rest and at maximum cycle-ergometer effort. Both ventricles were analysed by standard and speckle-tracking echocardiography.

**Results:** Endurance training induced similar structural and functional cardiac remodelling in MAs and FAs, characterized by bi-ventricular dilatation (~34%, left ventricle [LV]; 29%, RV) and normal bi-ventricular function. However, males had larger RV size ( $p<0.01$ ), compared to females: RV end-diastolic area ( $\text{cm}^2/\text{m}^2$ ):  $15.6\pm 2.2$  vs  $11.6\pm 1.7$  in athletes;  $12.2\pm 2.7$  vs  $8.6\pm 1.6$  in controls, respectively) and lower bi-ventricular deformation (RV global longitudinal strain (GLS) (%):  $-24.0\pm 3.6$  vs  $-29.2\pm 3.1$  in athletes;  $-24.9\pm 2.5$  vs  $-30.0\pm 1.9$  in controls, and LVGLS:  $-17.5\pm 1.4$  vs  $-21.9\pm 1.9$  in athletes;  $-18.7\pm 1.2$  vs  $-22.5\pm 1.5$  in controls, respectively,  $p<0.01$ ). During exercise, the increase in LV function was positively correlated ( $p<0.01$ ) with increased cardiac output ( $\Delta\%$ LV ejection fraction,  $r=+0.46$  and  $\Delta\%$ LVGLS,  $r=+0.36$ ). Improvement in RV performance was blunted at high workloads, especially in MAs.

**Conclusion:** Long-term endurance training induced similar bi-ventricular remodelling in MAs and FAs. Independently of training load, males had larger RV size and lower bi-ventricular deformation. Improvement in RV performance during exercise was blunted at high workloads, especially in MAs. The potential mechanisms underlying these findings warrant further investigation.

## **INTRODUCTION:**

High-intensity endurance training is associated with marked increases in cardiac output (CO) over periods of several hours. This workload promotes a high degree of stress on all myocardial structures, but especially on the right ventricle (RV) (La Gerche 2011), a heart cavity that typically works at low pressures at rest. In response to this long-term overload, a characteristic exercise-induced RV remodelling has been described in endurance athletes, characterized by larger RV size and lower RV inlet systolic strain (Teske 2009). Although structural and functional cardiac changes in response to exercise are classically considered adaptive and benign, a potential link between RV remodelling due to chronic training and increased prevalence of arrhythmias has been suggested among the sportive population (Benito 2011; Heidbüchel 2003). Data from clinical and experimental studies suggest a more favourable cardiac remodelling in females than in males in response to different scenarios of left ventricle (LV) pressure and volume overload (Weinberg 1999; Gardner 2002; Fliegner 2010). However, the influence of gender on RV remodelling has been scarcely studied. In addition, female athletes have typically been underrepresented in studies of cardiac adaptation to exercise. Exercise stress echocardiography offers an excellent tool to non-invasively evaluate real-time RV response to exercise, thus making it useful for estimating RV reserve (La Gerche 2012) and identifying athletes with potential pathological exercise-induced RV functional remodelling (La Gerche 2015).

The present study had two specific objectives: 1) to evaluate the influence of gender on RV structural and functional adaptation to chronic high-intensity endurance training; 2) to analyse RV performance during acute exercise in endurance athletes and evaluate the influence of gender on this behaviour. We hypothesized that long-term endurance training would promote similar structural and functional changes in the RV in both genders, with potentially more pronounced changes in male athletes. In addition, we hypothesized an increased performance during exercise in both ventricles, but expected that this improvement would be blunted for the RV at high exercise workload.

**Key words:** athlete's heart; sex; exercise; endurance training; right ventricle

**ABBREVIATIONS:**

**CO:** cardiac output

**EKG:** electrocardiogram

**FAs:** female athletes

**GLS:** global longitudinal strain

**HR:** heart rate

**LV:** left ventricle

**MAAs:** male athletes

**RV:** right ventricle

**RVFWLS:** right ventricle free wall longitudinal strain

**RVOT:** right ventricle outflow tract

**SV:** stroke volume

**METHODS:****Study population**

We included the first 20 female and 20 male endurance athletes (aged 20-45 years) who answered advertisements at local running clubs, had been performing >10 hours of intensive endurance exercise training per week for at least the last 5 years, and had competed in at least 4 long-distance running competitions (marathon, half ironman, ironman, ultra-trail race) in the last 2 years. We recruited 40 age-matched volunteers (20 women and 20 men) from hospital staff members. Those who responded to an advertisement were included if they engaged in regular recreational activity (mild to moderate non-competitive exercise, <3 hours/week). None of the respondents met the exclusion criteria of known cardiovascular disease, symptoms, or risk factors for cardiovascular disease.

The study protocol complied with the declaration of Helsinki and was approved by the Ethics Committee of our institution. All participants provided written informed consent.

### **Echocardiography**

All subjects underwent an exercise stress echocardiogram with an increment in workload of 25 W every 2 min until exhaustion and with reaching at least 85% of their maximum theoretical heart rate (HR). Exercise was performed on a semisupine cycle-ergometer (EE e-bike; GE Medical; Milwaukee, USA) with simultaneous 12-lead electrocardiographic recording. An echocardiogram was performed after at least 20 minutes of rest in pre-prandial condition and again during maximum effort. All echocardiographic images were acquired with a commercially available ultrasound system (Vivid Q; GE Medical; Milwaukee, USA). Images were acquired from the parasternal (long- and short-axis) and apical (4-, 3- and 2-chamber) views. Three consecutive cardiac cycles for each acquisition were digitally stored in a cine loop format for off-line analysis with commercially available software (EchoPac GE, Vingmed). Cardiac chamber dimensions were measured according to the standards of the European Association of Cardiovascular Imaging (Lang 2015) and indexed for body surface area according to the DuBois formula. LV volume and ejection fraction were derived using the biplane Simpson method. RV end-diastolic area and end-systolic area were estimated by tracing the endocardium from an apical 4-chamber view. RV fractional area change was then calculated. Maximal atrial volume were calculated using the biplane summed discs method (Lang 2015) for both left (LA) and right atrial (RA). RV and LV diastolic function were assessed by peak early (E) and atrial (A) flow velocities and annular velocities of the tricuspid and mitral valves (Lang 2015). Stroke volume (SV) was calculated with quantitative Doppler as the product of LV outflow tract area and velocity time integral of flow at that level (Baumgartner 2009).

### **Myocardial deformation imaging**

Myocardial deformation of both ventricles was evaluated from two-dimensional echocardiography using speckle tracking (2Dstrain, EchoPac, General Electric Healthcare, Milwaukee, WI, USA).RV peak systolic segmental strains were measured in the basal (inlet), mid and apical segments of the RV free wall (RV-FW); additionally, global RV peak systolic strain (RVGLS) was measured as an average of all six RV segments (3 RV-FW and 3 inter-ventricular septum) and

global RV-FW peak systolic strain (RVFWLS) as an average of the RV-FW segments. Left ventricle global longitudinal strain (LVGLS) was calculated as an average of LV systolic strain in 2-, 3- and 4- chamber apical views. Special care was taken to acquire zoomed images of the RV in apical views (60-80 frames per second) to ensure an adequate ratio of spatial/temporal resolution. Both at rest and during exercise, only segments with visually appropriate tracking were used for the analysis.

### **Statistical Analysis**

Data were analysed with SPSS Software for Windows (V.19.0, SPSS Inc., Chicago, New York, USA). A Gaussian distribution of all continuous variables was confirmed using a Kolmogorov–Smirnov test and values reported as mean and standard deviation (SD). Echocardiographic results at baseline (before exercise) were compared with a two-way ANOVA in which two main factors (Sex, Training status) and their interaction (Sex \* Training status) were included. No significant interactions were found for any of the variables tested and, thus, results for main effects are shown. Echocardiographic changes with exercise were also compared in all groups. In order to account for gender- and training- baseline differences, the percent change ( $\Delta$ ) from baseline was calculated for all echocardiographic parameters. Delta ( $\Delta$ ) values were compared with a two-way ANOVA in which two main factors (Sex, Training status) and their interaction (Sex \* Training status) were included. No significant interactions were found for any of the variables tested and, thus, results for main effects are shown. Those parameters significantly changing with exercise ( $\Delta \neq 0$ ) are shown with an asterisk (one sample t-test). Correlations between the different parameters were assessed with the Pearson rank test. Reproducibility was expressed as intraclass correlation coefficient.

## **RESULTS**

### **Baseline population characteristics**

Table 1 summarizes the population characteristics and echocardiographic parameters at rest in all four study groups. None of the study participants had a personal or family history of cardiovascular diseases. All four groups were of similar age. Body surface area was higher in men than in women, and systolic and diastolic blood pressure were slightly higher in men but within normal limits. Male and female athletes had a similar training load, evaluated by years of training and training hours per week. As expected, athletes had lower heart rates, compared to controls. Indexed SV was greater in athletes than in controls; as a result, there were no significant differences in indexed cardiac outputs at baseline between the four groups. All controls had normal electrocardiograms (ECG) and athletes had exercise-induced adaptive ECG changes: right bundle branch block and sinus bradycardia.

### **Resting left-sided cardiac performance.**

As expected, LA and LV indexed dimensions were greater in athletes as compared to controls, with no significant gender differences. As part of exercise-induced cardiac remodelling, athletes had enhanced LV diastolic function (higher E/A and e'/a' ratios) compared to controls; no significant differences were observed in LV volumetric function between the 4 study groups. Although high-intensity endurance exercise induced no significant changes in LV deformation, LVGLS values were significantly higher in women than in men.

### **Resting right-sided cardiac performance**

Long-term endurance training promoted an increase in all RA and RV indexed dimensions and a more spherical RV shape. Athletes had higher E/A tricuspid velocity ratios, compared to controls. However, e'/a' tricuspid annulus velocity ratios were similar between all 4 groups and no significant differences in RV volumetric function were observed. Athletes of both gender exhibited lower RV basal segmental strain values while no differences in RVGLS or apical and mid

segmental strains were shown between controls and athletes. However, women had higher RV segmental and global strain values compared to men, independently of training load.

### **Influence of gender in exercise-induced ventricular remodelling.**

Two-way ANOVA applied to athletes and controls showed no interaction between exercise and gender in determining ventricular dimensions and function (table 2). However, as it is depicted in figure 1, for the LV, males (independently of training load) cluster in a region with lower strain compared to female while athletes of both genders showed larger indexed sizes but similar strains compared to controls. However, for the RV, while for the females, the athletes assembly in larger sizes compared to the non-athletes, the males overall cluster in larger sizes. As for the LV, females (both athletes and controls) exhibited higher RV deformation values compared to males.

### **Ventricular performance and hemodynamic parameters during exercise.**

Table 2 summarizes hemodynamic and echocardiographic parameters during peak exercise in the 4 study groups. As expected, athletes had higher workload than controls. The increase in CO was similar between male and female athletes, although the males achieved a higher workload. In all 4 groups, this acute CO increase during exercise was mainly achieved by an increase in HR and to a lesser extent by an increase in SV. The % of the maximal theoretical HR achieved during effort was slightly greater in women (both athletes and controls) as compared to men. The increase in LV deformation and volumetric function was positively correlated with the increase in CO (correlation  $\% \Delta \text{CO}$  vs  $\% \Delta \text{LV}$  ejection fraction:  $r = +0.46$ ,  $p < 0.001$  and vs  $\% \Delta \text{LVGLS}$ :  $r = +0.31$ ,  $p = 0.02$ ), suggesting that the increase in LV function was proportional to exercise demand. However, in the whole population, the improvement in RV volumetric function and deformation showed no significant correlation with the increase in CO during exercise and was not proportional to the exercise demand (being significantly lower in male athletes despite their higher workload). In all 4 groups, the increase in RVGLS during exercise was mainly induced by an improvement in RV basal segmental strain, while RV apical segmental strain increased slightly in both groups of controls, showed no changes in female athletes, and decreased in male athletes. Including heart rate



as a covariate in the ANOVA analysis for bi-ventricular deformation changes during exercise, similar results were documented (data not shown). Both groups of athletes showed a slight decrease in LV size during exercise; no changes were documented in controls. No significant changes in RV size during exercise were observed in any of the 4 groups.

#### **Reproducibility of speckle-tracking analysis.**

Intraobserver and interobserver intraclass correlations were performed in 10 patients. Intraobserver and interobserver reproducibility for LVGLS was 0.96-0.94 at rest and 0.95-0.92 during exercise; for RVGLS, 0.94-0.90 at rest and 0.91-0.89 during exercise; for RVFWS, 0.92-0.89 at rest and 0.90-0.85 during exercise; for RVLS at basal segment, 0.93-0.90 at rest and 0.91-0.88 during exercise; for RVLS at mid segment: 0.91-0.89 at rest and 0.89-0.89 during exercise; and for RV apical segmental strain 0.93-0.90 at rest and 0.89-0.84 during exercise.

#### **DISCUSSION:**

The current exploratory study provides a comprehensive analysis of ventricular performance both at rest and during exercise, in male and female endurance athletes, compared to controls. The study has three key findings: a) long-term endurance training induced an increase in size in both ventricles and both atria, without significant changes in ventricular function, regardless of gender; b) independently of training, men had larger right heart cavities and lower bi-ventricular deformation values, compared to women; and c) the required increase of ventricular performance during exercise was blunted for the right ventricle at high exercise workload, especially in male athletes.

#### **Left-sided exercise-induced remodelling:**

Our results are in line with previous data confirming that long-term endurance training promotes significant LV and LA dilatation (La Gerche 2011; Whyte 2004; Utomi 2014) without changes in LV systolic function (Whyte 2004; Utomi 2014) and with enhanced LV diastolic function

(D'Ascenzi 2015). As reported by Peterson et al (2006), these structural and functional LV changes promoted by endurance exercise were of similar extent in both men and women. This finding contrasts with the unfavourable remodelling in response to different LV pressure overload in men, compared to women, documented by experimental and clinical studies (Weinberg 1999) and volume overload scenarios (Gardner 2002), but supports the physiologically adaptive nature of structural and functional exercise-induced changes in the LV. Our finding of higher LV deformation values in women (regardless of training load) is also in agreement with results from a study in 1266 healthy subjects by Dalen et al (2010) and suggests that values establishing LV deformation normality limits are not interchangeable between men and women.

#### **Right-sided exercise-induced remodelling:**

Our study provides additional evidence that long-term endurance training promoted significant RA and RV dilatation (Oxborough 2012; D'Andrea 2013; Utomi 2015). In accordance with D'Andrea et al (2013), the increase in RV size was dominant at the RVOT, especially in transverse heart diameters, and led to higher RV sphericity. In concordance with previous data (D'Andrea 2013; Utomi 2015), no differences in RV systolic volumetric function were observed, but lower deformation RV basal segmental strain was documented in athletes, compared to controls (Teske 2009; Sanz-de la Garza 2015). RV diastolic function in athletes is still a controversial issue (La Gerche 2015; Sanz-de la Garza 2015). In our study, endurance training promoted improved diastolic function in the LV but not in the RV. This finding requires further research, but suggests once again that exercise-induced remodelling differs in the right side of the heart, compared to the left. In accordance with Peterson et al (2006), structural and functional RV exercise-induced changes were similar in both men and women. However, in contrast with LV results, index RV size was significantly lower in female than in male athletes. In theory, this potential greater RV dilatation in men would be beneficial in responding to exercise demand (to increase SV), but according to the Laplace law this dilatation would ultimately occur at the cost of higher wall stress (Gabielli 2014; Marciniak 2007). As for the LV, and in agreement with previous studies from Chia and colleagues (Chia 2014), regardless of training load, women showed higher RV

deformation values compared to men. Furthermore, this findings has been confirmed in a MRI study by Lawton and colleagues (Lawton 2011). Thus, in establishing RV deformation normality limits, the influence of gender should be consider.

### **Biventricular performance during exercise**

Cardiac output is the result of a combination of HR and SV; in turn, SV is determined by myocardial deformation and cavity size (Bijnens 2012). Therefore, the acute increase in CO required during exercise (La Gerche 2012) can be achieved by an increase in HR, in cavity volume (dilatation), or a combination of these three elements. In the present study, the required increase in CO during exercise was achieved mainly by an increase in HR and to a lesser extent by an increase in SV. In addition, this acute increase in SV was achieved by an increase in bi-ventricular deformation. However, the behaviour of the two ventricles differed radically in our study: although we documented an increase in LV volumetric function and deformation proportional to the exercise demand in all the study groups, the improvement of RV performance (the increase in RV volumetric function and deformation) was blunted in athletes at higher workloads (higher increases in SV), especially in male athletes. Our findings suggest that the increase in contractility during exercise is limited in the RV, especially at higher workloads, when higher pulmonary artery pressure is reported (D'Andrea 2011; La Gerche 2012). In addition, despite similar increases in SV in both groups of athletes during exercise and even while women (both athletes and controls) achieved greater % HR of the maximal theoretical than men, this blunting in RV improvement in response to the exercise demand was more pronounced in male than in female athletes. Experimental and clinical studies have demonstrated that oestrogens have a vasodilator effect on pulmonary vasculature (Parker 2000; Tofovic 2010). As we couldn't estimate pulmonary artery pressure in our study, we could only hypothesize that this difference in RV performance response to exercise might be the result of a protective oestrogenic factor in female pulmonary vasculature. This limitation in RV contractility increase during exercise would constrain male athletes to RV and RA dilation in response to exercise demand and would explain why right heart cavities were larger in male than in female athletes in our study.

On the other hand, there were differences between the RV segments in their response to exercise demand. The basal segment had the major role in increasing SV during exercise, compared to the apex, confirming previous data (Sanz-de la Garza 2015). The apical segment of the RV is highly trabeculated and has a small volume (Ross 1977). Taking into account the small apical volume, the decrease in apical deformation we observed during exercise could be an adaptive response, preventing further apical deformation when all local volume has been ejected. Our finding that apical deformation decreased during exercise in male athletes, despite no changes in female athletes, would be in concordance with lower pulmonary artery pressures during exercise in females. The potential protective effect of oestrogenic hormones on female pulmonary vasculature remains to be elucidated and cannot be derived from the findings of the present study.

### **Conclusion**

Long-term endurance training promoted similar structural and functional cardiac remodelling in both male and female athletes. However, men had larger right heart cavities and lower bi-ventricular deformation independently of training load. In theory, this would constitute an advantage in terms of increasing SV in response to exercise demand, but it would ultimately generate higher wall stress. The improvement in RV performance during exercise was blunted at high workloads, especially in male athletes. The potential reasons that underline these findings warrant further investigation.

### **Limitations**

This observational study was carried out in a relatively small sample of participants, limiting its statistical power and generalizability. During exercise, the higher heart rates would result in less frames per cardiac cycle for speckle tracking analysis. Thus, bi-ventricular deformation values during exercise could be less accurate. However, both ventricles were analysed with the same technique so underestimated values would not explain the distinctly different response to exercise shown in RV deformation compared to LV. Additionally, ventricular deformation results for both

ventricles were unchanged after including the percentage change in HR as a covariate. An important limitation of the study is that we were unable to assess pulmonary artery systolic pressure accurately using the regurgitant tricuspid flow because most of the participants showed minimal tricuspid regurgitation, with inadequate Doppler signals for estimation. Using a contrast agent might have improved our acquisitions. In relation with deformation evaluation, only the longitudinal component was analysed and therefore the influence of changes in the circumferential component in the response to exercise could not be established. In the other hand, right ventricular morphology was only evaluated by 2-D echocardiography, whereas 3-D analysis would be more suited to take into account its complex geometry. We speculated that oestrogens could explain sex-related differences in the responses to exercise and ultimately in chronic right ventricle remodelling, but we did not measure hormone levels in the study population. More accurate functional and structural analysis of pulmonary vasculature and of RV geometry and function would be useful to better understand the influence of gender in RV adaptation to exercise.

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**Table 1: Population characteristics and baseline echocardiographic parameters in male and female athletes and controls**

	Male Athletes	Male Controls	Female Athletes	Female Controls	Gender	Sport	Interaction
Age (years)	38.0±3.5	36.2±3.5	37.4±6.3	36.9±4.6	0.98	0.25	0.53
BSA (m <sup>2</sup> )	1.88±0.09	1.91±0.17	1.60±0.10	1.62±0.11	<u>&lt;0.001</u>	0.35	0.80
HR (b.p.m)	57.5±8.1	66.5±8.9	59.9±5.1	74.9±7.6	0.06	<u>&lt;0.001</u>	0.11
SBP (mmHg)	125.0±10.5	119.0±6.4	111.7±11.5	110.6±13.1	<u>&lt;0.001</u>	0.15	0.30
DBP (mmHg)	79.0±5.3	77.9±4.9	73.3±8.4	71.3±8.8	<u>&lt;0.001</u>	0.33	0.77
SV (ml/m <sup>2</sup> )	49.3±4.9	41.6±3.7	48.6±4.3	39.8±3.8	0.20	<u>&lt;0.001</u>	0.55
CO (L/min/m <sup>2</sup> )	2.8±0.4	2.8±0.3	2.9±0.3	2.9±0.4	0.12	0.85	0.33
Training (hours/week)	13.5±1.6	NA	13.2±1.4	NA	0.71	<u>&lt;0.001</u>	0.69
Training (years)	10.2±3.4	NA	10.8±4.0	NA	0.56	<u>&lt;0.001</u>	0.56
RVEDA (cm <sup>2</sup> /m <sup>2</sup> )	15.6±2.2	12.2±2.7	11.6±1.7	8.6±1.6	<u>&lt;0.001</u>	<u>&lt;0.001</u>	0.63
RVOT (mm)	38.5±3.5	32.1±3.4	34.6±2.9	29.1±3.8	<u>&lt;0.001</u>	<u>&lt;0.001</u>	0.29
RVOT, indexed (mm/m <sup>2</sup> )	20.5±1.9	16.9±1.7	21.8±2.1	17.9±2.8	<u>&lt;0.001</u>	<u>&lt;0.001</u>	0.08
RV basal diameter (mm)	44.8±4.8	37.3±3.1	36.5±4.2	30.8±4.0	<u>&lt;0.001</u>	<u>&lt;0.001</u>	0.32
RV longitudinal diameter (base to apex) (mm)	77.3±6.5	72.6±5.1	61.8±5.7	57.5±7.0	<u>&lt;0.001</u>	<u>&lt;0.001</u>	0.83
RV sphericity index (basal/long diameter)(mm)	0.58±0.04	0.52±0.04	0.59±0.07	0.53±0.07	0.35	<u>&lt;0.001</u>	0.52
RVFAC (%)	47.9±5.1	49.6±6.1	49.3±5.1	47.3±5.8	0.62	0.82	0.12
RVFWLS (%)	-26.9±3.0	-26.6±2.6	-32.7±2.7	-32.4±2.1	<u>&lt;0.001</u>	0.98	0.57
RVGLS (%)	-24.0±3.6	-24.9±2.5	-29.2±3.1	-30.0±2.7	<u>&lt;0.001</u>	0.24	0.97
BASAL.RVLS	-22.8±3.0	-24.2±3.3	-26.6±2.1	-27.9±3.0	<u>&lt;0.001</u>	<u>&lt;0.001</u>	0.89
MID.RVLS	-27.1±3.6	-26.9±3.0	-34.0±2.6	-33.7±3.1	<u>&lt;0.001</u>	0.91	0.97
APICAL. RVLS	-30.5±3.6	-28.4±3.4	-37.4±2.7	-37.2±2.2	<u>&lt;0.001</u>	0.12	0.28
E/A tricuspid	1.80±0.47	1.38±0.22	1.80±0.28	1.48±0.20	0.49	<u>&lt;0.001</u>	0.47
e'/a' tricuspid	1.31±0.41	1.30±0.31	1.56±0.49	1.41±0.40	0.07	0.44	0.36
e' tricuspid	10.4±1.7	10.6±0.9	10.6±1.2	10.2±1.1	0.92	0.89	0.11
S' tricuspid	10.2±1.4	9.8±0.9	9.8±1.0	11.3±1.4	0.11	0.12	0.31
RAV (ml/m <sup>2</sup> )	30.8±11.02	21.9±7.5	22.3±4.3	14.2±4.5	<u>&lt;0.001</u>	<u>&lt;0.001</u>	0.80
LVEDV (ml/m <sup>2</sup> )	68.4±10.4	49.5±6.9	62.3±8.6	45.6±6.9	0.09	<u>&lt;0.001</u>	0.60
LVM (mg/m <sup>2</sup> )	89.8±15.7	80.8±12.9	68.7±10.9	57.8±7.8	<u>0.01</u>	<u>&lt;0.001</u>	0.73
LVEF (%)	56.1±4.2	57.1±5.1	55.8±3.5	58.6±5.1	0.57	0.09	0.41
LVGLS (%)	-17.5±1.4	-18.7±1.2	-21.9±1.9	-22.5±1.5	<u>&lt;0.001</u>	0.08	0.40
E/A mitral	1.97±0.31	1.58±0.35	1.82±0.39	1.56±0.32	0.30	<u>&lt;0.001</u>	0.40
e'/a' mitral	2.44±0.56	2.05±0.52	2.62±0.80	2.10±0.59	0.38	<u>&lt;0.001</u>	0.62



LAV (ml/m <sup>2</sup> )	25.0±6.7	18.7±5.1	27.1±6.2	15.8±4.5	0.76	<u>&lt;0.001</u>	0.09
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Underlined values signify p <0.05 by two-way ANOVA for the main factors: gender and sport and their interaction. **NA:** not applicable. **BSA:** body surface area. **HR:** heart rate. **SV:** stroke volume. **SBP:** systolic blood pressure. **DBP:** diastolic blood pressure. **CO:** cardiac output.

**RVEDA:** right ventricle end-diastolic area. **RVOT:** right ventricle outflow tract. **RVFAC:** right ventricle fractional area change. **RVFWLS:** right ventricle free-wall longitudinal strain.

**RVGLS:** right ventricle global longitudinal strain. **BASAL/MID/APICAL.RVLS:** Right ventricle longitudinal strain. **RAV:** right atrial maximum volume. **LVEDV:** left ventricle end-diastolic volume. **LVEF:** left ventricle ejection fraction. **LVGLS:** left ventricle global

longitudinal strain. **LAV:** left atrial maximum volume.

**Table 2: Percentage changes in hemodynamic and echocardiographic parameters during exercise in male and female athletes and controls.**

	Male athletes	Male Controls	Female athletes	Female Controls	Gender	Sport	Interaction
Workload(Watts)	221.3±40.1	171.3±22.1	173.8±29.0	123.3±25.7	<u>&lt;0.001</u>	<u>&lt;0.001</u>	0.62
	Δ%	Δ%	Δ%	Δ%			
HR (b.p.m)	+173.1±44.6*	+138.0±34.7*	+176.0±22.9*	126.4±24.2*	0.56	<u>&lt;0.001</u>	0.33
%HR maximum theoretical	87.7±2.6	88.2±2.8	90.1±3.2	91.3±3.3	<u>0.02</u>	0.15	0.51
SBP (mmHg)	+64.6±14.7*	+60.5±12.7*	+67.4±15.6*	+57.7±20.3*	0.97	0.07	0.43
DBP (mmHg)	-0.4±9.6	+3.0±11.8	+4.7±13.8	+6.3±13.2	0.17	0.45	0.83
SV (ml/m <sup>2</sup> )	+28.8±8.2*	+26.0±7.7*	+24.7±4.9*	+20.1±5.7*	<u>0.01</u>	<u>0.02</u>	0.56
CO (l/min/m <sup>2</sup> )	+252.2±59.1*	+200.8±40.8*	+243.9±28.9*	+173.0±33.1*	0.09	<u>&lt;0.001</u>	0.34
RVEDA (cm <sup>2</sup> /m <sup>2</sup> )	-1.3±7.9	-1.9±9.7	-3.9±5.4	+1.7±9.5	0.79	0.20	0.11
RVAFC (%)	+8.9±14.9*	+5.8±19.2	+17.2±16.4*	+12.5±15.3*	0.07	0.33	0.83
RVFWLS (%)	+4.5±12.9	+13.4±13.2*	+13.2±11.2*	+18.4±13.5*	<u>0.03</u>	<u>0.02</u>	0.44
RVGLS (%)	+8.5±13.4*	+14.7±13.0*	+13.3±10.9*	+20.0±12.7*	0.08	<u>0.04</u>	0.91
BASAL.RVLS (%)	+18.6±14.7*	+20.2±18.8*	+25.3±11.5*	+18.5±9.7*	0.48	0.49	0.21
MID.RVLS (%)	+5.0±14.7	+14.6±15.4	+10.9±15.0	+13.3±10.1*	0.51	0.08	0.26
APICAL.RVLS (%)	-6.8±15.5	+7.4±10.9*	+5.5±12.7	+13.3±9.1*	<u>0.03</u>	<u>0.01</u>	0.44
LVEDV (ml/m <sup>2</sup> )	-9.6±11.3*	-3.7±13.7	-9.1±8.7*	-5.9±9.7	0.78	0.07	0.66
LVEF (%)	+15.7±7.0*	+10.1±7.3*	+14.4±9.0*	+8.2±6.8*	0.45	<u>&lt;0.001</u>	0.92
LVGLS (%)	+28.6±6.3*	+24.6±8.9*	+30.3±11.5*	+22.1±9.3*	0.94	<u>0.01</u>	0.22

Underlined values signify  $p < 0.05$  by two-way ANOVA for the main factors: gender and sport and their interaction. \*  $p < 0.05$  by one sample T-test. Δ%: percentage change at peak of exercise.

**HR:** heart rate. **SBP:** systolic blood pressure. **DBP:** diastolic blood pressure. **SV:** stroke volume.

**CO:** cardiac output **RVEDA:** right ventricle end-diastolic area. **RVFAC:** right ventricle fractional area change. **RVFWLS:** right ventricle free wall longitudinal strain. **RVGLS:** right ventricle global longitudinal strain. **BASAL/MID/APICAL.RVLS:** Right ventricle longitudinal strain. **LVEDV:** left ventricle end-diastolic volume. **LVEF:** left ventricle ejection fraction.

**LVGLS:** left ventricle global longitudinal strain.

## **FIGURE LEGENDS**

**Figure 1:** Figure 1 depicts the relationship between size and deformation for the LV (A) and the RV (B) for athletes and controls. Athletes exhibited greater LV and RV size and lower deformation, compared to controls. Women presented higher bi-ventricular deformation values and lower indexed RV volumes, compared to men.

