Alterations in Cardiac Mechanics following Ultra-endurance Exercise: Insights from Left and Right Ventricular Area-Deformation Loops

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Highlights:

- This study provides data for temporal cardiac mechanics using area-strain loops.
- The loops assess the interaction between the ventricles following prolonged exercise.
- There is not a serial impact of the right ventricle on the left ventricle.
- This provides further mechanistic understanding of exercise-induced cardiac fatigue.

Abstract

Objective: The aim of this study was to utilise novel area-deformation (ε) loops to interrogate the interaction between the right and left ventricular mechanics following a 100 mile endurance run.

Methods: Fifteen participants (body mass 70.1 ± 8.8 kg, age 40 ± 8 years) were recruited for the study. Echocardiograms were performed pre-race, post-race and 6 hours into recovery. Right ventricular (RV) and left ventricular (LV) area and longitudinal ε were assessed using standard and speckle tracking echocardiography. Following cubic spline interpolation these variables were obtained across the same cardiac cycle and used to derive area-ε loops.

Results: The RV area-ε loop demonstrated a rightward shift post-race with increased RV area (26.0 to 27.1 cm^2) and reduced peak RV ε (-28.6 to -25.8%). The recovery RV area-ε loop was similar to post-race. A leftward shift was observed in the LV area-ε loop post-race secondary to reduced LV area (35.8 to 32.5 cm^2 respectively) and reduced peak ε (-18.3 to -16.6% respectively). In recovery, LV ε values returned towards baseline.

Conclusion: A 100 mile ultra-marathon resulted in a rightward shift in the RV area-ε loop as a result of RV dilatation. There was a concomitant leftward shift in the LV area-ε loop as a result of under-filling of the LV. At 6 hr post-exercise there was a partial recovery of the LV whilst RV function remained depressed. It appears that changes in RV function do not have a serial impact on the LV during recovery from ultra-endurance activity.

Keywords: echocardiography, endurance exercise, strain imaging, area-deformation loops, cardiac mechanics

66 **Abbreviation List**

Abbreviation	Definition
2D	two dimensional
3D	three dimensional
A	peak late diastolic trans-mitral blood flow velocity
A’	peak late diastolic myocardial tissue velocity
ASE	American Society of Echocardiography
BOO	atrial booster volume
BP	blood pressure
CON	atrial conduit volume
E	peak early diastolic trans-mitral blood flow velocity
E’	peak early diastolic myocardial tissue velocity
ECG	electrocardiogram
EDA	end diastolic area
EDV	end diastolic volume
EF	ejection fraction
EI	eccentricity index
ESV	end systolic volume
FAC	fractional area change
HR	heart rate
LA	left atrium
LV	left ventricle
PA	pulmonary artery
PASP	pulmonary artery systolic pressure
RA	right atrium
RES	atrial reservoir volume
RV	right ventricle
RVD_1	right ventricular inflow minor axis – basal level
RVD_2	right ventricular inflow minor axis – mid level
RVD_3	right ventricular major axis
RVD_{area}	right ventricular end diastolic area
$RVOT_1$	right ventricular outflow tract parasternal short axis at aortic valve level
$RVOT_2$	right ventricular outflow tract parasternal short axis at infundibulum
$RVOT_{plax}$	right ventricular outflow tract parasternal long axis at the aortic valve level
RVS_{area}	right ventricular end systolic area
S’	peak systolic myocardial tissue velocity
SV	stroke volume
TAPSE	tricuspid annular plane systolic excursion
TDI	tissue Doppler imaging
VOL ED	atrial volume at end diastole
VOL ES	atrial volume at end systole
VOL pre A	atrial volume prior to P wave
VTI	velocity time integral
ε	strain

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Introduction

The impact of prolonged strenuous exercise on cardiac function has received significant attention (1) with evidence of a transient, negative impact on both the right (RV) and left (LV) ventricles. A number of theories describing the possible mechanisms responsible for these findings have been proposed including beta-adrenergic receptor desensitization, oxidative stress and impaired calcium metabolism (2), however these have yet to be substantiated. A new theory has suggested that RV function may be depressed post-exercise due to the disproportionate changes in RV wall stress, subsequent to an increased pulmonary vascular resistance encountered during prolonged activity (3). In this instance, the RV is unable to maintain contractile force against an elevated afterload and to sustain stroke volume (SV), the RV dilates. A reduction in RV SV would have the effect of reducing blood volume through the pulmonary system reducing preload to the left atrium (LA). This in turn would impact on overall LV filling.

Echocardiographic techniques such as strain (ε) imaging have allowed a more comprehensive assessment of LV and RV function and these have recently been employed in the post-prolonged exercise setting (4-7). These studies have reported a reduction in peak LV and RV ε alongside alterations in chamber dimensions, but the impact of ultra-endurance exercise on temporal cardiac mechanics remains largely unknown. In this setting, the interaction of RV and LV structure and function has received limited attention and a comprehensive evaluation of simultaneous structure and ε throughout the cardiac cycle has not been attempted. The combination of echocardiographic modalities may help to reveal mechanical changes in cardiac function whilst offering a more comprehensive understanding of exercise-related structural and functional adaptation. The concept of assessing area-ε relationships (loops) within the ventricles is novel and provides the potential for determining the contribution of longitudinal deformation to area change in both ventricles.

In view of this, the current study utilises a novel approach by assessing echocardiographic derived temporal area-ε loops in conjunction with conventional 2D and Doppler indices, in order to establish any serial impact of changes in RV structure and function on and LV structure and function as well as any ventricular interaction following prolonged strenuous exercise (100 mile endurance run).

Furthermore, the study aims to establish whether any changes in cardiac mechanics persist 6 hours into recovery from the exercise bout.

Materials and methods

Sample Population

Fifteen elite runners (14 males, 1 female, body mass 70.1 ± 8.8 kg, height 179 ± 6 cm, age 40 ± 8 years) at the 2013 Western States 100 mile Endurance Run (Squaw Valley to Auburn, CA) were recruited and volunteered to take part in the study. Participants self-reported: no known cardiovascular disease, no prescribed medications and no comorbidities or family history of cardiovascular disease. The current training status (training days 6 ± 1 per week, 65 ± 12 miles/ 12 ± 3 hours per week) and number of completed ultra-marathons (38 ± 32) were documented. Written informed consent was obtained and ethics approval granted by the Liverpool John Moores University Ethics Committee.

Protocols

Participants were assessed pre-race (24 - 48 hours prior to the race) and immediately post-race (within 30 minutes of race completion). A sub-sample (n = 9) also returned for a recovery data collection at 6 hours post-race completion. Height, body mass, resting blood pressure (BP), a resting 12-lead electrocardiogram (ECG) and a supine echocardiogram were recorded at each time point. For the pre-race assessments, participants were requested to avoid vigorous training, alcohol for a minimum of 24 hours prior to the initial assessment and caffeine 4 hours prior to this time point. Throughout the race the participants were permitted to consume food and fluid *ad libitum* and temperature ranged from 73 to 102 °F. Race finishing time ranged from 18:55 to 23:55 hours.

Echocardiographic Assessments

All echocardiographic images were acquired using a commercially available ultrasound system (Vivid Q, GE Medical, Horten, Norway) with a 1.5-4 MHz phased array transducer. Images were obtained by a single experienced sonographer with the participant in the left lateral decubitus position. Images were recorded to DVD in raw DICOM format and data were analysed offline using commercially

available software (EchoPac version 7, GE Medical, Horten, Norway). A minimum of three cardiac cycles were averaged for all peak indices.

Conventional 2D, Doppler and Tissue Doppler Echocardiography

The RV was assessed in accordance with American Society of Echocardiography (ASE) guidelines (8) providing structural and functional indices at the outflow tract ($RVOT_{plax}$, $RVOT_1$ and $RVOT_2$) and at the inflow (RVD_1, RVD_2, RVD_3). RV diastolic area (RVD_{area}) and systolic area (RVS_{area}) were measured and the fractional area change calculated (RVFAC). RV SV was calculated from conventional pulsed wave Doppler using the volumetric equation $RVSV = (\pi r^2).RVOT_2VTI$ where (r = $RVOT_{2(systole)}$ / 2) and velocity time integral (VTI) is obtained sub-valvular. A pulsed wave tissue Doppler imaging (TDI) sample positioned at the tricuspid annulus allowed the assessment of peak myocardial velocities in systole (S'), early diastole (E') and late diastole (A'). RV systolic pressure was derived from the tricuspid regurgitant jet using continuous wave Doppler. Pulmonary artery (PA) systolic pressure (PASP) was calculated as ($PASP\ (mmHg) = RVS_p + 5mmHg$). RV and LV end-systolic wall stress was calculated using the formula $ES\text{-}\sigma = Pr/2h$ as previously described (3).

A comprehensive assessment of LV structure and function was undertaken in accordance with ASE guidelines (9). LV end diastolic (EDV) and systolic (ESV) volumes were estimated using Simpsons biplane methodology allowing the calculation of stroke volume (SV) and ejection fraction (EF). LV eccentricity index (EI) was calculated as a measure of interventricular septal displacement. LV diastolic function was assessed using trans-mitral Doppler providing peak velocities in early (E) and late diastole (A) and their ratio (E/A). Pulsed wave TDI assessment of the lateral and septal annulus provided S', E' and A' velocities and the average of both walls reported. E/E' was calculated as a non-invasive surrogate of left atrial (LA) pressure.

A full assessment of LA and RA structure and volumetric function was assessed using a Simpson biplane method as previously described (6). LA and RA volumes at end systole (VOL ES), end diastole (VOL ED) and pre A (VOL pre A) were calculated allowing the derivation of reservoir (RES), LA conduit (CON) and booster (BOO) volumes.

2D Myocardial Speckle Tracking

A focused apical four chamber orientation was acquired for assessment of the LV whilst a modified image with lateral transducer movement was acquired for assessment of the RV. For the assessment of LV circumferential function, rotation and torsion, images of the LV were acquired from a parasternal short axis view at the base, mid and apex. For all images the system was optimised as previously described (5). Offline analysis allowed the assessment of peak global longitudinal RV ε calculated as an average of 3 myocardial segments from base to apex of the RV lateral wall. LV global longitudinal ε is based on a 6 segment model from the four-chamber view only in order to allow the construction of simultaneous area-strain loops. Peak global LV circumferential ε was calculated as an average of 6 myocardial segments at basal mid and apical levels. Peak basal and apical rotation and rotation rates in systole and early and late diastole were obtained to allow the calculation of peak twist and twist rate as the net difference between basal and apical rotation and rotation rate respectively

Area-Deformation Loops

In order to standardise for variable heart rates (HR), temporal data was obtained throughout the entire cardiac cycle using cubic spline interpolation in Microsoft Excel (2010) to provide 300 data points for both systole and diastole as previously described (10). The splined data of longitudinal RV and LV ε were used to derive time points for the simultaneous area and ε calculations. Both systole and diastole were divided into 10% increments, essentially providing 20 time points and subsequent ε values across the full cardiac cycle. The original image and cardiac cycle that was used to derive the ε values was then re-analysed for RV/LV area in 2D at each corresponding time point, hence providing a simultaneous RV/LV ε and RV/LV area (see Figure 1). This was undertaken for each individual participant and the mean area-ε at percentage increments were calculated across the cohort. Data was plotted as area against ε (area-ε loop) for the whole cohort for RV and LV longitudinal motion using commercially available software (GraphPad Prism).

Polynomial regression analysis of the order $y=mx^2+mx+c$ was performed on each individual participants area-ε loops for systole and diastole independently at pre, post and post 6 hours. Using the polynomial equation ε values in systole and diastole were calculated for 10% increments of the chambers end diastolic area (EDA) within the range 40-90% for the LV and 60-90% for the RV to

reflect physiological functional area change in each ventricle. The difference between the same percentage of EDA in systole and diastole was calculated and termed *systolic-diastolic strain gradient*.

Reliability data for the RV and LV area-ε loops was assessed by a single operator constructing and analysing individual loops in a separate sample of 20 healthy control subjects on two separate occasions. Data from the RV and LV were similar across EDA ranges (40 to 80%) with coefficient of variation values ranging from 7-21% for simultaneous ε, area and systolic-diastolic gradient. Comprehensive reliability data for each 10% change in EDA is provided in Supplementary Tables 1-3).

Statistical Analysis

Due to the reduced sample size from post-race to post 6 hour data collection, pre-race versus post-race data were compared using Student's Paired T-tests and recovery data reported for descriptive purposes only. All statistical tests were performed using commercially available software (IBM SPSS version 21). Previous studies on a similar sample size have set alpha as $P < 0.05$ with no correction for multiple comparisons, in the current study alpha was set at $P < 0.01$ as a sensible balance between the likelihood of producing type I and II statistical errors.

Results

Demographics

Systolic and diastolic BP were significantly reduced post-race. Heart rate and body mass were not different at pre and post-race assessments (see Table 1).

Conventional 2D, Doppler and Tissue Doppler Echocardiography

There was a post-race increase of 13% in RV outflow and inflow dimensions (P = 0.004 and 0.002, respectively, see Table 2) whilst there was an 18% reduction in RV S' (P = 0.005; Table 2). RV SV was maintained with no significant reduction observed post-race as were RV FAC and RV E'. RV wall stress was elevated compared to baseline immediately post-race and in recovery and PAP was reduced post-race compared to pre-race measures albeit not significantly. There was an 11% decrease in LV EDV post-race (P = 0.005, see Table 2). There was an 18 % decrease in trans-mitral E (P = 0.001) and a subsequent 19% decrease in the E/A velocity ratio (P = 0.003). LV S', E' and A' were reduced by 10% post-race (P < 0.006). LV wall stress was reduced post-race and in recovery compared to pre-race values, albeit not significantly. LA VOL ES, pre A, ED, CON, RES and BOO volumes were not different post-race (P > 0.01). There was no change in RA VOL ES, pre A, ED, RES and BOO volumes pre to post-race (P > 0.01).

Myocardial ε Imaging

Peak RV longitudinal ε was reduced by 10 % pre to post-race (P = 0.007). LV longitudinal ε was reduced by 9% post-race (P = 0.01). LV basal, mid and apical circumferential ε were all reduced (19, 14 and 15%, P = 0.001, 0.008 and 0.01 respectively) pre to post-race as were basal and apical rotation, twist and systolic and diastolic twist rates (39, 46 and 46%, P = 0.007, 0.002, <0.001, 0.004 and <0.001 respectively, see Table 3).

Area-Deformation Loops

The RV area-ε loop demonstrated a rightward shift immediately post-race with increased RV area and reduced peak RV ε dictating that RV ε was elevated for any given area. That aside the polynomial regression equations were similar compared to baseline and the systolic-diastolic strain gradient was

unchanged reflected by the similar shape of the loop (see Table 4). The RV area-ε loop at 6 hr recovery was almost identical to the post-race loop (see Figure 2).

A leftward shift was observed in the LV area-ε loop post-race, secondary to reduced LV area and reduced peak ε. Hence for any given area, absolute ε values were lower. There was a change in LV longitudinal systolic-diastolic strain gradient post-race at 80, 70 and 40% EDA (see Table 4). This is also corroborated by the change in shape of the LV post-race area-ε loop. In recovery, the systolic-diastolic strain gradient returned close to baseline values, however the LV loop remained shifted to the left (see Figure 2).

Discussion

This is the first study to determine simultaneous area and ε relationships in the RV and LV in response to prolonged strenuous exercise. We observed that, 1) prolonged strenuous exercise resulted in RV dilatation and a reduction in contractility reflected by the rightward shift in the area-ε loop, although RV SV was maintained, and 2) post-exercise there is reduced filling in the LV as demonstrated by the leftward shift in the area-ε loop. The lack of change in the RV loop in the presence of a return towards baseline of the LV systolic-diastolic gradient at 6 hours recovery indicates an intrinsic reduction in relaxation that does not appear to be primarily driven by changes in RV structure and function such that there appears to be no serial impact of the RV on the LV.

Impact of Prolonged Strenuous Exercise

Previous studies on the LV and RV following prolonged strenuous exercise using conventional 2D and Doppler indices have reported a decrease in both LV and RV systolic and diastolic function (4, 5, 7). The data in the current study supports these findings with a depression in LV and RV systolic and diastolic function evident post-exercise. LV and RV structural indices in the current study are also in support of exercise-induced adaptation previously reported with a reduction in LV and increase in RV size previously documented (5-7).

The data from area-ε loops describe detailed changes in cardiac mechanics following prolonged endurance exercise whilst illuminating potential mechanisms. The visual representation of temporal cardiac mechanics provides further understanding of the ventricular interaction. The area-ε loops identify a post-exercise increase in RV size without any change in longitudinal contribution to area change. In view of an unchanged area-ε relationship and no change in the longitudinal systolic-diastolic strain gradient it is likely that the reduced peak contractility observed post-exercise is a consequence of the larger volume. Our findings of a maintained RV SV and no change in LA end systolic volume suggest a lack of intrinsic dysfunction of the RV myocardium. The LV area-ε loop data demonstrates post-exercise reduced filling of the LV with a concomitant reduction in peak longitudinal ε. Although systolic ε is lower at any given area post-exercise, it is clear the area-deformation relationship in systole is similar to baseline and is therefore likely to be a consequence of reduced filling. LV wall stress and blood pressure are both reduced post-race and therefore LV afterload is

reduced. In this instance, myocardial ε should increase due to a relative reduction in myocardial workload (11), in contrast we observed a reduction in post-race ε providing further support for an intrinsic reduction in function. There is a significant change in the longitudinal contribution in diastole post-race as demonstrated by an increased LV loop systolic-diastolic strain gradient. These changes in diastolic mechanics are in the presence of a reduced LA conduit volume and therefore may be partly responsible for the under-filling observed post-exercise. This is further evidenced by a maintenance of LA preload / volume and RV SV. These changes in the LV loop are supported by a reduction in circumferential strain, basal and apical rotation, twist and early diastolic untwist rate.

RV dilatation and dysfunction has been suggested to be secondary to a sustained exposure to a relatively elevated wall stress (3) and therefore the dysfunction observed in the post-exercise setting is likely to be a 'fatigue' of the myocardium resulting in a reduced stroke volume (5) with a serial negative impact on LV filling (6). Data from the current study significantly develops our knowledge of the post-prolonged exercise structure / function relationship of the RV but with only partial support of previous theories and no evidence indicating a serial impact of the RV on LV filling. Post-exercise wall stress in the current study is elevated, however the pulmonary artery pressure is reduced in recovery and therefore the increase in wall stress is likely as a result of the RV dilatation seen in recovery from prolonged strenuous exercise. The mechanistic theories postulated for LV dysfunction following prolonged endurance exercise are plentiful and include oxidative stress (12), myocardial damage (13), beta-receptor desensitization (14) as well as the impact from an enlarged, dysfunctional RV (3). The recovery loops provide further insight into the mechanisms underpinning LV dysfunction. Whilst the RV area-ε relationship remains similar to immediately post-exercise, the systolic-diastolic strain gradient of the LV loop returns to baseline level and provides strong evidence that the changes in longitudinal contribution to area change in diastole are intrinsic in nature and not secondary to a serial impact from the RV. That aside, the LV is still under-filled and therefore we must also speculate that there is an additional mechanism at play leading us to consider the multifactorial nature of LV post-exercise dysfunction.

A major contributing factor in LV filling is the ability of the ventricle to untwist, generating a sharp decline in LV pressure during early diastole (10). LV untwist is ultimately driven by its preceding twist

as potential energy is stored within the compressed titin molecule during ventricular systole (15) but also by the maintenance of LV structural integrity. It is apparent that any disruption to twist mechanics will impact on overall LV filling. Our data demonstrates a reduced twist and untwist immediately post-exercise which persists 6 hours into recovery. This may contribute to reduced LV filling immediately post-race and throughout the recovery period.

An alternative mechanism for the reduction in LV twist is a parallel RV impact on LV function, indicative of ventricular interdependence. This has been observed in the presence of increased RV volume/pressure and results in septal displacement in both systole and diastole (16). The displaced septum in diastole impacts on LV circumferential and torsional mechanics and reduces the ability of the LV to fill to capacity, thereby highlighting the interaction between the ventricles (17). Septal displacement has been observed in a few post-exercise studies (5, 7) as well as a recent case-report (18). The current data highlights an increased eccentricity index immediately post-exercise and theoretically, it could be argued that a 'parallel RV impact' has some influence on LV filling in the current study independent of any intrinsic reduction in LV relaxation.

Implications

Taking the current data, together with previous research, it is suggested that there is a possible cascade of cardiovascular events that result in changes in function. This cascade appears to be multifactorial, starting with diastolic filling abnormalities of the LV and RV at marathon level (6, 7, 19, 20) or moderate intensity shorter duration exercise (21). As exercise duration and/or intensity progress, this culminates in a combination of intrinsic LV and RV dysfunction and structural adaptation (3, 4, 5, 7, 22) alongside evidence of ventricular interdependence (3,5). Our data highlights the impact of extreme endurance exercise on RV and LV function and supports the notion of an interdependence between the RV and LV due to a displaced interventricular septum, due to RV overload, and the subsequent impact on LV mechanics. Previous data from our group have also demonstrated a negative correlation between finishing time and magnitude of RV enlargement at the inflow and dysfunction (5, 22). This raises the likelihood of exercise intensity being an important driver in acute RV adaptation and may also apply with respect to the LV. The relationship between increased previous experience and a reduced acute response is equally intriguing. This would imply

that RV remodeling through repeated exposure to an ultra-marathon results in chronic adaptation that may well be protective when faced with an acute exercise stimulus. What this means for the 'weekend warrior' is debatable but it would be sensible to consider this spectrum and the heterogeneous effects based on individual training, experience and race completion time. These findings lead us to consider that the magnitude of acute RV adaptation is very likely to be related to exercise volume (i.e. intensity x duration) particularly in those athletes that are less experienced.

Limitations

A 3 dimensional (3D) technique would overcome potential geometric limitations of the current 2D imaging, however the current frame-rates for real-time acquisition of 3D volume and ε are low and provide limited scope for detecting small changes in function. Global longitudinal ε in the current study was derived using a 6 segment model and therefore does not represent inferior, anterior, posterior or anterior septal function. The 6 segment model from the apical 4 chamber view provides global longitudinal strain that is representative of global function in athletes. RV and LV area-ε loops were only assessed in the longitudinal plane and therefore construction of circumferential area-ε loops may provide additional insight. The assessment of ventricular function and area-ε loops during exercise may reveal the timing of RV dilatation and determine whether LV intrinsic relaxation occurs prior to recovery. It would also be pertinent to assess the time course of RV and LV response in recovery from prolonged endurance exercise. The recovery time point in the current study indicates a partial recovery of the LV but not the RV and it is unclear how long these exercise-induced responses may persist for. Periodic assessments over the 24-48 hours following prolonged endurance exercise is an important consideration for future studies and has implications for sufficient recovery periods between training session and/or races. Due to the nature of this field based study, we were only able to assess a small sample of athletes and therefore the statistical power of the study is limited. In addition, six of the fifteen athletes assessed prior to and immediately following the race did not return for the 6 hour recovery time point, therefore recovery data could only be provided for descriptive comparison and is not included in any statistical analysis.

There are alterations is loading from pre to post-race, indicated by elevated heart rate and reduced blood pressure immediately following the race. A correlation between the change in heart rate and changes in the variables assessed in this study did not reveal any significant relationship. This indicates that the significant differences seen pre to post race are occurring independent of heart rate mediated loading conditions. Furthermore, previous studies have demonstrated that when afterload is reduced (as with a lower BP) then strain would be expected to increase as it is working against a lower afterload and therefore wall stress is reduced (11, 23). Our data reflects the opposite response with a reduction in strain when afterload is slightly altered suggesting that the changes in loading conditions are not solely responsible for these changes. In the event of reduced preload, strain may be reduced as a result of the Frank-Starling law. If there is reduced filling in the left ventricle (indicated by a reduction in EDV), then stroke volume and contractility are reduced. It would be pertinent to include the analysis of ventricular/vascular coupling to further understand the loading/function relationship.

Cardiac biomarkers were not measured during this study, however the inclusion of brain natriuretic peptide and/or cardiac troponins may aid the understanding of post-exercise changes in cardiac structure and function. Previous studies have linked post-exercise cardiac biomarker release to LV and more specifically RV dysfunction and investigating this relationship further may expose a mechanistic link. Blood sampling in our participants would also help to exclude perturbations to blood rheology such as rhabdomyolysis and hyponatremia, which could impact on cardiac function. That said, all participants were all self-ambulatory, had no physical signs and symptoms of sodium disturbance and all had voided their bladder during or after the race with no blood content.

Conclusion

There is evidence of a persistent post-exercise shift in the RV area-ε loop indicating RV dilatation with reduced contractility that is likely a consequence of RV structural adaptation rather than any intrinsic dysfunction. The LV area-ε loop is shifted left immediately post-exercise and the LV is under filled, likely as a result of intrinsically reduced longitudinal relaxation and impaired LV twist/untwist. The former mechanism is transient and returns to normal following 6 hours of recovery whilst LV

twist/untwist remains depressed which could explain a persistent LV under-filling, perhaps due to an RV/LV interaction. Importantly from a mechanistic insight, at 6 hr post-exercise there appears to be no obligatory serial impact of reduced RV function on LV mechanics. It may be that mechanical changes with prolonged exercise in the LV and RV are independent.

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Table and Figure Legends

Table 1 – Participant demographics pre and post-race and after 6h of recovery

Table 2 - Left and right ventricular and atrial structural and functional data pre-race, post-race and after 6 hours of recovery

Table 3 - Left and right ventricular ε data pre-race, post-race and after 6 hours of recovery

Table 4 - Systolic-diastolic strain gradients for right and left ventricles pre-race, post-race and after 6 hours of recovery

Figure 1 – Systematic methodology for generation of area-deformation loops

Figure 2 – Right and left ventricular area-deformation (ε) loops pre to post-race and post-race to recovery. Pre and post-race loops derived from n = 15, recovery loops derived from n = 9.

Table 1 – Participant demographics pre and post-race and after 6 hours of recovery

Parameter	Pre (n = 15)	Post (n = 15)	Recovery (n = 9)
Body mass (kg)	70.1 ± 8.8	68.8 ± 7.8*	66.1 ± 7.9
Systolic BP (mmHg)	134 ± 11	114 ± 12*	117 ± 12
Diastolic BP (mmHg)	84 ± 10	76 ± 8*	77 ± 8
Heart rate (bpm)	63 ± 10	70 ± 10	71 ± 12

* indicates statistical significance pre to post race ($P<0.01$. Data analysed using paired t-tests and presented as mean±SD. N.B. the 6 athletes who did not return for recovery measures reduce the mean body mass at the recovery time point.

Table 2 - Left and right ventricular and atrial structural and functional data pre-race, post-race and after 6 hours of recovery

Parameter	Pre (n = 15)	Post (n = 15)	Recovery (n = 9)
Right Ventricle			
$RVOT_{plax}$ (mm)	30 ± 4	33 ± 3*	33 ± 4
$RVOT_1$ (mm)	32 ± 4	36 ± 4*	35 ± 5
$RVOT_2$ (mm)	25 ± 2	28 ± 2	27 ± 3
RVD_1 (mm)	43 ± 4	48 ± 5*	47 ± 6
RVD_2 (mm)	32 ± 3	37 ± 3*	36 ± 3
RVD_3 (mm)	84 ± 6	83 ± 7	82 ± 6
RVFAC (%)	54.1 ± 5.8	48.8 ± 4.7	50.3 ± 8.2
TAPSE (mm)	24 ± 4	23 ± 4	26 ± 3
RV S' (cm/s)	17 ± 3	14 ± 3*	16 ± 1
RV E' (cm/s)	17 ± 2	14 ± 4	14 ± 3
RV A' (cm/s)	13 ± 5	12 ± 3	13 ± 3
RV SV (ml)	92 ± 25	89 ± 25	102 ± 35
PASP (mmHg)	25 ± 4	22 ± 8	23 ± 2
RV Wall Stress (kdynes/cm^2)	3.97 ± 1.93	4.39 ± 1.30	2.94 ± 2.24
Left Ventricle			
LV EDV (ml)	123 ± 15	109 ± 16*	112 ± 17
LV ESV (ml)	41 ± 5	47 ± 9*	39 ± 8
LV SV (ml)	82 ± 11	63 ± 11*	73 ± 11
LV EF (%)	66 ± 3	58 ± 6*	65 ± 3
MV E (m/s)	0.84 ± 0.17	0.69 ± 0.18*	0.74 ± 0.17
MV A (m/s)	0.50 ± 0.09	0.51 ± 0.11	0.53 ± 0.08
MV E/A	1.70 ± 0.38	1.37 ± 0.37*	1.38 ± 0.26
LV S' (cm/s)	13 ± 2	12 ± 1*	13 ± 2
LV E' (cm/s)	16 ± 2	13 ± 3*	15 ± 2
LV A' (cm/s)	10 ± 1	9 ± 2*	9 ± 2
E/E'	5.29 ± 1.01	5.20 ± 1.05	5.11 ± 1.26
EI Diastole	1.16 ± 0.11	1.22 ± 0.10	1.14 ± 0.08
EI Systole	1.09 ± 0.07	1.15 ± 0.12	1.14 ± 0.08
LV Wall Stress (kdynes/cm^2)	16.82 ± 2.34	14.42 ± 2.40	12.83 ± 1.66
Left Atrium			
LA VOL ES (ml)	55 ± 8	57 ± 11	60 ± 12
LA VOL pre A (ml)	33 ± 5	34 ± 8	37 ± 10
LA VOL ED (ml)	17 ± 3	21 ± 5	22 ± 6
LA RES (ml)	38 ± 6	36 ± 6	38 ± 8
LA CON (ml)	44 ± 13	26 ± 8	35 ± 5
LA BOO (ml)	16 ± 74	13 ± 4	15 ± 6
Right Atrium			
RA VOL ES (ml)	62 ± 23	62 ± 14	58 ± 22
RA VOL pre A (ml)	42 ± 14	46 ± 13	40 ± 13
RA VOL ED (ml)	28 ± 9	29 ± 11	27 ± 8
RA RES (ml)	34 ± 15	33 ± 9	31 ± 15
RA BOO (ml)	14 ± 7	17 ± 8	14 ± 7

*****indicates statistical significance pre to post race ($P<0.01$). Data analysed using paired t-tests and presented as mean±SD

Table 3 –Right and left ventricular ε data pre-race, post-race and after 6 hours of recovery

Parameter	Pre (n = 15)	Post (n = 15)	Recovery (n = 9)
RV longitudinal ε (%)	-28.6 ± 3.8	-25.8 ± 2.8*	-27.4 ± 4.1
LV longitudinal ε (%)	-18.3 ± 1.5	-16.6 ± 2.7*	-18.5 ± 2.4
LV basal circumferential ε (%)	-22.7 ± 2.0	-18.5 ± 3.7*	-21.2 ± 2.4
LV mid circumferential ε (%)	-20.4 ± 3.3	-17.6 ± 3.6*	-21.1 ± 2.7
LV apical circumferential ε (%)	-39.1 ± 8.1	-33.2 ± 6.6*	-35.9 ± 7.3
Basal rotation (^{0})	-8.7 ± 3.5	-5.3 ± 3.1*	-5.2 ± 3.2
Apical rotation (^{0})	16.5 ± 6.0	9.0 ± 5.0*	11.7 ± 3.2
Twist (^{0})	24.8 ± 6.6	13.5 ± 6.3*	16.5 ± 3.7
Systolic twist rate (^{0}/s)	121.7 ± 25.9	90.1 ± 25.8*	120.3 ± 16.3
Early diastolic twist rate (^{0}/s)	-150.6 ± 26.1	-83.8 ± 33.6*	-149.3 ± 38.5
Late diastolic twist rate (^{0}/s)	-79.0 ± 20.9	-78.5 ± 41.3	-81.9 ± 33.1

* indicates statistical significance pre to post race (P<0.01). Data analysed using paired t-tests and presented as mean±SD

Table 4 – Systolic-diastolic strain gradients for right and left ventricles pre-race, post-race and after 6 hours of recovery

% EDA	Pre Race (n = 15)	Post Race (n = 15)	Recovery (n = 9)
Right Ventricle			
90	-4.2	-4.2	-4.4
80	-5.8	-6.3	-6.4
70	-5.7	-6.2	-6.8
60	-4.1	-4.0	-5.4
Left Ventricle			
90	-1.0	-1.8	-0.7
80	-0.9	-2.8*	-0.9
70	-0.7	-2.4*	-0.9
60	-0.3	-0.5	-0.6
50	0.2	2.8	-0.2
40	0.8	7.5*	0.5

* indicates statistical significance pre to post race ($P<0.01$). Data analysed using paired t-tests.