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Right Ventricular Structure and Function in the Veteran Ultramarathon Runner: Is There Evidence for Chronic Maladaptation?

Right Ventricular Structure and Function in the Veteran Ultramarathon runner: Is there Evidence for Chronic Maladaptation?

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ABSTRACT

Background: It has been proposed that chronic exposure to prolonged strenuous exercise may result in maladaptation of the right ventricle (RV). The aim was to establish RV structure and function, including septal insertion points, using conventional echocardiography and myocardial strain (ε) imaging in a veteran population of ultramarathon runners (UR) and age and sex-matched controls.

Methods: A retrospective study design provided 40 UR (>35 years old; mean ± SD training experience: 18 ± 12 years) and 24 sedentary controls whom had previously undergone conventional 2D, tissue Doppler and speckle tracking echocardiography to measure RV size and function. Peak RV ε and strain rate (SR) were assessed from the base, mid, and apical lateral wall. SR were assessed during systole (SRs'), early diastole (SRe') and late diastole (SRa'). Regional assessment of RV insertion points were made at the basal inferoseptum and apical septum using left ventricular (LV) longitudinal ε, and at the anteroseptum and inferoseptum using LV circumferential and radial ε.

Results: All structural indices of RV size were significantly larger in UR. RV regional and global peak ε were not different between groups whereas basal RV SR was significantly lower in UR. UR had significantly higher peak LV circumferential ε (anteroseptum: -26 ± 8% vs -21 ± 6%; inferoseptum: -25 ± 6% vs -16 ± 9%), and higher peak LV longitudinal ε (apical septum; -28 ± 7% vs -22 ± 4%) compared to controls. There was regional heterogeneity in UR that was not observed in controls with significantly lower longitudinal ε at the basal inferoseptal insertion point when compared to the global ε (-19 ± 2% vs -22 ± 4%).

Conclusion: Myocardial ε imaging highlights no overt maladaptation in this cohort of veteran UR, although lower insertion point ε, compared to global ε, in UR may warrant further investigation.

Key Words: Echocardiography; Myocardial speckle tracking; Right ventricle; Strain imaging; Ultramarathon runner.

List of Abbreviations:

A':	Late diastolic myocardial tissue velocity
E':	Early diastolic myocardial tissue velocity
LV:	Left Ventricle
PLAX:	Parasternal Long Axis view
RV:	Right Ventricle
RVDarea:	Right ventricular end-diastolic area
RVFAC:	Right Ventricular Fractional Area Change
RVOT:	Right Ventricular Outflow Tract
RVSarea:	Right ventricular end-systolic area
ε:	Strain
S':	Systolic myocardial tissue velocity
SD:	Standard Deviation
SR:	Strain Rate
SRa':	Late diastolic strain rate
SRe':	Early diastolic strain rate
SRs':	Systolic strain rate
STE:	Speckle Tracking Echocardiography
TAPSE:	Tricuspid Annular Plane Systolic Excursion
UR:	Ultramarathon runners

INTRODUCTION

Regular exercise has been shown to positively affect risk factors for cardiovascular disease [1]. Despite this, the dose-response effect for exercise and cardiovascular health is controversial at high levels of training volume over many years [2,3]. There is evidence to suggest that a single bout of high volume endurance exercise can lead to a disproportionate wall stress on the right ventricle (RV), compared to the left ventricle (LV), that precipitates an RV dilatation and reduction in function in the acute post-exercise setting [4,5]. Typically, these changes are transient and physiological in nature [6] but the cumulative effect of lifelong exercise exposure of this nature is unknown [7].

Chronic RV adaptation in endurance athletes has been well documented [8,9,10,11] however there is some evidence to suggest that competitive endurance athletes have reduced regional function at the base of the RV compared to non-athletes [11]. These findings have generally been attributed to the physiological remodelling of the chamber rather than any intrinsic dysfunction [12]. Other evidence demonstrating potential maladaptation in the RV of athletes has been reported and suggested to reflect repeated extreme exercise exposure and insufficient recovery time [13]. In this setting, the potential for an exercise induced RV cardiomyopathy has been postulated [14]. There are some case series data in endurance athletes documenting myocardial fibrosis in the inter-ventricular septum at the RV insertion points [15] specifically those with greater RV structural remodelling and a greater training experience [16]. In addition, animal studies have demonstrated a relationship between exercise-induced RV remodelling and a propensity for RV arrhythmias [17]. This area requires more empirical evidence initially in

those athletes who have undertaken the largest volumes of exercise training and competition.

Although a recent study reported ventricular adaptations in the lifelong male endurance athlete [18], they did not assess regional RV strain rate (SR) or circumferential and radial strain (ε) at the RV insertion points. Since fibrosis is predominantly localised to the insertion point regions in lifelong endurance athletes, it may prove to be of some significance to assess tissue deformation from multiple planes in these regions. Speckle tracking echocardiography (STE) can measure global and regional function, providing ε and SR of tissue deformation from multiple planes of motion over time [19] including the ability to assess ε at the RV insertion points. It would therefore be novel and pertinent to explore these myocardial segments in detail. Furthermore, most descriptions of the RV phenotype of athletes reflect young athletic populations and often those competing in team sports or endurance events <26 miles [20,21,22]. There is a paucity of data in 'veteran' (> 35 years of age with prolonged exposure to extreme training volumes) ultramarathon runners (UR).

The aims of this study were to compare: 1) RV morphology and conventional measures of RV function 2) global and regional peak ε and peak SR of the RV lateral wall, and 3) peak regional ε in the interventricular septum at the segments where RV attachment occurs, between veteran UR and sedentary age and sex-matched controls. We tested the following hypotheses: 1) RV size will be larger in UR whilst conventional measures of RV function will be lower, 2) peak ε and SR across the RV lateral wall will be lower in UR, and 3) circumferential, radial and longitudinal ε, at the two RV insertion points, will be lower in UR.

METHODS

Study Population and Study Design.

The study utilised a cross-sectional, case-control design. Forty (33 men) retrospectively studied UR were recruited prior to undertaking one of three ultramarathons (2005 Comrades 87-km Run, Durban, South Africa; 2013 & 2014 161-km Western States Endurance Run, Squaw Valley, CA to Auburn, CA, United States). In addition, twenty-four (20 men) sedentary controls (defined as doing less than 2 hours structured exercise training per week) were recruited and assessed at the Research Institute for Sport and Exercise Science at Liverpool John Moores University. All participants were healthy non-smokers, aged between thirty-five and sixty-five, free from diabetes, hypertension, and any known cardiovascular, renal, liver, endocrinal, metabolic or respiratory disease. Participants were not currently taking any prescribed medication. The existence of pre-clinical coronary disease could not be excluded, but all participants self-reported no clinical symptoms and had no family history of premature coronary disease.

Participants were assessed on a single visit having refrained from consuming caffeine or alcohol and undertaking any vigorous exercise in the preceding 24 hours. The testing session involved the completion of a health and training questionnaire, assessment of height and weight allowing the calculation of body surface area [23], assessment of left brachial artery blood pressure, a resting 12-lead electrocardiogram and a comprehensive 2D, Doppler, tissue Doppler and speckle tracking echocardiogram. All participants had a normal resting electrocardiogram with no evidence of non-training related abnormalities as determined by European Society of

Cardiology guidelines [24]. Likewise, there was no evidence of valve disease, pulmonary hypertension or coronary artery disease on the resting echocardiogram. All athletes and controls with non-training related changes on the ECG or were symptomatic as determined by a health questionnaire were excluded. In addition, participants were excluded if they had any abnormal non-training related anomaly seen on the echocardiogram. Participants provided written informed consent and the study was granted approval from the Liverpool John Moores University Research Ethics Committee.

Echocardiographic Assessment

All echocardiograms were completed by a single highly experienced sonographer in accordance with American Society of Echocardiography guidelines using a commercially available ultrasound system (Vivid Q; GE Medical; Horten, Norway) and a phased-array transducer (1.5- to 4-MHz). Images were acquired with the participant in the left lateral decubitus position and exported to offline analysis software (EchoPac version 7.0; GE Medical) for subsequent analysis. Measurements were completed by a single experienced operator. This was true for all participants regardless of when and where the assessments took place.

Standard Echocardiography

RV structure and function was assessed in accordance with American Society of Echocardiography guidelines [25] (see Supplementary Figures). Specifically, this included linear measurements of the RV outflow tract from a parasternal long-axis view (RVOTPLAX) as well as proximal (RVOT1) and distal (RVOT2) dimensions from a parasternal short-axis orientation. The inflow of the RV was assessed using a right sided modified apical 4-chamber view at the base (RVD1), mid cavity (RVD2), and apical to annular length (RVD3). In the

same modified apical 4-chamber view, a measurement of RV end-diastolic area (RVDarea) and RV end-systolic area (RVSarea) were made from manually tracing the endocardium providing a calculation of RV fractional area change (RVFAC). All structural data were scaled to BSA allometrically using the rule of geometric similarity (linear dimensions to Body Surface Area$^{0.5}$; structural areas linearly to body surface area) as previously described [26]. Tricuspid annular plane systolic excursion (TAPSE) was assessed using M-mode and TDI was used to measure peak myocardial velocities through the cardiac cycle in systole (S'), early diastole (E') and late diastole (A'). All peak tissue Doppler data were scaled to RV length as previously recommended [27]. Due to the inability to obtain an adequate tricuspid regurgitant Doppler signal and its relatively poor accuracy for deriving pulmonary artery pressures [28] we chose to determine the probability of pulmonary hypertension based on a multifactorial assessment of echocardiographic signs as defined by European guidelines [29].

Two-Dimensional Speckle Tracking Echocardiography

To assess STE derived RV longitudinal ε and SR, a modified apical 4-chamber orientation was acquired. For all images, the frame rates were maintained as close to 90fps whilst the depth, frequency and the angle of insonation were kept consistent to reduce variability [19]. All ε and SR traces were assessed offline. A narrow region of interest was placed over the RV lateral wall from base to apex providing peak ε and peak SR in ventricular systole (SRs'), during early (SRe') and late diastole (SRa') from the 3 segments base, mid-level, and apex. A base to apex gradient was then calculated as (basal ε - apical ε). To assess LV circumferential and radial ε at the RV insertion points (see **Figure 1**), the parasternal short-axis view at the basal level was acquired. The region of interest was placed around the endocardium encompassing the whole of the myocardium and peak ε was calculated from the inferoseptum and anteroseptum. In

addition, an apical 4-chamber orientation focused on the LV was used to provide peak longitudinal ε from the basal inferoseptum and apical inferoseptum. The LV Global ε values were calculated as an average of the six segments in each plane of motion.

Statistical Analysis

Normality was tested by the Shapiro-Wilk test and by inspection of the graphical plots. An independent samples T-test was used to assess differences between groups (UR vs controls) using commercially available software (SPSS version 22, IBM, NY, United States) with statistical significance set at $P < 0.05$. In order to establish relative ε at the RV insertion points, the absolute values of circumferential, radial and longitudinal ε in these regions were compared to global LV ε in each group using a Paired Samples T-Test. Where data was not normally distributed, the appropriate non-parametric test was used. All data are presented as mean ± standard deviation (SD).

A previous intra-observer reliability study based on repeated acquisitions undertaken in our laboratory demonstrated coefficient of variation for RV ε, SRs', SRe' and SRa' of 7%, 13%, 17%, 15% respectively [30].

RESULTS

Participant demographics are presented in **Table 1**. UR and controls were matched for age (mean ± SD: 46 ± 8 vs 46 ± 7 years) and sex (82.5% vs 83.3% men), respectively. There was no difference in height between groups but the controls were significantly heavier and had a

significantly larger body surface area than UR. Resting heart rate was significantly lower in UR.

RV structural indices are presented in **Table 2**. UR had significantly larger linear dimensions throughout the RV outflow and inflow tracts as well as RVDarea and RVSarea compared to controls. None of the participants from both UR and controls had either an intermediate or high probability for pulmonary hypertension [29]

Conventional RV functional data are presented in **Table 3**. UR had a significantly higher RVFAC, peak myocardial tissue velocity in systole (S') and early diastole (E') compared to controls. There were no between group differences in TAPSE or peak A'.

All between group differences in regional and global peak ε for the RV lateral wall and septal insertion points are presented in **Table 4**. There were no differences in peak RV lateral wall ε at basal, mid, or apical levels or RV base-to-apex gradient between UR and controls. UR had significantly higher peak LV circumferential ε at the anteroseptum and inferoseptum compared to controls, but there were no differences in peak LV radial ε at either of the insertion points. Peak LV longitudinal ε at the apical septum was significantly higher in UR when compared to controls but this difference was not apparent in the basal inferoseptal segment.

All regional SR data for the RV lateral wall are presented in **Figure 2**. Basal SRs' (P=0.0001), SRe' (P=0.017), and SRa' (P=0.005) were all significantly lower in UR when compared to the

controls (see Figure 1a). Mid-level SRs' (P=0.003) and apical SRa' (P=0.012) were also significantly lower in UR whilst all other SR parameters were similar between groups.

All within-subject comparisons in regional insertion point ε compared to the global ε are presented in **Table 5**. Peak LV longitudinal ε at the apical septum was significantly higher than the global LV ε in both groups, but to a greater magnitude in UR. Peak LV longitudinal ε at the basal inferoseptum was lower than global ε in UR. This finding was not seen in the control group. An example case of ε curves from each group is presented in **Figure 3**. In addition, radial ε was also lower at the inferoseptum and anteroseptum compared to global radial ε in both UR's and controls. The magnitude of reduction was greater in the UR group for both the inferoseptum and anteroseptum respectively. However, circumferential ε at the inferoseptum was higher compared to global values in UR. This finding was not seen in the control group. Circumferential ε at the anteroseptum was significantly higher than the global circumferential ε in both UR and controls.

DISCUSSION

The main findings from this study are that veteran UR, compared with age and sex-matched sedentary controls, have 1) larger RV inflow and outflow dimensions, 2) normal global RV function and regional and global ε, 3) lower peak basal systolic and diastolic SR extending to the mid segment in systole, and the apical segment in late diastole, 4) higher values of insertion point ε, 5) regional heterogeneity of insertion point ε compared to global ε.

Right Ventricular Structural Adaptation

RV enlargement has previously been documented in endurance athletes compared to non-athletes with greater RV inflow dimensions, proximal and distal RVOT dimensions [8,31] and RV areas [30]. These findings have been substantiated when compared to published normative ranges of the non-athlete [10], with up to 50% of UR having abnormal RV inflow and outflow dimensions according to the American Society of Echocardiography guidelines [25]. A recent study has supported these findings in Olympic level athletes [32]. Our study extends the current empirical database to UR >35 years of age with a long history of training and competitive experience. Our data provide further support for chronic physiological RV enlargement in the endurance athletes but it is important to highlight that the magnitude of RV dimensions was not greater than those previously reported studies of endurance athletes *per se*. It could be postulated that absolute RV remodelling reaches a threshold, regardless of training longevity and accumulated volume.

The factors contributing to an enlarged RV in endurance and UR athletes have been discussed in detail previously [14,33]. La Gerche and colleagues measured a disproportionately larger increase in end-systolic stress on the RV during strenuous exercise [4] and suggested this could underpin evidence of disproportionate structural adaptation in the RV compared to the LV [10]. The relative elevation in wall stress in the RV is likely related to the lower compliance of the pulmonary vasculature compared to the systemic circulation [31]. It has also been suggested that the smaller mass of the thin walled RV has insufficient contractile reserve to cope with this increased demand [14]. If these mechanisms hold true, then RV adaptation is a normal physiological response to endurance exercise that is not exacerbated in the extremes of the athlete population.

Right Ventricular Functional Adaptation

The current study demonstrated that UR had higher conventional indices of global RV function when compared to controls, but with similar global or regional peak ε. Previous findings are contradictory with no significant differences observed in RVFAC [12,34] or even a reduced RVFAC seen in elite endurance athletes compared to a non-athlete population [11]. A study directly targeting UR demonstrated significantly higher S' [35] with these findings being reproduced in long distance swimmers [36]. More recently others have found no significant differences in S' between veteran elite endurance athletes and sedentary age and sex-matched controls [18,35] and no differences between endurance athletes and non-athletes [31]. The disparity in the literature may well be reflective of the heterogeneous athlete populations that have previously been studied and / or the inherent limitations of conventional echocardiography. Doppler measures of systolic function are angle dependent and assume that a single segment represents global function of the RV [25]. It is therefore clear that further work should aim to better define global RV systolic function across a range of athlete demographics.

We also noted a higher E' in UR. Some studies have highlighted the positive impact of endurance training on RV early diastolic function in young athletes [37,38], however, more recent studies found no differences in diastolic function between veteran athletes and veteran non-athletes [18,39]. Taken together these data suggest that a lifetime of extreme endurance exercise does not adversely impact on myocardial relaxation.

Peak regional and global RV longitudinal ε was not different between UR and controls. The application of this technique highlights that the overall magnitude of contraction and relaxation is not enhanced or reduced in UR. These findings were not expected given the increase in RV size and higher RVFAC, and may suggest a greater contribution of non-longitudinal RV ε in UR. Regional SR at the base, mid and apex were different between groups with lower values observed in UR. Lower resting basal SR*s*' in endurance athletes has been reported elsewhere [11,15]. Both these studies integrated an exercise stimulus to demonstrate enhanced contractile reserve demonstrating that the reduced resting basal SR is simply a physiological response to the increased size of the RV. This phenomenon is also compounded by slower heart rates which may, in part, contribute to the findings observed in this study. 3

Strain at the RV Insertion Points

A novel and primary outcome of this study was to assess the chronic effects of UR exercise on the functional mechanics of cardiac tissues at the RV insertion points, from multiple planes of motion. Our findings of an increased LV global and insertion point circumferential ε are at odds with a previous study that described a depression in regional LV circumferential ε occurring only at the anteroseptal and inferoseptal segments [40]. These contradictory findings may well be explained with the clear differences in population age (20 ± 1 years vs 46 ± 8 years), training stimulus (rowers vs runners), or study design whereby the 90 days of unsupervised endurance training is not directly comparable to the lifelong veteran UR, and is more likely part of an acute adaptation.

Our findings of increased global and apical septum longitudinal ε are not supported by another study that found no significant differences in global or regional LV longitudinal ε at the RV insertion points between a veteran cohort of endurance athletes and sedentary controls [18].

They also demonstrated no evidence of myocardial necrosis or fibrosis as determined by cardiac magnetic resonance imaging utilizing the late gadolinium enhancement technique. Fibrosis has been documented in highly trained animal models [17], and has previously been observed in a small number of highly trained veteran endurance athletes [41] and often confined to the inter-ventricular septum most frequently in the regions of RV attachment [4,15]. However, late gadolinium enhancement in ultra-endurance athletes may not necessarily represent fibrosis, and could be a reversible observation caused from the acute stress of prolonged exercise [42].

The finding that longitudinal ε in the UR at the basal inferoseptum was lower than global ε values in the same individuals may suggest the presence of subtle changes in regional function. Longitudinal fibers predominate in the subendocardium [43] which may be more susceptible to fibrosis in the lifelong endurance athlete. The greater magnitude of difference in radial ε at the insertion points compared to controls provides additional support for a measurable regional intrinsic dysfunction. We may speculate that increases in circumferential ε in the inferoseptum compared to global values, may partially compensate for the reduction in longitudinal ε. Overall, all regions of LV ε were still higher in UR than controls which may suggest enhanced LV performance and function. These differences may simply highlight a normal process of adaptation that occurs in the ventricle with long-term endurance training. It is well established that myocardial ε reduces with age and therefore the combination of ageing and endurance training may delay this natural decline. It is apparent that further work is required to elucidate the true nature of these findings.

Clinical and Long-Term Implications

The veteran UR in our study presented with increased RV dimensions of both the inflow and outflow tract, with some of the UR above normal ranges reported by the American Society of Echocardiography [25]. This may have implications when screening these individuals. It is important to note that this is in the presence of normal conventional indices of RV function and global longitudinal RV ε. Reductions in regional RV SR can be expected from those individuals with enlarged RV's. Our data suggest that regional myocardial contractility in the insertion points may be lower compared to global values in veteran UR, however this is in the presence of normal global function. Insertion point deformation was also increased above that of controls, however the within subject reductions in UR is worth consideration.

Limitations

There are several limitations associated with this study. This was a retrospective study which was based on data collection from 3 different ultraendurance events. This has the potential to introduce issues with information and selection bias, however all assessments were carried out by the same experienced sonographer and using the same equipment. In addition, we utilized EchoPac software that is not the current version. It is very likely that our findings will be reproduced using the most recent version but there is the potential that this may negatively impact on the external validity within this unique cohort.

We did not utilize cardiac magnetic resonance imaging for late gadolinium enhancement and so have no direct measure of fibrosis. In addition, regional segments used are relatively large when compared to small areas of fibrosis that are often seen. Small areas of fibrosis may not affect the overall peak deformation of each insertion point segment. A modest sample size was used and therefore it is important to consider the limited generalizability.

Participants in this study were predominantly male and so caution should be taken when comparing raw data to other study populations where sex percentages may not match those of the present study. Sex-based differences in ventricular structure and function can only be truly alleviated when allometrically indexing to lean body mass [44]. We have provided data scaled to body surface area allometrically using the rule of geometric similarity in the hope that all future researchers adopt this feasible and validated approach [26], relieving the burden of body size differences.

It has been well documented that an acute bout of prolonged strenuous exercise has a negative impact on RV structure and function [6]. Based on this, it is possible that the UR in the current study may have some cardiac lag from previous training. That aside previous data has demonstrated that the acute changes are of a lower magnitude and more transient in UR's that are more experienced. Based on the current training volume and duration it is sensible to assume that the UR's in our study were at the threshold of adaptation and less likely to 'suffer' from these acute changes. In addition, we ensured that our participants had refrained from training for 24 hours prior to examination with most data suggesting any transient adaptation to acute training will revert to baseline within 6 hours of cessation of exercise.

Conclusion

Veteran UR over the age of 35 years and with 18 ± 12 years of training and competition, presented with structural remodeling of the RV inflow and outflow tracts in the presence of normal / enhanced global systolic and diastolic function and absolute peak ε. These athletes

presented with lower regional SR which may be related to the chronic adaptation in RV size. Global LV and insertion point ε were enhanced in UR, however there was some evidence of lower insertion point deformation, compared to global deformation in the same individuals, and this requires further study.

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FIGURE AND TABLE LEGENDS

Table 1. Participant demographics

Table 2. Conventional Echocardiographic Structural Indices – Absolute and Scaled

Table 3. Conventional Echocardiographic Functional Data

Table 4. Regional and global strain from the RV free wall and RV insertion points

Table 5. Within-subject regional RV insertion point strain compared to global strain

Figure 1. Diagrammatic representation of RV insertion point locations (IS = inferoseptum, AS = anteroseptum)

Figure 2. Regional strain rates from the RV free wall at a) basal level, b) mid-level, and c) apical level.

RV, right ventricle; SR, strain rate; SRs', systolic strain rate; SRe', early diastolic strain rate; SRa', late diastolic strain rate.

Figure 3. Exemplar regional and average LV longitudinal strain curves from a) control, and b) UR. This figure shows lower basal inferoseptum strain compared to global strain in UR, but not controls.

Table 1. Participant demographics

PARAMETER	ULTRARUNNERS (Mean ± SD)	CONTROLS (Mean ± SD)	*P*-VALUE
Age (years)	46 ± 8	46 ± 7	0.99
Sex (% men)	82.5%	83.3%	0.93
Height (cm)	177 ± 8	174 ± 7	0.11
Weight (kg)	71 ± 10	85 ± 14	**0.0002**
BSA (m^2)	1.87 ± 0.16	2.02 ± 0.19	**0.002**
Ultramarathon Training (years)	18 ± 12	-	-
Training (hrs/week)	11 ± 4	-	-
Number of races > 50 miles	61 ± 80	-	-
Resting Heart Rate ($beats.min^{-1}$)	58 ± 8	68 ± 10	**0.0002**
Systolic Blood Pressure (mmHg)	125 ± 12	128 ± 13	0.357
Diastolic Blood Pressure (mmHg)	80 ± 11	78 ± 10	0.572

BSA: body surface area

Table 2. Conventional Echocardiographic Structural Indices

PARAMETER	ULTRARUNNERS (Mean ± SD)	CONTROLS (Mean ± SD)	*P*-VALUE
$RVOT_{PLAX}$ Index $(mm/(m^2)^{0.5})$	23 ± 3	21 ± 3	**0.043**
RVOT1 index $(mm/(m^2)^{0.5})$	24 ± 3	21 ± 3	**0.0005**
RVOT2 index $(mm/(m^2)^{0.5})$	18 ± 2	16 ± 2	**0.004**
RVD1 Index $(mm/(m^2)^{0.5})$	31 ± 4	26 ± 4	**< 0.0001**
RVD2 Index $(mm/(m^2)^{0.5})$	21 ± 3	16 ± 3	**< 0.0001**
RVD3 Index $(mm/(m^2)^{0.5})$	64 ± 5	55 ± 6	**< 0.0001**
RVD area index (cm^2/m^2)	13 ± 2	9 ± 2	**< 0.0001**
RVS area index (cm^2/m^2)	7 ± 2	5 ± 2	**0.0002**

RV: right ventricular; RVOTPLAX: RV outflow tract from parasternal long axis view; RVOT1 and 2: RV outflow tract 1 (proximal) and 2 (distal); RVD: RV dimensions 1 (base) 2 (mid) 3 (longitudinal); RVD & RVS area: RV diastolic and systolic area

Table 3. Conventional Echocardiographic Functional Data

PARAMETER	ULTRARUNNERS (Mean ± SD)	CONTROLS (Mean ± SD)	*P*-VALUE
RVFAC (%)	50 ± 9	44 ± 8	**0.013**
TAPSE (mm)	24 ± 4	23 ± 4	0.32
TDI S' (cm/s)	17 ± 3	13 ± 2	**< 0.0001**
S' Index (cm/s)/cm)	1.95 ± 0.39	1.71 ± 0.27	**0.011**
TDI E' (cm/s)	15 ± 3	12 ± 3	**0.0001**
`E' Index (cm/s)/cm)	1.83 ± 0.46	1.54 ± 0.40	**0.015**
TDI A' (cm/s)	16 ± 4	13 ± 3	**0.016**
A' Index (cm/s)/cm)	1.85 ± 0.55	1.69 ± 0.40	0.25

RVFAC: RV fractional area change; TAPSE: tricuspid annular plane systolic excursion; TDI: tissue doppler imaging during ventricular systole (S') and during early (E') and late (A') ventricular diastole.

Table 4. Regional and global strain from the RV free wall and RV insertion points

PARAMETER	ULTRARUNNERS (Mean ± SD)	CONTROLS (Mean ± SD)	*P*-VALUE
RV Basal ε (%)	-27 ± 5	-29 ± 4	0.22
RV Mid ε (%)	-28 ± 4	-30 ± 5	0.17
RV Apical ε (%)	-32 ± 4	-32 ± 5	0.82
RV Base to apex GRADIENT (%)	4.3 ± 5.4	3.2 ± 5.0	0.40
LV Circumferential	-	-	-
Global ε (%)	-21 ± 4	-16 ± 3	**<0.0001**
Basal Anteroseptum ε (%)	-26 ± 8	-21 ± 6	**0.006**
Basal inferoseptum ε (%)	-25 ± 6	-18 ± 5	**<0.0001**
LV Radial	-	-	-
Global ε (%)	51 ± 19	43 ± 13	**0.04**
Basal Anteroseptum ε (%)	39 ± 19	34 ± 17	0.162
Basal Inferoseptum ε (%)	43 ± 19	38 ± 18	0.141
LV Longitudinal	-	-	-
Global ε (%)	-22 ± 4	-19 ± 2	**<0.0001**
Basal Inferoseptum ε (%)	-19 ± 3	-18 ± 2	0.12
Apical Inferoseptum ε (%)	-28 ± 7	-22 ± 4	**< 0.0001**

ε indicates strain; RV, right ventricular; LV, left ventricular

Table 5. Within-subject regional RV insertion point strain compared to global strain

LV Longitudinal	-	-	-
GROUP	**Apical Inferoseptum ε (%)**	**Global ε (%)**	***P*-VALUE**
UR	-28 ± 7	-22 ± 4	**<0.0001**
Control	-22 ± 4	-19 ± 2	**<0.0001**
GROUP	**Basal Inferoseptum ε (%)**	**Global ε (%)**	***P*-VALUE**
UR	-19 ± 3	-22 ± 4	**< 0.0001**
Control	-18 ± 2	-19 ± 2	0.141
LV Circumferential	-	-	-
GROUP	**Inferoseptum ε (%)**	**Global ε (%)**	***P*-VALUE**
UR	-25 ± 6	-21 ± 4	**0.001**
Control	-18 ± 5	-16 ± 3	0.076
GROUP	**Anteroseptum ε (%)**	**Global ε (%)**	***P*-VALUE**
UR	-26 ± 8	-21 ± 4	**0.0001**
Control	-21 ± 6	-16 ± 3	**0.0002**
LV Radial	-	-	-
GROUP	**Inferoseptum ε (%)**	**Global ε (%)**	***P*-VALUE**
UR	43 ± 19	51 ± 19	**<0.0001**
Control	38 ± 18	43 ± 13	**0.008**
GROUP	**Anteroseptum ε (%)**	**Global ε (%)**	***P*-VALUE**
UR	39 ± 19	51 ± 19	**<0.0001**
Control	34 ± 17	43 ± 13	**<0.0001**

ε indicates strain; LV, left ventricular; UR, ultramarathon runner