Right and Left Ventricular Function and Mass in Male Elite Master Athletes

A Controlled Contrast-Enhanced Cardiovascular Magnetic Resonance Study

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Background—It is under debate whether the cumulative effects of intensive endurance exercise induce chronic cardiac damage, mainly involving the right heart. The aim of this study was to examine the cardiac structure and function in long-term elite master endurance athletes with special focus on the right ventricle by contrast-enhanced cardiovascular magnetic resonance.

Methods and Results—Thirty-three healthy white competitive elite male master endurance athletes (age range, 30–60 years) with a training history of 29±8 years, and 33 white control subjects pair-matched for age, height, and weight underwent cardiopulmonary exercise testing, echocardiography including tissue-Doppler imaging and speckle tracking, and cardiovascular magnetic resonance. Indexed left ventricular mass and right ventricular mass (left ventricular mass/body surface area, 96±13 and 62±10 g/m^2; P<0.001; right ventricular mass/body surface area, 36±7 and 24±5 g/m^2; P<0.001) and indexed left ventricular end-diastolic volume and right ventricular end-diastolic volume (left ventricular end-diastolic volume/body surface area, 104±13 and 69±18 mL/m^2; P<0.001; right ventricular end-diastolic volume/body surface area, 110±22 and 66±16 mL/m^2; P<0.001) were significantly increased in athletes in comparison with control subjects. Right ventricular ejection fraction did not differ between athletes and control subjects (52±8 and 54±6%; P=0.26). Pathological late enhancement was detected in 1 athlete. No correlations were found for left ventricular and right ventricular volumes and ejection fraction with N-terminal pro-brain natriuretic peptide, and high-sensitive troponin was negative in all subjects.

Conclusions—Based on our results, chronic right ventricular damage in elite endurance master athletes with lifelong high training volumes seems to be unlikely. Thus, the hypothesis of an exercise-induced arrhythmogenic right ventricular cardiomyopathy has to be questioned. (***Circulation*. 2016;133:1927-1935. DOI: 10.1161/CIRCULATIONAHA.115.020975.)**

Key Words: arrhythmogenic right ventricular cardiomyopathy ■ athletes ■ cardiac magnetic resonance imaging ■ myocardial injury ■ right ventricle

The beneficial effect of moderate regular exercise on cardiovascular health is well known and has led to recommendations for both primary and secondary prevention of cardiovascular diseases.[1–3] However, there is an incomplete understanding of the dose-response relationship, in particular, with regard to a safe upper-dose limit beyond which the adverse effects of exercise may outweigh its benefits.[4] Several studies have demonstrated that acute prolonged strenuous exercise such as a marathon, ultramarathon, or triathlon is associated with transient reductions in right ventricular ejection fraction (RVEF) and elevated cardiac biomarkers of myocardial injury, all of which return to normal within 1 week.[5–8] A study by Heidbüchel et al[9] identified a high prevalence of

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right ventricular (RV) structural and arrhythmic involvement in endurance athletes being evaluated in the context of symptoms like palpitations and dizziness. Thus, the hypothesis was put forward that long-term intensive endurance exercise training and competition may result in irreversible RV structural and functional changes termed exercise-induced arrhythmogenic RV cardiomyopathy (ARVC).[10] This hypothesis has been strongly discussed because these conclusions are mainly based on observational studies involving a small and selected group of symptomatic athletes.[11,12] Furthermore, several studies did

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not detect any evidence of myocardial RV damage in endurance athletes,[11,13–15] and increases in biomarkers are not necessarily linked to RV injury because the exercise-induced increases could also reflect a physiological mechanism.[16] Therefore, to date, long-term clinical consequences caused by repeated intensive endurance exercise remain speculative. Studies evaluating the clinical impact of long-term intensive endurance training and competition in high-level elite master athletes are rare.[17–20] In addition, information about training volume (hours per week) and history (years) are often lacking, and cardiopulmonary exercise testing with quantification of the aerobic capacity by measuring maximal oxygen uptake (Vo_2max) and power output for an assessment of sport-specific performance in professional elite endurance athletes with a long training history have not been performed so far.[17–19] Therefore, the aim of this study was to examine the cardiac structure and function with special emphasis on the RV by contrast-enhanced cardiovascular magnetic resonance (CMR) and complementary echocardiographic tissue Doppler imaging and strain data in long-term active, elite endurance master athletes including world class athletes.

We hypothesized that an exercise-induced RV cardiac damage (eg, ARVC) in these subjects would result in a RV overload with a disproportionate ratio of left ventricular end-diastolic volume (LVEDV) to right ventricular end-diastolic volume (RVEDV) in comparison with control subjects, an impairment of RV function, or late enhancement (LE) as an indicator of myocardial necrosis or fibrosis. Furthermore, we hypothesized that repeated exercise-induced RV damage resulting in a chronic ventricular overload should go along with an elevated brain natriuretic peptide concentration at rest in comparison with control subjects.

Methods

Study Population

Thirty-three healthy, white elite male master endurance athletes (age range, 30–60 years), still being in regular competition, with a recent continuous training history of ≥10 years and ≥10 hours per week were recruited. Of them, 16 athletes were former elite professional athletes, including a former ironman world champion and several second- and third-ranked professional athletes at the Hawaii Ironman, the world record holder at the long distance triathlon, a second-ranked cyclist of the Vuelta a España (Tour of Spain), 6 Olympic athletes in the triathlon and rowing disciplines, and a former winner of the Munich Marathon. The control group (exercising ≤3 hours/wk) consisted of 33 healthy white men pair-matched for age, and secondary for height (mean maximal tolerated deviation, ±5 cm) and weight (mean maximal tolerated deviation, ±5 kg). All athletes had to refrain from training for the last 48 hours before the examination. To exclude cardiovascular and other relevant diseases, each participant underwent a physical examination, resting ECG, blood pressure at rest, and echocardiography. In addition, blood samples were drawn at rest 30 minutes before the cardiopulmonary exercise test to determine standard blood parameters and high-sensitive troponin T (cobas e assay, Roche Diagnostics, Mannheim, Germany), and N-terminal pro-brain natriuretic peptide (cobas e assay, Roche Diagnostics, Mannheim, Germany), as well, to detect acute myocardial damage and maladaptation, respectively. Exclusion criteria for study participants included any history of cardiopulmonary disease (including cardiovascular risk factors such as hypertension, diabetes mellitus, and smoking), standard contraindications for CMR imaging (eg, claustrophobia, certain metallic implant devices, prior allergic reaction to gadolinium-contrast agents), and a Vo_2max <50 $mL \cdot kg^{-1} \cdot min^{-1}$ for athletes in the cycle/treadmill ergometry. All subjects denied the use of illicit substances and had not been tested positive for doping in their career. The study was approved by the ethics committee of the Saarländische Ärztekammer, Saarbrücken, Germany (SÄK), and all participants gave their written informed consent.

Cardiopulmonary Exercise Test

A cardiopulmonary exercise test until volitional exhaustion was performed to assess the maximal physical performance of athletes and control subjects by means of power output and Vo_2max. By doing this, we were able to examine if their physical performance matched their training history. Vo_2max was measured by using a gas-exchange device with breath-by-breath technology (Cortex MetaLyzer 3B, Leipzig, Germany). The device was calibrated before each test according to the manufacturer's guidelines. After a warm-up of 10 minutes, an individually adjusted ramp protocol was chosen to exhaust subjects within 10 to 15 minutes. Cyclists were tested by cycle ergometry (Lode Excalibur Sport, Groningen, Netherlands), and long-distance runners were tested by treadmill ergometry (Woodway, Weil am Rhein, Germany). Triathletes could choose the type of ergometry depending on their best discipline. Control subjects were tested according to the pair-matched athlete's choice of ergometry. All tested subjects had to meet 2 criteria for exhaustion (heart rate $[HR]_{max}$ cycle ergometry: 200 – age, or HF_{max} treadmill ergometry: 220 – age; maximal blood lactate concentration, >8 mmol/L; maximal respiratory exchange ratio, >1.10). Capillary blood samples for the determination of blood lactate concentrations as 1 criterion for exhaustion were taken at rest, 3 minutes and 5 minutes after cessation of the exercise test because peak values of blood lactate concentrations typically appear at 3 to 8 minutes postexercise when volitional exhaustion has been reached or at least approached.

Echocardiography

Echocardiography was performed on a GE System Vivid S6 (GE Healthcare, Solingen, Germany) according to the guidelines of the American Society of Echocardiography. M-mode echocardiography was used to determine the inner left ventricular end-diastolic diameter (LVEDD) and right ventricular end-diastolic diameter, interventricular septal thickness (IVST), posterior wall thickness (PWT), and fractional shortening. Total LVEDD (TEDD = LVEDD + IVST + PWT) was determined on the mitral valve plane ($TEDD_M$) and the papillary muscle plane ($TEDD_p$). Total left ventricular (LV) longitudinal diameter (TLD) was determined in the 4-chamber view. The LV total diastolic volume (TDV [milliliters]) and heart volume (HV [milliliters]) were calculated by the following formula[21]:

$$TDV = \left(\left[TEDD_M{}^2 x 0.785\right] + \left[TEDD_p{}^2 x 0.435\right)\right) \mathbf{x} TLD / 2000;\ HV = \left(TDV x 2.432\right) + 130.$$

Tricuspid and mitral annular plane systolic excursion was measured using a 4-chamber view with M-mode placed through the tricuspid and mitral annulus, respectively. Tissue Doppler imaging was recorded in an apical 4-chamber view by placing the sample volume at the septal and lateral corners of the mitral and tricuspid annulus, respectively. Tissue Doppler imaging velocities of the mitral and tricuspid annulus (s′, E′, A′) and the derived parameters (E′/A′ ratio) were obtained.

Two-dimensional speckle tracking echocardiography analysis was obtained from an apical 4-chamber view, using conventional 2-dimensional gray-scale echocardiography. Off-line analysis was performed by an experienced reader, blinded to the study, using a commercially available semiautomated 2-dimensional strain software (EchoPac, GE Healthcare, USA). After manually tracing along the endocardial border from base to apex and width setting to match the wall thickness, 3 segments (basal, middle, apical) for each wall were analyzed. If the automated 2-dimensional analysis appraisal of acceptable tracking quality indicated inappropriate tracking, retracing was performed. If that failed, segments were excluded. Longitudinal

strain values in the basal, mid, and apical segments, and the global longitudinal strain value, as well, for both ventricles were measured. Because speckle tracking echocardiography relies on good imaging quality, we had to exclude 1 athlete/control pair for LV longitudinal strain analysis and 7 athlete/control pairs for RV longitudinal strain analysis.

Cardiovascular Magnetic Resonance

CMR was performed by using a 1.5-tesla magnet (Magnetom Vision, Siemens, Erlangen, Germany). An advanced cardiac software package was used. Images were acquired with the subject in the supine position.

Double-oblique short-axis images were acquired for the measurement of LV and RV volumes, mass, wall thickness, and heart function. For this purpose, retrospectively, ECG-gated single-slice breath-hold steady-state free precession cine sequences (TrueFisp; repetition time, 60 ms; echo time, 1.89 ms; averages, 1; slice thickness, 6 mm; matrix size, 192×192; phases, 25; views per segment, 14; bandwidth, 965 Hz/pixel; and flip angle, 80°) were acquired with contiguous short-axis planes covering the LV, completed by the horizontal and vertical long-axis views. In addition steady-state free precession cine images of the RV and LV outflow tract were acquired.

For LE imaging, 5 to 10 minutes after contrast medium injection (0.1 mmol/kg BW MultiHance [Gd-BOPTA]), T1-weighted ECG-gated breath-hold inversion recovery sequences (repetition time, 750 ms; echo time, 4.8 ms; inversion time, 200–300 ms) manually regulated to provide optimal signal suppression over normal myocardium, slice thickness (7 mm) in short-axis orientation, matching the short-axis steady-state free precession sequences, were acquired.

Evaluation of LV and RV volumes, mass, wall thickness, and function was performed by using a commercially available software (SyngoVia, Siemens, Erlangen, Germany). To evaluate LV and RV volume and mass, manual tracing was used to outline endocardial and epicardial borders. Trabeculae and papillary muscles were included in the ventricular volumes (and excluded from the wall mass) for efficiency and reproducibility. To calculate mass, the interventricular septum was included as part of the LV. Epicardial fat and the pericardium were excluded from LV and RV mass. End-diastolic volumes (EDVs) and end-systolic volumes (ESVs) were used to determine stroke volume (SV = EDV – ESV) and ejection fraction (EF = EDV – ESV/EDV × 100). The LV and RV mass was determined by taking the sum of the EDVs within the epicardial and endocardial borders of the short-axis slices and multiplying the myocardial tissue volume by its specific density of 1.05 g/cm^3. In addition, all parameters were indexed to body surface area (BSA) for comparative analysis to minimize differences of cardiac parameters related to height and weight. Finally, criteria indicative of ARVC, such as isolated RV enlargement, wall motion abnormalities, or aneurysm formation, were noted.

Pattern and extent of LE were assessed by using short-axis views and were considered present if they were detectable in 2 orthogonal planes. LE patterns were defined as indicative of myocardial infarction if they were located predominantly in subendocardial areas, facultatively extending to midmyocardial and transmural regions, and attributable to coronary perfusion territories. Midmyocardial or subepicardial LE with patchy or spotty distribution was defined as a non-ischemic pattern. Two experienced radiologists/cardiologists visually judged the occurrence (absence versus presence), localization, and pattern of LE.

Statistical Analysis

Data were analyzed by using the statistical program Statistica. Univariate normality assumptions were verified with the Shapiro-Wilk test. Continuous, normally distributed data are expressed as mean±standard deviation or percentage values. Not normally distributed values are expressed as median (interquartile range). Differences between pairwise-matched endurance athletes and control subjects were measured by the paired *t* test. Pearson correlation coefficients were calculated for selected variables. The results were considered significant at $P<0.05$ for the α-error.

Results

We had to exclude 6 athletes because of poor ergometric/Vo_2max performance (3), hypertension (1), aneurysm of the ascending aorta (1), and claustrophobia during CMR (1). Five dropouts in the control subject group occurred because of concerns about the contrast agent (2), hypertension (1), mitral valve prolapse (1), and complete right bundle-brunch block (1). The final study population consisted of 33 athletes and 33 pair-matched control subjects. Table 1 provides information on anthropometric, sports-related, and exercise physiological characteristics of the study population. Electrocardiographically, 3 athletes showed findings unrelated to training with T-wave inversions beyond V_1 (2 athletes: V_1 to V_2; 1 athlete: V_1 through V_4). None of the athletes presented or had experienced atrial fibrillation. Echocardiographically, 22 athletes had an athlete's heart, defined as a heart volume ≥13 mL/kg body weight.[22]

Morphological Parameters

In athletes, left ventricular mass (LVM) and right ventricular mass (RVM) were significantly increased in comparison with control subjects (LVM, 188±26 and 124±23 g; $P<0.001$; RVM, 70±13 and 49±11 g; $P<0.001$). In addition, indexed LVM and RVM (values divided by BSA) at end-diastole showed similar

Table 1. Anthropometric, Sports-Related, and Exercise Physiological Characteristics of Endurance Athletes and Control Subjects

	Endurance Athletes (n=33)	Control Subjects (n=33)	*P* Value
Age, y	47±8	46±9	NS
Weight, kg	75±6	80±7	<0.001
Height, cm	182±5	181±6	NS
BSA, m^2	1.96±0.1	2.00±0.1	<0.05
Body fat, %	12.9±3.2	19.0±2.2	<0.001
Training volume, h/wk	16.7±4.4	–	<0.001
Training history, y	29±8	–	<0.001
Rest heart rate, bpm	48±7	65±11	<0.001
Systolic BP, mm Hg	128±8	127±8	NS
Diastolic BP, mm Hg	75±7	78±6	<0.05
Troponin T, pg/mL	5±2	4±2	<0.05
NT pro-BNP, pg/mL	37±22	43±28	NS
Peak power, W	422±48	240±41	<0.001
Peak velocity, km/h	17.1±1.4	11.2±1.7	<0.001
Vo_2max, mL·min^{-1}·kg^{-1}	60±5	37±6	<0.001
Peak heart rate, bpm	179±10	181±11	NS
Lactate max, mmol/L	9.7±2.1	9.5±2.8	NS
RER_{max}	1.23±0.1	1.27±0.1	<0.05

Data are presented as mean value±SD. BP indicates blood pressure; BSA, body surface area; NS, not significant; NT pro-BNP, N-terminal pro-brain natriuretic peptide; RER_{max}, maximal respiratory exchange ratio; and Vo_2max, maximal oxygen uptake.

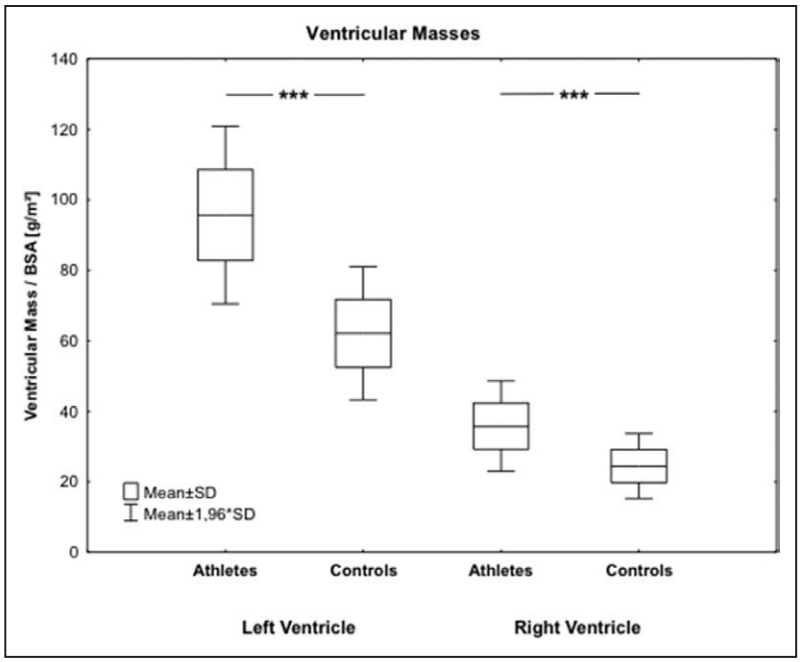

Figure 1. Indexed ventricular masses in endurance athletes and untrained control subjects. Data are expressed as mean value±SD. Error bars show mean value±1.96 SD, representing the lower and upper reference limit. ***P<0.001. BSA indicates body surface area; SD, standard deviation; and VM, ventricular mass.

differences (Figure 1). The ratio of LVM to RVM did not differ significantly for athletes and controls (Figure 2). LVM and RVM correlated significantly with Vo_2max (r=0.86 and 0.74, respectively).

Regarding ventricular volumes, LVEDV and RVEDV were significantly greater in athletes than in control subjects (LVEDV, 203±26 and 139±42 mL; P<0.001; RVEDV, 215±43 and 133±37 mL; P<0.001). Indexed LVEDV and RVEDV showed similar differences (Figure 3), resulting in greater SV (LVSV/BSA, 60±10 and 42±12 mL/m^2; P<0.001; RVSV/BSA, 57±13 and 36±10 mL/m^2; P<0.001). The LVEDV-to-RVEDV ratio differed significantly between athletes and control subjects (Figure 2). LVEDV and RVEDV correlated significantly with Vo_2max (r=0.77 for both parameters). Athletes had a significantly greater RVEDV than LVEDV (athletes, 215±43 and 203±26 mL; P<0.05), whereas, in control subjects, RVEDV and LVEDV did not differ significantly (controls, 139±42 and 133±37 mL; P=0.14).

Morphologically, most athletes showed a slight bulging in the basal to midventricular part of the RV free wall with a mild angular deviation, which is in keeping with the significantly increased RVEDV in comparison with control subjects. Three athletes had bulging of the apical RV free wall and suspicious trabecularization could be seen in one of them in CMR (Figure 4). However, no ARVC criteria such as isolated RV enlargement, wall motion abnormalities, or aneurysm formation were found in any of these athletes. Four control subjects had bulging of the apical RV free wall and 2 control subjects

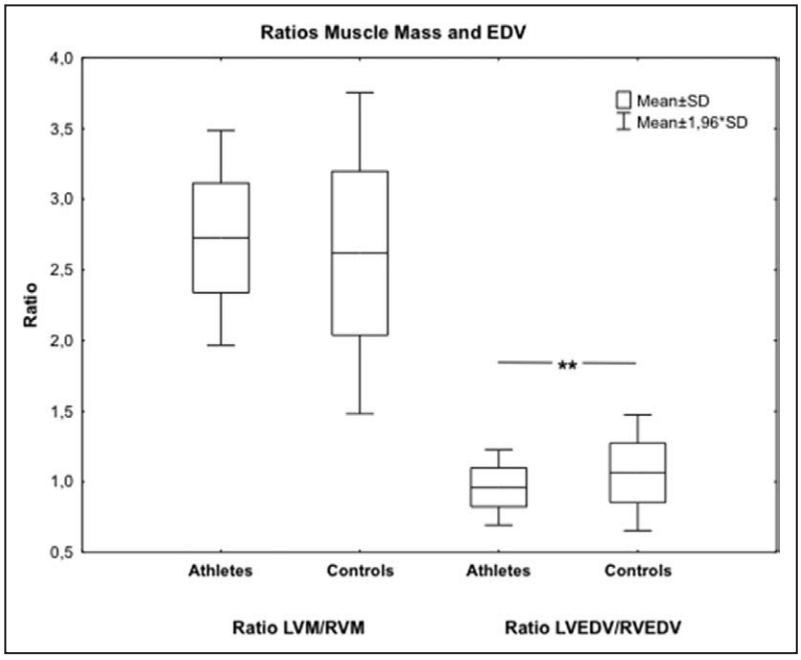

Figure 2. Ratio of left ventricular to right ventricular muscle mass (ratio LVM/RVM) and ratio of left ventricular to right ventricular end-diastolic volume (ratio LVEDV/RVEDV) in endurance athletes and untrained control subjects. Data are expressed as the mean value±SD. Error bars show mean value±1.96 SD, representing the lower and upper reference limit. **P<0.01. EDV indicates end-diastolic volume; MM, muscle mass; and SD, standard deviation.

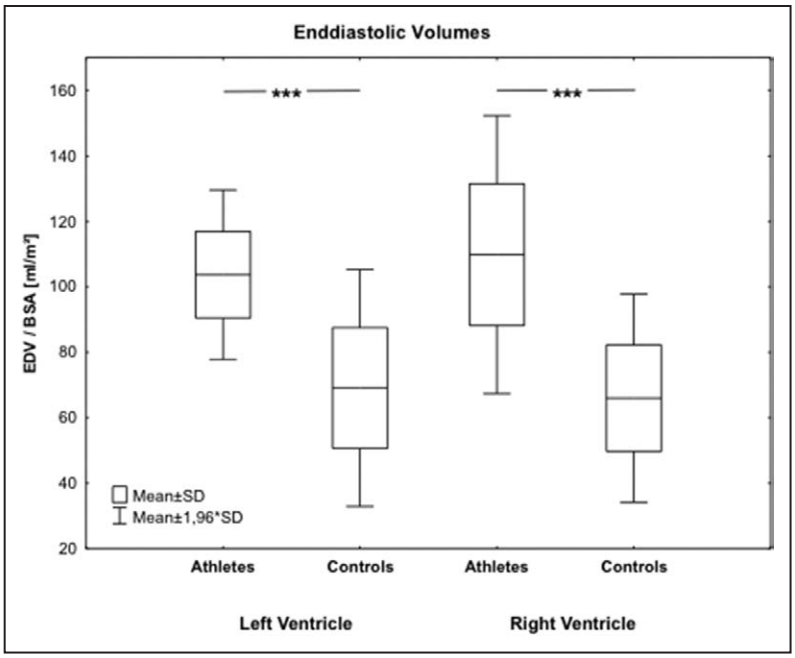

Figure 3. Indexed end-diastolic volumes in endurance athletes and untrained control subjects. Data are expressed as the mean value±SD. Error bars show mean value±1.96 SD, representing the lower and upper reference limits. ***P<0.001. BSA indicates body surface area; EDV, end-diastolic volume; and SD, standard deviation..

showed increased trabecularization. No ARVC criteria were fulfilled in the control group either.

Functional Parameters

Resting heart rate was significantly lower in athletes than in controls (48±7 and 65±11/min; P<0.001). Regarding echocardiographic functional metrics, tricuspid annular plane systolic excursion was significantly increased in athletes in comparison with control subjects (Table 2). However, tricuspid annular plane systolic excursion was still within the normal range in the control group. With the exception of A′, no significant difference was found for LV/RV tissue Doppler indices between athletes and controls (Table 2). LV and RV longitudinal strains did not differ between athletes and control subjects, with the exception of the RV basal longitudinal strain (Table 2). Regarding CMR, there was no significant difference between athletes and control subjects for LV ejection fraction (LVEF; 57±7 and 59±5%; P=0.19) and RVEF (52±8 and 54±6%; P=0.26). One athlete (3%) had a LVEF <45% (40%). This athlete also presented decreased LV longitudinal strain values at echocardiography. Five athletes (15%) and 3 control subjects (9%) had a RVEF <45%. None of these athletes/control subjects had a RVEF <40%. In addition, none of these athletes showed echocardiographically a decrease in RV longitudinal strain. Cardiac index at rest did not differ significantly between athletes and control subjects (2.8±0.6 and 2.6±0.8 $L \cdot min^{-1} \cdot m^{-2}$; P=0.23).

Late Enhancement

In 1 of 33 elite endurance athletes (3%), pathological LE was detected that could be localized subepicardially in the LV posteroinferior region on the short-axis view, corresponding to a nonischemic pattern (most likely because of a previous asymptomatic pericarditis). However, this athlete did not meet any of the revised Task Force Criteria for ARVC. One athlete showed a thinned myocardium in the inferior region of the LV, looking like a normal asymmetry, because no pathological LE was detected and the myocardial function was visually normal. All other athletes had no structural myocardial alterations suggestive

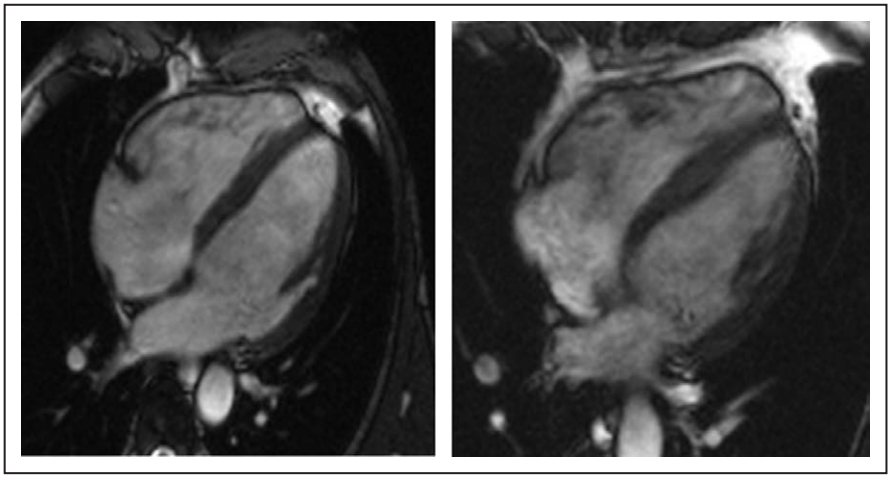

Figure 4. End-diastolic 4-chamber image from a former ironman world champion (**left**) and a multiple ironman winner (**right**). In comparison with the left heart, the right heart shows a more pronounced bulging of the apical and midventricular RV free wall, and increased trabecularization and a lower RVEF (41%), as well. RV indicates right ventricular; and RVEF, right ventricular ejection fraction.

Table 2. Echocardiographic Parameters of Endurance Athletes and Control Subjects

Echocardiography	Endurance Athletes	Control Subjects	*P* Value
Baseline parameters	n=33	n=33	
Heart volume, mL/kg	14.2±1.7	9.8±1.1	<0.001
LVEDD, mm	56.4±2.2	50.0±4.2	<0.001
RVEDD, mm	34.1±3.8	27.3±4.3	<0.001
IVST, mm	11.7±0.7	10.3±0.8	<0.001
PWT, mm	10.4±1.1	9.2±1.1	<0.001
Functional parameters			
M-Mode	n=33	n=33	
MAPSE lateral, mm	15±2	15±3	NS
MAPSE septal, mm	14±2	14±2	NS
TAPSE, mm	29±4	24±3	<0.001
TDI	n=33	n=33	
Left ventricle			
Mitral annulus septal			
E′, cm/s	9±3	10±3	NS
A′, cm/s	9±2	11±2	<0.01
E′/A′	1.1±0.4	1.0±0.5	NS
E/E′	7±2	7±2	NS
s′, cm/s	9±1	9±1	NS
Mitral annulus lateral			
E′, cm/s	14±3	14±3	NS
A′, cm/s	9±3	10±3	NS
E′/A′	1.6±0.7	1.5±0.6	NS
E/E′	5±1	5±1	NS
s′, cm/s	10±2	9±2	NS
Right ventricle			
Tricuspid annulus lateral			
E′, cm/s	15±2	14±3	NS
A′, cm/s	13±3	14±4	NS
E′/A′, cm/s	1.2±0.3	1.1±0.7	NS
s′, cm/s	15±3	15±3	NS
Speckle tracking			
LV longitudinal strains	n=32	n=32	
Global, %	−17±2	−18±2	NS
Basal septal, %	−15±2	−16±2	NS
Mid septal, %	−18±3	−18±2	NS
Apical septal, %	−20±4	−18±3	NS
Apical lateral, %	−15±4	−15±3	NS
Mid lateral, %	−17±3	−18±4	NS
Basal lateral, %	−19±4	−20±4	NS
RV longitudinal strains	n=26	n=26	
Global, %	−28±3	−28±5	NS
RV basal, %	−26±4	−30±5	<0.01
RV mid, %	−31±4	−30±6	NS
RV apical, %	−26±5	−23±7	NS

Data are presented as mean value±SD. IVST indicates interventricular septum thickness; LV, left ventricle; LVEDD, left ventricular end-diastolic diameter; MAPSE, mitral annular plane systolic excursion; NS, not significant; PWT, posterior wall thickness; RV, right ventricle; RVEDD, right ventricular end-diastolic diameter; SD, standard deviation; TAPSE, tricuspid annular plane systolic excursion; and TDI, tissue Doppler imaging.

of interstitial fibrosis or scarring. None of the control subjects showed LE.

Cardiac Biomarkers

N-Terminal pro-brain natriuretic peptide did not differ significantly between athletes and control subjects (37±22 and 43±28 pg/mL; P=0.32). High-sensitive troponin T was normal in all subjects, but significantly higher in the athlete group (5±2 and 4±2 pg/mL; P<0.05). No correlations were found between LVEF and RVEF and N-terminal pro-brain natriuretic peptide, nor high-sensitive troponin T. Regarding volumes, no correlations were found between LVEDV and RVEDV and N-terminal pro-brain natriuretic peptide, nor high-sensitive troponin T.

Discussion

To the best of our knowledge, this is the first study that systematically examined a unique cohort of long-time active elite master endurance athletes by means of detailed training volume/history, cardiopulmonary exercise testing with quantification of Vo_2max, and power output to elucidate the impact of their intense endurance training on myocardial structure and function by contrast-enhanced CMR and complementary echocardiographic tissue Doppler imaging and strain data. Researchers postulated that chronic intense endurance exercise with repeated bouts of high RV wall stress might promote adverse RV remodeling, which has led to the hypothesis of an exercise-induced ARVC that is currently under debate.[10–12] However, our results indicate that no signs of a chronic endurance exercise–induced RV maladaptation or acquired cardiac pathology occur in (asymptomatic) elite master endurance athletes with a professional training history of 29 years.

Morphological Parameters

As expected, endurance athletes showed significantly greater EDV and ESV of both ventricles in comparison with the control subjects, indicating exercise-induced cardiac remodeling. Our finding of a significantly greater RV than LV volume in the athlete group did not apply to the

control group, underlining that greater RV loading may be matched by greater RV remodeling. However, according to our results, this should not be interpreted as a sign of pathology because functional RV parameters by CMR and echocardiography were within the normal range and did not differ significantly from the control subjects. The lower LVEDV in comparison with RVEDV (ratios <1) have been confirmed by several other CMR studies.[23–26] Interestingly, our morphological finding of mild angular deviated bulging at the basal to midventricular part of the RV free wall in our athlete's cohort may signify that the RV dilation induced by long-term endurance training primarily involves the RV main body. A review by the study group of LaGerche[27] dealing with the athlete's heart also describes a bulging of the RV free wall in endurance athletes.

The ventricular masses were within the range described in the literature, and the ratio LVM/RVM did not differ between athletes and control subjects. In general, a wide variability in ventricular mass values has been described in the literature, ranging from 56±11 to 126±14 g/m^2 for LVM and 15±2 to 41±4 g/m^2 for RVM, respectively.[18,19,25,28] This wide range of extreme values can be explained by: (1) sex differences and study populations with the inclusion of female subjects; (2) different fitness levels and heart volumes of studied subjects; and (3) methodological differences in the off-line image analysis (eg, exclusion versus inclusion of papillary muscles for wall mass).

Functional Parameters

In the present study, there was no significant difference between athletes and control subjects for LVEF and particularly RVEF, corresponding well with results from previous CMR studies.[17,19,28] Five athletes had a RVEF <45% which is considered as the lower reference limit of normal for the left and right ventricular systolic ejection fraction in athletes, as measured by MRI.[27] However, lower values may also be physiological, at least in some endurance athletes with athlete's heart.[27] In general, RVEF in athletes (52±8%) was within the range reported by other studies,[19,23–25,29] whereas some studies showed even higher RVEFs for athletes.[17–19,24,28] These discrepancies may be attributable to the use of different methods of image analysis, thus affecting volume parameters and consecutively EF. Complementary echocardiographic functional metrics only showed a significant lower RV basal longitudinal strain in athletes in comparison with control subjects. However, a modest reduction in systolic deformation at the basal wall of the RV in athletes has also been described in a recent review by D'Ascenzi et al[30] and can be explained by different curvature changes in RV apex and basis. Moreover, LaGerche et al[31] postulated that, given that volume is greatest at the RV base, a lesser degree of deformation may be required to generate the same stroke volume, thereby explaining why RV deformation may be reduced in this region. A recent meta-analysis of postendurance exercise studies revealed that intense prolonged exercise is associated with a decrease in RV function possibly resulting in a chronic injury of the RV.[7] However, our CMR and echocardiographic findings clearly refute this hypothesis of chronic RV damage induced by prolonged intensive endurance exercise, and the fact that we did not find any correlation between cardiac biomarkers and RVEDV and RVEF further strengthens this notion.

Late Enhancement

Pathological LE was only detected in 1 athlete (3%). However, this asymptomatic athlete did not fulfill any of the revised Task Force Criteria for ARVC, and the nonischemic LE pattern is rather suggestive of a silent perimyocarditis in the past. Because of the low prevalence of LE in our studied subjects, we do not consider that exercise alone induced this clinical finding. However, it remains unclear if repeated extreme endurance exercise may affect adverse remodeling and scar formation in the presence of another trigger such as myocardial inflammation.

In general, there is a wide discrepancy in the literature regarding the prevalence of LE in endurance athletes. A study by Breuckmann et al[32] found that 12% of nonelite marathon runners had LE, which was 3-fold more than the sedentary controls. A small study by Wilson et al[17] demonstrated LE in 6 elite veteran male endurance athletes (50% of the study cohort) of which 5 showed a non–coronary artery disease LE pattern. Karlstedt et al[18] demonstrated LE in only 2 participants with evidence of coronary artery disease on subsequent cardiac computed tomography. Several other studies conducted with cardiac MRI among athletes did not detect any LE, whereas they confirmed chronic remodeling of both the LV and RV.[5,26,33] Our results demonstrate that, in the vast majority of elite endurance athletes with a long-term intensive training history, no signs of myocardial damage could be detected, thus indicating that even long-term intensive endurance training does not seem to induce myocardial necrosis or fibrosis at least in well-trained and exercise-adapted athletes. This finding is supported by the fact that none of the athletes had shown any arrhythmias during the cardiopulmonary exercise test up to exhaustion nor described any symptoms related to malignant arrhythmias in the past.

Task Force Criteria for ARVC

The accurate differentiation of normal athlete's heart from pathological conditions is challenging and largely depends on our knowledge of what constitutes normal. However, normal CMR values for endurance athletes are far less numerous than echocardiographic values. When applying the revised Task Force Criteria for ARVC using cardiac MRI, 16 athletes (48.5%) fulfilled the RVEDV index major criterion, whereas no athlete fulfilled the RVEF major criterion. Thus, RVEF seems to be a more suitable parameter to distinguish endurance athletes from ARVC patients. Regarding the athletes with a major criterion (RVEDV), none of them had shown LE or reported any cardiopulmonary complaints beforehand, and power output at cardiopulmonary exercise testing was within the expected range in all of them. However, we recommended additional diagnostic workup (stress MRI) in 1 athlete who presented a bulging of the apical RV free wall with apical trabecularizations and fulfilled the RVEF minor criterion for ARVC (RVEF, 41%, with LVEF also being decreased to 40%).

Study Limitations

An important limitation of this study is the use of a cross-sectional study design that may have led to a recruitment bias. However, as long as there is no true longitudinal study available (hardly achievable in the near future), a cross-sectional study design is, to date, the only conceivable methodical approach to detect cardiac structural and functional changes in a professional training life. Furthermore, it seems unlikely that those athletes who stopped their career because of cardiovascular symptoms all experienced exercise-induced cardiac diseases.

In terms of fibrosis, we cannot completely exclude subclinical fibrosis, because no T1 mapping was performed. Furthermore, we did not immediately perform additional diagnostic workups in subjects with major ARVC criteria or proven LE for practical reasons. Although we cannot completely rule out the use of illicit substances in our athlete cohort, none of them had ever been tested positive for prohibited substances according to the doping list, and the use of prohibited substances was denied by all the studied athletes. Finally, the present results only apply to white male athletes because we did not study black or female athletes.

Conclusions

This study found an expected exercise-induced cardiac remodeling in asymptomatic long-term elite master endurance athletes with no signs of maladaptation or acquired cardiac pathology. Thus, at least the cause-effect and dose-response relationship between intensive endurance exercise and the hypothesis of an exercise-induced ARVC has to be questioned.

Perspectives

As a perspective, follow-up examinations on highly trained master athletes with borderline or pathological findings are required to be able to better understand the long-term clinical consequences. Furthermore, large-scale longitudinal studies with different cohorts of endurance athletes should enable a better evaluation of the cause-effect and dose-response relationships between endurance exercise and cardiovascular events.

Disclosures

None.

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CLINICAL PERSPECTIVE

It is under debate whether the cumulative effects of years of high-intensity/high-volume exercise induce chronic cardiac damage, mainly involving the right heart. This study examined the cardiac structure and function by contrast-enhanced cardiovascular magnetic resonance and complementary echocardiographic tissue Doppler imaging and strain data in 33 elite male master endurance athletes including world-class athletes (age range, 30–60 years) with a training history of 29±8 years and a control group, pair-matched for age and secondary for height and weight. The athlete group demonstrated expected evidence of exercise-induced cardiac remodeling. However, cardiovascular magnetic resonance and echocardiographic functional parameters such as left ventricular ejection fraction/right ventricular ejection fraction and longitudinal strain values did not differ between athletes and controls. Pathological late enhancement was only detected in 1 asymptomatic athlete (nonischemic pattern suggestive of a silent perimyocarditis in the past), who did not meet any of the revised Task Force Criteria for arrhythmogenic right ventricular cardiomyopathy. No correlation was found for left ventricular and right ventricular volumes and ejection fractions with N-terminal pro-brain natriuretic peptide. In summary, in this study, no signs of a long-term exercise-induced cardiac maladaptation or pathology could be demonstrated in asymptomatic long-term elite master endurance athletes. Therefore, at least the cause-effect and dose-response relationship between long-term intensive endurance exercise and the hypothesis of an exercise-induced arrhythmogenic right ventricular cardiomyopathy has to be questioned.

Right and Left Ventricular Function and Mass in Male Elite Master Athletes: A Controlled Contrast-Enhanced Cardiovascular Magnetic Resonance Study

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