Structural and functional cardiac alterations in Ironman athletes: New insights into athlete's heart remodeling ☆

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The structure of the heart of athletes (ATHL) may differ from that of non-athletes, provided that a regular training of sufficient intensity and duration is performed [1]. Preparation for an Ironman (IM) triathlon consists of extreme endurance training with both dynamic and static components. This may impact cardiac remodeling more than typical of an athlete's heart. The available echocardiographic data on morphologic and functional cardiac alterations in IM-ATHL are limited and no data exist on application of echocardiographic criteria for specific cardiomyopathies to the remodeled hearts of these ATHL. In the present study, we assessed cardiac dimensions and functional parameters of both ventricles in IM-ATHL and controls by advanced echocardiography. Additionally, echocardiograms were analyzed searching for alterations resembling features usually observed in cardiomyopathies, such as left ventricular non-compaction (LVNC), arrhythmogenic right ventricular cardiomyopathy (ARVC), or hypertrophic cardiomyopathy (HCM).

Amateur ATHL participating in the Ironman Switzerland in 2010 were examined the day before the race. Healthy subjects not participating in regular sportive activities served as controls. Participants had no personal history of cardiovascular diseases and no family history of sudden cardiac death (SCD) or inherited heart disease. All subjects underwent a 12-lead electrocardiogram and a transthoracic echocardiogram. The study was approved by the local ethical committee. All participants provided written informed consent. The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology. Echocardiographic examination was performed according to the guidelines of the American and European Society of Echocardiography using a Vivid 9 ultrasound system (GE Medical Systems, Milwaukee, Wisconsin, USA) [2]. All echocardiograms were screened for presence of criteria for HCM, LVNC, or ARVC [3–5]. For strain and rotation analysis, the 2-D speckle tracking method was used [6,7]. The left ventricular (LV) global longitudinal strain (GLS) was automatically calculated from loops acquired from apical two-, three-, and four-chamber views. LV apical rotation was assessed in the parasternal short axis view at the apical level. Right ventricular (RV) 2-D longitudinal strain was assessed in the apical four-chamber view. The RV was divided into 6 segments. Longitudinal strain for each segment and RV GLS were calculated. Continuous data are presented as median (interquartile range). Continuous data were compared by Mann–Whitney test and categorical variables by chi-square test. A p-value of less than 0.05 was considered statistically significant.

IM-ATHL and controls were matched for age (both groups 36 [31–43] years, $p = 0.97$), gender (female: 7 [18%] vs. 5 [22%], $p = 0.72$), and body surface area (1.9 [1.8–2.0] vs. 1.98 [1.75–2.05] m^2, $p = 0.94$). The heart rate was lower in IM-ATHL (56 [50–64] vs. 73 [65–81] beats-per-minute, $p < 0.0001$). Data on cardiac dimensions are shown in Table 1. Screening for specific structural alterations revealed that no IM-ATHL fulfilled criteria for presence of HCM. Four (10%) IM-ATHL had a positive LVNC criterion of a >2:1 ratio between the hypertrabecularized and the compacted endocardial layer (Fig. 1A). IM-ATHL frequently exhibited enlargement of the RV outflow tract (RVOT). In the parasternal long-axis, 7 (18%) had a RVOT diameter ≥19 mm/m^2 and in the parasternal short-axis, RVOT diameter exceeded 21 mm/m^2 in 2 (5%). RV apical ectasia was found in 5 (13%) IM-ATHL (Fig. 1B). Five other IM-ATHL showed a prominent moderator band. Among those ATHL with a prominent moderator band, RVOT dilatation was observed in 3 (8%), and small RV sacculations were seen in 2. When applying the recently proposed modification of the Task Force criteria for the diagnosis of ARVC [5], 1 (3%) IM-ATHL would have met a minor criterion. Among those 7 ATHL exhibiting ectasia or sacculations in the RV, none had T-wave inversions or epsilon waves on electrocardiogram. Echocardiographic parameters of LV and RV function are summarized in Table 2. LV GLS was similar in IM-ATHL with and without a positive LVNC criterion (−20 [(−23)–(−16)] vs.−22 [(−24)–(−19)] %, $p = 0.28$). RV apical strain (lateral apical strain: −31 [(−32)–(−25)] vs.−29 [(−32)–(−27)] %, $p = 0.97$)

Table 1
Cardiac structural parameters in Ironman athletes and controls.

	Ironman athletes (n = 39)	Controls (n = 23)	p-value
LVEDVI, ml/m^2	67 (61–74)	49 (40–57)	<0.0001
LVMMI, g/m^2	92 (84–106)	74 (60–81)	<0.0001
LV septal thickness, cm	1.0 (0.8–1.1)	0.9 (0.8–1.0)	0.008
LV posterior wall thickness, cm	0.9 (0.8–1.0)	0.8 (0.7–0.9)	0.04
LAVI, ml/m^2	35 (31–38)	22 (20–25)	<0.0001
RVEDA, cm^2	23 (19–26)	17 (15–19)	<0.0001
PSAX RVOT, mm/m^2	17 (15–18)	15 (14–17)	0.001
PLAX RVOT, mm/m^2	17 (16–18)	16 (15–18)	0.11
RV free wall thickness, mm	5 (4–6)	4 (4–5)	0.1
RAVI, ml/m^2	32 (25–39)	20 (17–23)	<0.0001

Results are expressed as median (interquartile range).
LV denotes left ventricular, EDVI enddiastolic volume index, MMI myocardial mass index, LVH left ventricular hypertrophy, LAVI left atrial volume index, RV right ventricular, EDA enddiastolic area, PSAX parasternal short axis, PLAX parasternal long axis, OT outflow tract, and RAVI right atrial volume index.

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[1] All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

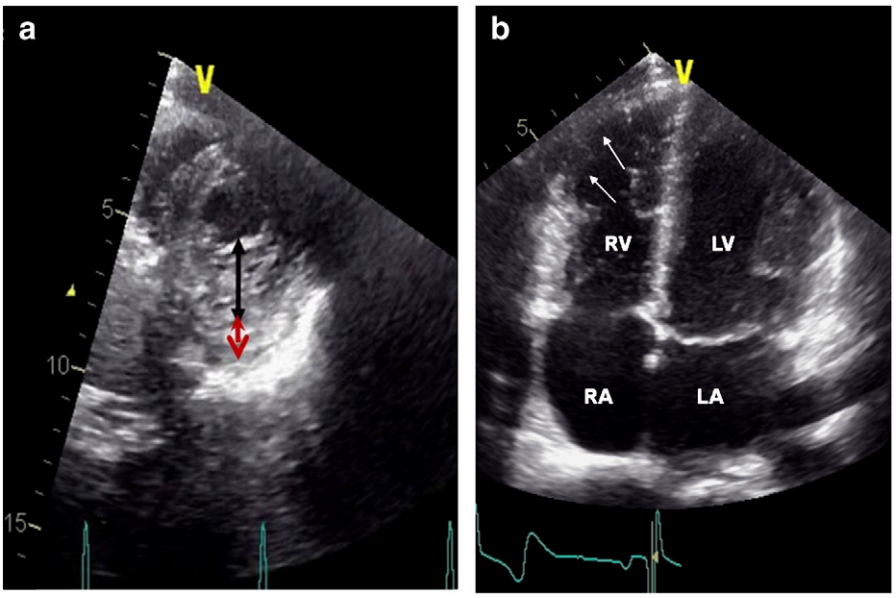

Fig. 1. a) Parasternal short-axis view of the apical region of the left ventricle showing a ratio of the hypertrabecularized non-compacted (black double-arrow) to the compacted myocardial (gray double-arrow) layer > 2 at endsystole. (b) Apical four-chamber view of an Ironman athlete exhibiting ectasia in the right ventricular apical region (white arrows). RV denotes right ventricle, LV left ventricle, RA right atrium and LA left atrium.

and RV GLS (−24 [(−25.4)–(−22)] vs. −24.4 [(−26.4)–(−22.4)]%, p = 0.67) were similar between IM-ATHL with and without structural RV apical alterations.

In the present study, IM-ATHL exhibited changes typical of athlete's heart with enlarged ventricles and atria and increased LV muscle mass. Besides these well known adaptive changes, the investigated IM-ATHL exhibited specific echocardiographic alterations of cardiac structure that are usually observed in cardiomyopathies. Thus, a positive LVNC criterion and structural changes resembling ARVC were frequently found in the remodeled hearts of IM-AHTL. Interpretation of these findings is challenging since differentiation to true cardiomyopathies may be cumbersome. Recent data suggest that speckle myocardial imaging may be a helpful tool to discriminate between cardiomyopathies and healthy hearts because intrinsic myocardial pathologies have been associated with impairment in 2D-speckle strain-derived functional parameters [8,9]. In our study, the observed structural changes in IM-ATHL were not associated with impaired cardiac function as assessed by conventional or speckle-strain echocardiographic parameters. Speckle imaging revealed similar GLS values in both ventricles in IM-ATHL and controls. Whereas none of the LV and RV segments exhibited significantly impaired deformation values, we even noted increased LV apical rotation and increased RV apical strain in IM-ATHL, suggesting that enhanced apical function in both ventricles might be a component of the cardiac adaptation occurring in the setting of a physiologic biventricular remodeling in IM-ATHL. Considering the normal or even higher than normal parameters of myocardial deformation in IM-ATHL and given the high prevalence of the observed changes resembling ARVC or LVNC in the presence of a negative family history for cardiac disease and SCD, it is unlikely that inherited cardiomyopathies caused the observed structural changes. Our data rather imply that the remodeling process in IM-ATHL results in structural adaptation that may mimic echocardiographic features usually observed in specific cardiomyopathies. Therefore, echocardiographic criteria for these cardiomyopathies have to be applied carefully in ultraendurance ATHL, taking global and regional myocardial functional parameters into account. In any case, when screening these ATHL by echocardiography, it may be important to

Table 2
Left and right ventricular function in Ironman athletes and controls.

	Ironman athletes (n = 39)	Controls (n = 23)	p-value
LVEF, %	63 (58–68)	60 (57–65)	0.14
LV GLS, %	−22.1 ([−23.6]–[−18.5])	−20.6 ([−21.7]–[−19.6])	0.38
LV peak apical rotation, %	8.5 (4.6–10.5)	5.1 (3.7–7.7)	0.02
LV E-velocity, cm/s	80 (68–90)	75 (62–85)	0.26
LV A-velocity, cm/s	47 (41–57)	51 (42–62)	0.30
LV septal e', cm/s	11 (10–12)	11 (9–12)	0.42
LV lateral e', cm/s	16 (13–19)	15 (12–16)	0.21
RV FAC, %	47 (40–50)	46 (40–52)	1.0
RV GLS, %	−24.3 ([−26.2]–[−22.4])	−23.3 ([−25.7]–[−21.7])	0.27
RV lateral basal strain, %	−25.0 ([−29.0]–[−22.0])	−26.0 ([−31.0]–[−24.0])	0.16
RV lateral midventricular strain, %	−28.3 ([−32.0]–[−25.0])	−28.5 ([−31.0]–[−25.0])	0.85
RV lateral apical strain, %	−29.3 ([−32.0]–[−27.0])	−26.0 ([−29.5]–[−23.0])	0.002
RV septal basal strain, %	−19.0 ([−22.0]–[−17.0])	−19.5 ([−21.5]–[−17.5])	0.86
RV septal midventricular strain, %	−20.0 ([−22.0]–[−18.0])	−18.5 ([−20.0]–[−18.0])	0.44
RV septal apical strain, %	−21.0 ([−25.0]–[−19.0])	−18.5 ([−22.0]–[−15.0])	0.01

Results are expressed as median (interquartile range).
LV denotes left ventricular, EF ejection fraction, GLS global longitudinal strain, E early mitral inflow, A atrial mitral inflow, *e'* early diastolic mitral annular velocity, RV right ventricular, and FAC fractional area change.

know these alterations. Moreover, in some cases exhibiting distinctive findings, further investigation may be warranted.

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Response to Commentary "Efficacy of inspiratory muscle training in chronic heart failure patients"

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In their letter [1] Plentz and colleagues attempt to highlight discrepancies between their review work and that of Smart et al. [2].

Plentz and colleagues [1] suggest that the search by Smart et al. [2] was too narrow. We challenge Plentz and colleagues to find omitted studies that were published in the stipulated time frame as, in addition to the stipulated search, extensive hand searching was conducted. The discrepancy between the previous works and the work of Smart et al. [2] may be explained by the fact that we only recorded papers where we were required to read more than the title (e.g. abstracts or full manuscripts) in order to come to a decision to exclude a study.

Second, Plentz and colleagues suggest our review included too many studies [1], which perhaps contradicts their comment above? We do however acknowledge that journal word limits permitting the inclusion of a sensitivity analysis (e.g. removal of studies of Winkelmann [3] and Laoutaris [4–7]) may have been helpful in teasing out any effects of heterogenic studies. We did conduct a sensitivity analysis as suggested by removing Winkelmann and Laoutaris' studies and can confirm that this did not alter the statistical significance of peak VO_2 MD 1.41 ml kg^{-1} min^{-1} (95% CI 0.79 to 2.04, $p<0.00001$). Another salient point here is that the inclusion of the study of Winkelmann (which utilized respiratory muscle training and aerobic training) actually reduced, rather than increased, the effect sizes for 6 min walk distance, Minnesota living with heart failure score and peak VO_2.

Plentz and colleagues suggest that a random effects model should be employed for the 6 min walk distance and V_E/VCO_2 analyses [1]. While Plentz and colleagues incorrectly refer to this as a sensitivity analysis, we recently conducted these analyses again with a random effects model and the statistical significance of both outcome measures were unchanged, although the 95% CI's were reduced therefore making the analyses more robust. In a related matter we argue that an I^2 value of 64% (being less than the commonly used 75% threshold) would not qualify as "considerable heterogeneity" and we refer to page 28 of the Cochrane handbook of systematic reviews [8].

Plentz and colleagues asked for an explanation of "high heterogeneity" (we note their classification of heterogeneity has changed from "considerable" to "high"). We would like to point out that it is not usual reporting protocol for meta-analysis authors to explain heterogeneity; they are merely expected to state what the I^2% values are for each analysis. Plentz and colleagues [1] should remember meta-analysis authors do not create the inter-study heterogeneity. Of course Plentz and colleagues have possibly overlooked that they have answered their own question as moderate to substantial (but not considerable) heterogeneity may be explained by the inclusion of the studies of Laoutaris and Winkelmann.

We can confirm that data extraction and assessment of study quality was performed by two reviewers as stated in Section 2.1 of our published review [2]. Moreover we do not feel that an adequate tool currently exists to assess quality of exercise training trials. Perhaps the most commonly used tool is the PeDRo scale which is specific to physiotherapy, but not exercise physiology—so there remain limitations in utilizing this tool in exercise training studies.

In their penultimate paragraph Plentz and colleagues again mention that the studies of Laoutaris and Winklemann should be excluded. It is not surprising that Plentz and colleagues also mention here that their analyses failed to show significant changes in peak VO_2 and quality of life

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