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Training-induced right ventricular remodelling in pre-adolescent endurance athletes: The athlete's heart in children

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ABSTRACT

Aims: Little is known about the adaptation of the right ventricle (RV) to endurance exercise in children. The aim of this study was to assess the effects of 5 months of intensive training on RV morphology and function in preadolescent endurance athletes.
Methods: Ninety-four children were evaluated in this study. Fifty-seven male competitive swimmers (aged 10.8 ± 0.2 years) were evaluated before (baseline) and after 5 months of the training (peak-training), and compared to 37 age- and sex-matched non-athlete children evaluated at baseline and after 5 months of natural growth. All subjects were asymptomatic, with negative family history for cardiomyopathies.
Results: At baseline no differences were found between athletes and controls for indexed RV outflow tract (RVOT) (18.5 ± 2.7 vs. 16.8 ± 5.0 mm/m^2, $p = 0.18$) and RV basal end-diastolic diameter (EDD) (24.9 ± 4.1 vs. 23.6 ± 3.0 mm/m^2, $p = 0.15$). After 5 months, indexed RVOT and RV basal EDD significantly increased in athletes (20.2 ± 2.9 mm/m^2 and 25.4 ± 3.3 mm/m^2, $p < 0.0001$ vs. baseline) while no differences were observed in controls ($p = 0.84$ and $p = 0.25$). Despite the increase in RV size, RV function remained normal in athletes, with no changes in RV fractional area change ($p = 0.97$), s′ value ($p = 0.22$), and RV longitudinal strain ($p = 0.28$).
Conclusions: Endurance training influences the growing heart of male preadolescent athletes with an addictive increase in RV dimensions, with a preserved RV function. Therefore, in children engaged in endurance sports the increase in RV size associated with normal RV function represents a physiological expression of the athlete's heart and should not be misinterpreted as an expression of incipient RV cardiomyopathy.

1. Introduction

Cardiac remodelling induced by athletic conditioning (i.e., athlete's heart) [1,2] has for long time been considered a physiologic adaptation to training with no clinical consequences [3–6]. However, recently, a special attention has been paid to right ventricular (RV) remodelling and possible detrimental effects of intensive exercise conditioning have been reported [7–9].

Most of the studies on 'athlete's heart' have been carried out in adults [1–9] or rarely in adolescent individuals [10–12], and little is known regarding the occurrence and extent, if any, of cardiac remodelling in pre-adolescent individuals. Data derived from adults cannot be transferable to preadolescent populations, as these young athletes are physically less mature and exposed to a shorter intensity and duration of training [12]. Furthermore, at the present time, data on the effects of regular exercise training on RV morphology and function in preadolescent athletes are lacking [13–15].

Considering the increasing number of children involved in competitive sports, the trend for more intensive training loads, and the very young age at which pre-adolescent are being encouraged to start competitive events, we believed timely and appropriate to investigate the cardiac consequences of endurance training on pre-adolescent athletes. Therefore, we sought to analyse: i) to what extent cardiac dimensions were altered as a consequence of endurance training and body growth in athletes and in controls during a competitive season; ii) whether changes in RV morphology and function occurred in pre-adolescent athletes.

2. Materials and methods

2.1. Study design

Sixty-two male pre-adolescent endurance athletes practicing competitive swimming at regional level were enrolled in this study. The mean age was 10.8 ± 0.2 (9–13 years).

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The swimmers trained once a day, over 5 or 6 days each week. The typical training started sessions have been previously described in details [16].

The evaluations were performed at the beginning of the season (September 2014, named hereafter 'baseline') and after 5 months of intensive and closely supervised training (February 2015, named hereafter 'peak-training'). During the 3 months preceding the baseline evaluation athletes were active, but not engaged in any training program. In the preceding year (winter/spring 2014), most of the participants had joined a supervised introductory swimming program of mild intensity and duration. Young athletes were excluded from the study if they had signs of heart disease (cardiomyopathies, shunts, ventricular septal defect or atrial septal defect, patent *ductus arteriosus*, complex ventricular arrhythmias), family history of sudden cardiac death or cardiomyopathies, or if they withdrew from the training program for >20 consecutive days. Accordingly, three athletes were excluded from the initial population because of musculoskeletal injuries and two for evidence of cardiac heart disease (1 with atrial septal defect and 1 with patent *ductus arteriosus*). Thus, the final athletes' population included 57 healthy subjects.

Thirty-seven sedentary age-matched male subjects were used as controls. The mean age was 10.2 ± 0.2 (9–13 years). Controls participated in recreational physical activities for <2 h per week and none was engaged in a regular training program.

The participants of the study underwent complete physical examination, ECG, echocardiography, and step ECG test. None of the participants showed evidence for cardiac disease, hypertension, type I diabetes mellitus, and/or endocrine disease. After the rationale and the study protocol were explained, the parents gave written informed consent for their offspring to participate in this study. The local Ethical Committee approved the investigational protocol.

2.2. Physical examination

Height, weight and body surface area (BSA) were obtained both at the beginning of the study and after 5 months [17]. The biological maturation of the participants was established using the Tanner's five stages of penile and testicular development [18], obtained at the two different time-points. The presence of cardiac symptoms, fatigue, or performance impairment was also investigated.

2.3. Twelve-lead ECG

A standard 12-lead ECG was performed using an ESAOTE P8000 Power Light, recorded at 25 mm/s in a supine position during quiet respiration. ECG was interpreted by an expert cardiologist, blinded to study time and without any knowledge of the echocardiographic findings. The ECG examination has been previously described in details [19]. Left axis deviation was defined as a QRS axis exceeding −30°, and right axis deviation was defined as a QRS axis exceeding +120°. Incomplete right bundle branch block (RBBB) was defined as QRS duration <100 ms, with r′ or R′ wave in lead V1 and S wave of greater duration than R wave or >40 ms in leads I and V6, while complete RBBB was defined as QRS duration >100 ms in presence of the criteria above described [20]. The presence of negative T waves in the peripheral leads and beyond V1 in the precordial leads was evaluated [21]. The presence of RV hypertrophy was defined by the sum of the R waves in V1 and the S waves in V6 exceeding 1.05 mV [22].

2.4. Echocardiographic examination

The echocardiographic examination was performed by one cardiologist using a high-quality echocardiograph (Vivid 9, GE, Milwaukee, WI, USA), equipped with a M4S 1.5–4.0 MHz transducer, and a one-lead ECG was continuously displayed. Off-line data analysis, from three stored cycles, was performed by two experienced readers, blinded to the study time-point, using a dedicated software (EchoPac, version 112, GE, USA).

RV chamber size was assessed as recommended [23]. Basal and mid-cavity end-diastolic diameters were obtained. RV outflow tract (RVOT) diameter was measured at the proximal level in the parasternal long-axis view, calculated from the anterior RV wall to the RV septum (RVOT PLAX) [24]; at subvalvular level in the parasternal short axis at the level of the aortic valve, calculating the maximum distance between the anterior aortic wall and the RV free wall (RVOT PSAX), and at pulmonic valve from the parasternal short-axis of pulmonary bifurcation view (RVOT distal diameter) [23]. RV end-diastolic and end-systolic areas were calculated by tracing the RV endocardium from a modified apical 4-chamber view, and RV fractional area change (FAC) was derived and expressed as percentage [24]. Tricuspid annular plane systolic excursion (TAPSE) was also calculated [23]. Left ventricular (LV) end-diastolic and end-systolic volumes and LV ejection fraction were calculated, as recommended [24] and indexed to BSA [25].

The *Z*-scores were calculated both in athletes and in controls to evaluate whether RVOT PLAX, RVOT distal diameter, and RV end-diastolic area exceeded the cut-off value reported for the normal population, i.e. ≤2 [26,27].

Pulsed-wave Doppler and Tissue Doppler imaging (TDI) evaluation were recorded in the apical four-chamber view by placing the sample volume at the tips of tricuspid valve and at the tricuspid annulus, respectively [28]. The following measurements of RV filling were considered: E peak and A peak velocities, E/A ratio, s′, e′, and a′ velocities, tricuspid E/e′ ratio.

The echocardiographic examination was completed by two-dimensional speckle-tracking echocardiographic analysis, a non-invasive imaging technique that has recently applied to athlete's heart, enhancing our understanding of biventricular and biatrial myocardial deformation in athletes [3,4,8,29–31]. Speckle-tracking echocardiography was performed on narrow-sector gray-scale images of both RV and LV from an apical four-chamber view with temporal resolution of 60–90 frames/s. All images were optimized with gain, compression, and dynamic range to enhance myocardial definition with standardized depth, frequency, and insonation angle for all participants [32]. Off-line analysis was performed by an experienced reader, blinded to the study time-point, using a commercially available semi-automated 2D strain software (EchoPAC PC, version 112, GE, USA) [32]. A region of interest was manually traced along the endocardial border of the RV free wall from the base to the apex, and excluding the interventricular septum. Width was set to match the wall thickness. If the automated 2D analysis appraisal of acceptable tracking quality indicated inappropriate tracking, retracing was performed until all segments were considered acceptable [33].

2.5. Statistical analysis

Normal distribution of all continuous variables was examined using the Shapiro–Wilk test, and data are presented as mean ± SD or median and interquartile range, as appropriate. Categorical variables are expressed as percentages. The unpaired *t*-test and the Mann–Whitney *U* test were used to assess the between groups significance, according to data distribution. The paired *t*-test and the Wilcoxon matched-pair test were used to assess the within subjects significance of baseline and peak-training measurements, as appropriate for data distribution. A *p* value <0.05 was considered significant. The potential differences in Tanner's group assignment between athletes and controls were adjusted using sampling weights so that the marginal totals on Tanner's group assignment in the athletes group agreed with the corresponding totals of the control population, according to raking ratio estimation [34].

Correlation analysis was performed to find association between continuous variables using the Spearman and Pearson methods, as appropriate for data distribution. The change of parameters between baseline and 5-month measurements were calculated and used as dependent or independent variables.

To assess the reproducibility of RV parameters, measurements were repeated, in a random sample of 20 subjects (10 athletes and 10 controls), by the same investigator (intra-observer variability). Inter- and intra-observer variability was assessed by the intraclass correlation coefficients (ICC) with 95% confidence intervals (CIs).

Statistics were performed using SPSS version 21.0 software for Windows (Statistical Package for the Social Sciences Inc., Chicago, IL).

3. Results

The demographic characteristics of athletes and controls are reported in Table 1. At baseline there were no significant differences between athletes and controls for height, weight, and BSA. After 5 months, a significant increase in height, weight, and BSA was found both in the athletes and in the controls ($p < 0.0001$).

At baseline, 46% ($n = 25$) of athletes were at stage 1 (pre-puberty) and the rest were at stages 2–5 (puberty). After 5 months, 9% ($n = 5$) of athletes reached the sexual maturity, with 37% remaining at the pre-pubertal stage ($n = 20$). At baseline the 43% ($n = 16$) of controls were at stage 1 (pre-puberty) while the 16% ($n = 6$) reached sexual maturity in the following 5 months with 27% remaining at pre-pubertal stage ($n = 10$).

3.1. 12-lead resting ECG

At baseline athletes had a lower resting HR as compared with controls and a further decrease in resting HR was observed at peak-training (Table 1). An incomplete RBBB was found in 19% of athletes both at pre- and peak-training time points and in 15% of controls both at baseline and after 5-month time points (p value athletes vs. controls = 0.69). At baseline, 6% of controls (but none of the athletes) showed negative T waves in the precordial leads V1 to V3, which reduced to 3% after 5-month ($p = 0.16$ vs. baseline). None of the athletes exhibited negative T waves from V1 to V3 either at baseline or at peak training evaluation. At baseline, T-wave inversion in the precordial leads from V1 to V2 were present in 18% of athletes and 17% of controls; after 5 months a significant decrease was observed in the former ($p = 0.002$). Neither athletes nor controls showed complete RBBB. None of the participants did fulfil the ECG criteria for RV hypertrophy.

3.2. Morphological adaptation

The baseline and peak-training measurements obtained in athletes and the baseline and 5-month data found in controls are reported in Table 2. At baseline, absolute and indexed RVOT PSAX did not differ

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