THE DEVELOPING ATHLETE'S HEART: A COHORT STUDY IN YOUNG ATHLETES TRANSITIONING THROUGH ADOLESCENCE

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ABSTRACT

Background: Athlete's heart is a term used to describe physiological changes in the hearts of athletes, but its early development has not been described in longitudinal studies. This study aims to improve our understanding of the effects of endurance training on the developing heart.

Methods: Cardiac morphology and function in 48 cross-country skiers were assessed at age 12 (12.1±0.2 years) and then again at age 15 (15.3±0.3 years). Echocardiography was performed in all subjects including 2D speckle-tracking strain echocardiography and 3D echocardiography. All participants underwent cardiopulmonary exercise testing at both age 12 and 15 to assess maximal oxygen-uptake and exercise capacity.

Results: Thirty-one (65%) were still active endurance athletes at age 15 and 17 (35%) were not. The active endurance athletes had greater indexed $VO_{2\ max}$ (62±8 vs 57±6mL/kg/min, $p<0.05$) at follow-up. There were no differences in cardiac morphology at baseline. At follow-up the active endurance athletes had greater 3D indexed left ventricular end-diastolic (84±11mL/m^2 vs. 79±10mL/m^2, $p<0.05$) and end-systolic volumes (36±6mL/m^2 vs. 32±3mL/m^2, $p<0.05$). Relative wall thickness (RWT) fell in the active endurance athletes, but not in those who had quit (-0.05ΔmL/m^2 vs. 0.00mL/m^2, $p=0.01$). Four active endurance athletes had RWT above the upper reference values at baseline; all had normalized at follow-up.

Conclusion: After an initial concentric remodeling in the preadolescent athletes, those who continued their endurance training developed eccentric changes with chamber dilatation and little change in wall thickness. Those who ceased endurance training maintained a comparable wall thickness, but did not develop chamber dilatation.

KEYWORDS

Cardiomegaly, Exercise-Induced (D059267); Echocardiography, Three-dimensional (D019560); Exercise Test (D005080)

AUTHOR CONTRIBUTIONS

SIS, TE, HEWL, JH and SL contributed to the conception or design of the work. All co-authors contributed to the acquisition, analysis, or interpretation of data for the work. AWB drafted the manuscript. All co-authors critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

INTRODUCTION

Increased cardiac dimensions and changes in haemodynamics in those engaging in endurance sports have been described as early as the beginning of the 20th century.[1] These changes include increased left ventricular (LV) wall thickness, LV mass and increased LV and right ventricular (RV) chamber size, and is generally referred to as the "athlete's heart".[2] Although the precise mechanisms have proved elusive, they are believed to be physiological adaptions to normalize wall stress after altered loading conditions.[3] The amount of aerobic endurance training is thought to be the strongest predictor for the degree of cardiac changes observed.[4, 5] A meta-analysis found greatest athlete's heart-associated cardiac changes in bicyclists and cross-country skiers.[6]

Altered cardiac morphology and function have been found even in very young athletes,[7, 8] and with increased competitiveness and professionalism, there has been an increasing demand to improve our understanding on how intense endurance training affects the developing heart.[9]

Our group recently published a cross-sectional study on the hearts of preadolescent cross-country skiers, in which we found all the hallmark features of the athlete's heart.[8] As these elite athletes transition into adolescence, their hearts are undergoing the concurrent processes of development into maturity and athletic remodeling.

Success in endurance sports is closely linked to cardiac performance, thus it may be that a lack of progression is due to the inability of an athlete's heart to further adapt. With a cohort of promising, preadolescent athletes, we aimed to describe the cardiac features of both those who continued regular endurance training, and those who did not.

In our baseline study, we found a concentric form of remodeling in preadolescent endurance athletes. We hypothesize that with continued endurance exercise, further cardiac changes will be primarily of an eccentric nature, similar to those found in adult elite endurance athletes.[6]

METHODS

Participants were recruited from skiing clubs in the southeast of Norway in April to May 2013 and underwent baseline examinations from May to June the same year. The baseline examinations were performed at 12 years of age, one year after the athletes were allowed to participate in organized national competitions by the Norwegian Olympic and Paralympic Committee and Confederation of Sports provisions on children's sport.[10] All participants were invited to the follow-up in 2016. At both baseline and follow-up, the participants filled out self-reported questionnaires on training intensity and duration as well as prior illnesses.

Written informed consent was given by the legal guardians of all study participants. The study complies with the Declaration of Helsinki and was approved by the Regional Committee for Medical Research Ethics (ref. 2011/659 S-08702d).

Transthoracic echocardiography

Both at baseline and at follow-up all participants underwent an echocardiographic study (Vivid E9, GE, Vingmed, Horten, Norway). Using greyscale harmonic imaging, standard echocardiographic views were obtained. Data were digitally stored for post hoc analysis (EchoPac, GE, Vingmed). All measurements were performed by a single, blinded observer. Using two-dimensional echocardiography (2DE) LV dimensions, ejection fraction (EF) ad modum Simpson and LV diastolic function parameters were assessed. Left atrial (LA) volume was measured using the biplane method. Right atrial (RA) area, RV basal and mid-ventricular diameter and RV fractional area change (FAC) were assessed in the 4-chamber view. Parameters were measured according to the recommendations of the European Association of Cardiovascular Imaging (EACVI),[11] including indexing all chamber dimensions to body surface area (BSA). LV mass was calculated using the Devereux' formula.[12] Left ventricular geometry was assessed by calculating relative wall thickness (RWT) as (2*LVPWT)/LVEDD. LV volumes, EF and mass were also calculated from the 3D data sets.

Two-dimensional strain echocardiography

Strain analysis was performed using 2DE. For assessment of longitudinal strain, the endocardial borders were traced in the end-systolic frame of the 2D images from the apical 4-, 2-chamber, and apical long axis views. Strain was evaluated on a frame-by-frame basis by automatic tracking of acoustic markers throughout the cardiac cycle. Segments that failed to track properly were manually adjusted by the operator. Any segment that subsequently failed to track was excluded. Peak systolic LV longitudinal strain was assessed in 16 LV segments and averaged to LV global longitudinal strain (GLS). Similarly, by tracing the endocardial borders in the parasternal short-axis view at the papillary muscle level, circumferential strain was evaluated. Peak systolic LV global circumferential strain (GCS) was assessed by averaging 6 LV segments. RV GLS was calculated by averaging 3 RV free wall segments in the apical 4-chamber view. The frame rate at baseline was 65±12 Hz and at follow-up 63±14 Hz.

Cardiopulmonary exercise testing

Maximal oxygen uptake ($VO_{2\ max}$) was determined by an incremental exercise test to exhaustion on a treadmill (Woodway Elg 70, Weil am Rhein, Germany). Speed and inclination were set to 7 $km \cdot h^{-1}$ and 6.3 % respectively and the participants walked/ran at this intensity for one minute. Subsequently both speed and inclination were increased by 1 $km \cdot h^{-1}$ and 1 % every minute until a speed of 11 $km \cdot h^{-1}$ was reached. Further increase in intensity was achieved by increasing the inclination. When the participant could no longer complete the desired workload, the test was terminated. Oxygen uptake was measured continuously with an automated system (Oxycon Pro, Jaeger-Toennis, Hochberg, Germany). The exercise test was accepted as maximal if the majority of the following termination criteria were met: respiratory exchange ratio (RER)>1.0, heart rate>200 beats/min, display of indicators of a maximal effort such as sweating and, despite strong verbal encouragement the participant was unable or unwilling to continue.

Statistical analysis

Analyses were carried out using SPSS version 21 (SPSS Inc., Chicago, IL, USA) and Stata 15.0 (StataCorp LLC, Texas, USA). Data were presented as mean±SD, and numbers and percentages, respectively. The $\chi 2$ test (categorical variables) and the Student's t-test (continuous variables) were used to determine differences between two groups at baseline and follow-up. Linear mixed models were used to assess impact of training group on $VO_{2\ max}$, LV EDV, LV ESV and RWT. Training group, time point and the interaction of these were added as fixed effects and the individual athlete as a random effect. The models were adjusted for sex. For intra-individual changes from baseline to follow-up, the paired t-test was used. Reproducibility was expressed as intraclass correlation coefficient.

RESULTS

Out of 76 participants in the baseline study, forty-eight (63 %) took part in the follow-up. Those who attended the follow-up had a higher indexed $VO_{2\ max}$ (64±7 vs 59±5mL/kg/min, $p<0.01$) at baseline, but did not differ in regards to other basic characteristics or echocardiographic data compared to those who did not return for follow-up. Two athletes failed to complete CPX at baseline due to issues with the mask. At follow-up, one former and one active endurance athlete failed to complete CPX due to injuries. One active endurance athlete was diagnosed with asthma. No other chronic illnesses were reported. All participants in the study were Caucasian.

Of the 48 athletes, 31 (65%) reported more than 5 hours of weekly endurance exercise, and were classified as active endurance athletes, while 17 athletes (35%) reported less than 5 hours of weekly endurance exercise and were classified as former endurance athletes. In the active group, 29 participated in cross-country skiing (94%), one in competitive rowing (3%) and one in orienteering (3%).

The active endurance athletes engaged in 10.3±2.2 hours of organized training per week, of which 7.4±1.9 hours were endurance training. The former endurance athletes reported 8.5±5.6 hours of organized training per week, of which 1.9±1.7 hours were endurance training. Of the 17 former endurance athletes, 3 (15%) had quit cross-country skiing after or during the previous season (0.5 – 1 year earlier), the rest at least 1.5 years earlier. All participants reported less than 3 hours of weekly strength training.

A comparison of basic characteristics between the active and former endurance athletes is summarized in Table 1. There were no significant differences in anthropometric data at baseline. At follow-up, the active endurance athletes had a lower resting heart rate.

Cardiopulmonary exercise testing

Cardiopulmonary exercise testing (CPX) data, comparing the two groups at baseline and follow-up are summarized in Table 1. With no difference at baseline, the active endurance athletes had greater indexed and absolute $VO_{2\ max}$ and time to exhaustion at follow-up. RER and maximal heart rate did not differ at any point of measurement.

With a mixed linear regression model with $VO_{2\ max}$ as the dependent variable, we found a greater increase in $VO_{2\ max}$ from baseline to follow-up in the active endurance athlete group (1101ΔmL/min vs. 683ΔmL/min, $p<0.005$). Both groups experienced a reduction in indexed $VO_{2\ max}$, but the reduction was less pronounced in the active endurance athletes (-3ΔmL/min/kg vs. -6ΔmL/min/kg, $p<0.05$).

Cardiac morphology and function

There was no difference in any morphological parameter between the two groups at baseline (Table 2). At follow-up the active endurance athletes had greater 3D indexed LV EDV and ESV. There

was also a trend towards greater indexed RV end-diastolic and end-systolic areas in the active endurance athletes at follow-up.

With a mixed linear regression model, we found a greater increase in indexed LV EDV from baseline to follow-up in the active endurance athletes (11ΔmL/m^2 vs. 4mL/m^2, p<0.05). For LV ESV there was a similar non-significant trend (3ΔmL/m^2 vs. 0mL/m^2, p=0.05). RWT fell in the active endurance athletes, but not in those who had quit (-0.05ΔmL/m^2 vs. 0.00mL/m^2, p=0.01).

There were moderate, positive correlations between weekly hours of endurance training and changes in $VO_{2\ max}$ (R=0.55, p<0.001), indexed LV EDV (R=0.45, p<0.01), LV ESV (R=0.35, p<0.05), RV EDA (R=0.39, p<0.01) and RV ESA (R=0.44, p<0.01). No correlation was found for weekly hours of non-specified exercise.

There was no significant intergroup difference in any functional parameter at neither baseline nor follow-up (Table 2).

Intra- and inter-observer intraclass correlations were performed in ten of the 12-year old athletes and were 0.99 and 0.95, respectively, for 3D LV EDV; 0.97 and 0.93 for 3D LV ESV; 0.93 and 0.94 for 3D LV mass; and 0.77 and 0.73 for 3D LV EF. For LV and RV strain, we have performed intra- and inter-observer variability analysis in earlier studies.[13]

DISCUSSION

Cardiac morphology

In this longitudinal follow-up study, we found no difference in either wall thickness or cardiac mass between those who continued competitive endurance sports and those who quit. However, ventricular volumes did differ. Those who continued to engage in competitive endurance exercise no longer experienced a concentric remodeling, as they did at baseline, but underwent balanced or even

eccentric remodeling. The morphological changes found at follow-up are in contrast to those found at baseline. At 12 years of age, we found the greatest differences in wall thickness and cardiac mass; not chamber dimensions when comparing our preadolescent athletes with age-matched controls. This led to higher RWT, with a subsection of young athletes even exceeding the normal range.[8] As a consequence of chamber dilatation, the RWT of the active endurance athletes at 15 year of age normalized (Figure 1). Of the four active endurance athletes in our cohort with RWT exceeding the reference value (RWT >0.42) at baseline, none did so at follow-up.

This early concentric remodelling is not predicted by the Morganroth-hypothesis, named after the hallmark paper by Morganroth et al. in 1975.[4, 14] Morganroth proposed that endurance athletes develop eccentric remodeling due to volume overload, while power athletes develop concentric remodeling due to increased afterload. If we were to look at the athletes at 15 years of age in isolation, ignoring the cardiac morphology at 12 years of age, it would fit well with this hypothesis; as would earlier studies in adult endurance athletes. Conversely, concentric remodeling in preadolescent endurance athletes would not fit into the same narrative.

In a recent CMR study, Barczuk-Falęcka et al. have found the same phenomenon in preadolescent, polish footballers. They found no differences with regards to chamber dimensions, but both LV mass and wall thickness were significantly greater in preadolescent athletes.[15] Similarly, Pelà et al. found an average RWT of 0.35 in 13 year old athletes, the same high value as the 12 year old athletes in our baseline study.[16]

This dynamic does not seem to be isolated to young athletes. In a recent experimental study, Arbab-Zadeh et al. demonstrated the same initial dynamic in the development of athlete's heart in adults. Previously untrained, healthy adults were exposed to intensive endurance training, and the initial cardiac response was concentric wall thickening. There was no eccentric chamber dilatation until after 6-9 months.[17]

Combined, these studies suggest a different mechanism in the development of athlete's heart in endurance athletes than a purely eccentric response to volume overload. It could very well be that the initial feature in the development of the athlete's heart is concentric remodeling, and that the dilated ventricles seen in the fully developed athlete's heart is in fact a late result of continued endurance training. Such a two-phased dynamic might explain the observed heterogeneity of athlete's heart morphology in young endurance athletes.

Cardiac function

Neither group saw any significant changes in LV deformation parameters, which is in accordance with the findings of a recent meta-analysis on LV function in the athlete's heart.[18] However, both groups saw a similar decline in RV GLS and TAPSE. While data on the subject is quite sparse, studies on RV GLS in preadolescent athletes have generally found greater deformation values than similar studies in adult athletes.[19, 20] The dynamics of RV remodelling might well be different in the developing heart, which could help explain both the findings from this study and the discrepancies in RV GLS between preadolescent and adult athletes seen in other studies. Furthermore, exercise have been found to be inversely correlated with RV GLS even in adult athletes.[21] It should be noted, however, that both RV GLS and TAPSE remained well within reference values and the changes from baseline to follow-up are small.

Clinical implications

With increasing professionalism and with more and more preadolescent athletes engaging in intense exercise, distinguishing physiological changes of the athlete's heart from pathological cardiac changes is becoming increasingly clinically relevant. There is evidence that intense endurance exercise not only hastens the onset and increases the burden of symptoms in hereditary heart disease like arrhythmogenic right ventricular cardiomyopathy (ARVC), but that overtraining in itself may induce arrhythmias through irreversible cardiac changes.[20, 22, 23] Identifying athletes at risk for

cardiac disease and sudden cardiac death is of vital importance, and the focal point of the recently published pre-participation guidelines from the European Heart Rhythm Association and the European Association of Preventive Cardiology.[24] However, in addition to accurately predict rare events in a large population, correctly identifying those *not* at risk might be an equally important task. Concentric remodeling might alarm a clinician expecting only eccentric changes in young endurance athletes. Our study suggests that concentric remodelling in conjunction with chamber dilatation can be considered normal in the early development of the athlete's heart, and that it is likely to normalize with continuing exercise.

LIMITATIONS

While the former endurance athletes engaged in less endurance exercise than the active endurance athletes, the group was far from sedentary. Everyone in this cohort was engaged in regular endurance training at 12 years of age, and most of the former endurance athletes were still exercising regularly. Some also pursued other non-endurance sports competitively. This could potentially mask cardiac changes that would be visible in a comparison to a sedentary population. Interestingly, however, only weekly hours of endurance exercise correlated with increases in $VO_{2\,max}$ and changes in cardiac morphology. Since this study does not have a sedentary control arm, the cardiac changes can not be controlled for cardiac maturation. The differences between the two groups may have been greater, had the former endurance athletes ceased exercising altogether. A third of the athletes from the baseline study were lost to follow-up, adversely affecting statistical power.

We estimated LV mass using 3DE, and while there is evidence that utilizing 3DE for assessing LV mass is more precise than traditional echocardiographic techniques, CMR is still the gold standard.[25]

CONCLUSION

In young athletes who performed high volume endurance training from the age of 12 to 15, after an initial concentric remodeling, the cardiac chambers started to dilate, and the relative wall thickness decreased and normalized. In contrast, those who ceased high volume endurance training did not see this dilation and did not experience a drop in relative wall thickness. Our results support the notion that the morphological changes described in the power athlete's and the endurance athlete's heart might be incorrect. According to our data, an early concentric remodeling in preadolescents followed by an eccentric chamber dilatation in adolescents should be expected in young endurance athletes.

FIGURES

figure1.jpg

Figure 1. Change in relative wall thickness from baseline to follow-up amongst those who continued endurance training and those who did not.

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