

Bjerring, A. W., Landgraff, H. E. W., Leirstein, S., Haugaa, K., Edvardsen, T., Sarvari, S., Hallén, J. (2020). From talented child to elite athlete: The development of cardiac morphology and function in a cohort of endurance athletes from age 12 to 18. *European Journal of Preventive Cardiology (EJPC)*, under utgivelse.
<https://doi.org/10.1177/2047487320921317>

Dette er siste tekst-versjon av artikkelen, og den kan inneholde små forskjeller fra forlagets pdf-versjon. Forlagets pdf-versjon finner du her:
<https://doi.org/10.1177/2047487320921317>

This is the final text version of the article, and it may contain minor differences from the journal's pdf version. The original publication is available here:
<https://doi.org/10.1177/2047487320921317>

FROM TALENTED CHILD TO ELITE ATHLETE: THE DEVELOPMENT OF CARDIAC MORPHOLOGY AND FUNCTION IN A COHORT OF ENDURANCE ATHLETES FROM AGE 12 TO 18

Anders W Bjerring MD^{a,c}, Hege EW Landgraaff MSc^b, Svein Leirstein^b, Kristina H Haugaa MD PhD^{a,c}, Thor Edvardsen MD PhD^{a,c}, Sebastian I Sarvari MD PhD^{a,c}, Jostein Hallén PhD^b

^a Department of Cardiology, Oslo University Hospital, Rikshospitalet, Oslo, Norway

^b Norwegian School of Sport Sciences, Oslo, Norway

^c Faculty of Medicine, University of Oslo, Oslo, Norway

Previous presentations: Preliminary data from this study was presented at EuroEcho 2019.

Funding: The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by South-Eastern Norway Regional Health Authority (Grant number 2017053).

Disclaimers: None

Corresponding author

Sebastian Imre Sarvari, MD, PhD

Department of Cardiology,

Oslo University Hospital, Rikshospitalet,

N-0027 Oslo, Norway

Phone: +4723071395. Fax: +4723073530

E-mail: sebastian.sarvari@rr-research.no

Word count: 4241

ABSTRACT

Background: Adult athletes undergo cardiac adaptations in what is known as the “athlete’s heart”.

Cardiac adaptations in young athletes have not been described in longitudinal studies but have previously been believed to be uniform in nature.

Methods: Seventy-six cross-country skiers were assessed at age 12. Forty-eight (63%) completed the first follow-up at age 15 and thirty-six (47%) the second follow-up at age 18. Comprehensive exercise-data was collected. Echocardiography with 3D measurements and cardiopulmonary exercise testing were performed at all time points. The cohort was divided into active and former endurance athletes, with an 8 hours of weekly endurance exercise cut-off at age 18.

Results: The athletes underwent eccentric remodeling between ages 12 and 15 and concentric remodeling between ages 15 to 18. At age 18, the active endurance athletes had greater increases in inter-ventricular wall thickness ($1.8 \pm 1.4 \Delta \text{mm}$ vs. $0.6 \pm 1.0 \Delta \text{mm}$, $p < 0.05$), left ventricular (LV) posterior wall thickness ($1.6 \pm 1.2 \Delta \text{mm}$ vs. $0.8 \pm 0.8 \Delta \text{mm}$, $p < 0.05$), LV mass ($63 \pm 30 \Delta \text{g}$ vs. $27 \pm 21 \Delta \text{g}$, $p < 0.01$), right ventricular (RV) end-diastolic area ($3.4 \pm 4.0 \Delta \text{cm}^2$ vs. $0.6 \pm 3.5 \Delta \text{cm}^2$, $p < 0.05$), RV end-systolic area ($1.0 \pm 2.3 \Delta \text{cm}^2$ vs. $-0.9 \pm 2.0 \Delta \text{cm}^2$, $p < 0.05$) and left atrial volume ($24 \pm 21 \Delta \text{mL}$ vs. $6 \pm 10 \Delta \text{mL}$, $p < 0.05$) and had greater indexed VO_2 max ($66.3 \pm 7.4 \text{ mL/min/kg}$ vs. $57.1 \pm 8.2 \text{ mL/min/kg}$, $p < 0.01$). There was no significant difference for LV volumes.

Conclusion: This study finds a shift in the development of the young athlete’s heart. Between ages 12 and 15, the active endurance athletes underwent eccentric remodelling. This dynamic switched to concentric remodeling between ages 15 and 18.

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.

INTRODUCTION

Athlete's heart (AH) is a term encompassing a range of mainly morphological, but also functional changes in the hearts of athletes. In the fully developed AH, all four chambers are dilated, usually in a balanced manner, but in some cases more pronounced in the right side of the heart.¹ Wall thickness is symmetrically increased, which in conjunction with the chamber dilation causes a substantially greater left ventricular (LV) mass. LV function is unaffected or slightly reduced, stroke volume is increased, and heart rate is lower at rest.^{2, 3}

While most studies of the athlete's heart has been performed in adult athletes, altered cardiac morphology and function have been found even in preadolescent athletes.^{4, 5} Increasing competitiveness have led to earlier and more intense endurance training in young age groups. As a consequence, there has been a growing demand to improve our understanding on how intense endurance training affects hearts that undergo the concurrent processes of development into maturity and athletic remodeling.⁶

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 AH. Surprisingly, the remodeling was concentric in nature, rather than the eccentric changes predicted by the classical Morganroth-hypothesis.^{5, 7, 8} In the follow-up study performed at age 15, the dynamic of remodeling had changed. Those who continued to engage in high-performance endurance sports underwent balanced or even eccentric changes, rather than experiencing increased wall thickness.⁹

In the present study, at age 18, cardiac maturation is largely complete. While drop-out in this age range is substantial, both in the general athletic population and in this study, several of the promising 12-year-old athletes in our cohort have become amongst the best junior cross-country skiers in Norway. For the first time, we are able to describe the cardiac development of the world-class endurance athlete from the very beginning of their athletic career.

Our aims are to describe the development of the AH from preadolescence to adulthood and to assess the impact of endurance and non-endurance exercise on cardiac parameters. We hypothesize that as these young athletes approach adulthood, their cardiac morphology will more closely approximate that of adult athletes, primarily through increased LV mass.

METHODS

Seventy-six athletes of both genders were recruited in 2013 from skiing clubs in the southeast of Norway. Participants had to turn 12 years the same year, have no prior medical conditions and be active members of a cross-country skiing club. They underwent baseline examinations from May to June the same year. All participants were invited to a follow-up in 2016 and 2019. 48 completed the first and 36 the second follow-up (Figure 1). At all three time points, the participants filled out self-reported questionnaires on sport discipline(s), exercise frequency, type, intensity and duration, as well as prior illnesses. All participants were subsequently interviewed by an experienced observer to ensure that the reported exercise data was accurate. Training was classified as endurance exercise and non-endurance exercise (technical, tactical and strength exercise). Typical endurance training was continuous or interval workouts, either running, skiing or biking.

Participants were classified as either active or former endurance athletes. At age 15, a cut-off of 5 hours of weekly endurance exercise was used. At age 18, after an AUC-analysis where weekly hours of endurance exercise were compared to indexed VO_2 max, 8 hours was chosen as the cut-off (AUC 0.79). At baseline, twenty-five age-matched, non-competing, healthy preadolescents were recruited as controls.

At the first follow-up one active endurance athlete reported a diagnosis of asthma. At the second follow-up, one active endurance athlete reported having undergone ablation for Wolff-Parkinson-White syndrome. No other illness was reported. All participants in this cohort were Caucasian.

Written informed consent was given by the legal guardians of the 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

At age 12, 15 and 18, the participants underwent echocardiographic studies (Vivid E9/E95, GE, Vingmed, Horten, Norway). Standard echocardiographic images were obtained from the parasternal long-axis, short axis, apical 4-, 3- and 2-chamber and subcostal views. All measurements were performed and analysed post-hoc using dedicated software (EchoPac, GE, Vingmed). A single, blinded observer performed all measurements. LV dimensions and diastolic function was assessed by two-dimensional echocardiography (2DE). Left atrial (LA) volume was measured using the biplane method. Right atrial (RA), right ventricular (RV) dimensions were measured in the apical 4-chamber view. All parameters were measured in accordance with the recommendations by the European Association of Cardiovascular Imaging (EACVI).¹⁰ All chamber dimensions were indexed to body surface area (BSA). Devereux' formula was used to calculate 2D LV mass.¹¹ Relative wall thickness (RWT) was calculated as $(2 * \text{LV posterior wall thickness}) / \text{LV end-diastolic diameter}$. LV volumes, stroke volume and ejection fraction were calculated from the 3D data sets using a semi-automatic technique.

For speckle-tracking strain analysis 2DE acquisitions were used. Peak systolic LV longitudinal strain was measured in 16 segments in the apical 4, 3- and 2-chamber views and averaged to LV global longitudinal strain (GLS). Peak systolic LV global circumferential strain (GCS) was measured by averaging 6 segments in the parasternal short-axis view at the papillary muscle level. RV GLS was calculated from 3 RV free-wall segments in the apical 4-chamber view. The frame rate was 63 ± 11 Hz on average.

Cardiopulmonary exercise testing

Maximal oxygen uptake (VO_2 max) was measured by an incremental exercise test on a treadmill (Woodway Elg 70, Weil am Rhein, Germany). Speed was initially set to 7 km/h and inclination to 6.3 %. After the participant had been running at this intensity for one minute, the speed was increased by 1 km/h and inclination by 1 % every minute until a speed of 11 km/h was reached. Subsequent increase in intensity was achieved by steeper inclination only. The test was terminated when the participant was unable to complete the current workload. VO_2 max was continuously measured for the whole duration of the exercise test (Oxycon Pro, Jaeger-Toennis, Hochberg, Germany).

Statistical analysis

Analyses were carried out using Stata 15.0 (StataCorp LLC, Texas, USA) and SPSS version 21 (SPSS Inc., Chicago, IL, USA). Data were presented as mean \pm SD, and numbers and percentages, respectively. Delta-values were calculated for changes between the first and second follow-up, and differences in the two groups were assessed using the χ^2 test (categorical variables) and the Student's t-test (continuous variables). Linear mixed models were used to assess the impact of exercise type on select variables, with hours of either endurance or all-types exercise, time point and the interaction of these as fixed effects and the individual athlete as a random intercept effect. Time was added as a random slope effect when it improved the Akaike's information criteria (AIC). Sex was included in the model when it was both significant and improved the AIC. Reproducibility was expressed as intraclass correlation coefficient.

RESULTS

The active endurance athletes reported both more hours of endurance exercise (11 ± 2 vs. 3 ± 3 , $p<0.001$) and more hours of all types of exercise per week (13 ± 2 vs. 9 ± 5 , $p<0.01$). Of the active

endurance athletes, 17 (85%) participated in cross-country skiing, 2 (10%) in orienteering and 1 (5%) in Nordic combined. Nine participants were reclassified from active endurance athletes at age 15 to former endurance athletes at age 18. Eight out of the nine competed in cross-country skiing at age 15, one participated in rowing. At age 18 four (44%) reported still participating in cross-country skiing, one (11%) participated in rowing, one (11%) participated in orienteering, one (11%) participated in football and two (22%) reported not participating in any sports at age 18.

Basic characteristics at age 18 are summarized in Table 1. No intergroup differences in age, sex, height, weight, BSI, BMI, resting heart rate or blood pressure was found.

Cardiopulmonary exercise testing

Cardiopulmonary exercise testing (CPX) data are summarized in Table 1. From age 15 to 18, the active endurance athletes had a greater increase in VO_2 max ($1134 \pm 475 \Delta mL/min$ vs. $578 \pm 510 \Delta mL/min$, $p < 0.01$) and a non-significant trend towards greater indexed VO_2 max ($3.5 \pm 5.8 \Delta mL/min/kg$ vs. $-0.6 \pm 4.9 \Delta mL/min/kg$, $p = 0.07$). The active endurance athletes also had higher absolute and indexed VO_2 max and time-to-exhaustion at 18 years.

Cardiac morphology and function

Changes in cardiac morphology and function from age 15 to age 18 are summarized in Table 2. Both groups had greater LV end-diastolic volume (EDV), LV end-systolic volume (ESV), LV mass, inter-ventricular septal diameter and LV posterior wall diameter at age 18 compared to age 15, but the active endurance athletes had significantly greater increases in LV mass, inter-ventricular septal diameter and LV posterior wall diameter. They also had greater increases in RV end-diastolic area (EDA) and RV end-systolic area (ESA).

At age 18, 8 (42%) active and 4 (25%) former endurance athletes exceeded the upper reference limit for indexed LV mass, while 13 (68%) active and 11 (68%) former endurance athletes

exceeded upper reference limits for indexed LV EDV. Twelve (63%) active and 7 (47%) former endurance athletes exceeded the upper reference limits for indexed RV EDA.¹⁰

While both groups underwent a minor reduction in both GLS and GCS, they remained within normal limits and there was no intergroup difference. No changes or intergroup difference was seen for other functional parameters.

There was a strong correlation between VO₂ max and several morphological parameters at age 18, most notably LV mass (R=0.89), LV end-diastolic volume (EDV) (R=0.81) and LV end-systolic volume (ESV) (R=0.77).

Impact of endurance exercise

Weekly hours of endurance training showed a moderate to strong positive correlation to change in LV mass from age 15 to age 18 (R=0.69, p<0.01). There was also moderate, positive correlation between weekly hours of endurance training and changes in inter-ventricular septal thickness (R=0.54, p<0.01), LV posterior wall diameter (R=0.47, p <0.05), RV EDA (R=0.47, p<0.05), RV ESA (R=0.53, p<0.01) and LA volume (0.43, p<0.05).

Using the full dataset from age 12 to 18 in a mixed model linear regression model adjusted for sex, with the individual athlete as random intercept and time as a random slope, we found that each weekly hour of endurance exercise increased LV mass by 3.6 g (p<0.01) between age 12 and 15 and by 6.4 g (p<0.001) between age 15 and 18. LV EDV increased by 2.3 mL (p<0.05) and LV ESV by 1.1 mL (p<0.05) per hour of endurance exercise between age 12 and 15. No significant association was found between weekly hours of endurance exercise and LV volumes from age 15 to 18. There was no significant impact of weekly hours of non-specified exercise on any parameter at any time point.

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.¹²

DISCUSSION

Cardiac morphology

The morphological development of the AH from preadolescence to young adulthood in elite athletes has not previously been described in longitudinal studies. In this study, we show a mainly concentric remodeling occurring in the hearts of elite endurance athletes from ages 15 to 18. Significant increases in both inter-ventricular and posterior wall thickness, as well as greater LV mass, are the main morphological features of the 18 years old athletes. This mainly concentric remodeling is in contrast to the eccentric remodeling in the active endurance athletes from age 12 to 15.⁹

In our baseline study, where we compared the then 12 years old athletes to age-matched sedentary controls, the athletes had significantly greater LV wall thickness and LV mass, but only slightly larger chamber volumes. As such, the RWT was greater in the athletes than in the controls (0.35 ± 0.05 vs. 0.29 ± 0.07 , $p<0.001$). Six of the athletes (13%) even exceeded the normal limit for RWT (>0.42), indicative of concentrically remodelled hearts. At the first follow-up at age 15, we found a marked increase in LV chamber volumes combined with a smaller increase in mass, resulting in a normalization of RWT in all participants. While the former endurance athletes did not see any change in RWT from age 12 to 15 (0.33 ± 0.05 to 0.33 ± 0.05 , $p=0.93$), the active did (0.35 ± 0.05 to 0.31 ± 0.04 , $p<0.001$).⁹

There appears to be a shifting and dynamic relationship between chamber volume and wall thickness throughout the development of the AH from preadolescence to young adulthood. We have

identified tiers in this development, but it is far from certain that our measurements have hit upon the precise maximal fluctuation in this relationship, or indeed uncovered all. Closer and more frequent follow-up could potentially have found even greater differences in RWT.

While this is the first time the development of the AH has been assessed longitudinally in young athletes, several studies have looked at cardiac remodeling in adult athletes using experimental models. Spence et al. randomized healthy, untrained adults to either six months of endurance or strength training.¹³ The only significant change identified in that study was increased LV mass and wall thickness in the participants undergoing endurance training. Similarly, Arab-Sadeh et al. exposed untrained adults to a 12 months training program. They found an initial concentric remodeling with increased LV mass and wall thickness. Importantly, only after 6-9 months could they identify any changes in chamber volumes.¹⁴

There are clear limitations in generalizing such experimental studies to a population of adult and, even more so, preadolescent and adolescent athletes. While you can randomize someone to engage in endurance exercise, you cannot randomize them into becoming world-class athletes. Both Spence and Arab-Sadeh induced impressive improvements in VO_2 max in their participants, but the maximal average values remained at 49.3 and 47.6 ml/kg/min, respectively. In comparison, the active endurance athletes in this study had an average VO_2 max of 66.3 ml/kg/min.

While longitudinal data in young athletes is scarce, several cross-sectional studies have examined the heart of preadolescent endurance athletes and these consistently show concentric remodeling. In a CMR study on preadolescent, polish footballers and age-matched controls, Barczuk-Falęcka et al. found no differences with regards to chamber dimensions, but both LV mass and wall thickness were significantly greater in the athletes.¹⁵

Even though the young athletes show extensive remodelling at age 18, similar to what has been described in adult endurance athletes, it is unlikely that their hearts have reached their zenith.

In the more than 800 world cup events organized by the International Ski Federation to date, not a single athlete under the age of 20 have won.¹⁶ It is thus likely that further cardiac adaptation will occur in the active endurance athletes in this cohort. While sex seems to have a limited impact on adjusted morphological parameters in sedentary controls, studies have found a substantial effect of sex in athletes. Further studies on the effect of sex are warranted.¹⁷

Impact of exercise type

The degree of AH development is closely linked to the sport being performed. Along with cyclists and swimmers, cross country skiers are consistently found to have the greatest changes in cardiac morphology.¹⁸ In the classical view, strength exercise would induce concentric remodeling due to the repeated bursts of increases in afterload, while endurance training would induce eccentric remodeling due to volume overload.^{7, 8} While the impact of endurance exercise is well documented, a meta-study concluded that there is no clear evidence for the “strength heart”, a position that has also been acknowledged in recent guidelines.^{3, 19, 20} Thus the question of whether strength exercise is a separate entity with a separate mechanism, or simply a less effective variation of endurance exercise, has been raised.⁹

We found significant correlations between weekly hours of endurance exercise and change in cardiac morphology, but not for all exercise combined or any other subcategory of exercise.

Clinical implications

With the number of young athletes engaging in intense exercise on the rise, distinguishing physiological changes of the AH from pathological cardiac changes, such as those seen in arrhythmogenic cardiomyopathy and hypertrophic cardiomyopathy, is becoming more important than ever.^{21, 22} A majority of the athletes in this study exceeded the upper reference limit for LV EDV and a third of the active endurance athletes exceeded the upper reference limit for LV mass.

Improved knowledge of the dynamic relationship between concentric and eccentric remodeling in young athletes may aid the clinician in decision-making, especially in the setting of serial evaluations.

LIMITATIONS

Even though the active endurance athletes engaged in far more endurance training, the former endurance athletes were not sedentary. At the time of inclusion, everyone in this cohort engaged in regular endurance training, and at both follow-ups, most former endurance athletes still exercised more than sedentary peers. This could potentially mask effects of training on changes in morphology. The lack of sedentary controls also means that cardiac changes cannot be controlled for maturation. A cohort of age matched non-athletes could potentially have shed more light on this aspect of the cardiac development in the athletes. However, recent data from the Pediatric Heart Network found, perhaps surprisingly, no clinically relevant effect of age or sex on echocardiographic parameters and concluded that adjustment for BSA is sufficient in pediatric populations.²³ Accordingly, adjusting parameters for BSA greatly mitigates the issue of cardiac maturation, but does not eliminate it completely. Furthermore, training responsiveness is partly dependent on genetic factors, and will most likely lead to lower rates of drop-out in those most able to benefit from endurance exercise.

CONCLUSION

The young, elite athletes in this study underwent extensive changes in cardiac morphology from preadolescence to young adulthood. At age 12, the endurance athletes tended towards concentric remodeling, with increased wall thickness and cardiac mass compared to sedentary peers. At age 15, this dynamic had transferred to an eccentric remodeling, with increased chamber volumes. Finally, those who continued high-level endurance sports switched back into concentric remodeling at age 18. Previously thought to be uniform in nature, and dependent on the sport practiced, this study finds a remarkable heterogeneity in the development of the young AH.

Moreover, this unbalanced remodeling appears constant across a whole cohort, indicating that there could be distinct phases in the development of the young AH.

FIGURE LEGENDS

Figure 1. Flow-chart of the participants at baseline and the two follow-up studies.

REFERENCES

1. Fagard R. Athlete's heart. *Heart (British Cardiac Society)* 2003; 89: 1455-1461. 2003/11/18.
2. Azevedo LF, Perlingeiro PS, Hachul DT, et al. Sport Modality Affects Bradycardia Level and Its Mechanisms of Control in Professional Athletes. *International journal of sports medicine* 2014; 35: e3. 2014/07/11. DOI: 10.1055/s-0034-1384589.
3. Caselli S, Di Paolo FM, Picicchio C, et al. Patterns of left ventricular diastolic function in Olympic athletes. *Journal of the American Society of Echocardiography : official publication of the American Society of Echocardiography* 2015; 28: 236-244. 2014/12/03. DOI: 10.1016/j.echo.2014.09.013.
4. Ayabakan C, Akalin F, Mengutay S, et al. Athlete's heart in prepubertal male swimmers. *Cardiology in the young* 2006; 16: 61-66. 2006/02/04. DOI: 10.1017/s1047951105002106.
5. Bjerring AW, Landgraff HE, Leirstein S, et al. Morphological changes and myocardial function assessed by traditional and novel echocardiographic methods in preadolescent athlete's heart. *European journal of preventive cardiology* 2018; 25: 1000-1007. 2018/05/23. DOI: 10.1177/2047487318776079.
6. Bergeron MF, Mountjoy M, Armstrong N, et al. International Olympic Committee consensus statement on youth athletic development. *British journal of sports medicine* 2015; 49: 843-851. 2015/06/19. DOI: 10.1136/bjsports-2015-094962.
7. Morganroth J and Maron BJ. The athlete's heart syndrome: a new perspective. *Annals of the New York Academy of Sciences* 1977; 301: 931-941. 1977/01/01.
8. Morganroth J, Maron BJ, Henry WL, et al. Comparative left ventricular dimensions in trained athletes. *Annals of internal medicine* 1975; 82: 521-524. 1975/04/01.
9. Bjerring AW, Landgraff HE, Stokke TM, et al. The developing athlete's heart: a cohort study in young athletes transitioning through adolescence. *European journal of preventive cardiology* 2019: 2047487319862061. 2019/07/10. DOI: 10.1177/2047487319862061.
10. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *European heart journal cardiovascular Imaging* 2015; 16: 233-270. 2015/02/26. DOI: 10.1093/ehjci/jev014.
11. Devereux RB, Alonso DR, Lutas EM, et al. Echocardiographic assessment of left ventricular hypertrophy: comparison to necropsy findings. *The American journal of cardiology* 1986; 57: 450-458. 1986/02/15.

12. Sarvari SI, Haugaa KH, Anfinson OG, et al. Right ventricular mechanical dispersion is related to malignant arrhythmias: a study of patients with arrhythmogenic right ventricular cardiomyopathy and subclinical right ventricular dysfunction. *European heart journal* 2011; 32: 1089-1096. 2011/03/17. DOI: 10.1093/eurheartj/ehr069.
13. Spence AL, Naylor LH, Carter HH, et al. A prospective randomised longitudinal MRI study of left ventricular adaptation to endurance and resistance exercise training in humans. *The Journal of physiology* 2011; 589: 5443-5452. 2011/10/05. DOI: 10.1113/jphysiol.2011.217125.
14. Arbab-Zadeh A, Perhonen M, Howden E, et al. Cardiac remodeling in response to 1 year of intensive endurance training. *Circulation* 2014; 130: 2152-2161. 2014/10/05. DOI: 10.1161/circulationaha.114.010775.
15. Barczuk-Falecka M, Malek LA, Krysztofiak H, et al. Cardiac Magnetic Resonance Assessment of the Structural and Functional Cardiac Adaptations to Soccer Training in School-Aged Male Children. *Pediatric cardiology* 2018; 39: 948-954. 2018/03/10. DOI: 10.1007/s00246-018-1844-5.
16. FIS. Ruka Preview, <https://www.fis-ski.com/en/cross-country/cross-country-news-multimedia/news/archive/article=ruka-preview-classic-interval-start> (2017, accessed 10.03 2020).
17. Finocchiaro G, Dhutia H, D'Silva A, et al. Effect of Sex and Sporting Discipline on LV Adaptation to Exercise. *JACC Cardiovascular imaging* 2017; 10: 965-972. 2016/11/21. DOI: 10.1016/j.jcmg.2016.08.011.
18. Spirito P, Pelliccia A, Proschan MA, et al. Morphology of the "athlete's heart" assessed by echocardiography in 947 elite athletes representing 27 sports. *The American journal of cardiology* 1994; 74: 802-806. 1994/10/15.
19. Utomi V, Oxborough D, Whyte GP, et al. Systematic review and meta-analysis of training mode, imaging modality and body size influences on the morphology and function of the male athlete's heart. *Heart (British Cardiac Society)* 2013; 99: 1727-1733. 2013/03/12. DOI: 10.1136/heartjnl-2012-303465.
20. Pelliccia A, Caselli S, Sharma S, et al. European Association of Preventive Cardiology (EAPC) and European Association of Cardiovascular Imaging (EACVI) joint position statement: recommendations for the indication and interpretation of cardiovascular imaging in the evaluation of the athlete's heart. *European heart journal* 2017 2017/10/14. DOI: 10.1093/eurheartj/ehx532.
21. Mont L, Pelliccia A, Sharma S, et al. Pre-participation cardiovascular evaluation for athletic participants to prevent sudden death: Position paper from the EHRA and the EACPR, branches of the ESC. Endorsed by APHRS, HRS, and SOLAECE. *European journal of preventive cardiology* 2017; 24: 41-69. 2016/11/07. DOI: 10.1177/2047487316676042.

22. Lie OH, Dejgaard LA, Saberniak J, et al. Harmful Effects of Exercise Intensity and Exercise Duration in Patients With Arrhythmogenic Cardiomyopathy. *JACC Clinical electrophysiology* 2018; 4: 744-753. 2018/06/23. DOI: 10.1016/j.jacep.2018.01.010.
23. Lopez L, Colan S, Stylianos M, et al. Relationship of Echocardiographic Z Scores Adjusted for Body Surface Area to Age, Sex, Race, and Ethnicity: The Pediatric Heart Network Normal Echocardiogram Database. *Circulation Cardiovascular imaging* 2017; 10 2017/11/16. DOI: 10.1161/circimaging.117.006979.

Baseline (12 years)
76 active athletes

≥5 hrs/week
31 (65%)

<5 hrs/week
15 (35%)

30 (39%) failed to respond or declined participation in the 1st follow-up. 8 (27%) of these participated in the 2nd follow-up.

1st follow-up (15 years)
31 active athletes

1st follow-up (15 years)
15 former athletes

9 (29%) failed to respond or declined further participation

9 (60%) failed to respond or declined further participation

≥8 hrs/week
13 (59%)
+
6 who did not complete the 1st follow-up

<8 hrs/week
9 (48%)

≥8 hrs/week
1 (17%)

<8 hrs/week
5 (83%)
+
2 who did not complete the 1st follow-up

2nd follow-up (18 years)
20 active athletes

2nd follow-up (18 years)
16 former athletes

Table 1. Basic characteristics and CPX parameters at age 18 in active and former endurance and athletes.

	Active endurance athletes (n=20)	Former endurance athletes (n=16)	p-value
Basic characteristics			
Age, years	18.3±0.3	18.3±0.3	0.98
Male sex, n (%)	15 (79)	9 (56)	0.15
Height, cm	180±9	180±10	0.96
Weight, kg	70±9	72±10	0.71
BSA, m ²	1.89±0.17	1.90±0.17	0.83
BMI, kg/m ²	22±2	22±3	0.53
Resting HR, bpm	55±7	56±11	0.63
Systolic blood pressure, mmHg	127±10	129±12	0.51
Diastolic blood pressure, mmHg	65±7	68±5	0.17
CPX parameters			
VO ₂ max mL/min	4685±906	4013±808	<0.05
VO ₂ max indexed, mL/min/kg	66.3±7.4	57.1±8.2	<0.01
RER	1.11±0.06	1.12±0.05	0.63
Time to exhaustion, min:sec	9:51±1:58	6:54±2:01	<0.001

BSA, body surface area; BMI, body mass index; HR, heart rate; VO₂ max, maximal oxygen uptake per minute; RER, peak respiratory exchange ratio. Data expressed as mean±SD. Right column shows P-values for the Student's t-test for continual parameters and the χ^2 for dichotomous parameters.

Table 2. Changes in echocardiographic parameters from 1st to 2nd follow-up in active and former endurance athletes.

	Active endurance athletes (n=15)	Former endurance athletes (n=13)	p-value
Morphology			
LA volume, ΔmL	24±21	6±10	<0.05
IVSd, Δmm	1.8±1.4	0.6±1.0	<0.05
LVIDd, Δmm	3.9±5.4	2.2±2.1	0.30
LVPWd, Δmm	1.6±1.2	0.8±0.8	<0.05
LV Mass, Δg	63±30	27±21	<0.01
3D LV EDV, ΔmL	30±18	21±22	0.30
3D LV ESV, ΔmL	14±9	11±12	0.45
RWT, Δ	0.04±0.08	0.02±0.03	0.28
RA area, Δcm ²	2.8±3.1	1.4±2.2	0.19
RV end-diastolic area, Δcm ²	3.4±4.0	0.6±3.5	<0.05
RV end-systolic area, Δcm ²	1.0±2.3	- 0.9±2.0	<0.05
LV systolic function			
3D LV EF, Δ%	- 1±3	- 2±4	0.70
3D LV SV, ΔmL	15±11	10±13	0.26

LV GLS, $\Delta\%$	- 2.2 \pm 1.7	- 1.7 \pm 2.4	0.53
LV GCS, $\Delta\%$	- 1.5 \pm 2.5	- 0.5 \pm 2.3	0.33
RV FAC, $\Delta\%$	4.9 \pm 5.7	3.5 \pm 4.3	0.49
TAPSE, Δ mm	0.3 \pm 0.4	0.2 \pm 0.4	0.13
RV GLS, $\Delta\%$	1.2 \pm 3.2	1.5 \pm 3.1	0.82

LV diastolic function

Mitral E velocity, Δ cm/sec	- 0.1 \pm 0.1	- 0.1 \pm 0.2	0.51
Mitral A velocity, Δ cm/sec	- 0.0 \pm 0.1	- 0.0 \pm 0.1	0.45
Mitral E/A-ratio, Δ	- 0.3 \pm 0.4	- 0.2 \pm 0.8	0.72
Mitral DT, Δ ms	- 29 \pm 27	- 54 \pm 41	0.08
E/e'-ratio, Δ	- 0.7 \pm 1.2	- 1.2 \pm 1.8	0.48

LA, left atrial; IVSd, inter-ventricular septum in end-diastole; LVIDd, left ventricular internal diameter in end-diastole; LVPWd, left ventricular posterior wall in end-diastole; LV, left ventricle; EDV, end-diastolic volume; ESV, end-systolic volume; RWT, relative wall thickness; RA, right atrial; RV, right ventricular; EF, ejection fraction; SV, stroke volume; GLS, global longitudinal strain; GCS, global circumferential strain; FAC, fractional area change; TAPSE, tricuspid annular plane systolic excursion; DT, deceleration time. Only athletes who completed both follow-ups are included. Data expressed as mean \pm SD. Right column shows P-values for the Student's t-test.
