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Electrical and structural adaptations of the paediatric athlete's heart: a systematic review with meta-analysis.

Electrical and structural adaptations of the paediatric athlete's heart: A systematic review and meta-analysis

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ABSTRACT

Aim: To describe the electrocardiographic (ECG) and echocardiographic manifestations of the paediatric athlete's heart, and examine the impact of age, race and sex upon cardiac remodelling responses to competitive sport.

Design: Systematic review and meta-analysis

Data sources: Six electronic databases were searched to May 2016: MEDLINE, PubMed, EMBASE, Web of Science, CINAHL and SPORTDiscus.

Inclusion criteria: 1) Male and/or female competitive athletes, 2) participants aged 6-18 years, 3) original research article published in English language.

Results: Data from 14,278 athletes and 1,668 non-athletes were included for qualitative (43 articles) and quantitative synthesis (40 articles). Paediatric athletes demonstrated a greater prevalence of training-related and training-unrelated ECG changes than non-athletes. Athletes ≥14 years were 15.8 times more likely to have inferolateral T-wave inversion than athletes <14 years. Paediatric black athletes had significantly more training-related and training-unrelated ECG changes than Caucasian athletes. Age was a positive predictor of left ventricular (LV) internal diameter during diastole, interventricular septum thickness during diastole, relative wall thickness and LV mass. When age was accounted for, these parameters remained significantly larger in athletes than non-athletes. Paediatric black athletes presented larger posterior wall thickness during diastole (PWTd) than Caucasian athletes. Paediatric male athletes also presented with larger PWTd than females.

Conclusions: The paediatric athlete's heart undergoes significant remodelling both before and during 'maturational years'. Paediatric athletes have a greater prevalence of training related and training-unrelated ECG changes than non-athletes, with age, race and sex mediating factors on cardiac electrical and LV structural remodelling.

Word count: 244

What is already known?

- Chronic training loads are associated with a number of electrophysiological, structural and functional cardiac adaptations in adult athletes.
- Race and sex significantly impact upon the cardiac remodelling of the adult athlete's heart.
- Paediatric athletes undergo significant growth and maturational changes; but unlike known musculoskeletal changes, there is limited information regarding how the heart may adapt to training before, during and after puberty.

What are the new findings?

- Paediatric athletes were up to 13 times more likely to have deep T-wave inversion (TWI) (≥2mm) than age-matched non-athletes
- Paediatric athletes ≥14 years of age were up to 16 times more likely to have inferolateral TWI (warranting further investigation) than athletes <14 years
- Paediatric black athletes were up to 36 times more likely to have extended anterior TWI (leads V1-V4) than Caucasians.
- Even after accounting for age, left ventricular structural parameters were larger among paediatric athletes than paediatric non-athletes

INTRODUCTION

Regular and sustained intensive physical activity is associated with a number of electrophysiological[1], structural and functional cardiac adaptations[2]; collectively referred to as the 'Athlete's Heart'. It is also well documented that race and sex significantly impact these manifestations of the adult athlete's heart[3,4]. Whilst previous systematic reviews and meta-analyses have detailed the adult athlete's heart phenotype[2,5], with some accounting for race and sex[6,7], data from paediatric (6-18 years) athletic populations is limited to original research; often restricted by inadequate sample sizes and heterogeneity to assess the impact of age, race and sex in tangent.

Sports academies are increasingly used by clubs and governing bodies alike to develop and nurture talented sports stars of the future. Consequently, there is increasing competitiveness, professionalism and training demands placed upon the paediatric athlete during the maturational period. The International Olympic Committee, amongst others, has called for more diligence to safeguard the physiological development of the paediatric athlete[8–10]. Performing a cardiac pre participation evaluation (PPE) within paediatric populations is controversial due to a lack of international consensus with regards to when, how, and who should undertake such examinations[11,12]. Whilst data from the USA indicate that paediatric black athletes are particularly susceptible to sudden cardiac death (SCD)[13] , there is a general lack of understanding as to which factors (e.g., physical growth, race and sex) have the potential to increase the likelihood of generating a false-positive diagnosis and unnecessary disqualification from competitive sport. Consequently, the distinction between paediatric athlete's heart and cardiac pathology associated with SCD is especially important for this population.

Therefore, the primary aim of this systematic review and meta-analysis was to describe the electrocardiographic (ECG), structural and functional manifestations of the paediatric athlete's heart compared to that of age-matched non-athletes. The secondary aims were to determine the impact of an athlete's chronological age, race, and sex on cardiac remodelling responses to intensive competitive sport.

METHODS

This review was conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[14].

Literature Searching

A systematic search was conducted using six electronic databases; (1) MEDLINE, (2) PubMed, (3) EMBASE, (4) Web of Science, (5) CINAHL, and (6) SPORTDISCUS. Databases were searched from inception, to May 2016. Search terms were mapped to relevant MeSH terms or subject headings under four concepts:

1) 'Paediatric'
2) 'Athlete',
3) 'Electrocardiography', 'Echocardiography', 'Magnetic Resonance Imaging'

4) ‘European Society of Cardiology Criteria’, ‘Seattle Criteria’, ‘Ventricle’, ‘Atrium’ and ‘Septum’.

Terms within each concept were combined with the Boolean operator ‘OR’, then concepts were combined with the ‘AND’ operator to, produce the search strategy (Supplementary Appendix A). To supplement the electronic database searching, we hand searched reference lists of eligible articles, ePublication lists of key journals, and undertook citation tracking using Google Scholar (Supplementary Appendix B). All identified articles were imported into Endnote X4 for application of selection criteria (Thomson Reuters, California, USA).

Selection Criteria

Titles and abstracts of potentially eligible articles were independently screened by two authors (GM and NR) against the selection criteria. For articles where it was not immediately clear from the title and/or abstract whether they should be included, we obtained the full text for independent screening. Discrepancies were resolved via consensus discussion, with a third reviewer (MW) consulted if consensus could not be reached.

Inclusion criteria were: 1) data reported for male and/or female competitive athletes, with or without comparison to non-athletes, 2) all participants were aged 6-18 years old at the time of assessment, and 3) an original research article published in English language. We defined a competitive athlete as:

"One who participates in an organised team or individual sport that requires regular competition against others as a central component, places a high premium on excellence and achievement, and requires some form of systematic (and usually intense) training"[15].

Participants not meeting this definition were classified as non-athletes. Articles were limited to English-language owing to translation costs. Articles that did not document athlete age range were excluded because of the risk of including athletes >18 years. If ECG and/or echocardiographic outcome data were not reported, or if professional guidelines for data acquisition were not observed or cited, articles were also excluded.

Risk of Bias Assessment

We developed a 15-item risk of bias assessment checklist (Supplementary Appendix C), comprising items from Downs & Black's 'Assessment of Methodological Quality of Randomised and Non-Randomised Studies' checklist[16], and a previously published athletes heart meta-analysis checklist[5]. The purpose was to identify articles of low methodological quality that could bias results[17]; with articles achieving ≤ 50% of total possible appraisal score, excluded from quantitative synthesis. Two reviewers (GM & NR) independently assessed all included articles. Discrepancies were resolved via consensus discussion and consistency was measured using an interclass correlation coefficient ($ICC_{2,1}$).

Data Extraction

All ECG and echocardiographic data were extracted by one reviewer using a predefined extraction form and reviewed by a second reviewer, with discrepancies resolved by consensus (Supplementary Appendix D). Data extraction included the calculated mean (SD) for continuous data and *n* for dichotomous data. If insufficient data were reported, corresponding authors were contacted to request additional data.

Data management

Demographics

Body surface area (BSA)[18] was extracted or manually calculated from the height and body mass reported in individual articles.

ECG

The 2010 European Society of Cardiology (ESC) recommendations for interpretation of the 12-lead ECG in athletes were applied, dividing ECG patterns into Group 1 training-related and Group 2 training un-related patterns accordingly[19]. T-wave inversion (TWI) was classified if ≥1mm and in ≥2 contiguous leads, localised as follows: anterior leads (V1–V3), extended anterior leads (V1–V4), inferior leads (Leads II–aVF), lateral leads (V5–V6/I–aVL) and infero-lateral leads (Leads II–aVF/V5–V6/I–aVL). Deep TWI was defined as a negative T wave ≥2 mm in ≥2 contiguous leads, (excluding leads III and aVR). ECG classification of left ventricular hypertrophy (LVH) was made according to the Sokolow–Lyon criteria[20]. Early repolarisation was defined as ST segment elevation (≥0.1 mV) and/or J point elevation manifested either as QRS slurring or notching, in ≥2 contiguous leads[21].

Echocardiography

Two-dimensional echocardiography data, where the American Society of Echocardiography paediatric guidelines were followed, were extracted[22,23]. On the basis of previous publications within the paediatric athlete's heart, participants with an LV wall thickness >12 mm were considered to have left ventricular hypertrophy (LVH)[24]. Left ventricular mass (LVM) was calculated according to the formula of Devereux[25]. Relative left ventricular wall thickness (RWT) was calculated and expressed as a fraction: [PWTd + IVSd)/LVIDd] posterior wall thickness during diastole (PWTd), interventricular septum thickness during diastole (IVSd) and left ventricular internal diameter during diastole (LVIDd). If IVSd was not reported, it was considered equal to PWTd[2].

Data synthesis

Data were analysed using StatsDirect (Altrincham, UK) and Stata V.12 (Stata Corp, College Station, Texas, USA). Demographic data were analysed using arithmetic means. Pooled dichotomous data were analysed using random-effects proportion meta-analyses (as we expected significant statistical heterogeneity), and presented as odds ratios (ORs) or risk ratios (RRs) as appropriate. We only pooled data for variables with a minimum of 3 articles reporting on the variable. Pooled continuous data were presented as standardised mean differences (i.e. effect size). The magnitude of pooled standardised mean differences were interpreted according to Cohen's guidelines; with small medium and large effects interpreted as ≥20%, ≥50% and ≥80% respectively[26]. A p-value of <0.05 was used to denote statistical significance.

Random-effects meta-regression (Kendall's non-parametric statistic) was utilised to explore and account for the impact of the covariates; age, race (black vs. Caucasian) and sex (Male vs. Female) upon ECG and echocardiographic variables. Random-effects meta-regression analysis was deemed inappropriate when <10 articles were available for synthesis[27].

Sub-analysis was used to explain the effect of the covariates; age (<14 years vs. ≥14 years), race (black vs. Caucasian), sex and where possible, the interaction of age (<14 years vs. ≥14 years) was explored within race and sex. With regards to maturational age, 14 years was set according to the attainment of selected development landmarks in boys (Mean age of peak height velocity = 14; Peak weight velocity = 14.3; Peak leg length velocity = 14.4; 90% of adult stature = 13.9; 95% of adult stature = 14.9; Genital stage IV = 14.6; and Pubic hair stage IV = 15.1) [28] and the onset of menarche within females (13.2 years)[29].

Data were combined as per Cochrane guidelines[30]. If data were reported for the same participants in more than one article, the data were extracted from the article with the largest cohort size (with corresponding author's confirmation). If an article reported multiple follow-ups, data were extracted from the latest visit (i.e. longest follow-up). When standard deviation (SD) was not reported, it was imputed from the average SD[30], only utilising articles containing ≥30 participants. To ensure results were not subsequently biased, sensitivity analysis was conducted omitting imputed SD data. Statistical heterogeneity was examined using the I^2 index[31].

RESULTS

Literature Search

The literature search identified 2030 potentially eligible articles, of which 972 were duplicates. After application of the selection criteria, 43 articles remained for qualitative analysis and 40 remained for quantitative analysis (Figure 1).

<INSERT FIGURE 1 HERE>

Risk of bias assessment

There was substantial agreement (71% 95% CI (49-84))[32] between the reviewers for the risk of bias assessment (Supplementary Appendix E). Most frequently, discrepancies occurred when assessing ‘professional guidelines’ and ‘missing data’ (77% 95% CI 61-68)). Risk of bias scores ranged from 4 to 13 out of a maximum possible score of 15. No articles reported ‘power analysis’ or ‘intra-observer reliability’, with non-athlete ‘activity levels’ poorly described in 44%. Three articles were excluded[33–35] from quantitative synthesis due to low methodological quality.

Demographic data

Data from 14,278 athletes (mean age 13.8 ± 1.3 years [range: 6-18]) and 1,668 non-athletes (mean age 12.6 ± 0.6 years [7-18]) were extracted from 43 articles. There were no differences in age or BSA between paediatric athletes and non-athletes. Athletes competed in 30 different sports, with football (soccer) predominating (33%). There were more males and Caucasians, but proportionately distributed among both athletes and non-athletes. In 2 articles, sex was not reported[35,36]. In 23 articles, race was not documented[33–56] and in 29 articles maturational status was not reported[24,33–46,49,50,53,55–67] (Table 1).

<INSERT TABLE 1 HERE >

Data management

Within the 40 articles that were quantitatively synthesised; two articles reported overlapping data from a group of 155 athletes[58,62], two articles reported overlapping data from a cohort of 158 athletes[43,44] and two articles reported overlapping data from a cohort of 900 athletes[24,68]. Four articles presented multiple follow-up data[40,59,64,69]. Adjustments were made, to account for this in the meta-analysis (Supplementary Appendix F).

Electrocardiographic characteristics

<u>Paediatric athlete vs. paediatric non-athlete</u>

Paediatric athletes had a significantly longer PR interval, and a significantly greater frequency of sinus bradycardia, 1st ^{o}AV block, incomplete right bundle branch block (IRBBB), voltage criteria for LVH and early repolarisation when compared to paediatric non-athletes (Table 2). The prevalence of TWI ≥1mm was similar between athletes and non-athletes (6.7% vs. 5.9%). However, athletes were 12.7 times more likely to have deep TWI ≥2 mm in ≥2 contiguous leads (except leads III and aVR) than non-athletes (4.7% vs. 0.3%). Athletes were 1.4 times more likely to have anterior TWI (6.5% vs. 5.7%) and 1.5 times more likely to have extended anterior TWI (1.4% vs. 0.9%) than non-athletes. Whilst inferior (0.9%) and lateral (0.2%) TWI was present among athletes, these were not observed in non-athletes. Other training un-related ECG patterns suggestive of underlining cardiac pathology including ST segment depression, abnormal Q waves, complete bundle branch blocks and abnormal QTc measurements were rarely observed in athletes (≤0.6%) and were not observed in non-athletes.

<INSERT TABLE 2 HERE>

Impact of paediatric athlete age

Paediatric athletes ≥14 years had a significantly longer QRS duration, and a significantly greater frequency of sinus bradycardia and voltage criteria for LVH than athletes <14 years (Table 3). Athletes ≥14 years were 1.3 times more likely to have TWI than athletes <14 years (6.9% vs 5.4%). Athletes <14 years were 1.2 times more likely to have anterior TWI than athletes ≥14 years (6.7% vs. 5.4%). Athletes ≥14 years were 3.1 times more likely to have extended anterior TWI (1.7% vs. 0.5%), and 15.8 times more likely to have inferolateral TWI (2.5% vs. 0.1%) than athletes <14 years.

<INSERT TABLE 3 HERE>

Impact of paediatric athlete race

Black paediatric athletes had a significantly greater frequency of sinus bradycardia, 1st °AV block, IRBBB, voltage criteria for LVH and early repolarisation compared to Caucasian athletes (Table 4). Black athletes were 4 times more likely to have TWIs (23.4% vs. 5.9%) and 2.6 times more likely to have deep TWIs (10.6 vs. 4.2%), than Caucasian athletes. Further, black athletes were 2.9 times more likely to have anterior TWI (12.2% vs. 4.2%), 36 times more likely to have extended anterior TWI (10.8% vs. 0.3%) and 6.5 times more likely to have inferolateral TWI (8.2% vs. 1.3%) than Caucasian athletes. Finally, black athletes were 5 times more likely to have abnormal Q waves (0.5% vs. 0.1%) and 2.9 times more likely to have LAE (5.7% vs. 2.0%) when compared to Caucasian athletes.

<INSERT TABLE 4 HERE>

Echocardiographic patterns

<u>Paediatric athletes vs paediatric non-athletes</u>

Athletes had a significantly greater LVIDd (+8.2%), LVID during systole (LVIDs) (+14.2%), IVSd (+12.9%), PWTd (+12.2%), relative wall thickness (RWT), (+5.6%) LV mass (LVM) (+27.6%), and left atrial diameter (LAD) (+12.3%) than non-athletes (Table 5). One percent of athletes (95% CI 0.3 - 2.3, 5 articles; n=4460) had LVH (LV wall thickness >12 mm). LVH was not observed in non-athletes. There were no significant differences in cardiac functional parameters between athletes and non-athletes. Using imputed SDs did not influence the results.

<INSERT TABLE 5 HERE>

<u>Impact of age: paediatric athletes vs paediatric non-athletes</u>

Age was a positive predictor of LVIDd, IVSd, PWTd, RWT and LVM in athletes and non-athletes ($P \leq 0.001$). After accounting for age, athletes had greater LVIDd, IVSd, RWT and LVM ($P \leq 0.05$) than non-athletes.

<u>Impact of paediatric athlete age</u>

Paediatric athletes ≥14 years had a significantly greater LVIDd (+13.5%), LVIDs (+15.9%), IVSd (+15.2%), PWTd (+21.3%), LVM (+38.7%), Aortic Root (+14.2%), and LAD (+15.6%) than athletes <14 years (Table 6). With the exception of E/A ratio (+13.6% greater in athlete's ≥14 years) there were no statistical differences with regards to left ventricle function.

<INSERT TABLE 6 HERE>

<u>Impact of paediatric athlete race</u>

Black athletes had a significantly greater PWTd (+12.4%) and LAD (+13.4%) than Caucasian athletes (Table 7). Prevalence of LVH (LV wall thickness >12 mm) was 17.1 times greater among black [2 articles, n=319] than Caucasian athletes [3 articles, n=3318] (7.1% vs. 0.4%).

<INSERT TABLE 7 HERE>

<u>Impact of paediatric athlete sex</u>

Male athletes had a significantly larger IVSd (+9.2%) than female athletes (Table 8). Prevalence of LVH was 2.6 times greater among male [5 articles; n=4028) than female athletes [2 articles; n=432] (1.2% vs. 0.4%).

<INSERT TABLE 8 HERE>

DISCUSSION

In the first systematic review and meta-analysis investigating the ECG, structural and functional manifestations of the paediatric athlete's heart, we found that 1) Paediatric athletes had a greater prevalence of training-related and training unrelated ECG changes than non-athletes, 2) Whilst the overall prevalence of TWI remained similar, the distribution and magnitude differed; 3) Paediatric athletes had larger echocardiographic derived LV dimensions than non-athletes, even after accounting for age; 4) Paediatric black athletes had increased levels of training and training unrelated ECG findings (particularly TWI); and finally 5) Paediatric black athletes had a greater prevalence of echocardiographic derived indices of LVH compared to Caucasian athletes.

ECG characteristics of the paediatric athlete

This study confirms that regular and prolonged physical training is associated with a high prevalence of bradycardia, repolarisation changes, atrial enlargement and ventricular hypertrophy in paediatric athletes[70]. However, the magnitude, prevalence and distribution of such changes are dependent on the chronological age of the paediatric athlete. Similar to adult athletes, race impacted ECG remodelling in the paediatric athlete[71]. Black paediatric athletes had significantly more training-related changes, anterior, extended anterior, inferolateral and deep TWIs, in addition to Q waves and LAE compared to Caucasian athletes[6].

T wave inversion in the paediatric athlete: impact of age and race

Inverted T-waves may represent the only sign of an inherited heart muscle disease even in the absence of any other features or before structural changes in the heart can be detected[63]. Yet, until complete formation of adult ventricular mass, T wave inversions may persist across leads V1-V3 within the paediatric population, owing to right ventricular dominance[72]. Our findings on over 9000 paediatric athletes and over 800 paediatric non-athletes, support this notion, with a relatively high, but similar prevalence of anterior TWI (V1-V3) observed in both athletes and non-athletes (6.5% vs. 5.7%) respectively; suggesting this is a maturational trait largely not resultant upon athletic training. The slightly higher prevalence of anterior TWI in athletes vs. non-athletes also suggests that regular exercise may exacerbate or prolong the presence of juvenile TWI. Nevertheless, paediatric athletes were 12.7-times more likely to present with deep TWI (≥2mm) than non-athletes. Deep TWI (≥2mm) in the precordial leads are a major concern as these ECG alterations are a recognised manifestation of hypertrophic cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy[73].

TWIs are uncommon among adult Caucasian athletes. Conversely, African/Afro–Caribbean black athletes have a higher prevalence of TWI, as well as more striking repolarisation changes and magnitude of voltage criteria for LVH than Caucasian athletes of similar age and size participating in identical sports[74,75]. Similar to their adult counterparts[76], we found that black paediatric athletes are 4 times more likely to exhibit any TWI and 36 times more likely to exhibit extended anterior TWI (V1-V4) than Caucasian paediatric athletes[63]; this likely represents an ethnic response to physiological adaptation to exercise rather than an effect of race alone, exuberated by right ventricular dominance during pubertal years.

When is anterior T-Wave inversion normal?

Recently updated international consensus standards for 12-lead ECG interpretations in athletes[77,78] recommends that TWI ≥ 1 mm in depth in two contiguous anterior leads (V2-V4) is abnormal (with the exception of TWI confined to leads V1-V4 in black athletes and leads V1-V3 in all athletes aged <16 years) and should prompt further evaluation for underlying structural heart disease. Our data support this recommendation, demonstrating a significantly reduced prevalence of anterior TWI (V1-V3) in athlete's ≥14 years likely as a consequence of maturation. Based on current evidence, TWI in the anterior leads (V1-V3) in paediatric athletes <14 years of age (or pre-pubertal athletes) should not prompt further evaluation in the absence of symptoms, signs or a family history of cardiac disease.

Our data also support the observation that like their adult counterparts, paediatric black athletes were 3 times more likely to have anterior TWI (V1-V3) and 36 times more likely to have extended anterior TWI (V1-V4) when compared to Caucasians. In adult black athletes, it is recognised that anterior TWI is a normal variant when preceded by J-point elevation and convex ST segment elevation[79], unlike in arrhythmogenic right ventricular cardiomyopathy where the J-point and/or ST segment is usually isoelectric or depressed prior to TWI. Appreciating the J-point and preceding ST segment may help differentiate between physiological adaptation and cardiomyopathy in athletes with anterior TWI affecting leads V3 and/or V4, and may prove to be especially useful in athletes of mixed race. A recent study compared black and Caucasian healthy athletes against hypertrophic cardiomyopathy and arrhythmogenic right ventricular cardiomyopathy patients, all of whom had anterior TWI. Within athletes, the combination of J-point elevation ≥1mm and TWI confined to leads V1-V4 excluded hypertrophic cardiomyopathy or arrhythmogenic right ventricular cardiomyopathy with 100% negative predictive value, regardless of race[79]. Conversely, anterior TWI associated with minimal or absent J-point elevation (<1 mm) may reflect a cardiomyopathy. Such detailed investigations have yet to be extended to the paediatric athletic population.

Inferior and/or lateral TWI warrants investigation

We were surprised by the high prevalence of inferolateral TWI in both black (8.5%) and Caucasian (1.3%) paediatric athletes. It is unlikely that all such athletes harbour a sinister cardiomyopathy and may represent a racial variant in black athletes. Despite this, lateral lead TWI should be viewed with caution. We recently investigated 155 athletes presenting with pathological TWI with clinical examination, ECG, echocardiography, exercise testing, 24h Holter ECG and cardiac magnetic resonance[80]. Cardiac disease was established in 44.5% of athletes (81% hypertrophic cardiomyopathy). Inferior and/or lateral TWI were the most commonly observed ECG abnormalities (83.9%) and were largely isolated findings without other ECG abnormalities (43.2%). In our experience, regardless of an increased frequency after 14-years and a higher prevalence in adolescent black athletes, inferolateral TWI should be considered pathological in all cases until proven otherwise. While exclusion from competitive sport is not warranted in the asymptomatic paediatric athlete without a family history of SCD and normal secondary examinations, annual follow-up is essential to ascertain possible disease expression.

Left ventricular morphology of the paediatric athlete

While most adult athletes have left ventricular structural changes that are considered physiological, there are a small proportion who develop pronounced morphological changes that overlap with phenotypic expressions of cardiac pathology associated with SCD. Several groups have produced algorithms to aid in this differentiation[81–83]. Data for these algorithms primarily derives from five large echocardiographic studies[75,84–87] examining 5053 elite, predominately male adult athletes; 134 (2.7%) had a maximal wall thickness ≥12 mm (of which 27 (0.5%) athletes had a maximum wall thickness of ≥13 mm). In absolute terms and regardless of an athlete's BSA, the upper limit of physiological hypertrophy for adult male athletes is considered ≥13 mm for maximal wall thickness and ≥65 mm for LVIDd.

Despite undergoing significant changes in anthropometry during maturation paediatric athletes have significantly larger cardiac diameters, wall thicknesses and LV mass than non-athletes even after adjusting for age. From 4460 paediatric athletes analysed, just 1.1% presented with a maximal wall thickness ≥12 mm; although a maximal wall thickness of 15mm was documented in one study. A pooled mean LVIDd of 47mm (<14 years: 44.2mm vs. ≥ 14 years: 51.1 mm) is similar to upper limits previously observed among paediatric hypertrophic cardiomyopathy patients (48mm)[88]. Thus, such adult upper limit criteria may not be applicable to the paediatric athlete. Regardless of race, values above these should be viewed with suspicion in paediatric athletes, particularly if the athlete also presents with cardiac symptoms, a family history of SCD and/or an abnormal ECG. Given the widely recognised impact of chronological age and somatic growth upon paediatric echocardiographic variables, it is our suggestion that Z scores (which account for the effects of body size and chronological age) are instead used for differential diagnosis when normative data are available[89–91], as previously suggested within paediatric specific echocardiographic guidelines[22].

Impact of chronological age on LV remodelling

Cardiac enlargement increased with chronological age, as demonstrated by our meta-regression as well as by others[92], and helps to explain the heterogeneity observed within this dataset. After accounting for age (using meta-regression), paediatric athletes had greater LV morphology than paediatric non-athletes, demonstrating the potent stimulus exercise has upon cardiac structure. These changes appeared to be exaggerated during the pubertal growth stage, suggesting a potential role of hormonal factors in cardiac remodelling[93]. We recognise that whilst chronologic age is a linear factor, growth and maturation are not[94], and thus maturational status for children of the same chronological age can differ dramatically[95,96]. Yet, assessment of maturational status was conducted among only 14 of the 43 (33%) articles included for qualitative synthesis, and relied largely on assessment by Tanner Scale (79%), regarded to be inappropriate by many due to obvious child protection concerns. In our experience, clinical interpretation of cardiac PPE data should be governed by biological age rather than chronological age. According to the International Olympic Committee consensus statement on youth athletic development[97], skeletal age is the most useful estimate of maturity status and can be used from childhood into late adolescence. However, this can only be confirmed by radiological hand-wrist imaging. Since this is not widely available in most cardiological units, alternative simple measures such as percentage of predicted mature (adult) height at the time of observation may provide an estimate of maturity status[98]. However care is warranted, as 1) predicted mature (adult) height only demonstrates moderate concordance with classifications of maturity status, based on skeletal age[99,100], and 2) historical height data of the patient is required to rule out sudden growth spurts.

Impact of race on LV remodelling

Data from the USA indicate that paediatric black athletes are particularly susceptible to SCD[13], and therefore, the distinction between athlete's heart and cardiac pathology is of particular relevance in this group. Consistent with previous observations in adults[75,101,102], we found that paediatric black athletes had increased LVH in response to chronic training loads compared to Caucasian athletes. This change is consistent with a concentric remodelling pattern. Furthermore, the likelihood of LVH was 17.1 times greater among black when compared to Caucasian athletes. We speculate that these ethnic-specific manifestations of the athlete's heart are the result of hemodynamic influences; specifically greater peripheral vascular resistance and a smaller nocturnal decline in BP[100].

Impact of sex on LV remodelling

The last three decades have witnessed an exponential rise in the number of females participating in high-level competitive sport[105]. Consistent with observations among adults[4], we found a reduced LVH response to chronic training loads in female athletes compared to males. This might be due to hormonal differences and lower testosterone concentrations[106]. However, the relative differences of sex across maturational years has yet to be fully elucidated among paediatric athletes. Females reach complete pubertal development at an earlier chronological age and thus we may expect such relative differences between female and male athletes to be smaller during the early stages of pubertal development.

Limitations

A high statistical heterogeneity (I^2) was observed; this may be because it was not possible to stratify data according to biological age, race or sex due to inconsistent methodology and designs implemented within the observational studies included. Because of this, a random-effects meta-analysis model was adopted to provide a more conservative pooled estimate. Activity levels of our non-athlete cohort are unknown and thus they may not actually be sedentary, however, in all cases, participants did not meet classification criteria for a competitive athlete.

Whilst we utilised the 2010 ESC recommendations for interpretation of the 12-lead ECG[19], at the time of publication, it was not intended to be used in athletes ≤12 years old. We recently observed that the 2014 'Refined Criteria' for ECG interpretation in athletes outperformed both the 2013 Seattle Criteria and the 2010 ESC recommendations, by significantly reducing the number of false-positive ECGs in Arabic, Black and Caucasian adult athletes while maintaining 100% sensitivity for serious cardiac pathologies[107]. Again, however, all three ECG criteria are only applicable for adult athletes and not paediatric athletes. Thus for paediatric cardiac PPEs, the attending cardiologist or sports medicine physician is left with the conundrum of which criteria should be used for ECG interpretation. Recently published International consensus standards for ECG interpretation in athletes[77] do account for age and race respectively. TWI in the anterior leads (V1-V3) in adolescent athletes <16 years of age (or pre-pubertal athletes) and black adult athletes with J-point elevation and convex ST segment elevation followed by TWI in V2-V4, would now not prompt further evaluation in the absence of symptoms, signs or a family history of cardiac disease. But in most non-black athletes age ≥ 16 years, anterior TWI beyond lead V2 would prompt further evaluation given the potential overlap with arrhythmogenic right ventricular cardiomyopathy.

Finally, echocardiographic data were largely limited to left ventricle structural variables, owing to insufficient data available for synthesis. Such limitations highlight the importance of further research in the paediatric athlete extending to other chambers of the heart, and beyond load dependent measurements of cardiac function (ejection fraction or fractional shortening) towards Tissue Doppler imaging and myocardial deformation (strain) imaging.

Conclusion

Similar to adult athletes, paediatric athletes had a greater prevalence of training related and training unrelated ECG changes than non-athletes. Significant cardiac remodelling in paediatric athlete occurs both before and during their 'maturational years'; with race and sex significantly impacting upon the pattern of remodelling observed. The results demonstrate the importance of adjusting for age when assessing LV morphology in paediatric athletes, whilst consideration for an athletes' race and sex is further required when differentiating between physiological and pathological cardiac remodelling.

Contributions: GM, NRR, CLA and MGW contributed to the conception and design of the review. GM applied the search strategy. GM, NRR and MGW applied the selection criteria. GM and NRR completed the assessment of risk of bias. GM, CLA and AF analysed the data. All authors contributed to data interpretation. GM and MGW wrote the manuscript. NRR, CLA, AF, GEP, VW, CA, KPG and DO critically revised the manuscript for important intellectual content. GM and MGW are responsible for the overall content as guarantors.

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Table 1 Article characteristics

Author, year	Athletes n	Chronological age Mean (range)	Biological age	Race (C:B:O)	Sex (M:F)	Sport	Non-Athletes n	Chronological age Mean (range)	Biological age	Race (C:B:O)	Sex (M:F)	Outcome data ECG	Outcome data ECHO
Agrebi 2015[67]	24	13.9 (11-17)	NR	0:0:24	24:0	Handball							
Attisani 2011[33]	1865	13.7 (6-18)	NR	NR	1865:0	Soccer/Gymnastics						Y	N
Ayabakan 2006[108]	22	11.0 (9-12)	Prepubertal	22:0:0	22:0	Swimming	21	10.7 (9-12)	Prepubertal	21:0:0	21:0	N	Y
Bartkevičienė 2015[56]	167	14.8 (12-17)	NR	NR	167:0							N	Y
Bessem 2014[57]	193	14 (10-19)	NR	134:29:30	193:0	Soccer						Y	N
Calò 2015[109]	2261	12.4 (8-18)	Peripubertal	2261:0:0	2261:0	Soccer						Y	Y
Csajági 2015[69]	18	13.7 (13-15)	Mid pubertal	18:0:0	8:7	Swimming	15	13.8 (13-15)	Mid pubertal	15:0:0	8:7	N	Y
Di Paolo 2012[58]	216	16.1 (14-18)	NR	63:153:0	216:0	Soccer						Y	Y
Dinu 2010[35]	40	12.7 (10-17)	NR	NR	NS	Athletics						N	Y
Hauser 2013[37]	26	12.6 (7-17)	NR	NR	18:8	Triathlon						N	Y
Hoogsteen 2003[38]	66	17.5 (17-18)	NR	NR	66:0	Cycling						N	Y
Kinoshita 2015[59]	34	16.5 (16-17)	NR	0:0:34	0:34	Middle / long-distance runners						N	Y
Koch 2012[39]	343	13 (10-15)	NR	NS	189:154	High school athletes						Y	Y
Konopka 2015[60]	78	14.3 (12-17)	NR	78:0:0	64:14	Soccer, Tennis, Rowing.						N	Y
Madeira 2008[53]	21	15.9 (15-16)	NR	NR	21:0	Soccer; Swimming						N	Y
Makan 2005[68]	900	15.7 (14-18)	Post pubertal	882:0:18	693:207	10 sporting disciplines (*Invasion games/ racket/ endurance/combat*)	250	15.5 (14-18)	Post pubertal	NR	177:48	N	Y
Medved 1986[36]	72	10 (8-14)	NR	NR	NR	Swimming	72	10 (8-14)	NR	NR	NS	N	Y
Meško 1993[40]	23	14.5 (14-15)	NR	NR	23:0	Hockey	17	14.5 (14-15)	NR	NR	17:0	N	Y
Migliore 2012[110]	2765	13.9 (8-18)	Peri pubertal	2765:0:0	1914:851	18 sporting disciplines (*Invasion games/ gymnastics/winter sports/horse-riding/racket/ endurance/combat*)						Y	N
Moarles 1992[34]	9	16.2 (14-17)	NR	NR	9:0	Basketball						N	Y
Obert 1998[41]	10	10.7 (10-11)	Pre pubertal	NR	4:6	Swimming	11	10.9 (10-11)	Prepubertal	NR	4:7	N	Y
Ozer 1994[42]	82	11.2 (7-14)	NR	NR	41:41	Swimming	41	10.8 (7-15)	NS	NR	22:19	N	Y

Papadakis 2009[111]	1710	16 (14-18)	Post-pubertal	1642:0:0	1414:291	15 sporting disciplines (Invasion games/ racket/ endurance/combat)	400	16 (14-18)	Post pubertal	385:0:0	330:70	Y	N
Pavlik 2001[112]	165	14.7 (10-18)	NR	165:0:0	165:0	7 sporting disciplines (*Endurance/invasion games/weightlifting*)	22	14.7 (10-18)	NR	22:0:0	22:0	N	Y
Pelà 2014[43]	138	14.3 (11-17)	NR	96:42:0	138:0	Soccer						Y	Y
Pelà 2015 [44]	206	13.8 (11-17)	NR	206:0:0	158:48	Soccer						Y	Y
Petridis 2004[61]	137	16.6 (15-18)	NR	NS	137:0	Swimming						N	Y
Rowland 1987 [45]	14	11 (8-14)	Prepubertal	NR	14:0	Swimming	19	10.4 (8 -13)	Prepubertal	NR	19:0	Y	Y
Rowland 1994[46]	10	12.2 (11-13)	Prepubertal	NR	10:0	Middle distance runners	18	11.3 (10–14)	Pre pubertal	NR	18:0	Y	Y
Rowland 1997[47]	9	12.2 (9-15)	Early pubertal	NR	9:0	Cyclists						N	Y
Rowland 2000[48]	8	11.9 (10-13)	Early pubertal	NS	8:0	Cyclists & Triathletes	39	12.2 (10-13)	Early pubertal	NR	39:0	N	Y
Schmied 2009[62]	155	16.4 (14-17)	NR	0:155:0	155:0	Soccer						Y	Y
Sharma 1999[70]	1000	15.7 (14-18)	Post-pubertal	998:8:4	730:180	9 Sporting disciplines (*Invasion games/ racket/ endurance/combat*)	300	15.6 (14-18)	Post pubertal	293:0:7	210:90	Y	N
Sharma 2002[24]	720	15.7 (14-18)	NR	706:14:0	540:180	10 Sporting disciplines (*Invasion games/ racket/ endurance/combat*)						N	Y
Sheikh 2013[63]	1232	16.4 (14-18)	NR	903:329:0	980:252	Swimming/Athletics	134	15.3 (14–18)	NR	0:134:0	88:46	Y	Y
Shi & Selig 2005[49]	13	15.3 (14-16)	NR	NR	13:0	Gymnastics/Swimmers						N	Y
Stoner 1997[64]	37	9.9 (7-11)	NR	NR	0:37	Athletics	22	9.1 (7-11)	NR	NR	0:22	N	Y
Sundberg & Elovainio 1982[50]	59	13.7 (10-17)	NR	NR	59:0	Athletics	81	13.9 (10-17)	NR	NR	81:0	Y	N
Telford 1988[51]	85	11.9 (11-12)	Pre-mid pubertal	NR	48:37	Hockey	106	12.3 (12-13)	Pre-mid pubertal		60:46	N	Y
Valente-Dos-Santos 2013[52]	73	15.4 (15-17)	Skeletal age 16.4	NR	73:0	Basketball						N	Y
Vasiliauskas 2006[65]	62	13.6 (8-17)	NR	62:0:0	62:0	Soccer						N	Y
Yildirim 2016[55]	140	14.3 (10-18)	NR	NS	107:33	Basketball, Soccer, Swimmers.	31	14.1 (10-18)	NR	NR	21:10	Y	Y
Zdravkovic 2010 [66]	94	12.9 (12-14)	NR	94:0:0	94:0	Soccer	47	12.9 (12-14)	NR	47:0:0	47:0	N	Y

Abbreviations: C, Caucasian; B, Black; O, Other; M, Male; F, Female; NR, Not reported; Y, Yes; N, No.

Table 2 ECG characteristics of Paediatric athletes and Paediatric non-athletes

Characteristics	Athletes	Non-athletes	% Difference
PR interval (ms)	148 (142 – 154)* [10; 5671] {98%}	139 (136- 141) [4; 737] {41%}	6.1%
QRS duration (ms)	86 (84 -88) [11; 6938] {97%}	83 (79 -86) [6; 952] {97%}	4%
QTc duration (ms)	396 (391-400) [11; 7018] {97%}	386 (375 - 398) [6; 902] {97%}	3%
QRS axis*, (degrees)	70 (63.1 - 76.1) [8; 5476] {99%}	70 (67.9 - 73.0) [4; 779] {60%}	0%
Group 1 ECG patterns			**Odds Ratio**
Sinus bradycardia (%)	37.4 (17.6 – 59.7)** [11; 9745] {99%}	19.2 (16.6 21.90) [3; 834] {0%}	2.5 (2.1 - 3.0)
Sinus arrhythmia (%)	45.8 (35.7 -56.0) [3; 2898] {95.9%}		
1st ºAV block (%)	2.2 (0.8 - 4.2)** [8; 9488] {97%}	0.4 (0.1 - 1.1) [3; 834] {26%}	4.6 (1.7 - 12.4)
2nd ºAV block (Morbitz Type I) (%)	0.2 (0.1 - 0.4) [3; 2898} {0%}		
Incomplete RBBB (%)	25.8 (18.2 - 33.7)** [10; 9736] {97%}	7.8 (4.2 - 12.4) [3; 834] {78%}	4.3 (3.5 – 5.6)
LVH (%)	35.2 (26.0 - 45.0)** [11; 9745] {98%}	24.1 (20.3 - 28.1) [3; 834] {41%}	1.7 (1.5 - 2.0)
ER (%)	37.1 (25.6 -49.2)** [10; 9736] {99.3%}	29.2 (17.2 – 43.0) [3; 834] {93.9%}	1.4 (1.2 -1.7)
Group 2 ECG patterns			**Risk Ratio**
TWI (≥1mm) (%)	6.7 (4.7 - 8.9) [7; 9372] {93.3%}	5.9 (2.2 – 11.2) [3; 834] {86.7%}	1.1 (0.8 – 1.5)
Deep TWI (≥2mm) (%)	4.7 (2.3 - 8.1)** [7; 6514] {95.9%}	0.3 (0.04 - 1.8) [2; 534] {60.3%}	12.7 (3.1 – 50.7)
Anterior (%)	6.5 (2.9 - 11.3) [7; 9372] {98.4%}	5.7 (2.2 - 10.6) [3; 834] {84.9%}	1.2 (0.9 – 1.5)
Extended Anterior (%)	1.4 (0.2 - 3.5) [4; 5391] {95.8%}	0.9 (0.2 - 2.2) [2; 534] {24.1%}	1.5 (0.6 – 3.6)
Inferior (%)	1.0 (0.3 - 2) [5; 7446] {93%}	0.0 [3; 834]	NC
Lateral (%)	0.3 (0.05 - 0.6) [5; 7446] {80%}	0.0 [3; 834]	NC
Infero-lateral (%)	2.0 (1.0 – 3.3) [8; 9256] {93%}	0.0 [3; 834]	NC
ST-segment depression (%)	0.03 (0.003 - 0.08) [6; 7615] {0%}	0.0 [3; 834]	NC
Abnormal Q waves (%)	0.1 (0.03 - 0.2) [10; 9902] {25%}	0.0 [3; 834]	NC
LAE (%)	3.5 (0.4 - 9.5) [8; 5804] {98%}		

RAE (%)	5.9 (0.9 - 14.8) [4; 2575] {98%}		
LAD (%)	0.4 (0.1 - 0.9) [6; 5683] {75%}		
RAD (%)	3.7 (0.1 -11.8) [5; 4352] {98%}		
RVH (%)	9.8 (7.0 -13.0) [3; 2420] {81%}		
Ventricular pre-excitation (%)	0.6 (0.2 - 1.1) [6; 7422] {79%}		
Complete RBBB (%)	0.5 (0.3 - 0.7) [8; 9715] {55%}	0.0 [3; 834]	NC
Complete LBBB (%)	0.1 (0.008 - 0.3) [7; 9499] {81%]	0.0 [3; 834]	NC
Long QT interval (%)	0.6 (0.1 - 1.3) [9; 10247] {57%}	0.0 [3; 834]	NC
Short QT interval (%)	0.4 (0.02 - 1.1) [4; 4108] {81%}	0.0 [3; 834]	NC
Brugada-like ER (%)	0.2 (0.03- 0.4) [5; 7079] {0%}		

Data are presented mean or percentage (95%CI) [number of articles; number of participants] {heterogeneity}

*p ≤0.05 Significantly greater or more prevalent in athletes than non-athletes

** p ≤0.001 Significantly greater or more prevalent in athletes than non-athletes

NC: Non-Computable

Abbreviations: AV, atrioventricular; RBBB: right bundle branch block; LVH: left ventricular hypertrophy; ER: early repolarisation; TWI: T-wave inversion; Anterior: V1–V3; Extended Anterior: V1–V4; Inferior: Leads II-aVF; Lateral: V4-V6/I-aVL; Infero-lateral: Leads II-aVF/V4-V6/I-aVL; LAE: left atrial enlargement; RAE: right atrial enlargement; LAD: left axis deviation; RAD: right axis deviation; LBBB: left bundle branch block

Table 3 ECG characteristics of Paediatric athletes: Impact of Age

Characteristics	**≥14 years**	**<14 years**	**% Difference**
PR interval (ms)	151 (140 - 162) [4; 1985] {99%}	142 (137 - 147) [4; 89] {58%}	6%
QRS duration (ms)	92 (91 -93)* [4; 1991] {59%}	74 (70 - 82) [3; 77] {88%}	9%
QTc duration (ms)	377 (354 - 400) [5; 4205] {99%}	394 (375 - 412) [3; 77] {6%}	-5%
QRS axis*, degree	76 (73 - 78) [4; 2816] {89%}	74.7 (61.4 - 88.0) [2; 63] {75%}	2%
Group 1 ECG patterns			**Odds Ratio**
Sinus bradycardia (%)	61.3 (46.3 - 75.3)** [5; 4205] {98%}	18.8 (12.1 - 26.7) [2; 109] {0%}	6.6 (4.1-10.7)
LVH (%)	48.0 (36.4 - 59.5)** [5; 4205] {98%}	20.7 (9.3 – 35.1) [2; 109] {30%}	3.4 (2.2 -5.5)
Group 2 ECG patterns			**Risk Ratio**
TWI (≥1mm) (%)	6.9 (3.7 - 10.9** [6; 5051] {96%}	5.4 (0.2 - 16.9) [2; 1272] {92%}	1.3 (1.0-1.7)
Anterior (%)	5.4 (1.4 - 11.8) [7; 6575] {98%}	6.7 (4.4 – 9.4)† [3; 2516] {78%}	1.2 (1.0 - 1.5)
Extended Anterior (%)	1.7 (0.4 – 4.0)* [4; 3823] {94%}	0.5 (0.1 - 3.0) [2; 1257] {68%}	3.1 (1.4 – 6.6)
Infero-lateral (%)	2.5 (1.0 - 4.6)** [5; 3710] {89%}	0.1 (0.01 - 0.4) [2; 1272] {0%}	15.8 (3.9 – 63.9)

Data are presented mean or percentage (95%CI) [number of articles; number of participants] {heterogeneity}
*p ≤0.01 Significantly greater or more prevalent in athletes ≥14 years than in athletes <14 years
** p ≤0.001 Significantly greater or more prevalent in athletes ≥14 years than in athletes <14 years
† ≤0.05 Significantly greater or more prevalent in athletes <14 years than in athletes ≥14 years
NC: Non-Computable
Abbreviations: LVH: left ventricular hypertrophy; TWI: T-wave inversion; Anterior: V1–V3; Extended Anterior: V1–V4; Infero-lateral: Leads II-aVF/V4-V6/I-aVL.

Table 4 ECG characteristics of Paediatric athletes: Impact of race			
Characteristics	**Black (10-18 years)**	**Caucasian (8-18 years)**	**% Difference**
PR interval (ms)	161 (146 -177) [2; 196] {91.6%}	141 (135 to 148) [3; 2529] {95%}	12%
QRS duration (ms)	86 (82 - 90)** [3; 525] {94.9%}	92 (88 - 95) [4; 3232] {98.3%}	-7%
QTc duration (ms)	394 (387 - 401) [3; 525] {95%}	398 (392 - 403) [4; 3232] {98.4%}	-1%
Group 1 ECG patterns			**Odds Ratio**
Sinus bradycardia (%)	38.2 (18.6 - 60.1)*** [3; 525] {95%}	29.3 (10.9 - 52.2) [5; 6197] {99%}	1.5 (1.3 - 1.8)
1st ^{o}AV block (%)	11.4 (6.9 - 16.9)*** [2; 483] {65%}	1.1 (0.25 - 2.5) [4; 5991] {92%}	11.6 (8.0 – 17.0)
Incomplete RBBB (%)	22.1 (13.1 - 32.7) [3; 525] {83%}	21.1 (15.0 - 27.9) [5; 6197] {97%}	1.1 (0.9 - 1.3)
LVH (%)	60.3 (11.0 - 98.3)*** [3; 525] {99%}	28.1 (20.2 - 36.7) [5; 6197] {97%}	3.9 (3.3 - 4.7)
ER (%)	74.3 (41.0 - 96.6)*** [3; 525] {98%}	31.0 (17.4 - 46.5) [5; 6197] {99%}	6.4 (5.2 – 7.9)
Group 2 ECG patterns			**Risk Ratio**
TWI (≥1mm) (%)	23.4 (19.8 – 27.1)*** [3; 512] {69%}	5.9 (5.3 - 6.6) [5; 5263] {71%}	4.0 (3.3 – 4.8)
Deep TWI (≥2mm) (%)	10.6 (5.5 -17.2)*** [3; 525] {73%}	4.2 (0.7 - 10.4) [4; 3936] {97%}	2.6 (1.9 – 3.4)
Anterior (%)	12.2 (8.2 -16.9)*** [3; 512] {43%}	4.2 (3.0 - 5.6) [4; 6063] {25%}	2.9 (2.2 – 3.8)
Anterior Extended (%)	10.8 (7.8 -14.2)*** [2; 358] {0%}	0.3 (0.03 - 0.8) [3; 3298] {66%}	36 (18 – 71)
Infero-lateral (%)	8.2 (6.0 - 10.7)*** [3; 512] {95%}	1.3 (0.3 - 3.1) [4; 6063] {0%}	6.5 (4.5 – 9.3)
Abnormal Q waves (%)	0.5 (0.0 - 2.0)* [3; 526] {52%}	0.1 (0.04 - 0.3) [4; 6135] {19%}	5.0 (1.3 - 19.3)
LAE (%)	5.7 (1.2 - 1.3)*** [4; 680] {91%}	2.0 (0.02 - 7.0) [4; 3936] {97%}	2.9 (2.0 - 4.2)
LAD (%)	0.8 (0.0 - 3.1) [2; 484] {70%}	0.7 (0.4 - 0.9) [2; 3668] {0%}	1.3 (0.4 - 3.6)
Complete RBBB (%)	0.3 (0.02 - 1.1) [2; 483] {0%}	0.3 (0.2 -0.6) [4; 5991] {46%}	1.2 (0.3 – 5.0)
Long QT (%)	1.1 (0.03 - 3.7) [3; 638] {79%}	0.1 (0.0 - 0.2) [4; 5991] {0%}	16.4 (4.8 – 56.0)

Data are presented mean or percentage (95%CI) [number of articles; number of participants] {heterogeneity}

*p ≤0.05 Significantly greater or more prevalent in black than Caucasian athletes

**p ≤0.01 Significantly greater or more prevalent in black than Caucasian athletes

*** p ≤0.001 Significantly greater or more prevalent in black than Caucasian athletes

Abbreviations: LVH: left ventricular hypertrophy; TWI: T-wave inversion; Anterior: V1–V3; Extended Anterior: V1–V4; Infero-lateral: Leads II-aVF/V4-V6/I-aVL.

Table 5 Echocardiographic patterns of Paediatric Athletes and Paediatric Non-athletes			
Parameter	**Athletes**	**Non-athletes**	**% Difference**
LVIDd (mm)	47.3 (46.2 - 48.3)*** [33; 6681] {99%}	43.4 (41.7 - 45.1) [18; 1042] {98%}	8.2
LVIDs (mm)	29.6 (28.4 - 30.8)*** [19; 3354] {98%}	25.4 (24.8 - 26.0) [7; 177] {64%}	14.2
IVSd (mm)	8.5 (8.2 - 8.8)*** [28; 5083] {99%}	7.4 (7.1 - 7.8) [16; 804] {98%}	12.9
PWTd (mm)	8.2 (7.8 - 8.6)** [29; 5168] {99%}	7.2 (6.6 - 7.8) [17; 908] {92%}	12.2
RWT	0.36 (0.34 - 0.37)*** [29; 6315] {99%}	0.34 (0.33 - 0.35) [16; 804] {99%}	5.6
LVM (g)	135.7 (122.2 - 149.1)*** [29; 5086] {99%}	98.2 (84.6 - 111.8) [17; 908] {99%}	27.6
LVEDV (ml)	106.8 (91.8 - 121.8) [6; 494] {98.3%}		
LVESV (ml)	38.3 (35.1 - 41.6) [5; 457] {86%}		
Aortic Root (mm)	26.3 (24.9 - 27.8)* [10; 3055] {99%}	23.5 (20.9 - 26.0) [6; 563] {99%}	10.6
LAD (mm)	30.2 (28.7 - 31.7)* [13; 5324] {99%}	26.5 (24.5 - 28.6) [8; 587] {97%}	12.3
EF (%)	65.6 (61.1 - 70.1) [11; 3150] {99%}	70.9 (63.8 - 77.9) [4; 130] {99%}	-8.1
FS (%)	37.2 (35.5 - 38.9) [14; 1829] {98%}	36.9 (34.7 - 39.1) [11; 666] {96%}	0.8
E Wave (m/s)	0.88 (0.81 - 0.96) [10; 1915] {0%}	0.91 (0.86 - 0.96) [4; 480] {93%}	-3.4
A Wave (m/s)	0.46 (0.43 - 0.49) [10; 1915] {98%}	0.49 (0.46 - 0.52) [4; 480] {84%}	-6.5
E/A ratio	2.1 (2.0 - 2.2) [14; 3634] {96%}	1.9 (1.8 - 2.1) [8; 672] {93%}	9.5
DT (ms)	133 (108 - 157) [4; 201] {97%}		
IVRT (ms)	60 (39 - 82) [3; 168] {99%}		

Data are mean (95% CI), [number of studies; number of participants] {heterogeneity}

*p ≤0.05 Significantly greater in athletes than non-athletes

**p ≤0.01 Significantly greater in athletes than non-athletes

*** p ≤0.001 Significantly greater in athletes than non-athletes

LVIDd, left ventricular cavity diameter in end-diastole; LVIDs, left ventricular cavity diameter in end-systole; IVSd, interventricular septum thickness in end-diastole; PWTd, posterior wall thickness in end-diastole; RWT, relative wall thickness; LVM, left ventricular mass; LVEDV, left ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; Ao, aortic root diameter; LAD, left atrial diameter; EF, ejection fraction; FS, fractional shortening; DT, Deceleration time; IVRT, interventricular septum relaxation time

Table 6 Echocardiographic patterns of Paediatric Athletes: Impact of Age

Parameter	≥14 years	<14 years	% Difference
LVIDd (mm)	51.2 (50.6 - 51.9)** [14; 2856] {93%}	44.3 (43.3 - 45.3) [14; 872] {94%}	13.5
LVIDs (mm)	32.8 (30.8 - 34.7)** [5; 288] {97%}	27.6 (25.9 - 29.2) [8; 363] {98%}	15.9
IVSd (mm)	9.2 (8.8 - 9.6)** [12; 1366] {97%}	7.8 (7.5 - 8.0) [13; 787 {96%}	15.2
PWTd (mm)	8.9 (8.5 - 9.3)** [12; 1378] {98%}	7 (6.6 - 7.3) [14; 872] {0%}	21.3
RWT	0.36 (0.33 - 0.39) [12; 2857] {99%}	0.35 (0.33 - 0.36) [13; 787] {96%}	2.8
LVM (g)	167 (153.5 - 180.4)** [12; 1378] {96%}	102.3 (91.8 - 112.8) [14; 872] {87%}	38.7
Ao (mm)	28.9 (27.3 - 30.4)** [5; 2396] {98%}	24.8 (23.7 - 25.8) [6 2420] {97%}	14.2
LAD (mm)	33.3 (32.0 - 34.5)** [6; 2462] {95%}	28.1 (27.0 - 29.2) [8; 601] {93%}	15.6
EF (%)	63.7 (59.1 - 68.2) [4; 285] {99%}	67.5 (55.2 - 79.8) [4; 217] {99%}	-6.0
FS (%)	35.8 (33.0 - 38.7) [3; 1052] {98%}	38.1 (37.0 - 39.2) [6; 226] {56%}	-6.4
E Wave (m/s)	0.86 (0.83 - 0.90) [10; 1915] {92%}	0.72 (0.56 - 0.88) [4; 480] {99%}	16.3
A Wave (m/s)	0.43 (0.39 - 0.46) [10; 1915] {95.3%}		
E/A ratio	2.2 (2.1 - 2.3)* [9; 2710] {92%}	1.9 (1.9 – 2.0) [5; 530] {77%}	13.6

Data are mean (95% CI), [number of studies; number of participants] {heterogeneity}
*p ≤0.05 Significantly greater in athletes ≥14 years than in athletes <14 years
** p ≤0.001 Significantly greater in athletes ≥14 years than in athletes <14 years
LVIDd, left ventricular cavity diameter in end-diastole; LVIDs, left ventricular cavity diameter in end-systole; IVSd, interventricular septum thickness in end-diastole; PWTd, posterior wall thickness in end-diastole; RWT, relative wall thickness; LVM, left ventricular mass; Ao, aortic root diameter; LAD, left atrial diameter; EF, ejection fraction; FS, fractional shortening.

Table 7 Echocardiographic patterns of Paediatric Athletes: Impact of race

Parameter	**Black (12-18 years)**	**Caucasian (8-18 years)**	**% Diff**
LVIDd (mm)	49.5 (47.0 - 51.9) [3; 525] {97%}	48.2 (46.3 – 50.0) [10; 3919] {99%}	2.6
IVSd (mm)	9.7 (9.5 - 9.9) [2; 196] {0%}	8.7 (8.0 - 9.3) [9; 3016] {99%}	10.3
PWTd(mm)	9.7 (9.4 - 10.1)* [2; 196] {44%}	8.5 (7.9 - 9.0) [9; 3016] {99%}	12.4
RWT	0.39 (0.38 - 0.40) [4; 680] {90%}	0.36 (0.34 - 0.38) [10; 3919]{ 99%}	7.7
LVM (g)	169.4 (143 - 195.9) [2; 196] {95%}	148.2 (129.0 -167.4) [9; 3016] {99%}	12.5
Aortic Root (mm)	29.7 (28.9 - 30.5) [3; 638] {90%}	26.9 (24.1 - 29.7) [4; 1137] {99%}	9.4
LAD(mm)	35.4 (34.6 - 36.1)** [3; 638] {81%}	30.5 (27.0 – 34.0) [4; 3320] {99%}	13.4
E/A	2.1 (1.9 - 2.3) [2; 483] {88%}	2.1(1.9 - 2.3) [5; 1207] {93%}	0.0

Data are mean (95% CI), [number of studies; number of participants]

*p ≤0.05 Significantly greater in black than Caucasian athletes

**p ≤0.01 Significantly greater in black than Caucasian athletes

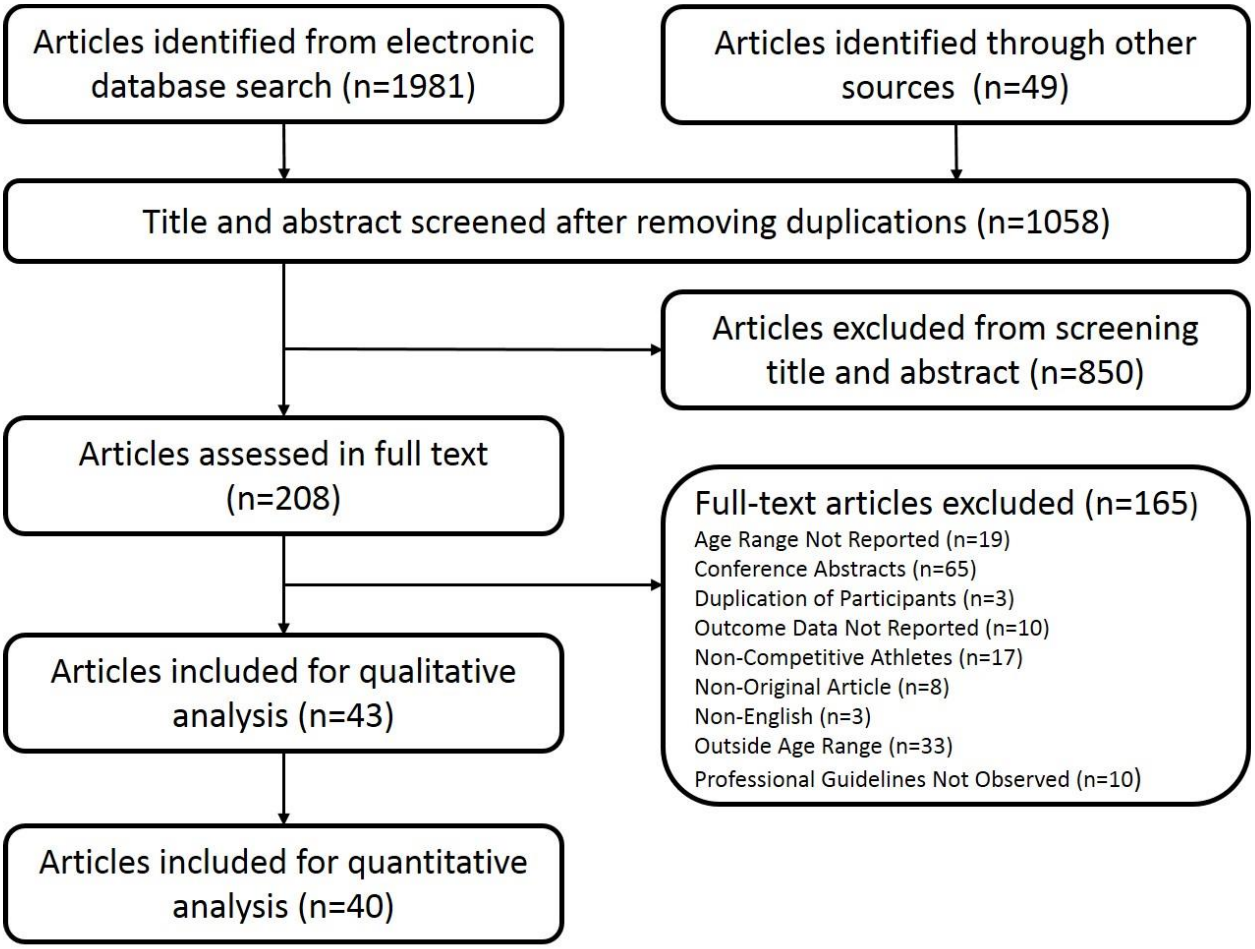
LVIDd, left ventricular cavity diameter in end-diastole; IVSd, interventricular septum thickness in end-diastole; PWTd, posterior wall thickness in end-diastole; RWT, relative wall thickness; LVM, left ventricular mass; Ao, aortic root diameter; LAD, left atrial diameter.

Table 8 Echocardiographic patterns of Paediatric Athletes: Impact of sex			
Parameter	**Male (8-18 years)**	**Female (10-18 years)**	**% Diff**
LVIDd (mm)	47.8 (46.5 - 49.2) [21; 4294] {99%}	45.3 (43.5 - 47.1) [6; 479] {98%}	5.2
LVIDs (mm)	30.2 (28.5 - 31.8) [12; 2879] {99%}	28.5 (25.2 - 31.9) [3; 92] {98%}	5.6
IVSd (mm)	8.7 (8.3 - 9.1)* [19; 4066] {99%}	7.9 (7.5 - 8.4) [6; 452] {96%}	9.2
PWTd (mm)	8.4 (7.8 - 8.9) [19; 4066] {99%}	7.8 (6.9 - 8.7) [6; 452] {99%}	7.1
RWT	0.36 (0.34 - 0.38) [19; 4066] {99%}	0.34 (0.33 0.36) [6; 452] {95%}	5.6
LVM (g)	137.5 (115.3 - 159.6) [14; 3482] {99%}	129.5 (99.8 - 159.2) [5; 298] {98%}	5.8
EDV (ml)	114.3 (108.0 - 120.7) [5; 409] {86%}	82.2 (69.0 - 95.4) [2; 85] {94%}	28

Data are mean (95% CI), [number of studies; number of participants]

*p ≤0.05 Significantly greater in Male than Female athletes

LVIDd, left ventricular cavity diameter in end-diastole; LVIDs, left ventricular cavity diameter in end-sytsole; IVSd, interventricular septum thickness in end-diastole; PWTd, posterior wall thickness in end-diastole; RLVWT, relative left ventricular wall thickness; LVM, left ventricular mass; LVEDV, left ventricular end-diastolic volume.



Articles identified from electronic database search (n=1981)
Articles identified through other sources (n=49)
Title and abstract screened after removing duplications (n=1058)
Articles excluded from screening title and abstract (n=850)
Articles assessed in full text (n=208)
Full-text articles excluded (n=165)
Age Range Not Reported (n=19)
Conference Abstracts (n=65)
Duplication of Participants (n=3)
Outcome Data Not Reported (n=10)
Non-Competitive Athletes (n=17)
Non-Original Article (n=8)
Non-English (n=3)
Outside Age Range (n=33)
Professional Guidelines Not Observed (n=10)
Articles included for qualitative analysis (n=43)
Articles included for quantitative analysis (n=40)

ONLINE APPENDIX

Supplementary appendix A

Full search strategy as applied to the MEDLINE electronic database

#	Query	Results
1	Adolescent/ or Child/ or Paediatrics/	2340649
2	(Girl* OR Boy* OR Junior* OR Juvenile* OR Teen* OR Paediatric* OR Prepubescent OR Pubescent OR Peri Pubertal).ti,ab,kw.	316474
3	Athlete/	4416
4	(Athlete* or Players).ti,ab,kw.	52511
5	Electrocardiography/	169256
6	(Electrocardiogram* or 12 Lead Electrocardiogram* or ECG* or 12 Lead ECG* or EKG* or 12 Lead EKG*).ti,ab,kw.	81490
7	Echocardiography, Doppler/ or Echocardiography, Doppler, Color/ or Echocardiography/ or Echocardiography, Transesophageal/ or Echocardiography, Doppler, Pulsed/	103453
8	(Echocardiogram* or Speckle Tracking or STE Resolution or 2D STE or 2DSTE or Speckle or STE).ti,ab,kw.	21310
9	Magnetic Resonance Imaging/	304307
10	(MRI* or CMRI*).ti,ab,kw.	162605
11	Ultrasonography/ or Ultrasonography, Doppler/ or Blood Flow Velocity/	52496
12	Ultrasound.ti,ab,kw.	167633
13	Ventricular Function/ or Hypertrophy, Right Ventricular/ or Ventricular Function, Left/ or Ventricular Function, Right/ or Ventricular Septum/ or Hypertrophy, Left Ventricular/ or Ventricular Remodeling/ or Myocardial Contraction/ or Heart Atria/	130852
14	(Ventric* or Atria* or Atrium or Septum).ti,ab,kw.	443254
15	Arteries/ or Brachial Artery/ or Radial Artery/ or Carotid Artery/ or Femoral Artery/ or Popliteal Artery/ or Vasodilation/ or Vasoconstriction/ or Vascular Resistance/ or Muscle Smooth, Vascular/ or Endothelium, Vascular/ or Arterioles/	282428
16	(Artery Structure or Artery Function or Arteriolar or Conduit Artery or Resistance Artery or Arterial Size or Arterial Wall Thickness or Intima Media Wall Thickness or Arterial Remodeling or Lumen Dimension or Vascular Function or FMD or Flow Mediated Dilation or Flow Mediated Dilatation or Shear Stress or Shear Pattern or Shear Rate).ti,ab,kw.	36920
17	(Heart rate or HR or PR Interval or QT Interval or QTc or QRS Duration or QRS or LVH or RVH or Sokolow or Cornell or Pediatric Specific or Romhilt Estes or Early Repolarization or ER or ST Elevation or J Point Elevation or J Wave* or ST Segment Elevation or QRS Slurring or Incomplete Right Bundle Branch Block or Incomplete RBBB or Incomplete Left Bundle Branch Block or Incomplete LBBB or T Wave Inversion or TWI or First Degree Atrio Ventricular Block or 1st Degree AV Block or Q Wave* or LAE or RAE or Left Atrial Enlargement or Right Atrial Enlargement or Bradycardia or Arrhythmia or Ectopic Atrial Rhythm or Junctional Rhythm or Mobitz Type I or Mobitz I or Wenckebach or Second Degree AV Block or 2nd Degree AV Block or Premature Ventricular Contraction* or PVC* or ESC Criteria or European Society of Cardiology Recommendation or Seattle Criteria or Refined Criteria or ECG Criteria).ti,ab,kw.	417843
18	OR/1-2	2470231
19	OR/3-4	53440
20	OR/5-12	842415
21	OR/13-17	1096521
22	AND/18-21	433

Supplementary appendix B

ePublication lists of key journals hand searched to supplement electronic database searching.

#	Journal	Yield
1	Journal of the American College of Cardiology	0
2	Circulation	0
3	Circulation: Arrhythmia and Electrophysiology	0
4	Circulation: Cardiovascular Imaging	0
5	European Heart Journal	0
6	European Heart Journal: Cardiovascular Imaging	0
7	American Heart Journal	0
8	Chest	0
9	Heart	0
10	British Journal of Sports Medicine	1
11	Nature Cardiology	0
12	The New England Journal of Medicine	0
13	European Journal of Preventive Cardiology	0
14	Journal of Electrocardiology	0
15	Journal of the American Society of Echocardiography	2
16	Scandinavian Journal of Sports Medicine	2
17	Europace	1
18	European Journal of Applied Physiology	2
19	Pediatric Exercise Science	0
20	Pediatric Cardiology	1
21	Cardiology in the Young	1
22	Pediatrics	0
23	European Journal of Pediatrics	1
24	American Journal of Hypertension	1
25	The Journal of Physiology	0
26	Journal of Applied Physiology	0
Total		12

Supplementary appendix C

15-item risk of bias assessment checklist

Study: ____

#	RISK OF BIAS ASSESSMENT ITEM	YES	NO/UNCLEAR
1	Sufficient power to detect clinically important effect where probability for difference being due to chance < 5% (*answer yes if sample size calculated and adequate to detect clinically important effect*)		
2	Are the inclusion and exclusion criteria clearly stated?		
	Test-control		
3	Are activity levels for the control group reported?		
4	Are the control group matched for age?		
5	If groups are unmatched, have statistical differences been controlled for? *(Answer yes if groups matched for age)*		
	Test-athletes		
6	Are athletes of competitive status? *"One who participates in an organised team or individual sport that requires regular competition against others as a central component places a high premium on excellence and achievement, and requires some form of systematic (and usually intense) training"*		
7	Are training details available? (*years, volume, duration/intensity*)		
	Data acquisition		
8	Is there detailed information to allow replication? *(Answer yes if professional guidelines cited)*		
9	Are the observer(s) stated?		
10	Are more than one observer used? If so is interobserver variability stated?		
	Measurement technique		
11	Are professional guidelines observed/cited		
	Reporting Data		
12	Is an explanation for missing data given? *(Score yes if none missing)*		
13	Is data clearly and accurately presented? (*Simple outcome data, including denominators and numerators, should be reported for all major findings*)		
14	Estimates of random variability in data provided for main outcomes? (*e.g. interquartile range, standard error, standard deviation, confidence intervals*)		
15	Are anthropometrics reported? (Height and weight or BSA (with formula presented))		
	Total Score		

Note:

Items 1,2,14 were selected from Downs & Black's Assessment of Methodological Quality of Randomised and Non-Randomised Studies checklist[1].

Items 3-5,7,10-13 were selected from a previously published athletes heart meta-analysis checklist[2].

Items 6,9,15 were written specifically for the purposes of this review.

Supplementary appendix D

Variables extracted for analysis

Primary Variables	ECG	Characteristics	Group 1: common and training-related ECG changes	Group 2: uncommon and training-unrelated ECG changes
		Heart rate, bpm	Sinus bradycardia (≥30 bpm)	T-wave inversion
		PR interval, ms	Sinus arrhythmia	ST-segment depression
		QRS duration, ms	1st degree AV block (PR interval>200 ms)	Pathological Q waves
		QTc duration, ms	Morbitz type 1 (Wenckeback) 2nd degree AV block	Left atrial enlargement
		QRS axis, degree	Incomplete RBBB (QRS duration, 120 ms)	Left axis deviation
		S V1 + R V5/6, mm	Early repolarisation (ST elevation, J-point elevation, J waves, notching or terminal QRS slurring)	Right axis deviation
			Isolated QRS voltage criteria for LVH (Sokolow-Lyon)	Complete LBBB or RBBB
				Long QT interval
				Ventricular pre-excitation
				Brugada-like early repolarization
	Echo parameters	**Structure**		**Function**
		LV end-diastolic internal diameter, mm		Ejection fraction, %
		LV end-systolic internal diameter, mm		Fractional shortening, %
		LV end-diastolic volume, ml		Stoke volume, ml
		LV end-systolic volume, ml		Cardiac output, lpm
		Interventricular septal wall thickness, mm		E wave (m/s)
		Posterior wall thickness, mm		A wave (m/s)
		Maximal wall thickness, mm		E/A
		Relative wall thickness.		

		Aortic root, mm
		RV end-diastolic area, cm^2
		RV basal dimension, mm
		RV mid-ventricular dimension
		RV longitudinal dimension
		RV outflow tract dimension (parasternal), mm
		RV outflow tract dimension (proximal), mm
		RV outflow tract dimension (distal), mm
		RV free wall thickness, mm
		Left atrial diameter, mm
		LV mass, grams
Secondary Variables	**Contextual Factors**	
		Age range
		Gender
		Ethnicity
		Height, cm
		Weight, kg
		BSA
		Sport
		Training Hours/Week, hours
		Training Years, years

Bpm: beats per minute; ms: milliseconds; mm; millimeters; cm; centimeters; LBBB: left bundle branch block; RBBB: right bundle branch block; LVH: left ventricle hypertrophy; LV: left ventricle; RV: right ventricle; m/s: meters per second; kg: kilograms; BSA: body surface area.

Supplementary appendix E

Risk of bias assessment

Article	Criterion 1 Power analysis	Criterion 2 Selection criteria	Criterion 3 Nonathlete activity levels	Criterion 4 Control age matched	Criterion 5 Statistical differences accounted for	Criterion 6 Competitive athletes	Criterion 7 Athlete training details	Criterion 8 Detailed data acquisition
Agrebi 2015[3]	N	Y	N	N	N	Y	Y	N
Attisani 2011[4]	N	Y	N	N	N	Y	N	N
Ayabakan 2006[5]	N	Y	Y	Y	Y	Y	Y	Y
Bartkevičienė 2015[6]	N	Y	Y	Y	Y	Y	Y	Y
Bessem 2014[7]	N	Y	N	N	N	Y	N	Y
Calò 2015[8]	N	Y	N	N	N	Y	Y	Y
Csajági 2015[9]	N	Y	Y	Y	Y	Y	Y	Y
Di Paolo 2012[10]	N	Y	N	N	N	Y	Y	Y
Dinu 2010[11]	N	N	Y	Y	Y	Y	N	N
Hauser 2013[12]	N	Y	N	N	N	Y	Y	Y
Hoogsteen 2003[13]	N	Y	N	N	N	Y	Y	Y
Kinoshita 2015[14]	N	Y	N	N	N	Y	Y	Y
Koch 2012[15]	N	Y	N	N	N	Y	Y	Y
Konopka 2015[16]	N	Y	N	N	N	Y	Y	Y
Madeira 2008[17]	N	Y	N	N	N	Y	Y	Y
Makan 2005[18]	N	Y	Y	Y	Y	Y	Y	Y
Medved 1986[19]	N	Y	Y	Y	Y	Y	Y	Y
Meško 1993[20]	N	Y	Y	Y	Y	Y	Y	Y
Migliore 2012[21]	N	Y	N	N	N	Y	N	Y
Moarles 1992[22]	N	Y	N	N	N	Y	N	Y
Obert 1998[23]	N	Y	Y	Y	Y	Y	Y	Y
Ozer 1994[24]	N	Y	Y	Y	Y	Y	Y	Y
Papadakis 2009[25]	N	Y	Y	Y	Y	Y	Y	Y
Pavlik 2001[26]	N	Y	N	N	Y	Y	Y	Y
Pelà 2014[27]	N	Y	N	N	N	Y	Y	Y
Pelà 2015 [28]	N	Y	N	N	N	Y	Y	Y
Petridis 2004[29]	N	Y	N	Y	Y	Y	Y	Y
Rowland 1987 [30]	N	Y	Y	Y	Y	Y	Y	Y
Rowland 1994[31]	N	Y	N	Y	Y	Y	Y	Y
Rowland 1997[32]	N	Y	N	N	N	Y	Y	Y

Article	Criterion 1 Power analysis	Criterion 2 Selection criteria	Criterion 3 Nonathlete activity levels	Criterion 4 Non-athlete age matched	Criterion 5 Statistical differences accounted for	Criterion 6 Competitive athletes	Criterion 7 Athlete training details	Criterion 8 Detailed data acquisition
Rowland 2000[33]	N	Y	Y	Y	Y	Y	Y	Y
Schmied 2009[34]	N	Y	N	N	N	Y	N	Y
Sharma 1999[35]	N	Y	Y	Y	Y	Y	Y	Y
Sharma 2002[36]	N	Y	Y	Y	Y	Y	Y	Y
Sheikh 2013[37]	N	Y	Y	Y	Y	Y	N	Y
Shi & Selig 2005[38]	N	Y	Y	Y	Y	Y	Y	Y
Stoner 1997[39]	N	Y	Y	Y	Y	Y	Y	Y
Sundberg & Elovainio 1982[40]	N	Y	N	Y	Y	Y	Y	Y
Telford 1988[41]	N	Y	Y	Y	Y	Y	Y	Y
Valente-Dos-Santos 2013[42]	N	Y	N	N	N	Y	Y	Y
Vasiliauskas 2006[43]	N	Y	N	N	N	Y	Y	Y
Yildirim 2016[44]	N	Y	Y	Y	Y	Y	Y	Y
Zdravkovic 2010 [45]	N	Y	Y	Y	Y	Y	Y	Y
No. of articles fulfilling each criterion (% of total included studies)	0(0%)	42(98%)	19(44%)	23(53%)	24(56%)	42(100%)	36(84%)	40(93%)
Proportions of agreement	100%(90-100)	88%(74-96)	84%(69-93)	91%(77-97)	86%(71-94)	91%(77-97)	91%(77-97)	95%(83-99)

Y = criterion fulfilled, N = criterion not fulfilled

Article	Criterion 9 Observer(s) stated	Criterion 10 Interobserver reliability	Criterion 11 Professional guidelines	Criterion 12 Missing data	Criterion 13 Data presentation	Criterion 14 Random variability	Criterion 15 Anthropometrics	Total
Agrebi 2015[3]	N	N	Y	Y	Y	Y	Y	8
Attisani 2011[4]	N	N	N	Y	Y	N	N	4
Ayabakan 2006[5]	Y	N	Y	Y	Y	Y	Y	13
Bartkevičienė 2015[6]	N	N	Y	Y	Y	Y	Y	12
Bessem 2014[7]	Y	N	Y	Y	Y	Y	Y	9
Calò 2015[8]	Y	N	Y	Y	Y	Y	Y	10
Csajági 2015[9]	Y	N	Y	Y	Y	Y	Y	13
Di Paolo 2012[10]	N	N	Y	Y	Y	Y	Y	9
Dinu 2010[11]	N	N	N	N	Y	Y	Y	7
Hauser 2013[12]	Y	N	Y	Y	Y	N	Y	9
Hoogsteen 2003[13]	Y	N	Y	N	Y	Y	Y	9
Kinoshita 2015[14]	Y	N	Y	Y	Y	Y	Y	10
Koch 2012[15]	Y	N	Y	Y	Y	Y	Y	10
Konopka 2015[16]	N	N	Y	Y	Y	Y	Y	9
Madeira 2008[17]	Y	N	Y	Y	Y	Y	Y	10
Makan 2005[18]	Y	N	Y	Y	Y	Y	Y	13
Medved 1986[19]	N	N	Y	Y	Y	Y	N	11
Meško 1993[20]	N	N	Y	Y	Y	Y	Y	12
Migliore 2012[21]	Y	N	Y	Y	Y	Y	N	8
Moarles 1992 [22]	N	N	Y	N	N	N	Y	5
Obert 1998 [23]	Y	N	Y	Y	Y	Y	Y	13
Ozer 1994[24]	Y	N	Y	Y	Y	Y	N	12
Papadakis 2009[25]	Y	N	Y	Y	Y	Y	Y	13
Pavlik 2001[26]	Y	N	Y	Y	Y	Y	N	10
Pelà 2014[27]	Y	N	Y	Y	Y	Y	Y	10
Pelà 2015[28]	Y	N	Y	Y	Y	Y	Y	10
Petridis 2004[29]	N	N	Y	Y	Y	Y	Y	11
Rowland 1987[30]	Y	N	Y	Y	Y	Y	N	12
Rowland 1994[31]	Y	N	Y	Y	Y	Y	Y	12
Rowland 1997[32]	N	N	Y	Y	Y	Y	Y	9

Article	Criterion 9 Observer(s) stated	Criterion 10 Interobserver reliability	Criterion 11 Professional guidelines	Criterion 12 Missing data	Criterion 13 Data presentation	Criterion 14 Random variability	Criterion 15 Anthropometrics	Total
Rowland 2000[33]	N	N	Y	Y	Y	Y	Y	12
Schmied 2009[34]	Y	N	Y	Y	Y	Y	Y	9
Sharma 1999[35]	N	N	Y	Y	Y	Y	Y	12
Sharma 2002[36]	Y	N	Y	Y	Y	Y	Y	13
Sheikh 2013[37]	Y	N	Y	Y	Y	Y	Y	12
Shi & Selig 2005[38]	N	N	Y	Y	Y	Y	Y	12
Stoner 1997[39]	N	N	Y	Y	Y	Y	Y	12
Sundberg & Elovainio 1982[40]	Y	N	N	Y	Y	Y	Y	11
Telford 1988[41]	N	N	Y	Y	Y	Y	Y	12
Valente-Dos-Santos 2013[42]	Y	N	Y	Y	Y	Y	Y	10
Vasiliauskas 2006[43]	Y	N	Y	Y	Y	Y	Y	10
Yildirim 2016[44]	N	N	Y	Y	Y	Y	Y	12
Zdravkovic 2010 [45]	Y	N	Y	Y	Y	Y	Y	13
No. of articles fulfilling each criterion (% of total included studies)	26(60%)	0(0%)	40(93%)	40(93%)	43(98%)	40(93%)	37(86%)	452 (70%)
Proportions of agreement	81%(66-91)	100%(90-100)	77%(61-88)	77%(61-88)	84%(69-93)	93%(80-98)	88%(74-96)	70%(47-83)

Y = criterion fulfilled, N = criterion not fulfilled

Supplementary appendix F

Articles with overlapping electrocardiographic data

First Author	Overlapping participants	Number of participants included
Di Paolo 2012[10]	Athlete (males, black; n=154)	155/155
Schmied 2009[34]	Athlete (males, black; n=155)	
Pelà 2015[28]	Athlete (males, Caucasian; n=158)	158/158
Pelà 2014[27]	Athlete (males, Caucasian; n=96)	

Articles with overlapping Echocardiographic data

First Author	Overlapping participants	Number of participants included
Di Paolo 2012[10]	Athletes (males, black; n=154)	155/155
Schmied 2009[34]	Athletes (males, black; n=155)	
Makan 2005[18]	Athletes (males, mixed race; n=693) Athletes (females, mixed race; n=207)	900/900
Sharma 2002[36]	Athletes (males, mixed race; n=540) Athletes (females, mixed race; n=180)	
Pelà 2015[28]	Athletes (male, Caucasian; n=158)	158/158
Pelà 2014[27]	Athletes (male, Caucasian; n=96)	

Articles reporting repeat echocardiographic measurements (within the same article)

First Author	Follow-up	Participants	Number of participants included
Csajági 2015[9]	Six repeat assessments: • Start • Endurance (GEP1) • Race 1 (RP1) • Detraining (DT) • Endurance (GEP2) • Race2 (RP2)	Athletes (mixed gender, Caucasian; n=15)	15/15
Meško 1993[20]	Four repeat assessments: • Year 1 • Year 2 • Year 3 • Year 4	Athletes (male; n=23) Nonathletes (males; n=17)	40/40
Stoner 1997[39]	Two assessments: • Pre-onset of training • 1 Year post onset of training	Athletes (male; n=37) Nonathletes (male; n=20)	57/57
Kinoshita 2015[14]	Five repeat assessments: • Baseline • 0.5 Years post • 1 Year post • 1.5 Years post • 2 Years post • 2.5 Years post • 3 Years post	Athletes (females, Japanese; n=51)	34/51

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