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Title: The Influence of Maturation on Exercise-Induced Cardiac Remodelling and Haematological Adaptation

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The Influence of Maturation on Exercise-Induced Cardiac Remodelling and Haematological Adaptation

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27

Key points

- It has long been hypothesised that cardiovascular adaptation to endurance training is augmented following puberty.
- We investigated whether differences in cardiac and haematological variables exist, and to what extent, between endurance-trained *vs*. untrained, pre- and post-peak height velocity (PHV) children, and how these central factors relate to maximal oxygen consumption.
- Using echocardiography to quantify left ventricular (LV) morphology and carbon monoxide rebreathing to determine blood volume and haemoglobin mass, we identified that training-related differences in LV morphology are evident in pre-PHV children, with haematological differences also observed between pre-PHV girls. However, the breadth and magnitude of cardiovascular remodelling was more pronounced post-PHV.
- Cardiac and haematological measures provide significant predictive models for maximal oxygen consumption ($\dot{V}O_{2max}$) in children that are much stronger post-PHV, suggesting that other important determinants within the oxygen transport chain could account for the majority of variance in $\dot{V}O_{2max}$ before puberty.

Abstract

Cardiovascular and haematological adaptations to endurance training facilitate greater maximal oxygen consumption ($\dot{V}O_{2max}$), and such adaptations maybe augmented following puberty. Therefore, we compared left ventricular (LV) morphology (echocardiography), blood volume, haemoglobin (Hb) mass (CO-rebreathe) and $\dot{V}O_{2max}$ in endurance-trained and untrained boys (*n*=42, age=9.0-17.1 years, $\dot{V}O_{2max}$=61.6±7.2 mL·kg·min, and *n*=31, age=8.0-17.7 years, $\dot{V}O_{2max}$=46.5±6.1 mL·kg·min, respectively) and girls (*n*=45, age=8.2-17.0 years, $\dot{V}O_{2max}$=51.4±5.7 mL·kg·min and *n*=36, age=8.0-17.6 years, $\dot{V}O_{2max}$=39.8±5.7 mL·kg·min, respectively). Pubertal stage was estimated via maturity offset, with participants classified as pre- or post-peak height velocity (PHV). Pre-PHV, only a larger LV end-diastolic volume/lean body mass (EDV/LBM) for trained boys (+0.28 mL·kg^{LBM}, *P*=0.007) and a higher Hb mass/LBM for trained girls (+1.65 g·kg^{LBM}, *P*=0.007) were evident compared to untrained controls. Post-PHV, LV mass/LBM (boys:+0.50 g·kg^{LBM}, *P*=0.0003; girls:+0.35 g·kg^{LBM}, *P*=0.003), EDV/LBM (boys:+0.35 mL·kg^{LBM}, *P*<0.0001; girls:+0.31 mL·kgLBM, *P*=0.0004), blood volume/LBM (boys:+12.47 mL·kg^{LBM}, *P*=0.004; girls:+13.48 mL·kg^{LBM}, *P*=0.0002.) and Hb mass/LBM (boys:+1.29 g·kg^{LBM}, *P*=0.015; girls:+1.47 g·kg^{LBM}, *P*=0.002) were all greater in trained *vs.* untrained groups. Pre-PHV, EDV (R^2_{adj}=0.224, *P*=0.001) in boys, and Hb mass and interventricular septal thickness (R^2_{adj}=0.317, *P*=0.002) in girls partially accounted for the variance in $\dot{V}O_{2max}$. Post-PHV, stronger predictive models were evident via the inclusion of LV wall thickness and EDV in boys (R^2_{adj}=0.608, *P*<0.0001), and posterior wall thickness and Hb mass in girls (R^2_{adj}=0.490, *P*<0.0001). In conclusion, cardiovascular adaptation to exercise training is more

pronounced post-PHV, with evidence for a greater role of central components for oxygen delivery.

Introduction

Cardiovascular adaptations to endurance training facilitate enhanced oxygen delivery while minimising cardiac work, in part setting the upper limit for endurance exercise performance (Lundby *et al.*, 2017). These adaptations to the central components of the oxygen transport chain include cardiac remodelling, which enhances stroke volume (Morganroth *et al.*, 1975; Pluim *et al.*, 2000), and an expansion in haemoglobin (Hb) volume, increasing oxygen carrying capacity in the blood (Remes, 1979; Montero *et al.*, 2017). In adults, cardiac and haematological adaptations to endurance training often occur concomitantly (Montero *et al.*, 2015; Skattebo *et al.*, 2020), although this is not always the case (Arbab-Zadeh *et al.*, 2014). An enhanced circulating haematological volume with endurance training further stimulates cardiac remodelling via an increased ventricular filling pressure (Morganroth *et al.*, 1975; Prior & La Gerche, 2012). Therefore, cardiac and haematological adaptations are not only key variables in determining maximal oxygen consumption, but cardiac remodelling may also be dependent on the extent and timing of haematological expansion in response to training.

Nearly 40 years ago, it was hypothesised that cardiovascular training adaptations were absent in children before puberty due to low levels of sex- and growth-related hormones that increase substantially following puberty (Katch, 1983), particularly in boys (Wood *et al.*, 2019). During adolescence, sex- and growth-related hormones result in a peak rate of lean tissue growth around the timing of peak height velocity (PHV) (Iuliano-Burns *et al.*, 2001; Wood *et al.*, 2019), and have also been associated with cardiovascular adaptation to exercise (Marsh *et al.*, 1998; Neri Serneri *et al.*,

2001; Hero *et al.*, 2005). Indeed, adult female athletes, who will naturally experience lower androgen levels, demonstrate less pronounced left ventricular (LV) hypertrophy in response to chronic endurance training in comparison to their male counterparts (Pelliccia *et al.*, 1996). Despite lower growth-related hormone levels, a high $\dot{V}O_{2max}$ has been observed in pre-pubertal endurance-trained children (Mayers & Gutin, 1979; Nottin *et al.*, 2002), and a recent meta-analysis demonstrated cardiac hypertrophy in athletes across the adolescent spectrum (McClean *et al.*, 2018). However, LV hypertrophy was less prevalent in younger athletes, and evidence for training-related haematological adaptations in pre-pubertal children is sparse, with very few having investigated the area (Prommer *et al.*, 2018). Therefore, speculation remains around whether puberty provides a window of opportunity for enhanced training-induced cardiovascular adaptation. If this is the case, haematological expansion with training around puberty could act as a physiological stimulus for enhanced cardiac remodelling compared with pre-puberty (Prior & La Gerche, 2012).

$\dot{V}O_{2max}$ responses with training are similar between pre- and post-pubertal groups (Baquet *et al.*, 2003; Runacres *et al.*, 2019). Given that cardiovascular training adaptations may differ between these stages of maturation, the relative contributions of the central components of oxygen transport are likely to be different. It was therefore hypothesised that: (i) LV morphology and haematological components would be greater in all endurance-trained *vs*. untrained groups, but the magnitude of difference would be greater in post-, compared with pre-PHV cohorts; (ii) that blood volume would have a stronger relationship with LV end-diastolic volume post- *vs*. pre-PHV in boys and girls; and (iii) the variance in aerobic exercise capacity would be accounted for by both cardiac and haematological variables, with an increased contribution from these central components post-PHV. This study therefore aimed to:

(i) investigate whether there are any differences in cardiac and haematological variables by training status and, if so, whether the magnitude differs between pre- and post-PHV children; (ii) examine whether blood volume is associated with end-diastolic volume pre- and post-PHV; and (iii) identify the proportion of aerobic exercise capacity that can be accounted for by cardiac and haematological parameters pre- and post-PHV.

Methods

Ethical approval

The study was approved by the Cardiff Metropolitan University Natural Sciences Research Ethics Sub-committee (PGR-1339). Parents or guardians provided written informed consent and children provided written informed assent to participate in the study, which conformed to the ethical standards of the *Declaration of Helsinki*, except for registration in a database.

Study participants

A total of *n* = 163 participants were recruited. Participants were excluded due to failing to complete all measurements (*n* = 3), or failing to meet our cohort health or physical activity criteria (*n* = 6). Based on self- and parental-reported exercise training and physical activity, *n* = 154 participants were assigned to either endurance-trained (boys: *n* = 42, age = 9.0-17.1 years; girls: *n* = 45, age = 8.2-17.0 years) or untrained (boys: *n* = 31, age = 8.0-17.7 years; girls: *n* = 36, age = 8.0-17.6 years) groups. Criteria to be included within the endurance-trained group were to be undertaking at least three hours of structured endurance exercise-training per week for ≥12 months with an endurance sports club (cycling, swimming, long-distance running, or triathlon), and competing in their respective sport. This was in addition to meeting the UK minimum physical activity guidelines of at least 60 minutes of moderate intensity physical activity per day across the week (Department of Health and Social Care, 2019). Training histories and typical weekly volumes were reported by participants and confirmed by their parents. Untrained individuals were defined as not meeting the UK minimum physical activity guidelines (Department of Health and Social Care, 2019). All participants were reported to be healthy, normotensive, non-

149 smokers, free from any known cardiac or systemic diseases and were deemed not
150 obese according to age- and sex-specific body mass index (BMI) cut-offs of the
151 International Obesity Task Force criteria (Cole *et al.*, 2000).

152 *Experimental design*

153 Participants visited the laboratory on two occasions. Parents or guardians were
154 asked to ensure their child refrained from heavy exercise and caffeine consumption
155 12 hours prior, and had not eaten a heavy meal within three hours prior to arrival.

156 During the first laboratory visit, body mass, height and sitting height were measured,
157 with leg length then derived from height minus sitting height. These variables were
158 then used to estimate maturity using sex-specific equations (Mirwald *et al.*, 2002). As
159 per the original recommendation of Mirwald *et al.* (2002), the maturity offset was
160 used to categorise participants as pre-PHV or post-PHV, depending on whether the
161 value was below or above zero, respectively. The equation has a typical error of 0.5
162 years; however, the accuracy of the prediction improves the closer participants are to
163 PHV, making incorrect categorisation of our participants less likely. Moreover, the
164 equation was found to be stable from -1 - +2 years predicted PHV (Koziel & Malina,
165 2018). Age from predicted PHV was used as a surrogate measure of puberty due to
166 the non-invasive nature of the maturity offset measurement. Additionally, given that it
167 relates to the point of maximal growth, it is the key stage of interest due to the
168 associated growth-related hormones driving this process (Wood, 2019) and thus,
169 potentially driving cardiac growth. Resting blood pressure was measured following
170 10 minutes supine rest using an automated sphygmomanometer (Omron Healthcare,
171 Hoofddorp, Netherlands). $\dot{V}O_{2max}$ and maximal heart rate (HR_{max}) were assessed
172 during a cardiopulmonary exercise test on an upright cycle ergometer (Lode,

Excalibur, Groningen, Netherlands). Body composition, resting echocardiography and carbon monoxide (CO)-rebreathing measures were obtained during the second laboratory visit.

Experimental measures

Cardiorespiratory fitness

Participants completed an incremental ramp protocol on a cycle ergometer (Lode Excalibur; Groningen, The Netherlands) with ventilatory gas exchange measures for $\dot{V}O_2$, using a breath-by-breath gas analysis system (Jaeger, Oxycon Pro, Warwickshire, UK). Incremental workload increments were determined by stature and training status (Ellis *et al.*, 2017) and began subsequent to a three-minute warm up cycling at 10 watts. For trained and untrained participants >150 cm, the incremental workloads were 25 and 20 watts per minute, respectively; 125-149.9 cm, were 20 and 15 watts, respectively; and 110-124.9 cm, were 15 and 10 watts, respectively. Participants cycled at 75-85 rpm until they were unable to continue, despite strong verbal encouragement. This was followed by 15 minutes of seated rest before a constant-load supramaximal verification test at 105% of achieved peak power output to verify that $\dot{V}O_{2max}$ was achieved as described by Bhammar *et al.* (2017). $\dot{V}O_{2max}$ was accepted as the highest 30-second average value attained from either the ramp incremental test or the supramaximal verification test.

Body composition

Body fat percentage was derived from the measurement of skinfold thickness and validated, youth-specific equations, with a typical error of 3.6 and 3.9 for boys and girls, respectively (Slaughter *et al.*, 1988). Body fat mass and lean body mass (LBM) were calculated from the body fat percentage and total body mass.

Resting echocardiography

After 10 minutes supine rest, echocardiography was performed with a Vivid E9 system (GE Vingmed Ultrasound, Horten, Norway) using a 1.5 – 4 MHz transducer. Two-dimensional images from the parasternal and apical acoustic windows were attained with participants in the left lateral decubitus position. Images were stored digitally for offline data analysis (Echopac, GE medical, Horton, Norway) by the principal researcher (DRP).

LV mass was calculated using the area-length method (Lang *et al.*, 2015). Relative wall thickness was calculated as (posterior wall thickness (LVPWd) + interventricular septal thickness (IVSd))/(LV internal diameter at end-diastole (LVIDd)). LV end-diastolic volume (EDV), and LV end-systolic volume (ESV) were calculated using the biplane modified Simpson's technique. Stroke volume (SV) was calculated as EDV-ESV and cardiac output (Q) was then calculated as a product of SV and heart rate (HR) taken from the ultrasound electrocardiograph. All measurements are presented as absolute and scaled values where appropriate. Where scaling has been implemented, linear measures were scaled to height and three-dimensional measures were scaled to LBM in a dimensionally consistent manner (Dewey *et al.*, 2008). This approach was chosen over an allometric approach due to the difficulty in calculating a common scaling exponent from our relatively small sample size, and the lack of published exponents across maturational groups. Intra-observer coefficient of variation for LV morphology variables were EDV: 4.2%; ESV: 6.7%; SV: 4.5%; IVSd: 8.2%; LVPWd: 6.3%; and LVIDd: 3.5%.

Carbon monoxide rebreathing

Haematological data were determined using the optimised carbon monoxide (CO)-rebreathe method as previously described (Schmidt & Prommer, 2005), after 15 minutes in a sitting position. Prior to commencing the procedure, participants were familiarised with the equipment (SpiCO, Blood tec GmbH, Bayreuth, Germany) and the rebreathing protocol. A nose clip was fitted to participants, and after exhaling, they positioned the spirometer with a 5-liter reservoir bag of pure oxygen attached ready for rebreathing. Participants were instructed to fully inhale, whilst a CO-bolus was administered, before holding a full lung volume for 10 seconds. Participants then continued rebreathing the CO and O_2 balance through the spirometer until two minutes. Upon completion of rebreathing, participants fully exhaled into the bag before valve closure to enable quantification of unabsorbed CO using a portable CO analyser (Dräger Pac 3500; Dräger Safety, Lübeck, Germany). The calculated CO-bolus was reduced compared to the adult dose from 0.8-1.2 mL·kg to 0.4-0.8 mL·kg for our paediatric participants, as per previous recommendations (Prommer & Schmidt, 2007). Fingertip capillary blood samples were acquired before and after two minutes of CO-rebreathing to determine haematocrit (Hct), Hb concentration and the percentage of carboxyhaemoglobin (ABL80, Radiometer, Crawley, UK). Expired CO was also quantified prior to rebreathing and at four minutes following the onset of rebreathing using a portable CO analyser (Dräger Pac 3500; Dräger Safety, Lübeck, Germany). The reliability for the CO-rebreathe protocol with the current investigator was assessed from a paediatric subgroup of six boys and six girls. Two sets of haematological data were obtained separated by two to seven days. Our intra-observer coefficients of variation for Hb mass and blood volume in a paediatric population were 2.1% and 3.2%, respectively.

Statistical analysis

Data are expressed as means ± standard deviations (SD), unless stated otherwise. To analyse how well matched pre- and post-PHV groups of the same sex and training status were, independent samples *t*-tests were used to assess reported training volume and history between trained groups. To explore the differences between trained and untrained participants, at pre- and post-PHV, two-way ANOVAs with training and maturity status as the fixed factors were run independently for boys and girls. Independent samples *t*-tests were used to identify differences where there was a significant main effect. Effect sizes (Cohen's *d*) were calculated to assess the magnitude of any group differences. As per convention, effect sizes of 0.2, 0.5, 0.8 and 1.2 were accepted as small, medium, large and very large, respectively (Cohen, 1988; Sawilowsky, 2009). Relationships between blood volume and EDV, pre- and post-PHV for boys (*n* = 35 and 33 included, respectively) and girls (*n* = 33 and 39 included, respectively) were assessed using linear regression analysis with pooled trained and untrained data. Trained and untrained data were pooled for these analyses to explore the relationship between blood volume and EDV across a range of fitness levels to identify whether these relationships differ between pre- and post-PHV. To identify the proportion of relative $\dot{V}O_{2max}$ ($mL \cdot kg^{LBM} \cdot min$) contributed to by cardiac and haematological variables for each pre- and post-PHV group, trained and untrained pooled relative data were converted to *z*-scores and bivariate relationships were identified with Pearson's correlation coefficients. Variables with high multicollinearity ($r > 0.85$ and variance inflation factor (VIF) > 10) were removed from subsequent analyses. The remaining variables associated with $\dot{V}O_{2max}$ were entered into stepwise multiple linear regression analyses. Statistical analyses were performed using the Statistical Package for Social Science Software (version 24,

Chicago, IL) and GraphPad (Prism Version 8.1.1, GraphPad Software, San Diego, CA), with α set *a priori* as 0.05.

Results

Training and physical activity characteristics

Trained groups were recruited from either cycling, swimming, running or triathlon clubs. The proportion of participants from each of these respective sports were as follows (% from cycling/swimming/running/triathlon): pre-PHV trained boys (56/21/17/4%); post-PHV trained boys (68/0/5/26%); pre-PHV trained girls (27/36/13/22%); and post-PHV girls (39/21/21/17%). Weekly endurance training volume was not significantly different between pre- and post-PHV trained boys (8.6 ± 2.7 *vs*. 9.9 ± 2.7 hrs·wk, $P = 0.125$), whereas it was lower in pre- compared with post-PHV trained girls (6.0 ± 2.5 *vs*. 8.9 ± 3.6 hrs·wk, $P = 0.003$). Weekly strength training volumes were low across all groups (Trained boys: pre-PHV, 0.1 ± 0.3 hrs·wk; post-PHV, 0.5 ± 0.7 hrs·wk; trained girls: pre-PHV, 0.4 ± 0.6 hrs·wk; post-PHV, 0.3 ± 0.6 hrs·wk). As expected, years of training were lower in pre- compared with post-PHV trained groups, irrespective of sex (3.8 ± 1.5 *vs*. 6.0 ± 2.8 years, $P = 0.002$, and 2.6 ± 1.5 *vs*. 4.4 ± 2.3 years, $P = 0.003$, for boys and girls, respectively). Untrained participants were undertaking a small amount weekly of physical activity (Untrained boys: pre-PHV, 1.1 ± 0.9 hrs·wk; post-PHV, 0.9 ± 1.1 hrs·wk; untrained girls: pre-PHV, 1.0 ± 0.9 hrs·wk; post-PHV, 0.6 ± 0.9 hrs·wk).

Participant characteristics and cardiorespiratory fitness

There were no differences in maturity offset, height, body mass or LBM between trained and untrained groups at either pre- or post-PHV (Table 1). Further, no differences were found for systolic or diastolic blood pressure between trained and untrained groups either pre- or post-PHV, for boys or girls. As expected, endurance-trained boys and girls had a higher cardiorespiratory fitness than their untrained counterparts both pre- and post-PHV.

297 *Left ventricular dimensions and systolic function*

298 LV dimensions are outlined for boys and girls in Tables 2 and 3, respectively and
299 both LV mass and EDV relative to LBM are depicted in Figure 1. In pre-PHV
300 children, no significant differences were found in wall thicknesses between trained
301 and untrained groups, aside from a greater IVSd/height in trained girls. Post-PHV,
302 both IVSd/height and LVPWd/height were greater in both trained groups *vs*.
303 untrained. Relative wall thickness was greater in trained *vs*. untrained girls post-
304 PHV, but no difference was observed pre-PHV, or between boys by training status
305 irrespective of maturity. Pre-PHV, there was no significant difference in LV mass
306 scaled to LBM between trained *vs*. untrained groups; however, a difference was
307 found post-PHV with large and very large effect sizes for both boys and girls,
308 respectively.

309 Irrespective of maturity status, EDV and SV normalised to LBM were higher in
310 trained *vs*. untrained boys, with a greater effect size post-PHV. In contrast, there was
311 no significant difference in EDV or SV normalised to LBM between trained *vs*.
312 untrained girls pre-PHV, however, both were higher in trained girls post-PHV,
313 compared with untrained.

314 *Haematological parameters*

315 Haematological variables are detailed for boys and girls in Tables 2 and 3,
316 respectively, and both blood volume and Hb mass relative to LBM are depicted in
317 Figure 1. There were no training-related differences in haematological variables
318 between pre-PHV boys. In contrast, pre-PHV trained girls had a higher relative Hb
319 mass, blood volume and plasma volumes than untrained girls. Post-PHV, trained
320 boys and trained girls had higher relative Hb mass, blood volume and plasma

volume when compared with untrained controls. Post-PHV, effect sizes were larger between trained and untrained boys compared with pre-PHV for relative measures of Hb mass, blood volume and plasma volume. Effect sizes were larger between trained and untrained girls post-PHV for relative blood volumes compared with pre-PHV, but similar between pre- and post-PHV groups for other relative haematological variables.

Relationship between end-diastolic volume and blood volume

No relationship was observed in pre-PHV boys between EDV, and blood volume normalised for LBM (R^2 = 0.051, P = 0.193), but a small, significant relationship was found with post-PHV boys (R^2 = 0.184, P = 0.013) (Figure 2). Similarly, a weak relationship was found between EDV and blood volume normalised for LBM with pre-PHV girls (R^2 = 0.124, P = 0.045), with a stronger relationship found with post-PHV girls (R^2 = 0.316, P = 0.0002).

Independent relationships with $\dot{V}O_{2max}$

Bivariate associations with $\dot{V}O_{2max}$ for cardiac structural and haematological variables are presented in Table 4. The only significant correlations identified for pre-PHV boys were ESV, EDV and SV (r = 0.42-0.49, P = 0.001-0.006). In post-PHV boys, significant correlations were found for IVSd, LVPWd, LVIDd, LV mass, ESV, EDV, SV, Hb mass and blood volume (r = 0.41-0.69, P < 0.0001-0.018). For pre-PHV girls, there were significant correlations between $\dot{V}O_{2max}$ and IVSd, LV mass, EDV, SV, Hb mass and blood volumes (r = 0.35-0.49, P = 0.004-0.034). In post-PHV girls, significant correlations were found for IVSd, LVPWd, LV mass, ESV, EDV, SV, Hb mass and blood volume (r = 0.23-0.59, P < 0.0001-0.023).

Multiple regression analysis

Multicollinearity of *z*-scores for relative variables were identified between LV volume measures for all groups, and haematological measures for pre- and post-PHV girls, and post-PHV boys. Multicollinear variables were removed as necessary prior to analyses. The only variable to contribute to a significant proportion of the variance in $\dot{V}O_{2max}$ for pre-PHV boys was EDV, which accounted for 22% of the variance. The variance in $\dot{V}O_{2max}$ was also accounted for by EDV, alongside IVSd and Hb mass for post-PHV boys, which significantly contributed 61% of the variance (Table 5). For pre-PHV girls, Hb mass and IVSd significantly contributed 32% of the variance in $\dot{V}O_{2max}$. Hb mass and LVPWd contributed a significant proportion of the variance in $\dot{V}O_{2max}$ for post-PHV girls, accounting for 49% of the variance. These models which account for the variance in $\dot{V}O_{2max}$ using *z*-scores are stronger post-PHV as demonstrated by greater adjusted R^2 values and smaller standard errors compared with pre-PHV groups, for boys and girls.

Discussion

In relation to our three hypotheses, the novel findings were: (i) cardiac and haematological differences between trained *vs.* untrained children appear more pronounced in post-PHV children compared to their pre-PHV counterparts, characterised by a larger magnitude of LV hypertrophy and higher blood volume in the older group; (ii) the relationship between blood volume and ventricular volumes was stronger post-PHV; and (iii) cardiac and haematological adaptations provide a substantially greater contribution to relative $\dot{V}O_{2max}$ post-PHV, suggesting a maturation-dependent shift towards the central components of oxygen delivery in the context of maximal oxygen consumption.

The influence of maturity on LV morphology with endurance training

It has long been speculated that puberty provides a window whereby cardiac adaptations to endurance exercise are enhanced due to the hormonal milieu at this stage of development (Katch, 1983; McClean *et al.*, 2018). In trained pre-PHV children, a larger LV volume in boys and greater interventricular wall thickness in girls was found, but no other evidence of remodelling. In contrast, a similar phenotype to the adult athlete's heart with greater LV mass, ventricular volumes and consistently thicker ventricular walls compared to untrained counterparts was found for the post-PHV group (Pluim *et al.*, 2000; Prior & La Gerche, 2012). Given the high training volume and $\dot{V}O_{2max}$ in our trained pre-PHV groups, this potentially suggests a limited capacity for exercise-induced cardiac remodelling compared to the adult heart. Previous research examining exercise-induced cardiac remodelling prior to the onset of puberty has found similar results to our study, with either LV dilation (Obert *et al.*, 1998; Obert *et al.*, 2001; Obert *et al.*, 2003) or increased wall thickness

(Geenen *et al.*, 1982; Ayabakan *et al.*, 2006; Larsen *et al.*, 2018) in isolation, rather than in combination. These isolated adaptations may reflect the beginning of phasic cardiac remodelling, similar to the adaptation process observed in adults (Weiner *et al.*, 2015).

In adult training studies, enhanced wall thickness or LV dilation have also been observed in isolation prior to an eventual LV eccentric hypertrophy (Arbab-Zadeh *et al.*, 2014; Weiner *et al.*, 2015). Arbab-Zadeh *et al.* (2014) found an initial increase in LV wall thickness during the first six to nine months of training in exercise naïve adults, with LV dilation observed thereafter. This is congruent with the present study, in which girls had an enhanced wall thickness pre-PHV and an increased volume post-PHV. Conversely, Weiner *et al.* (2015) observed LV dilation prior to increased wall thickness with training intensification in athletes, which is in accord with our observations between pre- and post-PHV cardiac adaptations in boys. The differential response in boys and girls could be explained by differences in training volume and intensity. For example, Arbab-Zadeh *et al.* (2014) demonstrated that lower training volumes and intensities lead to increased wall thicknesses, whereas high intensity and volume exercise results in volumetric adaptation. Pre-pubertal training studies have also demonstrated this with isolated wall thickness adaptation when a lesser training load was implemented (Larsen *et al.*, 2018), compared with LV dilation alone when sessions are longer and completed at >80% maximal heart rate (Obert *et al.*, 2003). In the current study, trained pre-PHV girls had a slightly, but significantly lower training volume than boys, which may explain the isolated wall thickness and LV dilation adaptations in each group, respectively. However, given that neither pre-PHV boys or girls presented with combined wall thickness and

406 volume adaptations, despite their extensive training volume, suggests that cardiac
407 remodelling is likely limited prior to puberty.

408 The maturity related differences in LV mass could also be related to blood pressure,
409 which increases from childhood to adolescence (Rosner *et al.*, 1993), as shown in
410 the present data. Importantly though, resting blood pressures were similar between
411 trained and untrained groups, regardless of maturity group. Although not measured
412 in the current study, a more likely influence on differences in LV morphology is the
413 systolic blood pressure response during exercise, which has a much stronger
414 association with LV mass (Lauer *et al.*, 1992) and is greater in post-pubertal children
415 (Wanne & Haapoja, 1988). This could indicate that although our post-PHV groups
416 are undertaking a similar training volume, they likely experience a far greater
417 afterload stimulus for remodelling.

418 *The influence of maturation on haematological adaptations to endurance training*

419 There was a difference in relative Hb mass and blood volume between trained and
420 untrained boys post-PHV, but not pre-PHV. Haematological studies examining
421 adaptations to endurance training in children and adolescents are sparse. However,
422 similar to the present data in boys, Prommer *et al.* (2018) found that trained children
423 under 12 years of age have no difference in these haematological components when
424 compared with untrained counterparts. Continued monitoring of the trained group for
425 a further 3.5 years revealed an exponential increase in Hb mass for boys after 12
426 years of age. Indeed, Prommer *et al.* (2018) found a relationship between Hb mass
427 and LBM, but observed a 7% increase in Hb mass that was unrelated to body size
428 and attributed to the effects of training. Although maturity status was not quantified,
429 Prommer *et al.* (2018) speculated that the increase in Hb mass was directly related

to increased testosterone. Erythropoiesis has been shown to be upregulated during puberty (Krabbe *et al.*, 1978) and related directly to androgens (Hero *et al.*, 2005; Coviello *et al.*, 2008). This could explain the relative difference in haematological components between trained and untrained boys that exists post-PHV, but not pre-PHV in the current study. In contrast, the scaled differences in haematological components between trained and untrained girls are similar pre- and post-PHV, rather than widening post-PHV. It could be postulated that such findings are a result of the markedly lower increase in testosterone in girls compared with boys at puberty (Handelsman *et al.*, 2018). Indeed, Prommer *et al.* (2018) also found that whereas boys had an exponential increase in Hb mass around 12 years of age, the trajectory for trained girls remained unchanged across the study period, but only a very small number of girls (n = 4) were studied making definitive conclusions problematic.

Enhanced blood volume as a stimulus for post-PHV LV adaptation

It is well established that endurance training leads to cardiac remodelling in adults (Fagard, 2003). This adaptation is partly attributed to the training-related increases in blood volume (Green *et al.*, 1991) and the associated increase in preload (Colan, 1997). In the present study, a stronger relationship between ventricular volumes and blood volumes was evident post-PHV when circulating blood volume was significantly larger in trained vs. untrained adolescents. These data indicate that the increase in circulating volume could provide an enhanced volume challenge further driving LV remodelling with endurance training post-puberty.

Cardiac and haematological determinants of $\dot{V}O_{2max}$ pre- and post-PHV

Cardiac and haematological attributes are known to underpin $\dot{V}O_{2max}$ in adults (La Gerche *et al.*, 2012; Montero *et al.*, 2015; Diaz-Canestro *et al.*, 2021), but there is a

paucity of data defining cardiovascular determinants of $\dot{V}O_{2max}$ in adolescents. This study found that pre-PHV, the only variables to significantly contribute towards the variance in $\dot{V}O_{2max}$ were EDV for boys, and Hb mass and IVSd for girls, highlighting that contributions to endurance performance in pre-pubertal children are potentially sex dependent. The isolated cardiac variable and absence of a haematological influence in pre-PHV boys could reflect the lack of testosterone before puberty (Wood *et al.*, 2019), given its stimulatory effect on erythropoiesis (Hero *et al.*, 2005) and its association with cardiac hypertrophy (Marsh *et al.*, 1998). Our findings post-PHV support this, with Hb mass and IVSd also emerging as significant contributors alongside EDV to partially account for $\dot{V}O_{2max}$ in the more mature boys. Interestingly, and in contrast to this finding, Hb mass was identified to significantly contribute to some of the variance in $\dot{V}O_{2max}$ in pre-PHV girls, alongside IVSd, partially accounting the variance. Although paediatric data are sparse, adult haematological adaptation to training appears to be similar between males and females (Montero *et al.*, 2017). However, females are known to have a blunted cardiac adaptation to endurance training compared with males (Howden *et al.*, 2015), which may explain the reduced proportion of $\dot{V}O_{2max}$ that IVSd accounts for pre-PHV girls compared with Hb mass. Therefore, oxygen carrying capacity rather than maximal cardiac output may be of greater importance in accounting for the variance in $\dot{V}O_{2max}$ for pre-pubertal girls. Further research is required to understand the temporal nature of haematological and cardiac adaptations to long-term endurance training in pre-pubertal boys and girls.

We found the strength of the $\dot{V}O_{2max}$ predictive models to be weaker in pre-PHV groups compared to post-PHV groups for both boys and girls, despite comparable cardiorespiratory fitness. Therefore, central factors appear to be of less importance

in contributing towards the variance in aerobic exercise capacity pre-, compared with post-puberty. It is well documented that aerobic energy metabolism is the predominant energy pathway in pre-pubertal children (Ratel & Blazevich, 2017) with anaerobic contributions increasing with maturity (Van Praagh & Dore, 2002). Compared with adults, pre-pubertal children have enhanced muscle oxidative potential which has been attributed to a higher oxidative enzyme activity (Haralambie, 1982), increased mitochondrial density (Bell *et al.*, 1980) and improved clearance rates of H^+ ions (Ratel *et al.*, 2008). Given that central parameters impart a relatively small contribution to $\dot{V}O_{2max}$ in our pre-PHV groups, we speculate that these other important determinants within the oxygen transport chain could account for the majority of variance in pre-pubertal aerobic exercise capacity. However, we acknowledge that adding more variables to the models would likely alter the proportions of the variance in $\dot{V}O_{2max}$ that the significant contributors in the current study account for.

Limitations

Due to the cross-sectional design, we were unable to establish causality for training related adaptations, however cardiac adaptations to training pre-puberty (Obert *et al.*, 2003) and during adolescence (Churchill *et al.*, 2020) have been observed. We were also unable to control for the greater training histories in post-PHV groups, nor the slightly higher training volume in post-PHV trained girls, and thus we cannot discount the potential influence of these factors. However, after removing trained participants with the highest and lowest historical training volumes to match pre- and post-PHV trained groups on these variables, we ran subgroup analyses for our key outcome measures. Using these subgroups of our trained participants with n = 13 in each pre- and post-PHV group, compared with the same untrained groups, there

were no significant changes to our results. To completely account for these training histories and volumes, longitudinal training interventions, and ideally twin training interventions are required with a focus on the influence of maturation. Additionally, the absence of atrial and right ventricular data is acknowledged as a limitation and future research is required to characterise these variables with training pre- and post-puberty. We also recognise that the gold standard technique for cardiac structure is magnetic resonance imaging (Grothues *et al.*, 2002). However, echocardiography is frequently used in the assessment of cardiac remodelling (Lang *et al.*, 2015) and has been validated in children (Lopez *et al.*, 2010). The aim of the current study was to identify how cardiac and haematology influence $\dot{V}O_{2max}$, but we acknowledge that additional measures would also contribute to the variance in $\dot{V}O_{2max}$. Future studies should consider other central and peripheral determinants within the oxygen transport chain, especially in pre-pubertal children. Finally, we acknowledge our indirect method of quantifying maturation and recognise that the assessment of skeletal maturity would have provided the most accurate measure (Lloyd *et al.*, 2014). Additionally, direct measures of hormones would have enabled direct associations with our key outcome variables. However, given the circadian fluctuations of sex- and growth-related hormones, multiple measures during the day and night would have been required for an accurate representation (Gupta *et al.*, 2000; Matchock *et al.*, 2007). Therefore, we did not include these in order to avoid too many disruptive and invasive measures in our young paediatric cohort.

Translational perspective

Given that competitive youth athletes undertake high training volumes throughout their developmental years, it is important to identify how such loads may present upon clinical examination at different stages of maturity. Our findings suggest that

when attempting to differentiate between physiological and pathological cardiac remodelling, stage of maturity should be considered alongside endurance training history. Critically, our data suggest that marked LV dilation and wall thickening is very uncommon pre-puberty and should be considered pathologic until proven otherwise. Continued endurance training throughout puberty would then be expected to lead to more pronounced LV wall thickening and dilation as a feature of normal adaptation in the young athlete's heart.

Conclusion

Some degree of cardiac remodelling and haematological adaptation to endurance training is evident before puberty but is more pronounced following puberty. As children progress from childhood through adolescence, we speculate there may be a shift in the balance from peripheral to central components to account for the majority of the variance in maximal of oxygen consumption. However, pre-pubertal children remain eminently trainable and capable of achieving high levels of aerobic fitness – albeit potentially through different mechanisms than their older counterparts.

Additional information

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests

The authors have no competing interests to declare.

Author contributions

DRP, RSL, RES, JLO and MS contributed to the conception and design of the study. All authors were involved with the acquisition, analysis, or interpretation of data. DRP and MS drafted the manuscript, and all authors were involved in revising it critically for important intellectual content. All authors approved the final version of the manuscript.

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Table 1. Participant characteristics and cardiorespiratory fitness

		Boys		Training status main effect	Training status posthoc *t*-tests (ET *vs.* UN)		Maturity status main effect	Maturity status posthoc *t*-tests (pre- *vs*. post-PHV)		Interaction (Training status X Maturity status)	Girls		Training status main effect	Training status posthoc *t*-tests (ET *vs.* UN)		Maturity status main effect	Maturity status posthoc *t*-tests (pre- *vs*. post-PHV)		Interaction (Training status X Maturity status)
Anthropometric Characteristics		Pre-PHV	Post-PHV		Pre-PHV	Post-PHV		ET	UN		Pre-PHV	Post-PHV		Pre-PHV	Post-PHV		ET	UN	
Age (years)	ET	11.7 ± 1.7	15.9 ± 1.1	*P* = 0.520	***P* = 0.046**	*P* = 0.095	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	***P* = 0.011**	10.6 ± 1.3	14.1 ± 1.4	*P* = 0.154	*P* = 0.122	*P* = 0.585	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.566
	UN	10.6 ± 1.6	16.0 ± 1.2		(*d* = 0.672)	(*d* = 0.593)		(*d* = 2.530)	(*d* = 3.893)		10.0 ± 1.2	13.8 ± 1.7		(*d* = 0.510)	(*d* = 0.170)		(*d* = 2.571)	(*d* = 2.581)	
Maturity offset (years)	ET	-2.1 ± 1.2	1.5 ± 1.0	*P* = 0.686	*P* = 0.121	*P* = 0.300	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.067	-1.3 ± 1.0	1.9 ± 1.1	*P* = 0.089	*P* = 0.115	*P* = 0.391	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.648
	UN	-2.7 ± 1.1	1.9 ± 1.1		(*d* = 0.517)	(*d* = 0.364)		(*d* = 3.288)	(*d* = 4.067)		-1.8 ± 0.9	1.6 ± 1.1		(*d* = 0.522)	(*d* = 0.269)		(*d* = 3.068)	(*d* = 3.342)	
Height (cm)	ET	148.6 ± 11.8	175.4 ± 8.6	*P* = 0.608	*P* = 0.457	*P* = 0.957	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.559	143.6 ± 9.6	164.7 ± 6.6	***P* = 0.016**	*P* = 0.061	*P* = 0.144	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.413
	UN	145.9 ± 10.1	175.6 ± 10.6		(*d* = 0.245)	(*d* = 0.019)		(*d* = 2.564)	(*d* = 2.872)		137.6 ± 9.6	161.7 ± 6.4		(*d* = 0.624)	(*d* = 0.461)		(*d* = 2.566)	(*d* = 2.995)	
Body mass (kg)	ET	38.9 ± 8.9	61.7 ± 9.7	*P* = 0.788	*P* = 0.913	*P* = 0.797	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.901	34.4 ± 6.1	54.0 ± 8.5	*P* = 0.922	*P* = 0.649	*P* = 0.876	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.719
	UN	39.3 ± 9.4	62.6 ± 10.3		(*d* = 0.036)	(*d* = 0.090)		(*d* = 2.450)	(*d* = 2.373)		33.6 ± 5.5	54.5 ± 12.1		(*d* = 0.148)	(*d* = 0.049)		(*d* = 2.645)	(*d* = 2.186)	
Lean body mass (kg)	ET	33.2 ± 7.3	53.8 ± 7.1	*P* = 0.066	*P* = 0.114	*P* = 0.301	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.762	28.2 ± 4.7	43.3 ± 6.0	***P* = 0.015**	*P* = 0.081	*P* = 0.078	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.699
	UN	29.8 ± 5.0	51.3 ± 6.2		(*d* = 0.526)	(*d* = 0.363)		(*d* = 2.860)	(*d* = 3.814)		25.8 ± 3.7	39.9 ± 6.2		(*d* = 0.580)	(*d* = 0.561)		(*d* = 2.815)	(*d* = 2.713)	
Blood Pressure																			
Systolic BP (mm Hg)	ET	104 ± 8	117 ± 9	*P* = 0.502	*P* = 0.394	*P* = 0.899	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.628	104 ± 8	111 ± 7	*P* = 0.131	*P* = 0.218	*P* = 0.385	***P* < 0.0001**	***P* = 0.003**	***P* = 0.001**	*P* = 0.725
	UN	102 ± 8	116 ± 7		(*d* = 0.284)	(*d* = 0.044)		(*d* = 1.454)	(*d* = 1.864)		101 ± 6	109 ± 6		(*d* = 0.416)	(*d* = 0.272)		(*d* = 0.958)	(*d* = 1.292)	
Diastolic BP (mm Hg)	ET	60 ± 7	64 ± 7	*P* = 0.521	*P* = 0.117	*P* = 0.553	*P* = 0.565	*P* = 0.114	*P* = 0.536	*P* = 0.130	62 ± 7	64 ± 7	*P* = 0.955	*P* = 0.831	*P* = 0.886	*P* = 0.242	*P* = 0.323	*P* = 0.490	*P* = 0.799
	UN	64 ± 6	62 ± 7		(*d* = 0.528)	(*d* = 0.207)		(*d* = 0.507)	(*d* = 0.225)		63 ± 5	64 ± 6		(*d* = 0.071)	(*d* = 0.045)		(*d* = 0.302)	(*d* = 0.237)	
Cardiorespiratory Fitness																			
HR_{max} (beats·min)	ET	191 ± 9	194 ± 11	*P* = 0.303	*P* = 0.771	*P* = 0.271	*P* = 0.056	*P* = 0.346	*P* = 0.080	*P* = 0.520	196 ± 8	191 ± 6	*P* = 0.150	*P* = 0.313	*P* = 0.302	***P* = 0.013**	***P* = 0.031**	*P* = 0.155	*P* = 0.945
	UN	192 ± 9	197 ± 8		(*d* = 0.096)	(*d* = 0.387)		(*d* = 0.296)	(*d* = 0.652)		198 ± 7	194 ± 10		(*d* = 0.336)	(*d* = 0.324)		(*d* = 0.667)	(*d* = 0.494)	
$\dot{V}O_{2max}$ (mL·kg·min)	ET	59.4 ± 5.9	64.2 ± 8.0	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	***P* = 0.017**	***P* = 0.029**	*P* = 0.217	*P* = 0.497	51.1 ± 6.3	51.7 ± 5.2	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.214	*P* = 0.737	*P* = 0.052	*P* = 0.093
	UN	45.2 ± 7.6	48.0 ± 3.8		(*d* = 2.136)	(*d* = 2.511)		(*d* = 0.704)	(*d* = 0.454)		41.9 ± 5.6	38.1 ± 5.4		(*d* = 1.549)	(*d* = 2.573)		(*d* = 0.101)	(*d* = 0.685)	
$\dot{V}O_{2max}$ (mL·kg^{LBM}·min)	ET	69.3 ± 6.1	73.2 ± 7.6	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.219	*P* = 0.070	*P* = 0.962	*P* = 0.194	62.0 ± 5.7	64.1 ± 5.2	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.954	*P* = 0.204	*P* = 0.275	*P* = 0.093
	UN	58.3 ± 6.4	58.2 ± 5.4		(*d* = 1.777)	(*d* = 2.235)		(*d* = 0.577)	(*d* = 0.017)		53.5 ± 5.3	51.2 ± 6.4		(*d* = 1.549)	(*d* = 2.235)		(*d* = 0.385)	(*d* = 0.377)	
$\dot{V}O_{2max}$ (% age predicted)	ET	127 ± 13	145 ± 18	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	***P* = 0.0004**	***P* = 0.018**	*P* = 0.344	112 ± 14	139 ± 14	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	***P* = 0.025**	***P* = 0.010**
	UN	97 ± 16	108 ± 9		(*d* = 2.136)	(*d* = 2.511)		(*d* = 1.198)	(*d* = 0.900)		92 ± 12	103 ± 14		(*d* = 1.549)	(*d* = 2.573)		(*d* = 1.963)	(*d* = 0.800)	

Key: *BP*, blood pressure; *ES*, effect size; *ET*, endurance trained; HR_{max}, maximal heart rate; *PHV*, peak height velocity; *UT*, untrained; $\dot{V}O_{2max}$, maximal oxygen uptake.

Data expressed as mean ± SD. Statistical comparisons were performed using two-way ANOVAs with training and maturity status as fixed factors. Independent samples *t*-tests were then used to identify differences where an interaction or main effect existed. Effect sizes calculated using Cohen's *d*. Participants for anthropometric characteristics included boys, pre-PHV (trained, *n* = 23 *vs.* untrained, *n* = 16) and post-PHV (trained, *n* = 19 *vs.* untrained, *n* = 15), girls, pre-PHV (trained, *n* = 22 *vs.* untrained, *n* = 17) and post-PHV (trained, *n* = 23 *vs.* untrained *n* = 19).

Group *n*'s did not change from those of anthropometric characteristics, aside from the following: blood pressure, pre-PHV boys (trained, *n* = 22), pre-PHV girls (trained, *n* = 21 and untrained, *n* = 16); cardiorespiratory fitness, pre-PHV girls (untrained, *n* = 16).

Table 2. Left ventricular and haematological parameters in boys

		Boys		Training status main effect	Training status posthoc *t*-tests (ET vs. UN)		Maturity status main effect	Maturity status posthoc *t*-tests (pre- vs. post-PHV)		Interaction (Training status X Maturity status)
Absolute LV Parameters		Pre-PHV	Post-PHV		Pre-PHV	Post-PHV		ET	UN	
IVSd (mm)	ET	5.4 ± 1.3	7.4 ± 1.3	***P* = 0.028**	*P* = 0.362	***P* = 0.033**	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.328
	UN	5.1 ± 0.7	6.6 ± 0.7		(*d* = 0.301)	(*d* = 0.768)		(*d* = 1.488)	(*d* = 2.159)	
LVIDd (mm)	ET	42.2 ± 4.3	50.2 ± 3.8	***P* = 0.029**	*P* = 0.087	*P* = 0.163	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.930
	UN	40.0 ± 2.9	47.9 ± 5.7		(*d* = 0.572)	(*d* = 0.493)		(*d* = 1.981)	(*d* = 1.752)	
LVPWd (mm)	ET	5.9 ± 1.5	7.8 ± 1.0	***P* = 0.036**	*P* = 0.638	***P* = 0.007**	***P* < 0.0001**	***P* < 0.0001**	***P* = 0.0008**	*P* = 0.165
	UN	5.7 ± 0.9	6.9 ± 0.8		(*d* = 0.155)	(*d* = 1.003)		(*d* = 1.485)	(*d* = 1.343)	
LV length (cm)	ET	7.1 ± 0.8	8.5 ± 0.6	***P* < 0.0001**	***P* = 0.0003**	***P* = 0.0002**	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.807
	UN	6.2 ± 0.5	7.6 ± 0.7		(*d* = 1.290)	(*d* = 1.474)		(*d* = 2.005)	(*d* = 2.174)	
LV mass (g)	ET	88.5 ± 25.0	155.6 ± 26.5	***P* < 0.0001**	***P* = 0.027**	***P* = 0.0004**	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.106
	UN	73.2 ± 10.2	123.1 ± 20.1		(*d* = 0.749)	(*d* = 1.356)		(*d* = 2.611)	(*d* = 3.171)	
Relative wall thickness	ET	0.27 ± 0.06	0.30 ± 0.05	*P* = 0.509	*P* = 0.871	*P* = 0.226	***P* = 0.044**	***P* = 0.047**	*P* = 0.422	*P* = 0.287
	UN	0.27 ± 0.04	0.28 ± 0.04		(*d* = 0.053)	(*d* = 0.426)		(*d* = 0.634)	(*d* = 0.293)	
EDV (mL)	ET	65.4 ± 17.5	104.2 ± 15.7	***P* < 0.0001**	***P* = 0.002**	***P* = 0.0002**	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.343
	UN	49.5 ± 8.4	81.6 ± 15.0		(*d* = 1.092)	(*d* = 1.471)		(*d* = 2.327)	(*d* = 2.668)	
ESV (mL)	ET	26.7 ± 6.8	42.6 ± 6.6	***P* < 0.0001**	***P* = 0.001**	***P* = 0.0002**	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.281
	UN	19.5 ± 4.3	32.1 ± 7.8		(*d* = 1.198)	(*d* = 1.464)		(*d* = 2.365)	(*d* = 2.021)	
SV (mL)	ET	38.7 ± 11.1	61.6 ± 10.8	***P* < 0.0001**	***P* = 0.007**	***P* = 0.001**	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.451
	UN	30.1 ± 5.4	49.5 ± 8.9		(*d* = 0.935)	(*d* = 1.206)		(*d* = 2.089)	(*d* = 2.654)	
Heart rate (beats·min)	ET	66 ± 12	51 ± 5	***P* = 0.001**	*P* = 0.369	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.154	***P* = 0.037**
	UN	69 ± 9	64 ± 10		(*d* = 0.296)	(*d* = 1.731)		(*d* = 1.520)	(*d* = 0.527)	
Q (litres·min)	ET	2.36 ± 0.43	3.16 ± 0.68	*P* = 0.209	***P* = 0.039**	*P* = 0.909	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.318
	UN	2.08 ± 0.37	3.13 ± 0.59		(*d* = 0.697)	(*d* = 0.040)		(*d* = 1.435)	(*d* = 2.165)	
Relative LV Parameters										
IVSd/height (mm·m)	ET	3.6 ± 0.6	4.2 ± 0.8	***P* = 0.038**	*P* = 0.501	***P* = 0.038**	***P* = 0.005**	***P* = 0.011**	*P* = 0.132	*P* = 0.220
	UN	3.5 ± 0.4	3.7 ± 0.4		(*d* = 0.221)	(*d* = 0.746)		(*d* = 0.832)	(*d* = 0.557)	
LVIDd/height (mm·m)	ET	28.4 ± 2.4	28.7 ± 2.2	***P* = 0.044**	*P* = 0.221	*P* = 0.114	*P* = 0.976	*P* = 0.737	*P* = 0.817	*P* = 0.692
	UN	27.5 ± 2.1	27.3 ± 2.8		(*d* = 0.405)	(*d* = 0.561)		(*d* = 0.105)	(*d* = 0.084)	
LVPWd/height (mm·m)	ET	3.9 ± 0.8	4.5 ± 0.6	*P* = 0.068	*P* = 0.907	***P* = 0.009**	*P* = 0.079	***P* = 0.017**	*P* = 0.939	*P* = 0.098
	UN	3.9 ± 0.6	3.9 ± 0.6		(*d* = 0.038)	(*d* = 0.960)		(*d* = 0.769)	(*d* = 0.028)	
LV length/height (cm·m)	ET	4.8 ± 0.3	4.9 ± 0.3	***P* < 0.0001**	***P* < 0.0001**	***P* = 0.0001**	*P* = 0.317	*P* = 0.304	*P* = 0.644	*P* = 0.833
	UN	4.3 ± 0.3	4.3 ± 0.4		(*d* = 1.631)	(*d* = 1.495)		(*d* = 0.323)	(*d* = 0.168)	
SV/LBM (mL·kg)	ET	1.16 ± 0.20	1.15 ± 0.12	***P* = 0.0002**	***P* = 0.033**	***P* = 0.001**	*P* = 0.377	*P* = 0.740	*P* = 0.383	*P* = 0.648
	UN	1.02 ± 0.19	0.97 ± 0.15		(*d* = 0.719)	(*d* = 1.282)		(*d* = 0.104)	(*d* = 0.318)	
Q/LBM (mL·kg^{LBM,} min)	ET	72.20 ± 9.90	58.59 ± 8.05	*P* = 0.751	*P* = 0.693	*P* = 0.385	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.075	*P* = 0.377
	UN	70.69 ± 13.86	61.77 ± 12.93		(*d* = 0.129)	(*d* = 0.304)		(*d* = 1.494)	(*d* = 0.665)	
Haematological parameters										
Hb mass (g)	ET	449 ± 112	770 ± 120	***P* = 0.007**	*P* = 0.198	***P* = 0.017**	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.304
	UN	400 ± 86	663 ± 122		(*d* = 0.468)	(*d* = 0.887)		(*d* = 2.777)	(*d* = 2.461)	
Hb mass/BM (g·kg)	ET	11.6 ± 1.5	12.5 ± 1.1	***P* < 0.0001**	*P* = 0.070	***P* < 0.0001**	*P* = 0.109	***P* = 0.032**	*P* = 0.729	*P* = 0.296
	UN	10.4 ± 2.0	10.6 ± 0.6		(*d* = 0.666)	(*d* = 2.033)		(*d* = 0.690)	(*d* = 0.138)	
Blood volume (mL)	ET	3742 ± 920	6084 ± 860	***P* = 0.001**	*P* = 0.169	***P* = 0.002**	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.184
	UN	3326 ± 613	5113 ± 764		(*d* = 0.501)	(*d* = 1.183)		(*d* = 2.621)	(*d* = 2.555)	
Blood volume/BM (mL·kg)	ET	96.8 ± 13.6	99.3 ± 9.5	***P* < 0.0001**	*P* = 0.070	***P* < 0.0001**	*P* = 0.749	*P* = 0.495	*P* = 0.354	*P* = 0.246
	UN	87.2 ± 15.9	82.7 ± 7.2		(*d* = 0.667)	(*d* = 1.930)		(*d* = 0.214)	(*d* = 0.372)	
Plasma volume (mL)	ET	2399 ± 593	3775 ± 536	***P* = 0.001**	*P* = 0.203	***P* = 0.001**	***P* < 0.0001**	***P* < 0.0001**	***P* < 0.0001**	*P* = 0.135
	UN	2151 ± 397	3130 ± 477		(*d* = 0.462)	(*d* = 1.260)		(*d* = 2.424)	(*d* = 2.215)	
Plasma volume/BM (mL·kg)	ET	62.1 ± 9.2	61.7 ± 6.6	***P* = 0.0001**	*P* = 0.104	***P* < 0.0001**	*P* = 0.152	*P* = 0.880	*P* = 0.099	*P* = 0.211
	UN	56.3 ± 10.3	50.8 ± 6.0		(*d* = 0.595)	(*d* = 1.714)		(*d* = 0.047)	(*d* = 0.675)	
Hb (g·dL)	ET	13.4 ± 1.0	14.1 ± 0.7	*P* = 0.737	*P* = 0.594	*P* = 0.279	***P* < 0.0001**	***P* = 0.007**	***P* = 0.001**	*P* = 0.260
	UN	13.2 ± 0.8	14.4 ± 0.9		(*d* = 0.192)	(*d* = 0.388)		(*d* = 0.877)	(*d* = 1.462)	
Hct (%)	ET	39.4 ± 2.1	41.7 ± 1.9	*P* = 0.800	*P* = 0.399	*P* = 0.272	***P* < 0.0001**	***P* = 0.001**	***P* = 0.001**	*P* = 0.165
	UN	38.8 ± 1.9	42.6 ± 2.7		(*d* = 0.304)	(*d* = 0.394)		(*d* = 1.117)	(*d* = 1.567)	

Key: *BM*, body mass; *EDV*, end-diastolic volume; *ES*, effect size; *ESV*, end-systolic volume; ET, endurance trained; *Hb*, haemoglobin; *Hct*, haematocrit; *IVSd*, interventricular septum diastole; *LV*, left ventricle; *LBM*, lean body mass; *LVIDd*, LV internal diameter diastole; *ET,* endurance trained; *LVPWd*, LV posterior wall diastole; *PHV*, peak height velocity; *SV*, stroke volume; *Q*, cardiac output; *UT*, untrained.

Data expressed as mean ± SD. Statistical comparisons were performed using two-way ANOVAs with training and maturity status as fixed factors. Independent samples *t*-tests were then used to identify differences where an interaction or main effect existed. Effect sizes calculated using Cohen's *d*. Participants for cardiac parameters included boys, pre-PHV (trained, *n* = 23 *vs.* untrained, *n* = 16) and post-PHV (trained, *n* = 19 *vs.* untrained, *n* = 15). Paricipants for haematological parameters included boys, pre-PHV (trained, *n* = 23 *vs.* untrained, *n* = 12) and post-PHV (trained, *n* = 19 *vs.* untrained, *n* = 14).

Table 3. Left ventricular and haematological parameters in girls

		Girls		Training status main effect	Training status posthoc *t*-tests (ET vs. UN)		Maturity status main effect	Maturity status posthoc *t*-tests (pre- vs. post-PHV)		Interaction (Training status X Maturity status)
Absolute LV Parameters		Pre-PHV	Post-PHV		Pre-PHV	Post-PHV		ET	UN	
IVSd (mm)	ET	5.3 ± 1.0	6.7 ± 1.2	***P* < 0.0001**	***P* = 0.007** (*d* = 0.929)	***P* = 0.001** (*d* = 1.146)	***P* < 0.0001**	***P* < 0.0001** (*d* = 1.297)	***P* < 0.0001** (*d* = 1.510)	*P* = 0.415
	UN	4.5 ± 0.6	5.6 ± 0.8							
LVIDd (mm)	ET	40.6 ± 3.4	45.5 ± 3.3	***P* = 0.010**	*P* = 0.106 (*d* = 0.535)	***P* = 0.046** (*d* = 0.645)	***P* < 0.0001**	***P* < 0.0001** (*d* = 1.443)	***P* = 0.001** (*d* = 1.162)	*P* = 0.705
	UN	38.8 ± 3.2	43.1 ± 4.1							
LVPWd (mm)	ET	5.7 ± 1.0	7.1 ± 1.3	***P* < 0.0001**	***P* = 0.016** (*d* = 0.812)	***P* < 0.0001** (*d* = 1.533)	***P* < 0.0001**	***P* = 0.0002** (*d* = 1.244)	***P* = 0.014** (*d* = 0.860)	***P* = 0.046**
	UN	5.0 ± 0.7	5.5 ± 0.6							
LV length (cm)	ET	6.4 ± 0.7	7.5 ± 0.6	***P* = 0.001**	*P* = 0.091 (*d* = 0.561)	***P* = 0.005** (*d* = 0.940)	***P* < 0.0001**	***P* < 0.0001** (*d* = 1.717)	***P* < 0.0001** (*d* = 1.642)	*P* = 0.346
	UN	6.0 ± 0.4	6.9 ± 0.6							
LV mass (g)	ET	80.2 ± 16.2	126.0 ± 30.5	***P* = 0.0002**	***P* = 0.011** (*d* = 0.867)	***P* = 0.003** (*d* = 0.975)	***P* < 0.0001**	***P* < 0.0001** (*d* = 1.873)	***P* < 0.0001** (*d* = 2.176)	*P* = 0.193
	UN	67.7 ± 11.6	101.1 ± 18.0							
Relative wall thickness	ET	0.27 ± 0.05	0.30 ± 0.04	***P* = 0.001**	*P* = 0.098 (*d* = 0.548)	***P* = 0.002** (*d* = 1.053)	*P* = 0.053	***P* = 0.034** (*d* = 0.660)	*P* = 0.333 (*d* = 0.328)	*P* = 0.833
	UN	0.25 ± 0.04	0.26 ± 0.04							
EDV (mL)	ET	48.9 ± 11.4	75.7 ± 13.3	***P* < 0.0001**	*P* = 0.089 (*d* = 0.565)	***P* < 0.0001** (*d* = 1.384)	***P* < 0.0001**	***P* < 0.0001** (*d* = 2.155)	***P* = 0.0003** (*d* = 1.341)	***P* = 0.030**
	UN	42.9 ± 9.5	57.8 ± 12.4							
ESV (mL)	ET	18.1 ± 4.7	30.0 ± 6.8	***P* < 0.0001**	*P* = 0.308 (*d* = 0.334)	***P* < 0.0001** (*d* = 1.421)	***P* < 0.0001**	***P* < 0.0001** (*d* = 2.049)	***P* = 0.014** (*d* = 0.862)	***P* = 0.003**
	UN	16.7 ± 3.9	21.0 ± 5.8							
SV (mL)	ET	30.8 ± 7.9	45.7 ± 7.8	***P* = 0.0001**	*P* = 0.054 (*d* = 0.643)	***P* = 0.001** (*d* = 1.159)	***P* < 0.0001**	***P* < 0.0001** (*d* = 1.886)	***P* < 0.0001** (*d* = 1.585)	*P* = 0.202
	UN	26.2 ± 5.8	36.8 ± 7.4							
Heart rate (beats·min)	ET	72 ± 10	61 ± 7	***P* = 0.001**	*P* = 0.104 (*d* = 0.538)	***P* = 0.0002** (*d* = 1.275)	***P* < 0.0001**	***P* < 0.0001** (*d* = 1.321)	***P* = 0.034** (*d* = 0.736)	*P* = 0.681
	UN	79 ± 16	70 ± 7							
Q (litres·min)	ET	2.17 ± 0.60	2.79 ± 0.49	*P* = 0.117	*P* = 0.572 (*d* = 0.184)	*P* = 0.089 (*d* = 0.546)	***P* < 0.0001**	***P* = 0.001** (*d* = 1.119)	***P* = 0.024** (*d* = 0.787)	*P* = 0.529
	UN	2.07 ± 0.56	2.50 ± 0.55							
Relative LV Parameters										
IVSd/height (mm·m)	ET	3.7 ± 0.6	4.1 ± 0.6	***P* = 0.0001**	***P* = 0.041** (*d* = 0.684)	***P* = 0.001** (*d* = 1.124)	***P* = 0.040**	***P* = 0.040** (*d* = 0.639)	*P* = 0.395 (*d* = 0.288)	*P* = 0.333
	UN	3.3 ± 0.6	3.5 ± 0.4							
LVIDd/height (mm·m)	ET	28.3 ± 2.3	27.6 ± 1.6	*P* = 0.277	*P* = 0.912 (*d* = 0.036)	*P* = 0.137 (*d* = 0.475)	***P* = 0.019**	*P* = 0.258 (*d* = 0.346)	***P* = 0.041** (*d* = 0.708)	*P* = 0.362
	UN	28.2 ± 2.0	26.7 ± 2.4							
LVPWd/height (mm·m)	ET	4.0 ± 0.6	4.3 ± 0.7	***P* < 0.0001**	*P* = 0.097 (*d* = 0.550)	***P* < 0.0001** (*d* = 1.552)	*P* = 0.587	*P* = 0.094 (*d* = 0.516)	*P* = 0.143 (*d* = 0.501)	***P* = 0.033**
	UN	3.7 ± 0.5	3.4 ± 0.3							
LV length/height (cm·m)	ET	4.4 ± 0.4	4.5 ± 0.3	***P* = 0.049**	*P* = 0.746 (*d* = 0.105)	***P* = 0.011** (*d* = 0.837)	*P* = 0.966	*P* = 0.319 (*d* = 0.304)	*P* = 0.269 (*d* = 0.375)	*P* = 0.134
	UN	4.4 ± 0.3	4.3 ± 0.4							
SV/LBM (mL·kg)	ET	1.09 ± 0.21	1.06 ± 0.16	***P* = 0.010**	*P* = 0.173 (*d* = 0.449)	***P* = 0.006** (*d* = 0.907)	*P* = 0.138	*P* = 0.627 (*d* = 0.147)	*P* = 0.052 (*d* = 0.672)	*P* = 0.520
	UN	1.01 ± 0.12	0.92 ± 0.14							
Q/LBM (mL·kg^{LBM}· min)	ET	76.66 ± 14.60	64.92 ± 11.21	*P* = 0.815	*P* = 0.497 (*d* = 0.222)	*P* = 0.553 (*d* = 0.188)	***P* < 0.0001**	*P* = 0.005 (*d* = 0.902)	*P* = 0.001 (*d* = 1.201)	*P* = 0.364
	UN	80.19 ± 17.57	62.84 ± 10.96							
Haematological parameters										
Hb mass (g)	ET	351 ± 70	527 ± 82	***P* < 0.0001**	***P* = 0.016** (*d* = 0.924)	***P* = 0.001** (*d* = 1.093)	***P* < 0.0001**	***P* < 0.0001** (*d* = 2.317)	***P* < 0.0001** (*d* = 1.799)	*P* = 0.480
	UN	285 ± 73	434 ± 89							
Hb mass/BM (g·kg)	ET	10.3 ± 1.5	10.0 ± 1.4	***P* < 0.0001**	***P* = 0.0004** (*d* = 1.421)	***P* = 0.0001** (*d* = 1.370)	*P* = 0.562	*P* = 0.484 (*d* = 0.216)	*P* = 0.894 (*d* = 0.050)	*P* = 0.739
	UN	8.2 ± 1.4	8.1 ± 1.2							
Blood volume (mL)	ET	2979 ± 575	4459 ± 580	***P* = 0.0003**	*P* = 0.079 (*d* = 0.658)	***P* = 0.001** (*d* = 1.193)	***P* < 0.0001**	***P* < 0.0001** (*d* = 2.563)	***P* = 0.001** (*d* = 1.401)	*P* = 0.238
	UN	2550 ± 776	3647 ± 788							
Blood volume/BM (mL·kg)	ET	87.6 ± 12.9	84.4 ± 10.9	***P* < 0.0001**	***P* = 0.008** (*d* = 1.028)	***P* < 0.0001** (*d* = 1.561)	*P* = 0.165	*P* = 0.387 (*d* = 0.267)	*P* = 0.289 (*d* = 0.403)	*P* = 0.749
	UN	73.2 ± 15.9	68.1 ± 9.8							
Plasma volume (mL)	ET	1941 ± 371	2855 ± 371	***P* = 0.003**	*P* = 0.131 (*d* = 0.562)	***P* = 0.006** (*d* = 0.931)	***P* < 0.0001**	***P* < 0.0001** (*d* = 2.463)	***P* = 0.002** (*d* = 1.284)	*P* = 0.391
	UN	1693 ± 548	2416 ± 572							
Plasma volume/BM (mL·kg)	ET	57.1 ± 8.5	54.1 ± 7.1	***P* = 0.0002**	***P* = 0.018** (*d* = 0.903)	***P* = 0.003** (*d* = 1.013)	*P* = 0.159	*P* = 0.208 (*d* = 0.390)	*P* = 0.435 (*d* = 0.295)	*P* = 0.987
	UN	48.5 ± 11.2	45.4 ± 10.2							
Hb (g·dL)	ET	12.9 ± 0.6	13.1 ± 0.7	*P* = 0.412	*P* = 0.112 (*d* = 0.577)	*P* = 0.650 (*d* = 0.145)	***P* = 0.008**	*P* = 0.291 (*d* = 0.327)	***P* = 0.021** (*d* = 0.888)	*P* = 0.150
	UN	12.5 ± 0.9	13.2 ± 0.7							
Hct (%)	ET	38.3 ± 1.6	39.5 ± 2.3	*P* = 0.148	*P* = 0.073 (*d* = 0.655)	*P* = 0.698 (*d* = 0.124)	***P* = 0.001**	***P* = 0.049** (*d* = 0.620)	***P* = 0.006** (*d* = 1.070)	*P* = 0.371
	UN	37.2 ± 1.8	39.2 ± 2.0							

Key: *BM*, body mass; *EDV*, end-diastolic volume; *ES*, effect size; *ESV*, end-systolic volume; ET, endurance trained; *Hb*, haemoglobin; *Hct*, haematocrit; *IVSd*, interventricular septum diastole; *LV*, left ventricle; *LBM*, lean body mass; *LVIDd*, LV internal diameter diastole; *ET,*

endurance trained; *LVPWd*, LV posterior wall diastole; *PHV*, peak height velocity; *SV*, stroke volume; *Q*, cardiac output; *UT*, untrained.

Data expressed as mean ± SD. Statistical comparisons were performed using two-way ANOVAs with training and maturity status as fixed factors. Independent samples *t*-tests were then used to identify differences where an interaction or main effect existed. Effect sizes calculated using Cohen's *d*. Participants for cardiac parameters included girls, pre-PHV (trained, *n* = 22 *vs.* untrained, *n* = 17) and post-PHV (trained, *n* = 22 *vs.* untrained, *n* = 19). Participants for haematological parameters included girls, pre-PHV (trained, *n* = 21 *vs.* untrained, *n* = 12) and post-PHV (trained, *n* = 22 *vs.* untrained, *n* = 18).

Table 4. Bivariate associations with $\dot{V}O_{2max}$ (mL·kg^{LBM}·min) using pooled trained and untrained *z*-score values

	Boys				Girls			
	Pre-PHV		Post-PHV		Pre-PHV		Post-PHV	
	r	*P*-value	*r*	*P*-value	*r*	*P*-value	*r*	*P*-value
IVSd/height	0.14	0.389	0.45	**0.007**	0.41	**0.010**	0.47	**0.002**
LVPWd/height	0.04	0.814	0.47	**0.005**	0.31	0.056	0.59	**<0.0001**
LVIDd/height	0.25	0.119	0.41	**0.018**	0.14	0.386	0.19	0.229
LV mass/LBM	0.30	0.066	0.65	**<0.0001**	0.35	**0.034**	0.46	**0.002**
ESV/LBM	0.49	**0.001**	0.64	**<0.0001**	0.27	0.106	0.43	**0.005**
EDV/LBM	0.49	**0.001**	0.69	**<0.0001**	0.39	**0.014**	0.43	**0.006**
SV/LBM	0.43	**0.006**	0.60	**0.0001**	0.41	**0.011**	0.35	**0.023**
Hb mass/LBM	0.16	0.373	0.54	**0.001**	0.49	**0.004**	0.48	**0.002**
Blood volume/LBM	0.15	0.386	0.49	**0.004**	0.39	**0.026**	0.45	**0.003**

Key: *EDV*, end-diastolic volume; *ESV*, end-systolic volume; *Hb*, haemoglobin; *IVSd*, interventricular septum diastole; *LBM*, lean body mass; *LV*, left ventricle; *LVIDd*, LV internal diameter diastole; *LVPWd*, LV posterior wall diastole; *PHV*, peak height velocity; *SV*, stroke volume.

Bivariate correlation analysis was performed to identify independent associations with $\dot{V}O_{2max}$ using pooled trained and untrained *z*-score values. Analysis of cardiac structural variables included boys, pre-PHV (total, *n* = 39 (trained, *n* = 23; untrained, *n* = 16)) and post-PHV (total, *n* = 34 (trained, *n* = 19; untrained, *n* = 15)), girls, pre-PHV (total, *n* = 39 (trained, *n* = 22; untrained, *n* = 17)) and post-PHV (total, *n* = 41 (trained, *n* = 22; untrained, *n* = 19)). Analysis of Hb mass and blood volume included boys, pre-PHV (total, *n* = 35 (trained, *n* = 23; untrained, *n* = 12)) and post-PHV (total, *n* = 34 (trained, *n* = 19; untrained, *n* = 14)), girls, pre-PHV (total, *n* = 33 (trained, *n* = 21; untrained, *n* = 12)) and post-PHV (total, *n* = 40 (trained, *n* = 22; untrained, *n* = 18)).

Table 5. Regression analyses with $\dot{V}O_{2max}$ (mL·kg^{LBM}·min) as the dependent variable for each pre- and post-PHV group using trained and untrained pooled *z*-score values

Group	Model	*b*	$r_{partial}$	*P*-value	R^2 Change	R^2_{adj}	*P*-value	*SE*	Constant Equation
Pre-PHV boys	EDV/LBM	0.494	0.494	**0.001**	0.244	0.224	**0.001**	0.893	y = 0.494x - 0.0001
Post-PHV boys	EDV/LBM	0.516	0.620	**0.0002**	0.481	0.608	**<0.0001**	0.639	y = 0.516x + 0.295x 0.282x + 0.015
	IVSd/height	0.295	0.437	**0.014**	0.098				
	Hb mass/LBM	0.282	0.395	**0.028**	0.066				
Pre-PHV girls	Hb mass/LBM	0.427	0.478	**0.007**	0.243	0.317	**0.002**	.0.799	y = 0.489x + 0.413x + 0.013
	IVSd/height	0.336	0.394	**0.028**	0.118				
Post-PHV girls	LVPWd/height	0.607	0.613	**<0.0001**	0.339	0.490	**<0.0001**	0.772	y = 0.607x + 0.416x - 0.043
	Hb mass/LBM	0.416	0.519	**0.001**	0.178				

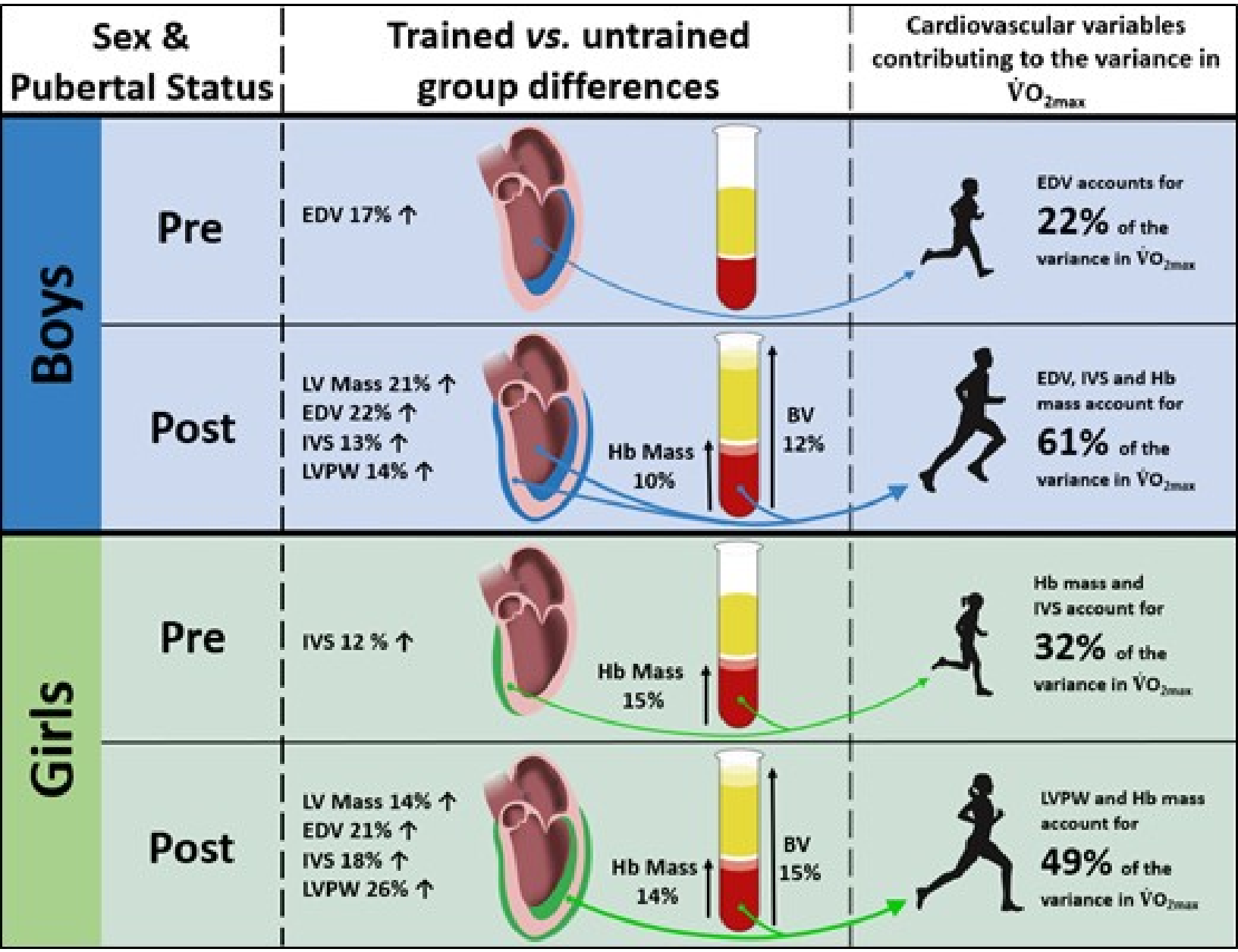
Key: *EDV*, end-diastolic volume; *Hb*, haemoglobin; *IVSd*, interventricular septum diastole; *LBM*, lean body mass; *LV*, left ventricle; *LVPWd*, LV posterior wall diastole; *PHV*, peak height velocity.

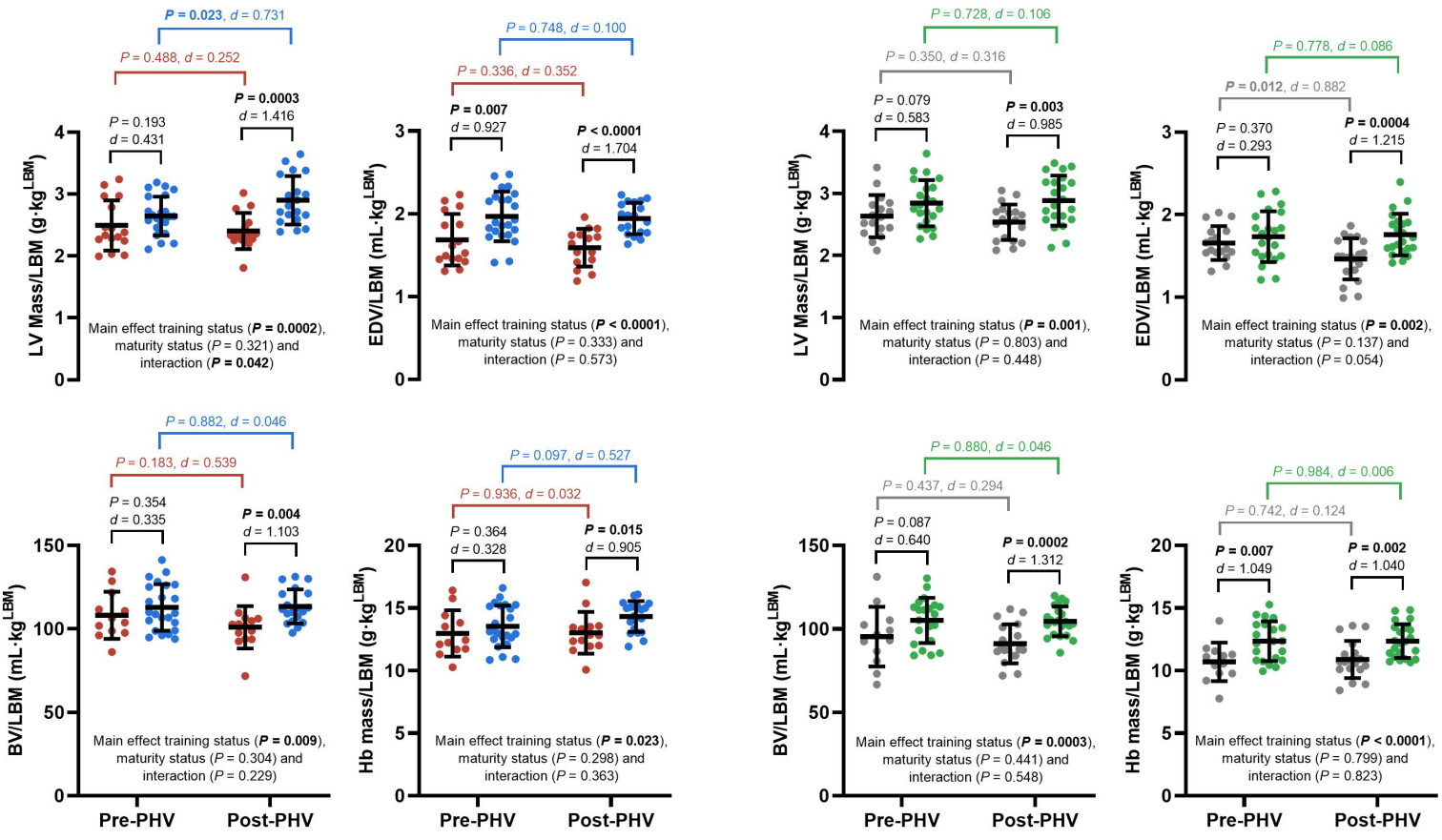
Stepwise multiple linear regression analyses were used to identify regressions models which best account for the variance in $\dot{V}O_{2max}$ using pooled trained and untrained *z*-score values. Analysis of cardiac structural variables included boys, pre-PHV (total, *n* = 39 (trained, *n* = 23; untrained, *n* = 16)) and post-PHV (total, *n* = 34 (trained, *n* = 19; untrained, *n* = 15)), girls, pre-PHV (total, *n* = 39 (trained, *n* = 22; untrained, *n* = 17)) and post-PHV (total, *n* = 41 (trained, *n* = 22; untrained, *n* = 19)). Analysis of Hb mass and blood volume included boys, pre-PHV (total, *n* = 35 (trained, *n* = 23; untrained, *n* = 12)) and post-PHV (total, *n* = 34 (trained, *n* = 19; untrained, *n* = 14)), girls, pre-PHV (total, *n* = 33 (trained, *n* = 21; untrained, *n* = 12)) and post-PHV (total, *n* = 40 (trained, *n* = 22; untrained, *n* = 18)).

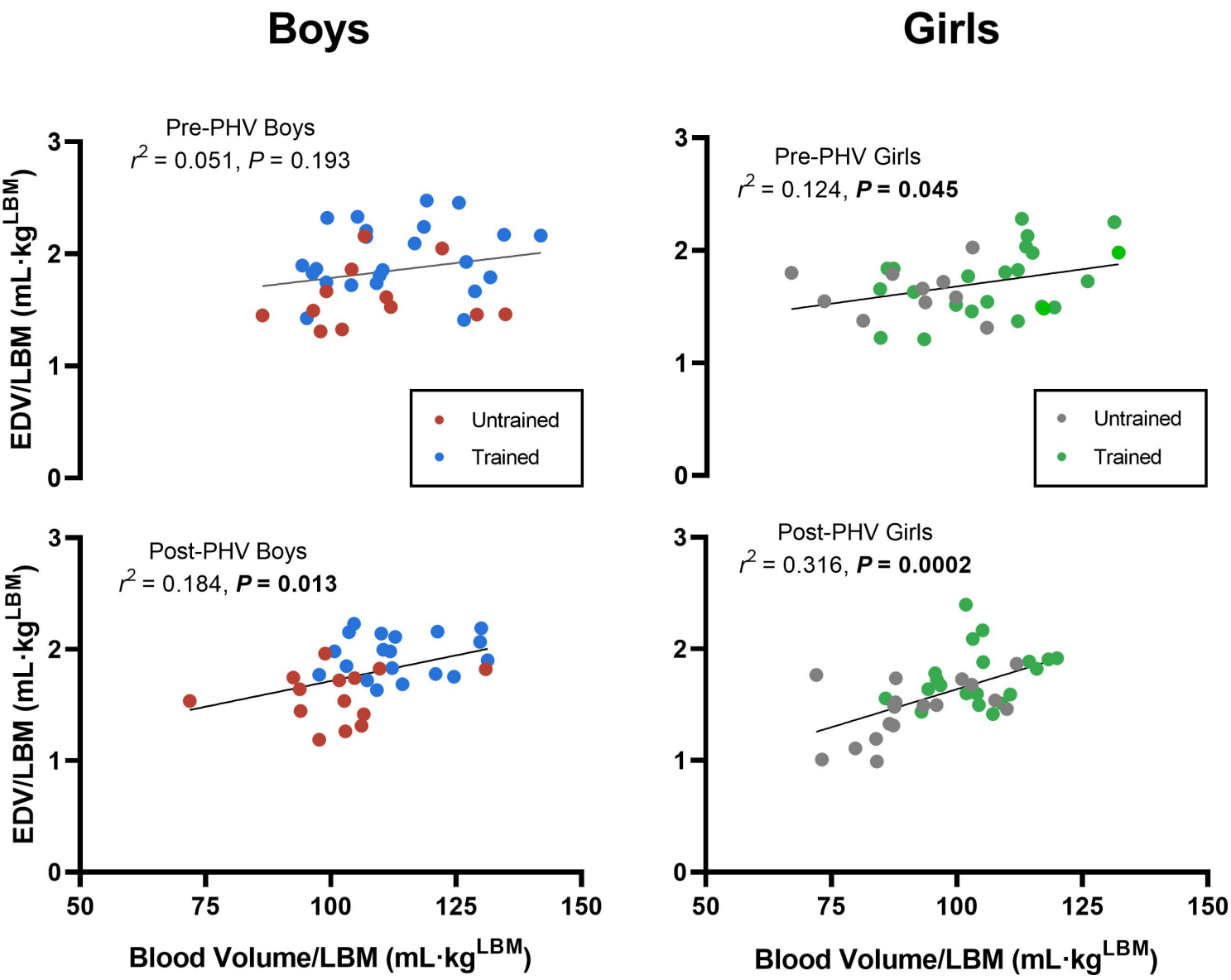
Abstract figure legend. Schematic diagram depicting cardiac structural and haematological differences between trained and untrained boys and girls, pre-peak height velocity (PHV) and post-PHV alongside cardiac and haematological variables contributions to the variance in $\dot{V}O_{2max}$. Cardiac and haematological variables are greater in trained *vs*. untrained pre-pubertal children, and a greater number and magnitude of differences are observed at post-PHV. These variables provide significant predictive models for maximal oxygen consumption in children and are much stronger post-PHV, suggesting that other important determinants within the oxygen transport chain could account for the majority of variance in $\dot{V}O_{2max}$ before puberty.

Figure 1. Endurance-trained *vs*. untrained between-group differences in left ventricular (LV) mass, end-diastolic volume (EDV), blood volume and haemoglobin (Hb) mass for boys and girls, pre-peak height velocity (PHV) and post-PHV. Statistical comparisons were performed using two-way ANOVAs with training and maturity status as fixed factors. Independent samples *t*-tests were then used to identify differences where a main effect or interaction existed. Effect sizes calculated using Cohen's *d*. Participants for LV mass and EDV comparisons included boys, pre-PHV (trained, *n* = 23 *vs.* untrained, *n* = 16) and post-PHV (trained, *n* = 19 *vs.* untrained, *n* = 15), girls, pre-PHV (trained, *n* = 22 *vs.* untrained, *n* = 17) and post-PHV (trained, *n* = 22 *vs.* untrained *n* = 19). Participants for blood volume and Hb mass comparisons included boys, pre-PHV (trained, *n* = 23 *vs.* untrained, *n* = 12) and post-PHV (trained, *n* = 19 *vs.* untrained, *n* = 14), girls, pre-PHV (trained, *n* = 21 *vs.* untrained, *n* = 12) and post-PHV (trained, *n* = 22 *vs.* untrained, *n* = 18).

Figure 2. Linear regression analysis between end-diastolic volume (EDV) and blood volume for boys and girls, pre-peak height velocity (PHV) (total boys, *n* = 35 (trained, *n* = 23; untrained, *n* = 12) and total girls, *n* = 33 (trained, *n* = 23; untrained, *n* = 10)) and post-PHV (total boys, *n* = 33 (trained, *n* = 19; untrained, *n* = 14) and total girls, *n* = 39 (trained, *n* = 21; untrained, *n* = 18)). Statistical significance on the figures are from the linear regression analyses to indicate slope significance, with the r^2 also reported to indicate the relationship strength.


Sex & Pubertal Status
Trained vs. untrained group differences
Cardiovascular variables contributing to the variance in $\dot{V}O_{2max}$
Boys
Pre
EDV 17% ↑
EDV accounts for 22% of the variance in $\dot{V}O_{2max}$
Post
LV Mass 21% ↑
EDV 22% ↑
IVS 13% ↑
LVPW 14% ↑
Hb Mass 10%
BV 12%
EDV, IVS and Hb mass account for 61% of the variance in $\dot{V}O_{2max}$
Girls
Pre
IVS 12 % ↑
Hb Mass 15%
Hb mass and IVS account for 32% of the variance in $\dot{V}O_{2max}$
Post
LV Mass 14% ↑
EDV 21% ↑
IVS 18% ↑
LVPW 26% ↑
Hb Mass 14%
BV 15%
LVPW and Hb mass account for 49% of the variance in $\dot{V}O_{2max}$


Boys
Girls
LV Mass/LBM (g·kg^LBM)
EDV/LBM (mL·kg^LBM)
BV/LBM (mL·kg^LBM)
Hb mass/LBM (g·kg^LBM)
P = 0.023, d = 0.731
P = 0.488, d = 0.252
P = 0.193
d = 0.431
P = 0.0003
d = 1.416
Main effect training status (P = 0.0002), maturity status (P = 0.321) and interaction (P = 0.042)
P = 0.748, d = 0.100
P = 0.336, d = 0.352
P = 0.007
d = 0.927
P < 0.0001
d = 1.704
Main effect training status (P < 0.0001), maturity status (P = 0.333) and interaction (P = 0.573)
P = 0.728, d = 0.106
P = 0.350, d = 0.316
P = 0.079
d = 0.583
P = 0.003
d = 0.985
Main effect training status (P = 0.001), maturity status (P = 0.803) and interaction (P = 0.448)
P = 0.778, d = 0.086
P = 0.012, d = 0.882
P = 0.370
d = 0.293
P = 0.0004
d = 1.215
Main effect training status (P = 0.002), maturity status (P = 0.137) and interaction (P = 0.054)
P = 0.882, d = 0.046
P = 0.183, d = 0.539
P = 0.354
d = 0.335
P = 0.004
d = 1.103
Main effect training status (P = 0.009), maturity status (P = 0.304) and interaction (P = 0.229)
P = 0.097, d = 0.527
P = 0.936, d = 0.032
P = 0.364
d = 0.328
P = 0.015
d = 0.905
Main effect training status (P = 0.023), maturity status (P = 0.298) and interaction (P = 0.363)
P = 0.880, d = 0.046
P = 0.437, d = 0.294
P = 0.087
d = 0.640
P = 0.0002
d = 1.312
Main effect training status (P = 0.0003), maturity status (P = 0.441) and interaction (P = 0.548)
P = 0.984, d = 0.006
P = 0.742, d = 0.124
P = 0.007
d = 1.049
P = 0.002
d = 1.040
Main effect training status (P < 0.0001), maturity status (P = 0.799) and interaction (P = 0.823)
Pre-PHV
Post-PHV


Boys
Girls
Pre-PHV Boys
r^2 = 0.051, P = 0.193
Pre-PHV Girls
r^2 = 0.124, **P = 0.045**
Post-PHV Boys
r^2 = 0.184, **P = 0.013**
Post-PHV Girls
r^2 = 0.316, **P = 0.0002**
Untrained
Trained
EDV/LBM (mL·kg^{LBM})
Blood Volume/LBM (mL·kg^{LBM})
0
1
2
3
50
75
100
125
150