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Age at start of endurance training is associated with patterns of left ventricular hypertrophy in middle-aged runners

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ABSTRACT

Background: Left ventricular hypertrophy (LVH) is a physiological adaptation to long-term endurance training. We investigated the impact of age at start of endurance training on LV geometry in a cohort of male, middle-aged, non-elite endurance athletes.

Methods: A total of 121 healthy, normotensive, Caucasian participants of a 10-mile race were recruited and assessed with an echocardiogram and a comprehensive interview. Athletes were classified based on patterns of LVH.

Results: Thirty-five athletes (31%) had LVH. Athletes with eccentric LVH (16%) were significantly younger at start of endurance training compared to athletes with concentric LVH (15%, 14 ± 5 years vs. 31 ± 8 years; $P < 0.001$). Although the yearly volume of endurance training was comparable between athletes with eccentric and concentric LVH, athletes with eccentric LVH had shorter race times. All athletes with an increased LV end diastolic volume index (LVEDVI; ≥74 ml/m^2) started endurance training before or at age 25.

Conclusions: In our cohort of non-elite middle-aged runners, eccentric LVH was found only in athletes with an early start of endurance training. In case of a mature starting age, endurance training may, contrary to what is commonly assumed, also lead to concentric LVH. The consideration of endurance training starting age may lead to a better understanding of morphological adaptations of the heart.

1. Introduction

Regular long-term exercise results in a series of adaptations of cardiac structure. This phenomenon, also called the athlete's heart, has been known for over a century and observed in different athletic populations [1–4]. The 'Morganroth Hypothesis' (MH) formed a milestone for the understanding of these adaptations and was subsequently widely adopted. This hypothesis states that the type of training plays a central role in the differential adaptation to exercise stress: Endurance training is proposed to lead, as a consequence of volume overload, to eccentric left ventricular hypertrophy (LVH), whereas strength training, as a consequence of pressure overload, to concentric LVH [5]. Despite ample evidence, the MH has been challenged by at least 6 recent studies. Utomi et al. and Spence et al. described a lack of concentric LVH in strength-trained athletes [6–8]. Caselli et al. demonstrated a balanced adaptation of LV mass and LV volume regardless of type of training [9]. Arbab-Zadeh et al. showed that the LV responded to endurance training with initial concentric but not eccentric remodeling during the first 6 to 9 months after commencement, with a normalization of mass-to-volume ratio thereafter [10]. Finally, Finocchiaro et al. observed that a significant proportion of endurance-trained elite athletes showed concentric LVH [11].

Concentric LVH is characterized by an overproportional increase in wall thickness compared to the cavity dimensions. Eccentric LVH, on the other hand, is the result of a proportionate increase in LV cavity dimensions and wall thickness [12,13]. A multivariate analysis based on data of a large Italian elite athlete population showed that 72% of variability in LV cavity dimension was attributable to non-genetic factors, such as body surface area (BSA), type of sport, gender and age [1]. The remaining 25% of variability could not be explained and was ascribed to genetic factors [14,15].

While the MH was primarily based on studies in young elite athletes [16], studies on middle-aged amateur athletes are rare. Whether findings from young athletes can be translated to previously sedentary persons starting endurance training at an advanced age is questionable. It is a relatively recent phenomenon that previously sedentary persons take up participation in endurance competitions requiring a large volume of training, which may be why studies including older and previously sedentary athletes are rare. It is plausible that the adaptive responses of the heart and the cardiovascular system may differ between peripubertal

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and mature aspiring athletes, similar to what has been well established in bone [17,18].

The central hypothesis of the present study was that the morphological cardiac adaptation to endurance training is a function of age at start of endurance training, with athletes starting endurance training at a more mature age having a lesser potential for cavity enlargement. Therefore we assessed the effect of starting age on LV geometry in a cohort of male, middle-aged, non-elite endurance athletes.

2. Methods

2.1. Participants and protocol

The Grand Prix of Bern is a popular 10 mile race in Switzerland with over 30,000 participants annually. Male non-elite runners were recruited for two studies on endurance exercise and atrial remodeling as previously described [19,20]. Runners aged 30 years and older, with and without a history of former long-distance runs, were included. Exclusion criteria were a history of cardiovascular disease, medication intake, or cardiovascular risk factors, in particular arterial hypertension, defined as an office blood pressure (BP) ≥140/90 mm Hg at the initial visit [21].

Athletes included in the above cited studies were contacted by e-mail and/or postal mail to arrange a comprehensive phone interview on their sports history. The interview included questions regarding their sports disciplines based on the Mitchell classification [22,23], starting age of the concerned disciplines and average volume of training per week of concerned sports disciplines on a year by year basis. The calculation of average training hours was determined by the athletes' estimation and/or exercise diary. Age at start of endurance sports career and, if applicable, average volume of competitions per year (in hours), as well as longer training interruptions were also recorded and accounted for in the calculations. Endurance training starting age was defined as the age when athletes performed at least 2 h of endurance training per week. Lifetime cumulative training hours according to Mitchell sports categories were calculated using the following formula: average training hours per sports category and per week × 52 × training years [19,20], calculated on a year by year basis if volume varied. Mitchell classes CI-CIII were further subdivided in cumulative lifetime ball sports including soccer, tennis, handball, field hockey, badminton, basketball, ice hockey, and cumulative lifetime endurance training including running, orienteering, cross-country skiing, swimming, rowing, cycling and triathlon. All athletes provided written informed consent and the protocol was approved by the local ethics committee.

2.2. Transthoracic echocardiography

Standard two-dimensional TTE was performed on a Phillips iE33 System (X5-1 transducer, Phillips Medical Systems, Zurich, Switzerland). LV internal diameter (LVID), interventricular septum (IVS) and posterior wall thickness (PWT) were measured in M-mode from the parasternal long-axis view at end-diastole. LV mass was calculated based on the cube formula: LV mass $= 0.8 \times 1.04 \times [(IVS + LVID + PWT)^3 - LVID^3] + 0.6$ g and indexed for BSA [12]. LVH was defined as LV mass/BSA ≥ 116 g/m^2 [12,24].

LV end-diastolic (LVEDV), and LV end-systolic volumes (LVESV) were calculated using the biplane method of disks summation technique. Volume measurements were based on tracings of the blood-tissue interface in the apical four- and two-chamber views. At the mitral valve level, the contour was closed by connecting the two opposite sections of the mitral ring with a straight line. LV length was measured from this line to the apical point of the LV contour. All volumes were indexed for BSA [12,13].

Phenotypic characterization of the LV geometry was based on the 4-tiered classification for LVH as recently proposed by Khouri and co-workers [25]. Echocardiographic thresholds for increased concentricity were ≥ 9.1 g/ml$^{2/3}$ and for increased LVEDV/BSA ≥76 ml/m^2 [24].

LV systolic function was expressed as ejection fraction (EF), derived from the LVEDV and LVESV. LV diastolic function was assessed by pulse-wave and tissue Doppler in the apical four-chamber view. Peak early and late diastolic velocities at the septal and lateral side of the mitral annulus were recorded and the mean value was calculated and defined as E′ mean and A' mean [12].

2.3. Data analysis

The data was analysed with SPSS Software for Windows (Version 17.0, SPSS Inc., Chicago, USA). The normality of quantitative variables was inspected visually and homogeneity of variances tested by Levene test. Normally distributed data were presented as mean ± standard deviation (SD), and non-normally distributed variables as median and interquartile range (IQR).

All athletes were classified by patterns of LVH [26] and resulting groups were compared with regard to anthropometric and echocardiographic data, as well as detailed sports history. Normally distributed variables with homogenous variances were compared by univariate ANOVA with Tukey post-hoc testing or Dunnet T3 post-hoc testing if variances were heterogeneous. Between group comparison of data with non-parametric distribution was performed by Kruskal-Wallis tests with Bonferroni-adjusted Mann-Whitney-U post-hoc testing.

We performed linear regression models for the dependent variable LVEDV. Rather than performing models for LVEDV indexed by BSA, we decided to enter BSA as an independent variable into the models. This allowed a direct comparison with the model presented by Pelliccia and colleagues [14]. To identify the independent parameters for forced inclusion into the models we performed a correlation matrix with Pearson and Spearman correlation coefficients between LVEDV and the following variables: BSA, BMI, HR at rest, systolic BP, age, age at start of endurance training, hours of endurance training per year, 10 mile race time, cumulative lifetime training hours for all, high dynamic, and endurance sports. We only entered independent parameters with significant linear relationship to LVEDV into the models. In case of collinearity between independent parameters, we chose to enter only the parameter with the stronger association with LVEDV. Further, we performed a logistic regression model for athletes with LVH with eccentric and concentric LVH as binary dependent variable and the three training variables age at start of endurance training, cumulative lifetime endurance training, and yearly endurance training as independent variables. We also performed univariate logistic regression models with the same dependent variable and the independent training variables entered individually into the models. Alpha was set at 0.05.

3. Results

3.1. Study subjects

A total of 174 male runners were contacted by mail. An interview lasting approximately 45 min was performed with 121 athletes, of whom 98 completed the interview by phone and 23 chose to complete a questionnaire by postal mail. Mean and SD of age was 42 ± 8 years. A broad spectrum of endurance athletes was included, ranging from leisure-time runners with a first participation in a 10 mile race up to semi-professional long-distance runners with >20,000 cumulative lifetime endurance training hours (median 3692, IQR 1963-8398).

3.2. LV geometry

Baseline characteristics and echocardiographic data are shown in Table 1 stratified according to patterns of LVH. Athletes with eccentric LVH had a lower HR and greater LVEDVI than all other athletes. Furthermore, athletes with eccentric LVH had a significantly lower posterior and relative wall thickness than athletes with concentric LVH.

Characteristics of sports history, stratified according to patterns of LVH, are shown in Table 2. Thirty-five athletes (31%) had LVH. Significant differences between groups were found for age at start of endurance training, 10 mile race time and cumulative lifetime training hours for all, high dynamic, and endurance sports. Athletes with eccentric LVH had significantly more cumulative lifetime endurance training hours compared to athletes with concentric LVH. However, the amount of endurance training hours per year did not differ between athletes with eccentric and those with concentric LVH. Athletes with eccentric LVH were younger at start of endurance training and had shorter race times compared to athletes with normal LV geometry or concentric LVH.

The influence of age at start of endurance training on LV geometry can be seen in Fig. 1. All athletes with eccentric LVH started endurance training at an age ≤ 25 years (mean 14 ± 5 years). On the other hand, age at start of endurance training in athletes with concentric LVH was considerably older (31 ± 8 years), and only three athletes (17%) in this group started endurance training between age 17–25. Similarly all athletes with an increased LVEDVI (≥74 ml/m^2) started endurance training at an age ≤ 25 years (mean 14 ± 5 years).

3.3. Determinants of LV cavity size

There was a significant association between LVEDV and the following parameters: Age (Spearman correlation coefficient − 0.30), BSA (0.19), HR at rest (−0.46), age at start of endurance training (−0.46), endurance training per year (0.25), 10 mile race time (−0.44) and cumulative lifetime training hours for all (0.27), high dynamic (0.29), and endurance sports (0.32, all $P < 0.01$, except BSA $P < 0.05$). The variables most strongly related to LVEDV were age at start of endurance training and HR at rest. Age and age at start of endurance training were correlated (0.35, $P < 0.001$). Age at start of endurance training