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Differentiating hypertrophic cardiomyopathy from athlete's heart: An electrocardiographic and echocardiographic approach $\overset{\diamond}{\sim}, \overset{\diamond}{\sim} \overset{\diamond}{\sim}$

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Abstract Differential diagnosis of hypertrophic cardiomyopathy (HCM) vs athlete's heart is challenging in individuals with mild-moderate left-ventricular hypertrophy. This study aimed to assess ECG and echocardiographic parameters proposed for the differential diagnosis of HCM. The study included 75 men in three groups: control (n = 30), "gray zone" athletes with interventricular septum (IVS) measuring 13–15 mm (n = 25) and HCM patients with IVS of 13–18 mm (n = 20). The most significant differences were found in relative septal thickness (RST), calculated as the ratio of 2 x IVS to left ventricle end-diastolic diameter (LV-EDD) (0.37, 0.51, 0.71, respectively; p < 0.01) and in spatial QRS-T angle as visually estimated (9.8, 33.6, 66.2, respectively; p < 0.01). The capacity for differential HCM diagnosis of each of the 5 criteria was assessed using the area under the curve (AUC), as follows: LV-EDD < 54 (0.60), family history (0.61), Twave inversion (TWI) (0.67), spatial QRS-T angle > 45 (0.75) and RST > 0.54 (0.92). Pearson correlation between spatial QRS-T angle > 45 and TWI was 0.76 (p 0.01). The combination of spatial QRS-T angle > 45 and RST > 0.54for diagnosis of HCM had an AUC of 0.79. The best diagnostic criteria for HCM was RST > 0.54. The spatial QRS-T angle > 45 did not add sensitivity if TWI was present. No additional improvement in differential diagnosis was obtained by combining parameters. © 2016 Elsevier Inc. All rights reserved.

Keywords: Hypertrophic cardiomyopathy; Athlete's heart; Echocardiography; Spatial QRS-T angle

Introduction

High-intensity training is associated with morphological and functional cardiovascular changes (athlete's heart) due to an increment in the hemodynamic load. These adaptive changes show high interindividual variability between athletes, depending on individual susceptibility and the type of training in terms of frequency, intensity and time [1].

In general, these changes are mild, but in some highly trained athletes, cardiac remodeling has characteristics similar to hypertrophic cardiomyopathy (HCM). The differential diagnosis of these two entities has important clinical implications, as HCM is the leading cause of sudden death among athletes younger than 35 years [2], and has important psychological and economic consequences because it is the basis for disqualification from competitive sport [3].

The differential diagnosis of athlete's heart vs HCM can be difficult in situations where a "gray zone" (13-15 mm wall thickness) exists between these two entities [4]. Recently, the utility of vectorcardiography for measuring the spatial angle formed between the QRS and the T-wave has been described as a prognostic factor in cardiomyopathies [5] and has also been used to improve the ECG-based screening of HCM in pediatric patients compared to the Italian or Seattle criteria. [6]. Nonetheless, current criteria for electrocardiographic (ECG) diagnosis of left-ventricular hypertrophy (LVH) have a low diagnostic accuracy: hypertrophy affects action-potential morphology and intraventricular conduction, and therefore changes in the axes of the QRS and T-waves may manifest as an increase in spatial ORS-T angle. Adding echocardiographic variables to ECG analysis may yield an accurate diagnosis of LVH.

 $[\]stackrel{\text{\tiny them}}{\Rightarrow}$ The first 2 authors contributed equally to this article.

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Likewise, the measurement of peak voltage QRS complex and T-wave in three leads (II-V2-V6) using a simple visual technique [7] has shown good correlation with the vectorcardiogram method described by Kors et al. to assess Frank XYZ leads [8].

The aim of our study was to establish the value of each of the most frequently used criteria for differential diagnosis, with the addition of two new variables, the spatial QRS-T angle and relative septal thickness (RST) calculated as the ratio between 2 x interventricular septum (IVS) and left-ventricle end diastolic diameter (LV-EDD) in the differential diagnosis.

Methods

A total of 75 Caucasian men were divided into three groups: a) control (n = 30 sedentary individuals); b) athletes participating in competitive sports with IVS of 13-15 mm, recruited in the pre-participation screening at three high-performance centers as follows: Basketball, 3; Cycling, 2; Gymnastics, 1; Handball, 3; Ice Hockey, 1; Rugby, 1; Soccer, 7; Swimming, 3; Tennis, 1; Athletics, 3 (n = 25); and c) University Hospital patients with HCM and IVS of 13-18 mm (n = 20). The study conformed to the guidelines for reporting observational studies and to the standards set by the Declaration of Helsinki. Approval was granted by the Research Ethics Committee of Hospital Clinic, Barcelona. All participants underwent a medical evaluation that included a personal and family history, physical examination, 12-lead ECG (Fukuda Denshi Co. Ltd., Japan), and Doppler echocardiography (Vingmed Vivid-7, General Electric, Milwaukee, Wisconsin, USA or Aplio 400, Toshiba, Japan).

We calculated the spatial QRS-T angles through utilization of the reduced-lead visual estimation technique described by Cortez et al. [7]. that employs the quasiorthogonal transform of Kors' et al. [8].

The following variables were compared between the three study groups: family history of HCM, T-wave inversion, spatial QRS-T angle, left atrial (LA) diameter, LV-EDD, IVS, relative wall thickness (RWT): (2 x PW/LD-EDD); RST: (2 x IVS/LV-EDD), IVS/posterior wall (PW) ratio, index left-ventricular mass.

The diagnosis of HCM was based on the assessment of family history, ECG, echocardiography and cardiac magnetic

resonance (CMR). The RST (Fig. 1) and the spatial QRS-T angle using visual estimation of the regression Kors (Fig. 2) were calculated for each participant.

Differential diagnostic ability was assessed by sensitivity, specificity, and area under the curve (AUC) in the study population for the items described in previous studies as suggesting the diagnosis of HCM and for the variables that differed significantly between groups. The point of greatest sensitivity and specificity was identified using the Youden index; continuous variables were then transformed into dichotomous.

Statistical analysis

A general descriptive analysis was carried out. Quantitative variables were expressed as mean \pm standard deviation. Discrete variables were presented as number of cases and percentages. The features in all three study groups were compared using one-way ANOVA with Bonferroni post-hoc analysis to determine differences between each group. Youden index was used to calculate the best cut-off point for the new variables proposed. All data were analyzed using the statistical package IBM SPSS (version 19, SPSS Inc., Chicago, New York, USA).

Results

Baseline characteristics of the 3 groups are shown in Table 1. Mean age was similar for all participants (35.7 ± 5.86 , 29.7 ± 7.87 , 35.4 ± 15.4 , respectively; p-ANOVA 0.058); while the other characteristics regarding family history, ECG and echocardiography were significantly different among groups. Left-ventricular indexed mass was similar between athletes and HCM patients; however, LV-EDD was lower and LA diameter was higher in the HCM group. The RST and spatial QRS angle were useful to differentiate these two groups.

We evaluated the differential diagnostic ability of the parameters previously described and those obtained using the Youden index for our population, which generated two new criteria: RST > 0.54 and spatial QRS-T angle >45 (Table 2). The best predictor variables for HCM were RST > 0.54 (AUC 0.92); and spatial QRS-T angle >45 (AUC 0.75); however, we observed a high Pearson correlation between the presence of negative T-waves and spatial QRS-T angle >45 (0.74; p = 0.01).



Fig. 1. Parasternal long view with an example of each group: A) control, B) athlete with IVS of 13–15 mm, C) HCM patient with IVS of 13–15 mm (the arrows show the increase of IVS and decrease of LV-EDD in the HCM group). IVS, interventricular septum; HCM, hypertrophic cardiomyopathy; LV-EDD, left ventricle end-diastolic diameter.

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