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Prominent left ventricular trabeculations in competitive athletes: A proposal for risk stratification and management☆

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ABSTRACT

Background: Recently, an unexpectedly large prevalence of Left Ventricular Non Compaction (LVNC) has been reported in athletes, raising the question of the appropriateness of current diagnostic criteria. We sought to describe prevalence and clinical characteristics of athletes with suspected LVNC in a large cohort of Olympic athletes.

Methods: Over 29 months, 2501 consecutive athletes underwent a cardiac evaluation including physical examination, ECG, exercise test and echocardiography. Additional investigations (Cardiac Magnetic Resonance and/or genetic testing) were selectively performed in athletes with abnormal ECGs, ventricular arrhythmias, borderline LV dysfunction or positive family history.

Results: Of the 2501 athletes, 36 (1.4%) showed prominent trabeculations suggestive for LVNC. Of these, 3 (0.1%) were considered to be affected by LVNC, based on presence of LV dysfunction (ejection fraction < 50%) and/or positive family history and genetic testing; these athletes were cautiously restricted from competitions and entered a clinical follow-up program. The remaining 33 athletes, in the absence of LV impairment or familial cardiac diseases, were considered normal ($n = 24$) or unlikely affected ($n = 9$), regardless of the extent of the trabeculations.

Conclusions: In a large athlete population, a marked LV trabecular pattern was seen in 1.4%. Only a small subset of these athletes (0.1%) showed familial, clinical and morphologic changes supporting the diagnosis of LVNC. In the vast majority of the athletes, the increased trabeculations were not associated with LV dysfunction and/or positive family history, likely representing a morphologic LV variant, deprived of clinical significance.

1. Introduction

Over the last years an increasing attention has been paid to left ventricular non-compaction (LVNC), phenotypically characterized by a double-layered myocardial wall, with a thinner epicardial compact layer and a thicker endocardial one, increased trabeculations and deep intertrabecular recesses [1–5]. Most recently, as a likely consequence of sophisticated contemporary imaging techniques as well as increased awareness of this condition, an unexpectedly large number of individuals with imaging suggestive for LVNC have been described worldwide, including young and asymptomatic subjects [6–8].

Diagnosis of LVNC is particularly relevant in the setting of cardiovascular (CV) evaluation of competitive athletes, in consideration of the potential morphologic overlap between this pathologic condition and the prominent trabeculations, which may occasionally be observed in the context of the physiologic remodeling of the athlete's heart [9–11].

Differentiation of innocent morphologic variants from true LVNC represents a new task for clinicians and cardiologists, and may be challenging on an individual basis. While it is important to correctly identify LVNC, in consideration of the potential adverse clinical consequences, misdiagnosis of clinically benign phenocopies may lead to unwarranted restriction from competitive sport of otherwise healthy athletes, with detrimental psychological, social and economic consequences [11–13].

In the present study, therefore, we sought to describe prevalence, morphologic features and clinical presentation of the prominent trabeculation pattern suggestive for LVNC in a large cohort of competitive athletes, with the aim to define the criteria for differential diagnosis and appropriate management.

☆ The authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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2. Methods

2.1. Study population

From January 2012 to May 2015, 2501 consecutive highly-trained athletes, members of the Italian National Team were evaluated at the Institute of Sports Medicine and Science in Rome, in the context of preparticipation screening for the London 2012 Olympic games, Sochi 2014 Winter Olympic Games, and Baku 2015 European Games. The mean age of the athletes was 25 ± 6 years (range, 15 to 45 years), 1550 were males (62%) and the large majority were Caucasians (99%).

All have been competing for ≥3 years prior entering our program, and were training regularly at the time of our evaluation. Cardiovascular evaluation included clinical history, physical examination, resting and exercise 12-lead electrocardiogram (ECG) and two-dimensional Doppler echocardiography.

Athletes were classified in 4 subgroups according to the predominant characteristics of training, as previously reported [14]: 1. skill (i.e. primarily technical activities, $n = 593$) including golf, table tennis, equestrian sports, shooting, karate, taekwondo and sailing; 2. power (i.e. primarily isometric activities, $n = 453$) including weightlifting, wrestling and short-distance running (100–200 m); 3. mixed (e.g. disciplines with both isometric and isotonic components; $n = 685$), including soccer, basketball, volleyball, handball, water polo, tennis and fencing; 4. endurance (e.g. primarily isotonic activities; $n = 734$) including rowing, canoeing, swimming, long-distance running and marathon, cycling, triathlon and pentathlon [14].

The study protocol was approved by the locally appointed ethics committee. Informed consent was waived for all athletes (or their legally authorized representative).

2.2. Electrocardiography

Standard 12-lead electrocardiography was performed with the subject in the supine position and recorded at 10 mV and 25 mm/s. Analysis of the ECG tracings was performed according to the most recent updated criteria [15].

2.3. Echocardiography

Two-dimensional echocardiography was performed using commercially available equipment (iE33 or EpiQ, Philips Medical Systems, Andover, MA) with a 5 MHz probe. Examinations were performed by two cardiologists with specific training and experience in the evaluation of LVNC (SC and AP). Two-dimensional measurements of LV cavity diameters, wall thickness, left atrial transverse diameter, and aortic root diameters were performed according to the European Association of Cardiovascular Imaging and American Society of Echocardiography criteria. [16] LV ejection fraction was measured using the biplane Simpson's method from the apical four- and two-chamber views. Assessment of left ventricular filling and diastolic function was performed using Pulse-Wave Doppler (PW) and Tissue Doppler Imaging (TDI) from the apical 4-chamber view as previously reported [14].

For the scope of this study we identified athletes with prominent LV trabeculations, if they fulfilled all the following criteria: 1) a double layered appearance of the myocardium with a compact epicardial layer and non-compact endocardial layer; 2) >3 prominent trabeculous formations, defined as muscle bundles of >3 mm in diameter raising from the left ventricular endocardial border in end-diastole (distinct from papillary muscles) 3) these trabeculations moved synchronously with the compacted myocardium; 4) perfusion of the intertrabecular spaces from the ventricular cavity in end-diastole on color-Doppler echocardiography (Fig. 1) [2,17].

The athletes who matched these inclusion criteria underwent additional echocardiographic investigation with the assessment of the following parameters: 1) thickness of the compact layer in diastole and systole; [13,18] 2) location of trabeculations using a 16 segments model; [19] 3) assessment of the Chin index (i.e., X/Y ratio in diastole, where X is the compact layer and Y is the distance between epicardial surface and peak of trabeculation); [4] 4) and the Jenni index, consisting of N/C ratio in systole (where N is the non-compacted layer and C is the compact layer) [2].

Additional testing, i.e., Cardiac Magnetic Resonance with late gadolinium enhancement (CMR with LGE), 24-h ECG Holter monitoring, genetic testing were selectively performed to assess risk stratification in athletes with reduced LV systolic (EF 55% or less), and/or associated ECG abnormalities (most commonly, diffusely flat or inverted T-wave), and/or ventricular tachyarrhythmias (i.e., ≥1 premature ventricular contraction (PVC) on baseline and/or ≥3 on exercise ECG), and/or positive family history for sudden death or a specific cardiomyopathy [20,21]. Neurologic evaluation was part of the general physical examination in all athletes.

2.4. Statistical analysis

Continuous data are expressed as mean ± standard deviation and categorical data as frequencies. Two-tailed p value < 0.05 was considered statistically significant. Differences between mean values for continuous variables were assessed using independent samples T test or Analysis of Variance (ANOVA) with multiple post hoc Bonferroni's tests. Differences in terms of categorical variables were assessed using X^2 tests. Statistical analysis was performed using SPSS version 22.0 (SPSS, Inc., Chicago, IL, USA).

3. Results

3.1. Demographic and clinical characteristics

Out of the overall population of 2501 athletes, 36 (1.4%) presented with a pattern of heavy trabeculations, consistent with the phenotypic diagnosis of LVNC. (Fig. 2) [22].

Demographic and clinical characteristics of this group are reported in Table 1. Of the 36 athletes, family history was positive in 2 athletes respectively for hypertrophic cardiomyopathy and for sudden cardiac death of unknown cause. On personal inquiry, 3 athletes referred palpitations. None complained syncope, angina or dyspnea. No athlete reported a family history for neuromuscular disorders.

Physical examination was normal in all; a mild systolic murmur was detected in 7 (19%) athletes with increased trabeculations, without the evidence of valvular disease on echocardiographic examination. Neurologic evaluation did not show abnormalities in any athlete.

3.2. LV morphologic characteristics

Athletes with prominent trabeculations showed LV thickness, cavity size and mass within normal limits (in relation to body size and sport participated), and not different from the remaining group. Ejection fraction was within normal limits, although mildly lower. Indexes describing diastolic function were also normal, and not different from athletes with normal LV morphology (Table 1).

The number of LV segments showing prominent trabeculations ranged from 2 to 11, averaging 5 ± 2, most commonly involving the apex. The minimum thickness of the compact layer was 5 ± 1 mm in

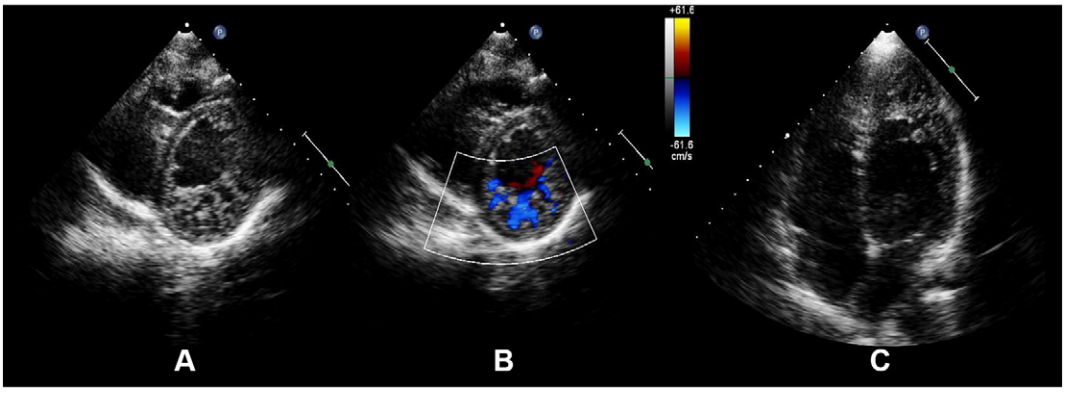

Fig. 1. Echocardiographic images from a 33 year-old male Caucasian cyclist. Short axis images (A and B) show the double layer appearance of the LV ventricle in end-diastole with a thin epicardial layer and a thicker and hypertrabeculated endocardial layer with evidence of color Doppler filling the recess from the LV cavity (B). Panel C shows the 4-chambers view; the athlete had impaired LV systolic function with ejection fraction of 45%. The Chin index was 0.26 and Jenni index was 2.20; the LV compact layer measured 4 mm in diastole and 5 mm in systole. Due to LV dysfunction he was restricted from training and competition and entered a periodic follow-up program.