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Left Ventricular Noncompaction

Anatomical Phenotype or Distinct Cardiomyopathy?

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ABSTRACT

BACKGROUND There is considerable overlap between left ventricular noncompaction (LVNC) and other cardiomyopathies. LVNC has been reported in up to 40% of the general population, raising questions about whether it is a distinct pathological entity, a remodeling epiphenomenon, or merely an anatomical phenotype.

OBJECTIVES The authors determined the prevalence and predictors of LVNC in a healthy population using 4 cardiac magnetic resonance imaging diagnostic criteria.

METHODS Volunteers >40 years of age (N = 1,651) with no history of cardiovascular disease (CVD), a 10-year risk of CVD < 20%, and a B-type natriuretic peptide level greater than their gender-specific median underwent magnetic resonance imaging scan as part of the TASCFORCE (Tayside Screening for Cardiac Events) study. LVNC ratios were measured on the horizontal and vertical long axis cine sequences. All individuals with a noncompaction ratio of ≥2 underwent short axis systolic and diastolic LVNC ratio measurements, and quantification of noncompacted and compacted myocardial mass ratios. Those who met all 4 criteria were considered to have LVNC.

RESULTS Of 1,480 participants analyzed, 219 (14.8%) met ≥1 diagnostic criterion for LVNC, 117 (7.9%) met 2 criteria, 63 (4.3%) met 3 criteria, and 19 (1.3%) met all 4 diagnostic criteria. There was no difference in demographic or allometric measures between those with and without LVNC. Long axis noncompaction ratios were the least specific, with current diagnostic criteria positive in 219 (14.8%), whereas the noncompacted to compacted myocardial mass ratio was the most specific, only being met in 61 (4.4%).

CONCLUSIONS A significant proportion of an asymptomatic population free from CVD satisfy all currently used cardiac magnetic resonance imaging diagnostic criteria for LVNC, suggesting that those criteria have poor specificity for LVNC, or that LVNC is an anatomical phenotype rather than a distinct cardiomyopathy. (J Am Coll Cardiol 2016;68:2157–65) © 2016 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Left ventricular noncompaction (LVNC) is characterized as a primary genetic cardiomyopathy by the American Heart Association, but is characterized by the European Society of Cardiologists as an "unclassified cardiomyopathy," aptly demonstrating some of the controversy that surrounds this condition (1–3). Previously considered a rare cardiomyopathy, there has been a rapid

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ABBREVIATIONS AND ACRONYMS

BNP = B-type natriuretic peptide

CMR = cardiac magnetic resonance imaging

CVD = cardiovascular disease

LVEDV = left ventricular end-diastolic volume

LVEF = left ventricular ejection fraction

LVESV = left ventricular end-systolic volume

LVGFI = left ventricular global function index

LVMVR = left ventricular mass volume ratio

LVNC = left ventricular noncompaction

LVSV = left ventricular stroke volume

proliferation in publications regarding this entity, raising the question of whether this is a result of better identification of those with the disease or whether it is being overdiagnosed due to the rapid expansion in the utilization of cardiac imaging and the ever-improving visualization of cardiac structures (4,5). More than 8% of athletes meet 1 of the 3 current echocardiographic criteria for LVNC, whereas 43% of a healthy population cohort meet the most commonly used cardiac magnetic resonance imaging (CMR) threshold for diagnosis measured on long axis cine sequences as proposed by Peterson et al. (6–8). In addition, a high prevalence of LVNC has been observed in both dilated and hypertrophic cardiomyopathies (9,10).

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Since the original CMR criteria was proposed by Petersen et al. (7), several other groups have developed alternate diagnostic criteria with improved sensitivity and specificity, utilizing measurements on both short axis systolic and diastolic views of the left ventricle as well as quantifying the compacted-to-noncompacted myocardial mass ratio (11–13). However, given the earlier findings from multiple studies utilizing multiple imaging modalities of significant noncompaction in asymptomatic cohorts free from known cardiovascular disease (CVD), it is not clear whether these new criteria help identify those with genuine disease, or whether, when applied to the general population, they will serve to further strengthen the notion of LVNC as an anatomical phenotype rather than a pathological entity. This is of significant clinical importance due to the long-term implications that currently receiving a diagnosis of LVNC entails—impacting insurance costs and necessitating long-term monitoring and follow-up. The aim of this study was to determine the prevalence of the population exhibiting LVNC, the predictors for the presence LVNC, and the physiological implications of noncompaction on cardiac function.

METHODS

STUDY POPULATION. Following local ethical committee approval, a cohort of 2,047 volunteers was invited to the imaging arm of the TASCFORCE (Tayside Screening for Cardiovascular Events) study. Volunteers were enrolled into the study if they: 1) were more than 40 years of age; 2) were free from CVD or other indication for statin therapy as recommended by the Scottish Intercollegiate Guidelines Network (SIGN) report 97 for "Risk Estimation and the Prevention of Cardiovascular Disease" published in February 2007; 3) had a serum B-type natriuretic peptide (BNP) level greater than their gender specific median; and 4) had a 10-year risk of coronary heart disease <20% as predicted by the Adult Treatment Panel III algorithm (14). Exclusion criteria included the following: 1) pregnancy; 2) known primary muscle disease; 3) known atherosclerotic disease—including angina, previous myocardial infarction, peripheral arterial disease, amputation, previous revascularization surgery, hypertension, heart failure, or cerebrovascular event; 4) known diabetes; 5) active liver disease; 6) other known illness or contraindication to magnetic resonance imaging (MRI); 7) participation in another clinical trial; 8) inability to give informed consent; 9) known alcohol abuse; and 10) a blood pressure >145/95 mm Hg. Details of the TASCFORCE study arms and design are encapsulated within **Figure 1**.

IMAGE ACQUISITION. The MRI protocol has been described in detail elsewhere (15). In brief, imaging was performed using a 3-T Magnetom Trio Scanner (Siemens, Erlangen, Germany). Whole-body magnetic resonance angiography was performed using a dual-bolus injection technique with the CMR cines performed before the first contrast injection, and the late gadolinium enhancement sequences performed between the first and second contrast bolus injections. For CMR, a body matrix radiofrequency coil (6 elements) was used in combination with a spine array (up to 24 elements).

Electrocardiograph (EKG)-gated segmented breath-hold cinematic (CINE) TrueFISP (Siemens, Erlangen, Germany) images were acquired in the horizontal and vertical long axes, and in the short axis from the atrioventricular ring to the left ventricular (LV) apex using a 2-dimensional ECG-gated breath-hold segmented (CINE) TrueFISP sequence. Retrospective ECG gating was used, with 25 cardiac phases reconstructed (25 lines per segment) and 2 image slices acquired per breath-hold. Parallel imaging was also implemented (integrated parallel acquisition technique [iPAT x2]).

IMAGE ANALYSIS. LV mass and volume quantification was performed as previously described (15). Values were normalized to height$^{1.7}$. For noncompaction assessment, each of the 4 diagnostic criteria was measured as follows (**Central Illustration**):

1. Long axis noncompaction (LAX) was measured on the horizontal and vertical LAX cine sequences, which were analyzed at end-diastole. The thickness of the compacted and noncompacted