Reproducibility of Echocardiographic Diagnosis of Left Ventricular Noncompaction

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Background: Left ventricular noncompaction (LVNC) cardiomyopathy is variably defined by numerous trabeculations, deep intertrabecular recesses, and noncompacted-to-compacted (NC/C) ratio >2. Limited studies exist on the reproducibility of diagnosing LVNC.

Methods: Clinical records of patients diagnosed with LVNC by echocardiography were reviewed. Blinded review of the index echocardiogram for all patients and a 1:1 match without LVNC was performed independently by two observers, measuring the number of trabeculations and the NC/C ratio.

Results: A total of 104 patients with LVNC were included in the study, 52 with no congenital heart disease (NCongHD) and 52 with congenital heart disease (CongHD). The duration of follow-up was 7.2 years (range, 0.5–23.1 years) for NCongHD and 8.2 years (range, 0–33.3 years) for CongHD. Agreement between observers in determining zero to three versus more than three trabeculations was 59% (NCongHD) and 73% (CongHD). Agreement in measuring an NC/C ratio ≤ 2 versus > 2 was 79% (NCongHD) and 74% (CongHD). Agreement with the original reader in diagnosing LVNC was 67%. There was no association between the number of trabeculations or the NC/C ratio and the likelihood of a major event. Patients with moderate or severe left ventricular dysfunction at the time of diagnosis were more likely to undergo cardiac transplantation or die compared with those with normal or mild dysfunction (NCongHD, 22% vs 0%, $P = .01$; CongHD, 39% vs 3%, $P = .001$).

Conclusions: The reproducibility of making measurements to diagnose LVNC by accepted criteria is poor. Heart transplantation and death are associated with significant ventricular dysfunction and not with increased trabeculations or NC/C ratios. (J Am Soc Echocardiogr 2012;25:194-202.)

Left ventricular (LV) noncompaction (LVNC) has been recognized as a primary, genetic cardiomyopathy by the American Heart Association, though little consensus exists on the etiology, diagnostic criteria, incidence, or clinical outcomes associated with LVNC.[1-16] Multiple diagnostic schema (Figure 1) have been proposed since the original description, including the following three that are most widely used: (1) Jenni *et al.*,[8] noncompacted-to-compacted (NC/C) ratio ≥ 2 measured in end-systole, no coexistent cardiac abnormalities, predominant localization to midlateral, apical, and midinferior walls, and deep perfused intertrabecular recesses; (2) Chin *et al.*,[5] decreasing X/Y ratio from the papillary muscle to the apex measured in end-diastole (where X is the distance from the epicardial surface to the trough of the trabecular recess, and Y is the distance from the epicardial surface to the peak of trabeculation); and (3) Stöllberger *et al.*,[14] more than three prominent trabeculations apical to the papillary muscle and surrounded by intertrabecular spaces perfused from the ventricular cavity.[5,8,14,17,18] All of these criteria have been developed on the basis of relatively small numbers of patients with limited subsequent validation studies and no independent means of verification.

There is increasing recognition of significant overlap in echocardiographic findings in LVNC and other cardiomyopathies as well as the normal population.[4,9,10,19] Associated mortality, cardiac transplantation rates, LV dysfunction, thromboembolic events, and arrhythmias vary greatly in the literature, as do risk factors attributed to such outcomes.[2,3,5-7,10-16,20] The purposes of this study were to describe a large population of patients who have been diagnosed with LVNC by echocardiography and to determine interobserver reproducibility of making such a diagnosis and the measurements proposed by the various criteria. Risk factors for adverse outcomes, including heart transplantation and death, were assessed.

METHODS

Identifying Cases

The records of all patients who received coded diagnoses of LVNC or excessive trabeculations by echocardiography from 1989 to 2006 at the Children's Hospital of Boston were reviewed. Patients were included in the study if the index echocardiogram (on which the

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Abbreviations

ASD = Atrial septal defect

CongHD = Congenital heart disease

ICD = Implantable cardioverter-defibrillator

LV = Left ventricular

LVNC = Left ventricular noncompaction

NCongHD = No congenital heart disease

NYHA = New York Heart Association

diagnosis of noncompaction was based) and at least one other echocardiogram were available for review. Patients with congenital heart disease (CongHD) and those with no congenital heart disease (NCongHD) were included in the study. The institutional review board for clinical research approved the use of patient medical records for this retrospective review. The following data were collected for each patient: demographics, age of diagnosis, length of follow-up, reason for cardiology referral, family history of cardiomyopathy, diagnosis of Barth syndrome, New York Heart Association (NYHA) classification, thromboembolic events, heart transplantation, and death.

Diagnostic Studies

The index echocardiograms of all patients were reviewed for qualitative assessment of function, dilation, hypertrophy, and distribution of trabeculations. Ejection fraction (based on systolic and diastolic volume calculated as 5/6 × area × length) and shortening fraction were recorded when available from the original report. Function on the basis of ejection fraction was defined as normal (>55%), mildly depressed (45%–55%), moderately depressed (35%–45%), or severely depressed (<35%). Subsequent and prior echocardiograms were reviewed for functional changes, phenotypic changes (i.e., ventricular dilation or hypertrophy, by *Z* scores on the basis of body surface area), and changes in the distribution, number, and sizes of trabeculations. When available, fetal echocardiograms were also reviewed. The results of Holter monitors, looping and event recorders, and electrophysiologic studies were recorded for all patients. The rationale for the placement of a pacemaker or an implantable cardioverter-defibrillator (ICD) was ascertained.

Identifying Controls

Patients described above given the diagnosis of LVNC by echocardiography are referred to as cases. A matching patient without LVNC, referred to as a control, was elicited for each case on the basis of the following criteria: (1) age (acceptable limits of match, <10% difference), (2) degree of LV dysfunction (on the basis of ejection fraction as categorized above), and (3) similarity of CongHD. Blinded reviews of the index echocardiogram for all cases and the matched control echocardiograms were performed by two observers. The following were recorded: number of trabeculations from the apical and parasternal views, NC/C ratio, X/Y ratio (Figure1), study quality score (1 = excellent, 2 = good, 3 = fair, 4 = poor, 5 = nondiagnostic), and qualitative opinion on the diagnosis of LVNC.

Statistical Analysis

The percentage agreement between the two observers and between each observer and the original report were calculated for the number of trabeculations and the NC/C ratio. Initially, the number of trabeculations was dichotomized as zero to three versus more than three, and the NC/C ratio was dichotomized as ≤2 versus >2; additional cut points were also explored. Using the original cut points of more than three for the number of trabeculations and >2 for the NC/C ratio, associations between diagnostic criteria and clinical outcomes, including heart transplantation and death, were evaluated using Fisher's exact test. Similarly, associations between moderate or severe LV dysfunction and clinical outcomes were assessed using Fisher's exact test.

RESULTS

A total of 104 cases with LVNC were included in the study, 52 NCongHD and 52 CongHD. The median age of diagnosis of LVNC was 11.0 years (range, 0.0–19.1 years) and 1.8 years (range, 0.0–30.4 years) in the NCongHD and CongHD groups, respectively. The duration of follow-up was 7.2 years (range, 0.5–23.1 years) in the NCongHD group and 8.2 years (range, 0–33.3 years) in the CongHD group. The most frequent reasons for initial referral in the NCongHD group included arrhythmia, congestive heart failure, positive family history of cardiomyopathy, and murmur. Specific congenital cardiac lesions in the CongHD group are listed in Table 1. Barth syndrome was diagnosed in four cases in the NCongHD group and none in the CongHD group. Positive family histories for cardiomyopathy were reported in 16 of 52 cases (30.8%) in the NCongHD group, including dilated ($n = 10$), noncompaction ($n = 3$), hypertrophic ($n = 1$), and unspecified ($n = 2$). In the CongHD group, three of 52 patients (5.7%) had family histories of cardiomyopathy, two with noncompaction and one with an unspecified cardiomyopathy.

Imaging

Index echocardiograms were qualitatively reviewed for all 104 cases, as well as echocardiograms at noted points of change of function, dilation, or hypertrophy per report. In total, 295 echocardiograms were reviewed. Fetal echocardiograms were obtained in two of 52 (4%) and 15 of 52 (29%) cases in the NCongHD and CongHD groups, respectively. LV hypertrabeculation was noted in utero retrospectively in two cases with CongHD, and the remaining fetal studies were considered nondiagnostic for LVNC on report and repeat review. Changes in function from the initial to the last follow-up echocardiographic study for both groups are shown in Figure 2. No case with normal or mildly depressed function at the beginning of the study had severe dysfunction at the end. Cases with severe dysfunction at the beginning of the study showed some improvement with time, more pronounced in the NCongHD group.

Initial echocardiograms were reviewed for the distribution of LV trabeculations according to standard myocardial segmentation and are listed in Table 2.[21] Phenotypic changes with time are listed in Table 3 and illustrated in Figure 3. Changes in LV dilation and hypertrophy correlated with removal of shunt lesions or relief of obstructions in some, but not all, cases with CongHD. New development of LVNC compared to prior echocardiography was seen in three cases (CongHD group): two with left-sided obstructive lesions after endocardial fibroelastosis removal and one after ventricular septal defect closure and coarctation repair (Figure 4).

Rhythm Abnormalities

Arrhythmias were common in both groups (NCongHD, $n = 18$; CongHD, $n = 19$; Table 4), often with multiple arrhythmias presenting in an individual. Tachyarrhythmias were predominantly present at the diagnosis of LVNC, although in a few patients in the NCongHD group, they presented up to 5.7 years later. In the same