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Comparison of Echocardiographic Diagnostic Criteria of Left Ventricular Noncompaction in a Pediatric Population

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Abstract

Background—There is controversy regarding the best echocardiographic diagnostic criteria for left ventricular noncompaction (LVNC). We assessed the diagnostic utility and reproducibility of the previously proposed echocardiographic diagnostic criteria in a pediatric population using a segmental approach.

Methods—Echocardiograms were matched for patients with and without a clinical diagnosis of LVNC. Blinded reviews of echocardiograms measured 1) depths of intertrabecular recesses (X/Y), 2) noncompaction-to-compaction ratio (NC/C), and 3) number of trabeculations, using a segmental approach. Measurements were analyzed for area under the receiver operating characteristic curves (AUC), sensitivity, and specificity

Results—There were 30 echocardiograms in the initial cohort (15 LVNC cases, 15 controls). Median age was 1.7 years (IQR 0.2–6.9 years) and systolic function was decreased in 40%. Comparison of diagnostic criteria demonstrated the best interrater agreement and AUC with an X/Y ratio measured in end-diastole in the parasternal short axis in the apical anterolateral segment (κ 0.72, CI 0.43–1.00, p-value <0.001), yielding 100% sensitivity and 70 to 86% specificity, among readers. The least predictive and reproducible method was the NC/C ratio. A validation cohort confirmed the superiority of the X/Y ratio, though the interrater agreement and AUC decreased.

Conclusion—Measurements according to existing LVNC diagnostic criteria vary by echocardiographic view and segment. Modification of the Chin *et al.* criteria [1] using an X/Y ratio <0.5 had the greatest interrater reliability and predictive validity when measured in end-

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diastole in the parasternal short axis in the apical anterolateral segment. The NC/C ratio had the lowest reliability and predictive validity.

Keywords

Left ventricular noncompaction; Echocardiography; Cardiomyopathy; Segment model; Pediatrics

Introduction

Isolated left ventricular noncompaction (LVNC) is characterized by a two-layered myocardium with a noncompacted layer of prominent ventricular trabeculae and a thinner layer of compacted epicardium. Isolated LVNC was first identified by echocardiography in 1984 by Engberding and Bender as a “persistence of isolated myocardial sinusoids” and while several diagnostic echocardiographic criteria have been proposed since then, there remains no “gold standard” against which to compare for diagnostic accuracy [2].

The three most commonly cited echocardiographic LVNC diagnostic criteria (Figure 1) measure the depths of intertrabecular recesses (Chin *et al.* criteria), the ratio of noncompacted to compacted myocardium (Jenni *et al.* criteria), and the number of trabeculations (Stöllberger *et al.* criteria) [1,3–5]. The application of these proposed echocardiographic criteria has demonstrated poor reproducibility, with interobserver agreement in diagnosing LVNC ranging from 67–87% [6,7]. There are limited studies comparing the diagnostic criteria to each other [6,8,9]. Furthermore the optimal echocardiographic view and ventricular segment within which to perform the measurements are not known, as the original diagnostic methods did not evaluate their criteria using a segmental model [6,8]. The purpose of this study was to assess the diagnostic utility and reproducibility of the most commonly cited LVNC echocardiographic criteria within multiple echocardiographic views using a left ventricular segment model in a pediatric population. We hypothesized that one of the currently accepted diagnostic criteria, or a combination of criteria, will prove more reproducible than the others, particularly when utilized within a certain echocardiographic view and myocardial segment.

Material and Methods

This study was a single-center, retrospective case-control study, approved by the Institutional Review Board at Columbia University Medical Center, with waiver of informed consent.

Study Population

LVNC cases and controls were identified by searching our echocardiogram database for patients aged 0–19 years evaluated at NewYork-Presbyterian/Morgan Stanley Children’s Hospital between 2006 and 2015. Given the lack of a gold standard, cases were assumed to meet inclusion criteria for LVNC if they were identified as having LVNC in the echocardiography report as well as clinically interpreted to have a diagnosis of LVNC in documentation by the primary cardiology/cardiomyopathy team, and by pathology data when available. LVNC cases were excluded if they had significant congenital heart defects (other than atrial communications, ventricular septal defects or patent ductus arteriosus) or

inadequate echocardiographic image quality for analysis. Control subjects were identified from the echocardiogram database with normal echocardiograms or dilated cardiomyopathy (DCM). Cases and controls were matched 1:1 by sex, body surface area (within 0.1m²), age range (infant, child, adolescent), and left ventricular ejection fraction (EF) functional group (normal >55%, mildly-moderately decreased 35–54%, and severely decreased <35%). Pathology reports when available from autopsy or explanted hearts were reviewed.

Echocardiographic Measurements

All patients underwent complete standard echocardiograms according to the American Society of Echocardiography recommendations using Philips iE33 ultrasound systems [10]. Echocardiograms were de-identified and two-dimensional clips were pre-selected to include the apical four-chamber, apical three-chamber, apical two-chamber, mid-papillary parasternal short-axis, and apical parasternal short-axis views.

Two experienced pediatric cardiologists (W.L. and S.C.) performed blinded review of echocardiograms, and reported the following:

1. X/Y Ratio (Chin *et al.* criteria): epicardial surface to trabeculation trough (X distance) divided by epicardial surface to trabeculation peak in end-diastole (Y distance) [1].
2. NC/C Ratio (Jenni *et al.* criteria): thickness of noncompacted (NC) to compacted (C) myocardium in systole [3].
3. Number of trabeculations that move synchronously with two-layered myocardium in end-diastole (Stöllberger *et al.* criteria) [4].

Echocardiographic study quality was also graded using a scoring system of 1=poor, 2=fair, 3=good, and 4=very good. The two readers met to review the diagnostic criteria and standardize measurement techniques using sample cases at the beginning of the study.

Using the 18-segment model of the left ventricle, readers performed the measurements in each segment at the mid-papillary and apex levels in both apical long and parasternal short axes (total 12 segments from 2 echocardiographic views) [11]. Both readers performed all continuous measures twice. Ejection fraction by 5/6 area $\times$ length method was calculated by a third pediatric cardiologist (D.H.).

The mean of the two measurements for each diagnostic test was calculated for each reader and as an average measurement in each segment in both the apical long and parasternal short echocardiographic views. The continuous data from these measurements were converted to categorical data using diagnostic cut-off thresholds. For the Jenni *et al.* and Stöllberger *et al.* criteria, the previously reported LVNC diagnostic criteria of NC/C ratio >2 and trabeculations >3 were used, respectively. The Chin *et al.* criteria did not originally specify a diagnostic cut-off value, however; and varying X/Y ratio cut-off thresholds (in 0.1 increments between 0.1–0.9) were tested to maximize the area under the receiving operating characteristic curve (AUC).

Statistical Analysis

All analyses were performed using Stata version 14 (StataCorp LP, College Station, Texas) and SAS version 9.4 (SAS Institute, Inc. Cary, NC). Clinical, demographic, and echocardiographic variables were described using standard summary statistics. To determine which diagnostic tests were most reproducible, we assessed interrater reliability using intraclass correlation for continuous data and Cohen's kappa statistic for categorical data. A kappa >0.20 was considered fair agreement, >0.40 moderate agreement, >0.60 substantial agreement, and >0.80 almost perfect agreement [12]. Once the most reproducible tests were determined (kappa >0.60), we compared means and medians using student's t-test and Mann-Whitney U tests as appropriate to assess the associations between each of the diagnostic criteria and LVNC or control diagnoses. The sensitivity and specificity of each diagnostic test were reported for each reader. The AUC was calculated for each diagnostic test. An overall diagnostic score was then developed by combining the diagnostic measurements with the best AUC and kappa values.

Validation Cohort

Given the concern that multiple comparisons have the potential to yield significant results when analyzing several echocardiographic diagnostic tests in multiple views and segments, we performed a follow-up validation in a second cohort, assessing the best diagnostic tests. Following the initial statistical analyses, the same readers analyzed a validation cohort of 30 additional echocardiograms of LVNC cases matched with controls. In the validation cohort, only the three best diagnostic measurements were tested, as determined in the initial study cohort. Data acquisition and statistical analyses were performed as described above.

Results

Patient Characteristics

A total of 30 echocardiograms were included in the initial study cohort, with 15 LVNC cases matched with 15 controls (Table 1). Median age was 1.7 years, ranging from 2 weeks of age to 18 years old. Systolic function was decreased in 40% of echocardiograms in LVNC cases and controls. Race was not reported in this study as it was poorly documented in the medical records during the study time period. One patient in the LVNC group had a ventricular septal defect. There were no congenital heart defects in the control group. The control group consisted of 10 normal echocardiograms and 5 echocardiograms reported as dilated cardiomyopathy with decreased systolic ventricular function (and without mention of noncompaction or hypertrabeculation). Pathology reports from explanted hearts were available for 5/15 LVNC cases and 3/15 DCM controls, and all were consistent with the LVNC or DCM diagnoses, respectively.

Echocardiographic Evaluation

Echocardiographic Quality—Echocardiographic quality was similar in LVNC cases and the controls (p-value >0.1). The mean echocardiographic quality score was 2.5 ± 0.3 across echocardiographic views. It was highest in the apical 4-chamber view (2.8 ± 0.6) and lowest in the apical 2-chamber view (2.2 ± 0.4 , p-value <0.0001).

Interrater Reliability—Comparing continuous data for all echocardiographic measurements of each diagnostic criteria obtained by the two readers, the intraclass correlation (ICC) was generally poor with an average ICC for LVNC cases of 0.13, likely due to the small magnitude of measurements obtained which are then divided into a ratio. The ICC correlated significantly in only 19% of the 53 echocardiographic measurements (24 measurements each for X/Y and NC/C ratio measurements and five measurements for each trabeculation count). ICC was best among LVNC echocardiograms for number of trabeculations counted in the parasternal short axis view at the apical level (ICC 0.8, CI 0.51–0.93, p-value <0.0001).

Measurements were converted to a categorical result using the previously reported diagnostic cut-offs (Jenni *et al.*: NC/C ratio >2, Stöllberger *et al.*: trabeculations >3). As the Chin *et al.* criteria did not report a diagnostic cut-off, we tested varying X/Y ratios and found the cutoff that yielded the highest AUC was an X/Y ratio <0.5 in the apical measurements (modified Chin *et al.* criteria), which is consistent with cut-offs used in other studies [9,13]. When data were reported as categorical outcomes, there was significant interrater agreement in 12 of the echocardiographic diagnostic tests (Table 2). Interrater agreement was best when the X/Y ratio was measured in the parasternal short axis in the apical anterolateral segment and when assessing number of trabeculations in the parasternal short axis at the apical level (κ 0.72, CI 0.43–1.00; κ 0.71, CI 0.46–0.97, respectively; p-value <0.001). Interrater agreement was lowest among the diagnostic tests using the Jenni *et al.* criteria with a NC/C ratio >2.

Diagnostic Tests—Four diagnostic tests had substantial interrater agreement, as determined by a Cohen's Kappa statistic >0.60 and were included for further analyses. The median values for each diagnostic test all had significantly different medians between LVNC cases compared with controls (Table 3). The median X/Y ratio (Chin *et al.* criteria) in the apical anterolateral region measured in the parasternal short axis was smaller in LVNC cases compared with controls (0.35 [0.30–0.44] versus 0.62 [0.56–0.75], p-value =0.0001), consistent with Chin *et al.*'s original findings (Figure 2). Number of trabeculations was greater in LVNC cases compared with controls, however was more pronounced at the apical level, consistent with Stöllberger *et al.*'s proposed diagnostic cut-off of >3 (5.3 [3.5–7.5] versus 1.5 [0.5–2], p-value =0.0001) (Figure 3). The NC/C ratio measured in the parasternal short axis in the anterior region of the mid-ventricular level was not statistically higher in LVNC cases compared with controls (0.96 [0.53–1.08] versus 0.73 [0.32–0.92], p-value =0.07). The only segments with median NC/C ratios >2 were the apical lateral segments assessed from the apical-3 chamber and apical 4-chamber views; however these measurements were previously determined to have low interrater agreement (κ <0.40).

We determined the diagnostic test with the highest AUC to be a modification of the Chin *et al.* criteria using an X/Y ratio <0.5 at the apical level, as it yielded the highest AUC and had 100% sensitivity among the two readers, with specificity ranging from 70% to 86% (Table 4). The second best diagnostic test was the Stöllberger *et al.* criteria when there were >3 trabeculations measured in the parasternal short axis at the apical level with moderate sensitivity ranging from 79% to 80% and specificity ranging from 79% and 93% among the 2 readers. Counting number of trabeculations at the mid-ventricular level had high

specificity but low sensitivity. The Jenni *et al.* criteria using NC/C ratio >2 as the diagnostic cutoff had the lowest AUC (0.54) and was an insensitive test.

Comparison of Diagnostic Tests—Comparison of diagnostic criteria demonstrated the greatest AUC and inter-rater agreement with the following LVNC diagnostic echocardiographic tests, assessed from the parasternal short axis in end-diastole (Table 4):

- a. X/Y ratio cut-off <0.5 in the apical anterolateral region (modified Chin *et al.* criteria)
- b. Number of trabeculations >3 at the apical level (Stöllberger *et al.* criteria)
- c. Number of trabeculations > 3 at the mid-ventricular level (Stöllberger *et al.* criteria)

These three diagnostic tests were then combined to create a novel LVNC echocardiographic score. A positive score was achieved if at least two of the three above diagnostic tests were positive for LVNC, with an AUC of 0.87 and sensitivity / specificity of 87% / 87% for reader 1 and 73% / 100% for reader 2 (κ 0.6 CI 0.32–0.88, $p < 0.001$).

Validation Cohort—The validation cohort included 15 LVNC cases and 15 controls. The interrater agreement dropped from substantial agreement with the first cohort to fair-moderate agreement with the validation cohort (κ range 0.39–0.46) (Table 5). The test with the highest AUC was again determined to be the modified Chin *et al.* criteria with an X/Y ratio <0.5 measured in the parasternal short axis in the apical anterolateral region in end-diastole with an AUC of 0.86 for reader 1 and 0.77 for reader 2. Analysis of the LVNC diagnostic score in this validation cohort with at least two of the three diagnostic tests positive for LVNC yielded an AUC 0.82 for reader 1 and 0.79 for reader 2.

Discussion

We found that among the previously proposed echocardiographic LVNC diagnostic criteria (Figure 1), which measured the depths of intertrabecular recesses (Chin *et al.* criteria), the ratio of noncompacted to compacted myocardium (Jenni *et al.* criteria), and the number of trabeculations (Stöllberger *et al.* criteria), that the reproducibility and interrater reliability was best in the parasternal short axis using the X/Y ratio in the apical anterolateral region and when counting number of trabeculations at the apex (Figure 4); however, the interrater reliability decreased in the follow-up validation cohort. Out of all the diagnostic tests measured in multiple echocardiographic views and segments, the modified Chin *et al.* criteria with an X/Y ratio <0.5 measured in the parasternal short axis at end-diastole in the apical anterolateral region had the highest AUC (ranging from 0.77–0.93) with sensitivity and specificity ranging from 79–100% and 54–92%, respectively among two experienced cardiologists in two tested cohorts. A positive echocardiographic LVNC score, in which two out of the three diagnostic tests are positive (parasternal short axis: X/Y ratio <0.5 in apical anterolateral, trabeculations >3 at apex and mid-ventricular level) was associated with sensitivity between 64 and 86% and specificity between 71 and 100%. The criterion with the lowest reproducibility and diagnostic validity was the Jenni *et al.* criteria, which assessed the NC/C ratio at end-systole.

Given the rarity of the diagnosis, many of the original LVNC diagnostic criteria were based on small numbers of patients. In 1990, Chin *et al.* were the first to define echocardiographic criteria for the diagnosis of LVNC [1]. They analyzed echocardiograms of only eight pediatric patients with isolated LVNC compared to normal echocardiograms, for which they had pathology data for 3 of the LVNC cases (Figure 1). They reported that in end-diastole, the ratio measuring from the epicardial surface to the trough compared to the peak of trabeculations (X/Y ratio) progressively decreases from the level of the mitral valve towards the apex compared with normal controls. While they found statistically smaller X/Y ratios in LVNC patients, particularly at the apical level, a diagnostic cutoff value was not proposed. Other studies have since extrapolated from the original data and have used a diagnostic cut-off <0.5 at the apical level, without validation.[9,13] In our study, testing values between 0.1 and 0.9, we confirmed that a cut-off of 0.5 optimized the AUC. Chin *et al.* proposed measuring X/Y ratios at the apical level in the long axis, either from the subcostal or apical 4-chamber views. We found, in contrast, that this test had the highest interrater reliability when measured in the parasternal short axis, and was most sensitive and specific when measured in the apical anterolateral region when using an 18-segment model of the ventricle.

In 2001, Jenni *et al.* analyzed echocardiograms and pathology data of only seven adult patients with LVNC compared to 19 dilated and hypertrophic ventricle controls and identified a NC/C ratio >2 measured in the short-axis during systole as diagnostic for LVNC [3]. They described that the maximal thickness was predominately localized in the mid-lateral, apical, and mid-inferior regions of the ventricle. In our study, using a NC/C ratio >2 had low levels of interrater reliability, with the highest kappa of 0.65 noted in the parasternal short axis in the anterior region at the mid-ventricular level. This region did not demonstrate maximal NC/C ratio and had low sensitivity and specificity for diagnosing LVNC, possibly because measurements obtained at this level are affected by the close proximity to the papillary muscles. We noted that individual readers found a median NC/C ratio >2 in LVNC cases most frequently in the apical lateral segments measured in the apical 3-chamber and apical 4-chamber views, although the interrater reliability of these measurements was low. Punnett *et al.* measured NC/C ratios using the 16-segment model and found the apical regions in the parasternal short axis had the highest NC/C ratios, but they did not report interrater reliability with these measurements [8].

First in 2002, and then refined in 2013, Stöllberger *et al.* proposed LVNC diagnostic criteria using >3 trabeculations from the left ventricle with evidence on color Doppler imaging of perfusion of the intertrabecular spaces after analyzing echocardiograms from 62 and 115 adults with LVNC with no control group [4,5]. These authors noted that trabeculations should come from the noncompacted layer of the two-layered myocardium and move synchronously with the myocardium. This group has suggested that the optimal view for assessing the number of trabeculations might be in end-diastole, using the parasternal short-axis view at the apical level. Our findings support this hypothesis, with the highest reliability and AUC observed in this echocardiographic view and ventricular region.

A common issue among echocardiographic diagnostic criteria for LVNC is that the interrater reliability tends to be sub-optimal. Saleeb *et al.* compared 104 LVNC cases to 100 controls

and found agreement between observers in counting trabeculations >3 and NC/C ratio >2 ranged from 53–77 percent agreement, which statistically does not incorporate the possibility of chance agreement [6]. Stöllberger *et al.* recently assessed interrater reliability among three observers assessing 100 echocardiograms of patients with LVNC and reported kappa ranges from 0.63 to 0.79 with disagreement in 35% of cases [7]. Relevant to all LVNC diagnostic studies assessing validity and interrater reliability is the lack of a gold standard for diagnosis, as many of these studies relied on an original echocardiographic diagnosis as their inclusion criteria, whereas we had pathology data for one third of LVNC cases in our initial study cohort. Furthermore, these echocardiographic diagnostic tests may be too sensitive as suggested by Kohli *et al.* who reported that 23.6% of patients presenting to their heart failure clinic met at least one of the three echocardiographic criteria for LVNC, including 8.3% of control subjects [9].

The issue of whether to assess the myocardium for evidence of noncompaction in systole or diastole has not been established, and varies between echocardiographic diagnostic criteria. Paterick *et al.* have proposed measurements of the two-layer myocardium be performed in end-diastole, as they have observed more precise measurements of the thickness of each layer and note that this approach is in line with the American Society of Echocardiography recommendations to measure ventricular wall-thickness at end-diastole [14]. This suggestion is also consistent with our observations that the NC/C ratio measurements performed in end-systole were the least reproducible with low interrater reliability, while the X/Y ratio and counting number of trabeculations, which were measured in end-diastole, tended to perform best. As Paterick *et al.* have suggested, it might be helpful to compare NC/C ratios measured in end-diastole instead of end-systole to see how it changes the diagnostic validity of the test; their group has reportedly modified their laboratory guidelines to reflect this suggestion. Their laboratory also notes that the best place to assess the noncompaction layer is in the parasternal short axis in the apicolateral region, similar to our finding using the 18-segment model with the best X/Y ratio noted in the parasternal short axis in the apical anterolateral region.

Our study was the first to compare all three commonly cited echocardiographic diagnostic criteria for LVNC with pediatric cases and controls using the 18-segment model of the left ventricle. Similar to previously reported data, we found that number of trabeculations >3 (Stöllberger *et al.* criteria) and the most prominent 2-layer myocardium was best measured in the apical regions, particularly when assessing the X/Y ratio <0.5 in the apical anterolateral region in the parasternal short axis (modified Chin *et al.* criteria). Both of these tests are performed in end-diastole, as opposed to the NC/C ratio measured in end-systole as proposed by Jenni *et al.*, which might suggest that the optimal phase in which to assess LVNC performs better in diastole. A diagnostic score that combines the top echocardiographic measurements could be potentially useful to address variability in measurements and overdiagnosis of LVNC. In terms of clinical applicability, the modified Chin *et al.* criteria may be more applicable as a screening test as it optimizes sensitivity, whereas a diagnostic score could be utilized to rule in a diagnosis of LVNC as it optimizes specificity. The drop in interrater reliability between readers from the original cohort to the validation cohort points to a need for further clarification and training on acquisition of these measurements. Now that we have identified the apical level of the parasternal short axis in

end-diastole as potentially the best segment and view to assess for LVNC, further training and refinement of the criteria could potentially be focused on this area to improve reliability and diagnostic validity.

There are several limitations to our study. The most obvious concern with identifying LVNC cases to assess echocardiographic diagnostic criteria rests on the lack of an existing gold standard for diagnosing LVNC. Our inclusion criteria identified LVNC cases and controls by prior echocardiography, clinical documentation, and pathology data when available, however; it is possible that cases were included that were not, in fact, “disease-positive”. Similarly, we matched patients for function which included controls with DCM, and it is possible that some of our control patients could have had LVNC that was not identified on prior echocardiogram or by the clinical team. This was a retrospective analysis and the quality of the previously acquired echocardiographic views were overall determined to be “fair” to “good” quality, with some studies noted to have limited apical views or parasternal short axes clips taken in an improper oblique plane which may have affected the accuracy of the measurements. Interrater reliability decreased over time as evidenced by the drop in kappa noted in the validation cohort. While readers met at the onset of the study to review measurement technique, it is possible that in the months that passed from the original cohort to the validation cohort that reader technique might have differed more, leading to the inconsistent findings.

Conclusions

In conclusion, we found that, of the three most commonly cited echocardiographic diagnostic criteria for LVNC, the Chin *et al.* criteria measuring the X/Y ratio in end-diastole in the parasternal short axis at the apical anterolateral region had the highest sensitivity and specificity and that the Jenni *et al.* criteria assessing NC/C ratio in systole had the lowest reproducibility and diagnostic validity. In our initial cohort of patients, interrater reliability was best in the parasternal short axis for X/Y ratio <0.5 in the apical anterolateral region and trabeculations >3 at the apical level; however, interrater reliability decreased in a follow-up validation cohort, suggesting that further training and refinement of acquiring these measurements are needed. Further research is needed to follow-up our finding and others’ suggestion that LVNC two-layer measurements may be best obtained in end-diastole in the parasternal short axis at the apical level. Future directions should continue to work towards clear echocardiographic measurement guidelines or development of an echocardiographic score that improves the diagnostic validity of LVNC.

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Appendix

Appendix Table 1

Validation Cohort: Patient demographics

Variable*	LVNC (n=15)	Control (n=15)
Age, year	5.6 [0.7–17.2]	5.7 [0.5–14.5]
Male, n (%)	9 (60%)	9 (60%)
Height, cm	112 [53–174]	87 [64–163]
Weight, kg	19.0 [4.4–64.5]	12.3 [5.5–53.0]
BSA, cm/m ²	0.77 [0.24–1.81]	0.71 [0.31–1.62]
Function Group:		
Normal	5 (33%)	5 (33%)
Mild-moderately decreased	6 (40%)	6 (40%)
Severely decreased	4 (27%)	4 (27%)
5/6 AL EF, %	44 [33–56]	47 [21–64]
Other Diagnoses:		
ASD	1 (7%)	0 (0%)
PDA	1 (7%)	0 (0%)

Data are expressed as median [IQR] or as number (percentage).

* There were no significant differences between LVNC and Controls for any patient characteristics.

LVNC: Left ventricular noncompaction; ASD: atrial septal defect; PDA: patent ductus arteriosus; EF: ejection fraction.

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	Chin <i>et al.</i> [1]	Jenni <i>et al.</i> [3]	Stöllberger <i>et al.</i> [4,5]
Measurement Example
Diagnostic Criteria	<ul style="list-style-type: none"> Decreasing X/Y ratio* from base to apex No specific cut-off reported 	<ul style="list-style-type: none"> a) Two-layer myocardium with NC/C* ratio >2 b) Non-compaction predominantly located in mid-lateral, apical, and mid-inferior regions c) Perfusion of intertrabecular spaces demonstrated by color Doppler d) Absence of coexisting cardiac abnormalities 	<ul style="list-style-type: none"> a) >3 prominent trabeculations b) Trabeculations move synchronously with myocardium c) Trabeculations part of noncompacted layer of the two-layered myocardium d) Perfusion of intertrabecular spaces demonstrated by color Doppler
Cardiac Phase	End-diastole	Systole	<ul style="list-style-type: none"> Trabeculations: End-diastole Two-layered myocardium: End-systole
Echocardiographic View/Segment	<ul style="list-style-type: none"> Parasternal long-axis at level of mitral valve and papillary muscle; Subcostal long-axis or apical four-chamber view at level of apex 	Parasternal short-axis	<ul style="list-style-type: none"> Trabeculations: Parasternal short axis, apical level Two-layered myocardium: "Atypical apical 2-chamber view"
LVNC Cases (n)	8	7	62[2], 115[3]
Control group (n)	8 (normal echocardiograms)	<ul style="list-style-type: none"> 10 with DCM* 9 with LVH* 	0
Pathology data (n)	3 out of 8 LVNC cases	<ul style="list-style-type: none"> 7 out of 7 LVNC cases 19 out of 19 Control cases 	0
Age range	11 months – 22 years	22 – 61 years	18 – 87 years

Figure 1.

Comparison of echocardiographic LVNC diagnostic criteria

* *X/Y ratio* = distance from epicardial surface to trough of trabeculation (X) divided by the distance from the epicardial surface to peak of trabeculation (Y); *NC/C ratio*: non-compaction to compaction ratio; *DCM*: dilated cardiomyopathy; *LVH*: left ventricular hypertrophy.

Figure 2.

Median X/Y ratio

Median X/Y ratio (Chin *et al.* criteria) measured in the parasternal short axis in the apical anterolateral region in LVNC cases compared with controls. Median values displayed with interquartile ranges (box) and upper/lower adjacent values. LVNC= Left ventricular noncompaction.

Figure 3.

Median number of trabeculations

Median number of trabeculations (Stöllberger *et al.* criteria) counted in the parasternal short axis at the apical level in LVNC cases compared with controls. Median values displayed with interquartile range (box) and upper/lower adjacent values. *LVNC* = Left ventricular noncompaction.

Figure 4.

Best LVNC echocardiographic diagnostic tests using the 18-Segment model of the left ventricle

The best LVNC echocardiographic diagnostic tests were measured in the parasternal short axis with the X/Y ratio <0.5 in the apical anterolateral region (red) and trabeculations >3 in the apical region (blue).

Table 1

Initial Cohort: Patient demographics

Variable [*]	LVNC (n=15)	Control (n=15)
Age, year	1.8 [0.2–9.2]	1.5 [0.2–6.9]
Male, n (%)	7 (47%)	7 (47%)
Height, cm	73 [59–125]	78 [55–121]
Weight, kg	8.1 [5.2–20]	9.8 [5.2–21]
BSA, cm/m ²	0.5 [0.3–0.9]	0.5 [0.3–0.9]
Function Group:		
Normal	4 (26.7%)	4 (26.7%)
Mild-moderately decreased	2 (13.3%)	2 (13.3%)
Severely decreased	9 (60.0%)	9 (60.0%)
5/6 AL EF, %	59 [32–66]	65 [27–68]
Other Diagnoses:		
VSD	1 (7%)	0 (0%)

Data are expressed as median [IQR] or as number (percentage).

^{*} There were no significant differences between LVNC and Controls for any patient characteristics.

LVNC: Left ventricular noncompaction; VSD: ventricular septal defect; EF: ejection fraction.

Table 2

Comparison of interrater reliability among LVNC echocardiographic diagnostic tests

Echocardiographic View & Ventricular Segment	Kappa (95% CI)	p-value
Modified Chin <i>et al.</i> criteria (X/Y ratio) <0.5:		
Parasternal Short/Apical Anterolateral	0.72 (0.43, 1.00)	<0.001
Parasternal Short/Apical Anterior	0.51 (0.13, 0.88)	<0.01
Parasternal Short/Apical Inferolateral	0.50 (0.16, 0.84)	<0.01
Parasternal Short/Apical Inferoseptal	0.49 (0.10, 0.87)	<0.01
Parasternal Short/Apical Inferior	0.43 (0.11, 0.75)	<0.001
Stöhlberger <i>et al.</i> criteria (trabeculations >3):		
Parasternal Short/Apical	0.71 (0.46, 0.97)	<0.001
Parasternal Short/Mid	0.63 (0.30, 0.96)	<0.001
Apical 4 Chamber	0.40 (0.08, 0.72)	<0.05
Jenni <i>et al.</i> criteria (NC/C ratio >2):		
Parasternal Short/Mid-Anterior	0.65 (0.02, 1.00)	<0.001
Apical 3 Chamber/Mid-Anteroseptum	0.47 (−0.13, 1.00)	<0.01
Parasternal Short/Apical inferior	0.36 (−0.05, 0.78)	<0.05
Apical 3 Chamber/Apical lateral	0.36 (−0.01, 0.74)	<0.05

LVNC: Left ventricular noncompaction; NC/C ratio: noncompaction to compaction ratio.

Table 3

Comparison of measurements obtained with LVNC echocardiographic diagnostic criteria in LVNC cases versus controls

Echocardiographic View & Ventricular Segment	Reader 1		Reader 2		Average		p-value
	LVNC	Control	LVNC	Control	LVNC	Control	
Chin <i>et al.</i> criteria (X/Y ratio):							
Parasternal Short/Apical Anterolateral	0.40 [0.33–0.44]	0.59 [0.53–0.77]	0.33 [0.29–0.45]	0.60 [0.50–0.70]	0.35 [0.30–0.44]	0.62 [0.56–0.75]	0.0001
Stöllberger <i>et al.</i> criteria (trabeculations):							
Parasternal Short/Apical	5 [4–7]	2 [1–3]	6 [4–7]	0 [0–2]	5.25 [3.5–7.5]	1.5 [0.5–2]	0.0001
Parasternal Short/Mid	3 [2–5]	2 [1–3]	3 [1–4]	1 [0–2]	2.5 [2–4.5]	1.75 [1–2]	<0.01
Jenni <i>et al.</i> criteria (NC/C ratio):							
Parasternal Short/Mid-Anterior	0.96 [0.69–1.17]	0.50 [0.39–0.80]	0.67 [0.43–1.00]	0.66 [0.39–1.25]	0.96 [0.53–1.08]	0.73 [0.32–0.92]	0.07

Data are expressed as median [IQR]. LVNC: Left ventricular noncompaction; NC/C ratio: noncompaction to compaction ratio.

Table 4

Initial cohort: comparison of LVNC echocardiographic diagnostic criteria

Echocardiographic View & Ventricular Segment	Reader 1			Reader 2		
	AUC (95% CI)	Sensitivity	Specificity	AUC (95% CI)	Sensitivity	Specificity
Modified Chin <i>et al.</i> criteria (X/Y ratio) <0.5:						
Parasternal Short/Apical Anterolateral	0.93 (0.83, 1.00)	100%	86%	0.85 (0.70, 1.00)	100%	70%
Stöllberger <i>et al.</i> criteria (trabeculations >3):						
Parasternal Short/Apical	0.79 (0.64, 0.95)	80%	79%	0.86 (0.73, 0.99)	79%	93%
Parasternal Short/Mid	0.70 (0.55, 0.85)	47%	93%	0.70 (0.57, 0.83)	40%	100%
Jenni <i>et al.</i> criteria (NC/C ratio >2):						
Parasternal Short/Mid-Anterior	0.54 (0.47, 0.61)	8%	100%	0.50 (0.41, 0.59)	7%	93%
Positive Diagnostic Score (2 out of 3):						
Parasternal Short Axis:						
a) X/Y <0.5, Apical Anterolateral						
b) Trabeculations >3, Apex	0.87 (0.74, 0.99)	87%	87%	0.87 (0.75, 0.98)	73%	100%
c) Trabeculations >3, Mid-ventricular						

AUC: Area under receiver operating characteristic curve; CI: Confidence interval; NC/C ratio: noncompaction to compaction ratio.

Table 5

Validation cohort: comparison of LVNC echocardiographic diagnostic criteria

Echocardiographic View & Ventricular Segment		Reader 1			Reader 2		
	Kappa	AUC (95% CI)	Sensitivity	Specificity	AUC (95% CI)	Sensitivity	Specificity
Modified Chin <i>et al.</i> criteria (X/Y ratio) <0.5:							
Parasternal Short/Apical Anterolateral	0.41	0.86 (0.72, 0.99)	79%	92%	0.77 (0.63, 0.91)	100%	54%
Stöllberger <i>et al.</i> criteria (trabeculations >3):							
Parasternal Short/Apical	0.39	0.82 (0.69, 0.95)	64%	100%	0.77 (0.61, 0.92)	80%	73%
Parasternal Short/Mid	0.46	0.75 (0.61, 0.89)	50%	100%	0.77 (0.61, 0.92)	67%	87%
Positive Diagnostic Score (2 out of 3):							
Parasternal Short Axis:							
a) X/Y <0.5, Apical Anterolateral	0.39	0.82 (0.69, 0.95)	64%	100%	0.79 (0.63, 0.94)	86%	71%
b) Trabeculations >3, Apex							
c) Trabeculations > 3, Mid-ventricular							

AUC: Area under receiver operating characteristic curve; CI: Confidence interval; NC/C ratio: noncompaction to compaction ratio.