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ORIGINAL RESEARCH

Comparison of Systolic and Diastolic Criteria for Isolated LV Noncompaction in CMR

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OBJECTIVES This study used cardiac magnetic resonance (CMR) to compare standard criteria for left ventricular noncompaction (LVNC).

BACKGROUND LVNC as a distinct cardiomyopathy is supported by a growing number of publications. Echocardiographic and CMR criteria have been established to diagnosis LVNC but have led to concerns of diagnostic accuracy.

METHODS Trabeculation/possible LVNC by CMR was retrospectively observed in 122 consecutive cases. We compared the standard end-systolic noncompacted-to-compacted ratio (ESNCCR), end-diastolic noncompacted:compacted ratio (EDNCCR), and trabecular mass-to-total mass ratio (TMTMR) along with deaths, embolic events, congestive heart failure (CHF) readmissions, ventricular arrhythmias, myocardial thickening (MT), left ventricular ejection fraction (LVEF), 3-dimensional sphericity index (3DSi), and left ventricular end-diastolic volume index. Adjusting for age, race, sex, body surface area, diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, and CHF, logistic regression was used to compare combined events (death, CHF readmission, embolism, ventricular arrhythmia) between ESNCCR, EDNCCR, and TMTMR. Adjusting for same covariates except CHF, logistic regression was used to compare the odds of CHF for those who met criteria and those who did not. Using analysis of covariance, adjusted means for LVEF, MT, 3DSi, and left ventricular end-diastolic volume index were generated.

RESULTS ES criteria had a higher odds ratio (8.6; 95% confidence interval [CI]: 2.5 to 33) for combined events than ED criteria (1.8; 95% CI: 0.6 to 5.8) or TMTMR criteria (3.14; 95% CI: 1.09 to 10.2). The odds ratio of CHF for those who met ESNCCR criteria was 29.4 (95% CI: 6.6 to 125), but the odds ratio of CHF for those who met EDNCCR criteria was 3.3 (95% CI: 1.1 to 9.2). After adjustment, those who met criteria for noncompaction by ESNCCR had a lower LVEF and less MT than those who did not ($p = 0.01$ and $p = 0.003$, respectively), but there was no difference between those who met criteria for EDNCCR or the TMTMR criteria and those who did not.

CONCLUSIONS ES measures of LVNC have stronger associations with events, CHF, and systolic dysfunction than other measures. (J Am Coll Cardiol Img 2013;6:931–40) © 2013 by the American College of Cardiology Foundation

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Interest in left ventricular noncompaction (LVNC) as a distinct form of cardiomyopathy has increased over the past decade after several publications established a congenital/genetic abnormality of myocardial compaction (1,2). Reliable imaging criteria are central to defining a specific phenotype of LVNC. As imaging techniques improve, spatial resolution of the endocardial borders, differentiation of noncompacted from compacted myocardium, and distinction of trabeculation from normal anatomic variants has become easier (3), and, therefore, identification of LVNC continues to change (4). This evolution of imaging modalities has led to some concerns that LVNC may be overdiagnosed (5,6). Complicating this situation, LVNC cardiomyopathy shares many of the clinical features associated with other forms of dilated cardiomyopathy (7). Therefore, an ideal imaging modality would both differentiate myopathic noncompaction (NC) from normal variants as well as other pathological cardiomyopathies, thus establishing a unique imaging phenotype.

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ABBREVIATIONS AND ACRONYMS

3DSi = 3-dimensional sphericity index

BSA = body surface area

CHF = congestive heart failure

CMR = cardiac magnetic resonance

ED = end-diastolic

EDNCCR = end-diastolic noncompacted-to-compacted ratio

ES = end-systolic

ESNCCR = end-systolic noncompacted-to-compacted ratio

LV = left ventricular

LVEDVi = left ventricular end-diastolic volume index

LVEF = left ventricular ejection fraction

LVNC = left ventricular noncompaction

MT = myocardial thickening

NC = noncompaction

TMTMR = trabecular mass-to-total mass ratio

In 2000, Oechslin et al. (2) published the seminal paper defining the echocardiographic criteria for the diagnosis of LVNC cardiomyopathy, the hallmark of which was to measure the end-systolic noncompacted-to-compacted ratio (ESNCCR) in myocardium. In 2005, these criteria were validated using a unique population (8). During this same time interval, the application of cardiac magnetic resonance (CMR) as a diagnostic modality led to several publications redefining LVNC (9). Initial attempts to measure end-systole by CMR were limited due to image quality, temporal resolution, and image sequences (10). As such, Petersen et al. (11) presented CMR criteria of LVNC based on the end-diastolic noncompacted-to-compacted ratio (EDNCCR). The difference in end-diastolic (ED) and end-systolic (ES) criteria has led to confusion regarding the true phenotypic expression of LVNC, and, therefore, current trends with CMR criteria (EDNCCR) may lead to greater sensitivity with limited specificity. More recently, some investigators have also introduced a trabecular mass–to–total mass ratio (TMTMR) to diagnose individuals with LVNC (12).

We postulate that CMR measures of ESNCCR are feasible and, compared with EDNCCR and TMTMR, may improve the clinical recognition of LVNC from other forms of cardiomyopathy.

METHODS

Study population. After obtaining institutional review board approval, we retrospectively queried the clinical CMR database at Wake Forest Baptist Hospital for descriptions of trabeculations or NC. A total of 4,762 patients had CMR studies performed between January 2007 and April 2011, of which 122 original patients (2.5%) had reports that included descriptions of trabeculations or noncompaction, and our study population comprised these clinical cases. Clinical and demographic data were extracted from the electronic medical records.

Cardiac magnetic resonance. Images were acquired on a 1.5-T unit (Avanto, Siemens Medical Solutions, Erlangen, Germany) using steady-state free precession. Cine images (echo time/repetition time, 1.5/3.0 ms, respectively; flip angle, 60°) were acquired in 3 long-axis views (i.e., 2-, 3-, and 4-chamber views), planned on short-axis pilots at 60° angles to each other. Multislice cine views were also acquired in the short-axis plane from the base to the apex to visualize all 17 segments according to the American Heart Association recommendation (13).

CMR NC measurements. Using short-axis cine images, the noncompacted and compacted layers were visually identified, and the papillary muscles were specifically excluded from measurement. The region with the largest noncompacted-to-compacted ratio was measured in end-diastole (Fig. 1) and end-systole (Fig. 1) using WebPAX (Heart Imaging Technologies, LLC, Durham, North Carolina). Apical short-axis views 16 to 24 mm from the true apical slice were used for all measurements due to the risk of overestimating the noncompacted-to-compacted ratio in more apical slices. Short-axis views were used to prevent identifying a papillary muscle or its attachments as isolated trabeculation on long-axis views. Longitudinal views were only used to assess involvement in the true apical segment, but no measurements were recorded. In accord with previously published standards, individuals were categorized as ES NC if the ESNCCR was ≥2, and individuals were categorized as ED NC if the EDNCCR was ≥2.3 (2,11). The number of segments with associated trabeculation was also measured.

Trabecular mass-to-total mass ratio. The trabecular mass and its ratio was calculated based on the

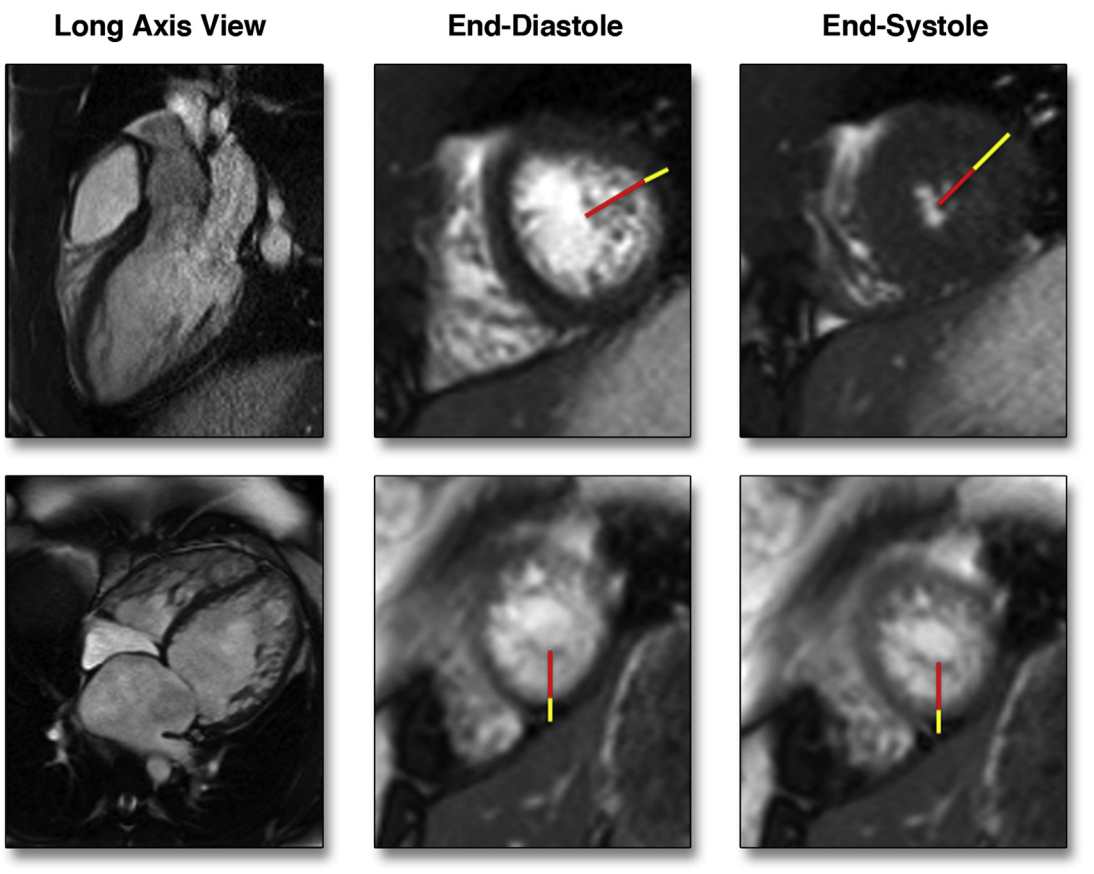

Figure 1. Still Cardiac Magnetic Resonance Images From End-Diastole and End-Systole With Demonstration of How Measurements Were Taken

The **yellow line** measures the compacted layer; the **red line** measures the noncompacted layer. **(Top)** Images obtained from an asymptomatic 40-year-old man who met end-diastolic criteria but not end-systolic criteria. **(Bottom)** Images obtained from a 35-year-old woman with congestive heart failure who met both end-diastolic and end-systolic criteria.

methods published previously (12). To measure the TMTMR, the trabecular border and papillary muscles were measured at end-diastole. The papillary muscles were included because it was difficult to distinguish between papillary muscle and trabeculations in the more densely trabeculated left ventricles. The trabeculated mass was calculated by subtracting the nontrabeculated left ventricular (LV) cavity volume from the LV end-diastole volume, which contained the entire LV cavity contained by the compacted myocardium. The trabecular volume was multiplied by the specific gravity to calculate the trabecular mass. Total LV mass was calculated by subtracting the nontrabeculated LV cavity from the LV epicardial volume and multiplying by the specific gravity. The trabeculated mass-to-total LV mass ratio was calculated. The previous study established 20% as a cutoff, but because papillary muscles were included in the trabeculated mass, the cutoff used for our analysis was 40%. Previous LV mass studies estimated that papillary muscle inclusion could increase the total LV mass by 10% (14).

Papillary muscle classification system. Using the mid-level short axis cine images at end-diastole, the papillary muscles were identified. The papillary muscles were grouped into 3 different categories (Fig. 2): 0, no identifiable papillary muscle or small muscular band contained within trabeculations; 1, 1 papillary muscle appears fully developed and independent of trabeculations, whereas the remaining papillary muscle is either not identified or contained within trabeculations; 2, both papillary muscles appear fully developed and independent of surrounding trabeculations.

CMR volume measurements. LV ED volume, ES volume, and left ventricular ejection fraction

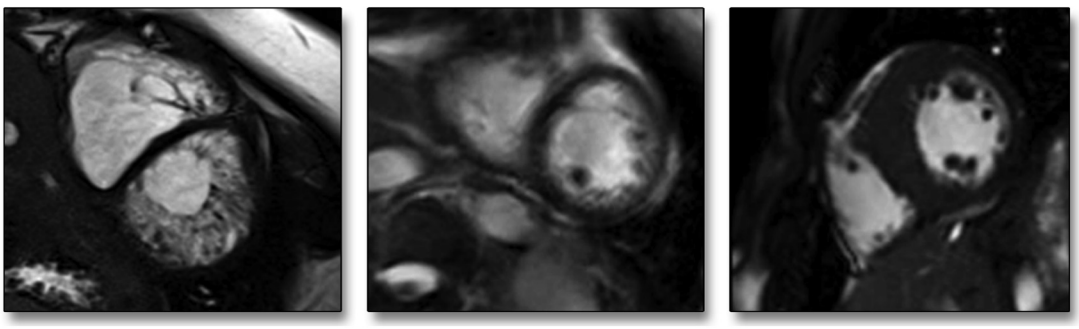

Figure 2. Cardiac Magnetic Resonance of the Different Papillary Muscle Groupings

From **left to right**, groups 0, 1, and 2.

(LVEF) were measured using commercialized software (Argus version 4.02, Siemens Medical Systems). ED and ES frames were defined as the frames in which the cavity sizes were largest and smallest by retrospective image review (15–17). The endocardial border was manually traced in the selected image frames. The papillary muscles and LV trabeculae were excluded from the endocardium and included in the LV cavity volume (18). At the base of the heart, slices were considered to be within the left ventricle if the blood volume was surrounded by ≥50% of ventricular myocardium (3).

Myocardial thickening (MT) was calculated by the following equation from the compared layer measurements obtained at the apex where the noncompacted-to-compacted ratio was measured: ED compacted layer thickness (mm) − ES compacted layer thickness (mm)/ED compacted layer thickness (mm).

The 3-dimensional sphericity index (3DSi) was calculated by the following equation (19,20): ES volume/$[4/3 \times \pi \times (D/2)^3]$ and the left ventricular end-diastolic volume index (LVEDVi) as EDV/body surface area (BSA).

Clinical events. Congestive heart failure (CHF) was defined as having a clinical diagnosis of CHF by medical record. Data were also gathered concerning death, heart failure readmission, embolic events, and ventricular arrhythmias, events previously described as being associated with LV noncompaction (2). To assess death, both the medical chart and the Social Security Death Index were searched. To assess heart failure readmission rates, the medical chart was reviewed, and a readmission was counted if they had been admitted for CHF after undergoing CMR to identify the trabeculations. To assess embolic events, the medical chart was reviewed for radiologic reports, neurology evaluations, and other notations for any description of an embolic event. To assess for ventricular arrhythmias, the medical chart was reviewed for cardiology consultations and device interrogations. Heart failure readmissions, death, ventricular arrhythmias, and embolic events were pooled for statistical power and represented a clinical phenotype of LVNC cardiomyopathy.

Covariates. Diabetes was defined as a participant who had a diagnosis of diabetes or was taking glucose-regulating medication. Hypertension was defined as a diagnosis of hypertension. Given that many of the medications used to treat CHF are also antihypertensives, we could not use antihypertensive medications as an indication of hypertension. Hyperlipidemia was defined as a diagnosis of hyperlipidemia or taking a lipid-lowering medication. Coronary artery disease (CAD) was defined as documented obstructive coronary artery stenosis, a history of percutaneous coronary intervention, or a history of coronary artery bypass graft surgery.

Statistical analysis. All CMR baseline data were presented as mean ± SD. Nominal data were tested using the chi-square test. Baseline variables were compared between those who met criteria for ES NC and those who did not and between those who met criteria for ED NC and those who did not.

Categorical data were analyzed using logistic regression. The dependent variables used were baseline CHF and combined clinical events. Covariates used for adjustment included age, race, sex, BSA, diabetes mellitus, hypertension, hyperlipidemia, CHF, and CAD. When CHF was the dependent variable, the logistic regression model was not adjusted for CHF.

Continuous data were analyzed using Pearson correlation and analysis of covariance to generate adjusted means. Separate models were used to compare the effects of ED NC and ES NC.

Outcomes included MT, LVEF, 3DSi, and LVEDVi. Analysis adjusted for age, race, sex, BSA, diabetes mellitus, hypertension, hyperlipidemia, CAD, and CHF. Of note, in the analysis involving LVEDVi, there was no adjustment for BSA. A p value <0.05 was considered statistically significant. Correlations were also used to describe unadjusted linear relationships. All statistical analyses were performed using SAS software version 9.1 (SAS Institute, Inc., Cary, North Carolina).

To describe the relationship between papillary muscle structure and different measures of NC, the chi-square test was used to compare the overall significance of the association of the papillary muscle groups with the different diagnostic criteria for NC.

To assess interobserver and intraobserver agreement, a subset of cases were randomly selected and interpreted by a second reader blinded to all information (n = 20). Interobserver and intraobserver agreement was assessed with Spearman's correlation analyzing the ED and ES thickness of the compacted and noncompacted layers. Spearman's correlation was also used to assess intraobserver and interobserver agreement regarding the TMTMR. Table analysis was used to assess interobserver and intraobserver agreement for the papillary muscle classification system. Agreement between ED and ES NC measures was also performed with table analysis and the kappa statistic.

RESULTS

Baseline characteristics are presented in Table 1. The overall population is older compared with previous investigations for LVNC (age, 57 ± 17 years), predominantly white (69%) with approximately one-third having CHF and one-fourth having CAD. The LVEF is 44 ± 16% and LVEDVi is 87 ± 37 ml/m^2. We analyzed the CMR data for relevant trends after separating the overall population into diagnostic criteria of ESNCCR, EDNCCR,

Table 1. Baseline Characteristics: Overall Study Population With Breakdown by Those Who Met End-Diastolic or End-Systolic Criteria

	Baseline Characteristics						
		End-Systolic Noncompacted-to-Compacted Ratio		End-Diastolic Noncompacted-to-Compacted Ratio		Trabecular Mass-to-Total Mass Ratio	
	Overall (N = 122)	<2.0 (n = 91)	≥2.0 (n = 31)	<2.3 (n = 88)	≥2.3 (n = 34)	<40% (n = 52)	≥40% (n = 70)
Age, yrs	57 ± 17.5	57.8 ± 16.9	54.6 ± 19.5	59.7 ± 15	49.9 ± 20*	55.4 ± 17	60.4 ± 16
African American	31	31	32	30	35	40	25
Female	50	50	52	45	62	49	52
BSA, m^2	2.0 ± 0.4	2.0 ± 0.3	1.9 ± 0.2	2.0 ± 0.3	1.9 ± 0.2	2.0 ± 0.27	1.9 ± 0.24
Diabetes	21	17	32	18	27	17	24
Hypertension	56	60	45	57	52	66	29
Hyperlipidemia	35	34	39	35	36	32	39
CHF	36	20	80*	28	57*	29	42
CAD	15.7	13	24	13	24	12	18
Hospitalizations	2 ± 3.4	1.6 ± 2.5	3.1 ± 5*	1.7 ± 3.1	2.6 ± 4.0	1.9	2.1
Death	6	4	10	7	3	4	7.6
Embolic event	10	5	23*	9	11	3.9	14.5*
Heart failure readmission	14	6	38*	8	2*	10	16.7*
Ventricular arrhythmia	6	1	20*	2	14	2	8.7
BNP, pg/ml	667 ± 795	450 ± 744	923 ± 793*	569 ± 891	817 ± 613	675 ± 890	662 ± 749
LVEF	44 ± 16	48.5 ± 14.6	30 ± 11.7*	46 ± 15	37 ± 16.8*	43.8 ± 15	43.7 ± 15
LVEDVi, ml/m^2	87 ± 37	78 ± 30	120 ± 39*	78 ± 30	111 ± 43*	79.4 ± 31.5	94 ± 37.6*
3DSi	0.36 ± 0.1	0.33 ± 0.1	0.46 ± 0.13*	0.35 ± 0.12	0.41 ± 0.15*	0.33 ± 0.10	0.39 ± 0.14*
Noncompacted segments	6.2 ± 2.7	5.4 ± 2.3	8.0 ± 2.5*	5.7 ± 2.6	7.4 ± 2.4*	5.5 ± 2.6	6.7 ± 2.7
MT	−36 ± 25	−46.8 ± 24	−5.6 ± 30*	−35.2 ± 18	−39.2 ± 30	−38.4 ± 41.5	−32.9 ± 37.8

Values are mean ± SD or %. *Statistical difference with $p < 0.05$ in comparison between those who met the respective criteria and those who did not.
BNP = B-type natriuretic peptide; BSA = body surface area; CAD = coronary artery disease; CHF = congestive heart failure; LVEDVi = left ventricular end-diastolic volume index; MT = myocardial thickening; 3DSi = 3-dimensional sphericity index.

and TMTMR. A clinical diagnosis of CHF was statistically more common among those who met the ESNCCR (80% vs. 20%) and EDNCCR (57% vs. 28%) criteria. There were slightly more who had CHF in those who met the TMTMR (42% vs. 29%), but it was not statistically significant. The individuals who met either ESNCCR or EDNCCR criteria had a lower LVEF than those who did not (48.5 ± 14.6 vs. 30 ± 11.7 and 46 ± 15 vs. 37 ± 16.8, ESNCCR and EDNCCR, respectively). However, those who met criteria with the TMTMR did not have a difference in LVEF compared with those who did not meet criteria (43.7 ± 15 vs. 43.8 ± 15). ESNCCR, EDNCCR, and TMTMR were associated with increased LVEDVi and 3DSi. Only individuals who fulfilled the ESNCCR criteria had statistically significant differences in MT parameters (−5.6 ± 11.6% vs. −46.8 ± 24%). The MT parameters in both subgroups evaluated by EDNCCR criteria were not different (−39.2 ± 25% vs. −35.2 ± 18%), nor were they different for the TMTMR criteria (−32.9 ± 37.8 vs. −38.4 ± 41.5). With MT, both groups for TMTMR and EDNCCR were comparable to the subgroup of patients who did not meet the ESNCCR criteria (−46.8 ± 24%). A scatterplot analysis with simple linear regression lines depicts the relationship between ESNCCR and EDNCCR with LVEF and MT (Fig. 3). Furthermore after analyzing both groups, ESNCCR continued to outperform EDNCCR and TMTMR with regard to LVEF, MT, and 3DSi.

LV size and function. The analysis of covariance models for ESNCCR, EDNCCR, and TMTMR presented in Table 2 is adjusted for age, race, sex, BSA, tobacco use, diabetes mellitus, hypertension, hyperlipidemia, CAD, and CHF. Those who met criteria for ESNCCR demonstrated statistically lower LVEF (31.8 ± 6% vs. 40.4 ± 8.8%), whereas those who met criteria for EDNCCR or TMTMR did not. Of note, not adjusting for CHF with 3DSi demonstrated significant results, which suggests that sphericity may be in the causal pathway between ESNCCR and CHF.

CHF and combined clinical events. After logistic regression analysis of the data based on the 2 criteria used, subjects who met ESNCCR criteria had greatest odds ratio for the presence of clinical heart failure after adjustment for the covariates listed above (odds ratio [OR]: 29.4, 95% confidence interval [CI]: 6.6 to 125) (Table 3). Logistic regression also

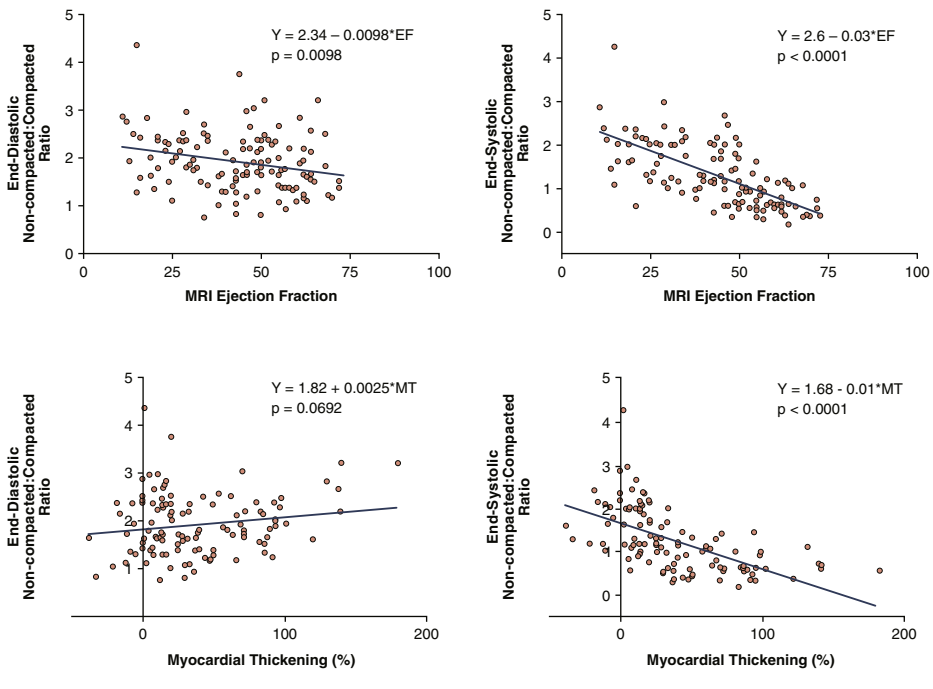

Figure 3. Scatterplots of Relationships Between End-Diastolic and End-Systolic Measures of Noncompaction With Ejection Fraction and Myocardial Thickening

Simple unadjusted linear regression lines applied to demonstrate relationship, if any. Myocardial thickening multiplied by "-" to allow for easier visual comparison with MRI ejection fraction. MT = myocardial thickening.

Table 2. ANCOVA to Generate Adjusted Means With 95% Confidence Intervals

	Adjusted Means for EF, MT, LVEDVi, and 3DSi Compared Between Different Noncompaction Criteria									
	LVEF (%)	p Value	MT, %	p Value	LVEDVi, ml/m^2	p Value	3DSi* (Without CHF)	p Value	3DSi* (With CHF)	p Value
ES NC:C ratio ≥2	31.8 ± 6	0.01	−9.4 ± 16.2	0.003	116 ± 14	0.008	0.47 ± 0.05	<0.001	0.42 ± 0.05	0.2
ES NC:C ratio <2	40.4 ± 8.8		−37.2 ± 12		93 ± 9		0.36 ± 0.05		0.38 ± 0.04	
ED NC:C ratio ≥2.3	36.4 ± 5.4	NS	−37.3 ± 12.3	0.07	116 ± 12	<0.001	0.44 ± 0.05	0.02	0.41 ± 0.05	0.2
ED NC:C ratio <2.3	38.4 ± 4.5		−27.0 ± 14.8		91 ± 11		0.37 ± 0.05		0.38 ± 0.05	
TrabM:TM ratio ≥40%	38.0 ± 4.1	NS	−25.9 ± 11.6	NS	100.7 ± 9.8	0.054	0.42 ± 0.04	0.015	0.41 ± 0.04	0.03
TrabM:TM ratio <40%	36.5 ± 4.8		−26.5 ±13.6		89.1 ± 11.6		0.36 ± 0.05		0.36 ± 0.04	

Adjusted for age, race, sex, body surface area, diabetes mellitus, hypertension, hyperlipidemia, coronary artery disease, and CHF. Without adjusting 3DSi for CHF, there is a significant relationship, which suggests that sphericity may be in the causal pathway between differing measures of noncompaction and CHF. *3DSi measured at end-systole.
ANCOVA = analysis of covariance; ED = end-diastolic; LVEF = left ventricular ejection fraction; ES = end-systolic; NC:C = noncompacted-to-compacted; TrabM:TM = trabeculated mass–to-total mass; other abbreviations as in Table 1.

demonstrated that ESNCCR had a higher OR (OR: 8.6; 95% CI: 2.5 to 33) for combined clinical events than TMTMR (OR: 3.14; 95% CI: 1.09 to 10.4) and EDNCCR (OR: 1.8; 95% CI: 0.6 to 5.8) (Table 3). To determine which aspect of the ratio was more significant, the same logistic regression model was performed with combined clinical events as the dependent variable with separate models run for ED noncompacted layer, ED compacted layer, ES noncompacted layer, ES compacted layer, trabecular mass, and total LV mass. The ES noncompacted layer and the ES compacted layer had higher odds of having clinical events ($p = 0.0008$ and $p = 0.002$, respectively), and there was also higher odds for increased trabecular mass ($p = 0.02$). However, there were not higher odds for ED noncompacted layer, ED compacted layer, or total LV mass. Using analysis of covariance, the adjusted mean of ES noncompacted layer for those who had clinical events was 14.5 ± 0.75 (95% CI) mm versus 9.9 ± 0.6 mm ($p = 0.0004$), and the adjusted mean of the ES compacted layer for those who had clinical events was 8 ± 0.6 mm versus 10.2 ± 0.4 mm ($p = 0.004$).

Papillary muscle groups and noncompaction criteria. In evaluating the relationship between the papillary muscle groups and the different diagnostic criteria, there was more abnormal papillary muscle structure noted in those who met criteria by ESNCCR and EDNCCR ($p < 0.0001$ for both comparisons). The TMTMR had a more modest association with the papillary muscle groups ($p = 0.017$) (Table 4).

Agreement between ED and ES criteria. The kappa statistic was used to compare ED and ES NC measures (Table 5). The kappa statistic was 0.43, which is only fair to moderate agreement. Both measures categorized participants in the same group 77% of the time.

Interobserver and intraobserver agreement. The interobserver agreement on ED compacted and noncompacted layer thickness by Spearman's correlation was 0.8 and 0.81, respectively. The interobserver agreement for the ES compacted and noncompacted layer measures was 0.82 and 0.78, respectively. The interobserver agreement for TMTMR was 0.85, and the interobserver agreement for papillary muscle classification had a kappa statistic of 0.82, which is good agreement (>90% classified in the same group). The intraobserver agreement on ED compacted and noncompacted layer thickness by Spearman's correlation was 0.82 and 0.84, respectively. The intraobserver agreement for the ES compacted and noncompacted layer measurements was 0.84 and 0.83, respectively. The intraobserver agreement for TMTMR was 0.87, and the intraobserver agreement for papillary muscle classification had a kappa statistic of 0.8, which is good agreement.

Table 3. Logistic Regression Analysis Used to Generate ORs (CIs) for CHF and Combined Clinical Events Separately

	ORs (CIs) for CHF and Clinical Events Associated With Noncompaction		
	ES NC:C Ratio ≥2.0	ED NC:C Ratio ≥2.3	TrabM:TM Ratio ≥40%
CHF	29.4 (6.6–125)	3.3 (1.13–9.2)	1.99 (0.82–5.0)
Combined events	8.6 (2.5–33)	1.8 (0.57–5.8)	3.14 (1.09–10.2)

Combined events included having at least one of the following: death, multiple heart failure hospitalizations, embolic events, or ventricular arrhythmias. Adjusted for age, race, sex, BSA, tobacco use, diabetes mellitus, hypertension, hyperlipidemia, CAD. Combined events also adjusted for CHF.
ORs = odds ratios; other abbreviations as in Tables 1 and 2.

DISCUSSION

This study highlights the difference in information provided by the noncompacted-to-compacted ratio measured at end-systole versus end-diastole using

Table 4. Percentage of Each Papillary Muscle Group Present in Those Who Fulfilled and Did Not Fulfill Different Criteria for Noncompaction

Association Between Papillary Muscle Groups and Different Measures of Noncompaction						
Papillary Muscle Group	**ES NC:C Ratio <2**	**ES NC:C Ratio ≥2**	**ED NC:C Ratio <2.3**	**ED NC:C Ratio ≥2.3**	**TrabM:TM Ratio <40%**	**TrabM:TM Ratio ≥40%**
0 (%)	37.5	62.5	46.9	53.1	31.3	68.7
1 (%)	84.2	16.8	52.6	47.4	33.3	66.7
2 (%)	88.7	11.3	88.7	11.3	50	50

By chi-square analysis, both the ES NC:C ratio and ED NC:C ratio had a p value <0.001, but the TrabM:TM ratio had a p value of 0.017.
Abbreviations as in Table 2.

CMR as well as the TMTMR. Four important observations are supported by the data. First, end-systole data generated by CMR LVNC are attainable in an unselected population of patients who underwent cardiac evaluation for various etiologies. Second, CMR measures of LVNC using the ESNCCR compared with the EDNCCR and the TMTMR criteria had stronger associations with LVEF and MT, imaging variables associated with cardiac dysfunction. Both ESNCCR and EDNCCR were associated with LVEDVi, a marker of ventricular remodeling, but only ESNCCR was associated with a greater sphericity index. Third, CMR ESNCCR criteria used to identify LVNC have the greatest OR (OR: 29.4) for clinical heart failure and those clinical events (OR: 8.6) classically associated with LVNC cardiomyopathy (heart failure readmissions, ventricular arrhythmias, embolic events). Fourth, different criteria were associated with abnormal papillary muscle structure, which may indicate abnormal development. Thus, we advocate adopting the ESNCCR criteria presented as the CMR phenotype for LVNC cardiomyopathy.

The most rigorously tested criteria for diagnosing NC cardiomyopathy was proposed by Jenni et al. using echocardiography (2,8). They proposed 4 imaging criteria to establish the diagnosis: 1) the myocardial wall has to be thickened with a 2-layered structure and an ESNCCR >2 from the parasternal short-axis view; 2) the predominant location of the pathology is apical, mid-lateral, and mid-inferior; 3) the absence of coexisting cardiac abnormality; 4) the demonstration of color Doppler flow in the recesses of the trabeculations. The original data included 38 patients, and subsequently the criteria were validated using a second population of 18 patients. The ES measures were found to be significantly related to ventricular arrhythmias (21), CHF (1,2), and thromboembolic phenomenon (1,2). Our population was not rigorously or prospectively evaluated for the clinical phenotype associated with LVNC. However, we did demonstrate significant differences in LVEF, MT, 3DSi, and clinical diagnosis of heart failure, as well as a strong association of clinical events classically associated with LVNC.

Table 5. Frequency Table: Kappa Agreement Statistic Was 0.43, Which Is Fair to Moderate Agreement

Comparison of Agreement Between ES and ED Measures of Noncompaction			
Measure	**ED NC:C Ratio <2.3**	**ED NC:C Ratio ≥2.3**	**Total**
ES NC:C ratio <2	76	15	91
ES NC:C ratio ≥2	12	19	31
Total	88	34	122

Assuming ES measures as standard, the ED measures' positive predictive value is 56%, and the negative predictive value is 86%.
Abbreviations as in Table 2.

In the early 2000s, an effort was made to correlate ES measures between echocardiography and CMR (10). However, due to small sample size and less-than-optimal CMR imaging sequences, the authors were unable to demonstrate significant correlations. Subsequently, Petersen et al. (11) evaluated 6 patients with LVNC and proposed CMR criteria of EDNCCR >2.3. Fazio et al. (22) extended this research and proposed CMR criteria of EDNCCR >2.5. Following these publications, many centers adopted ED measurements to define the imaging criteria for LVNC. This trend has led some authors to believe that LVNC is overdiagnosed as a phenotype, which could carry significant clinical implications (6). Although ED cutoff points are commonly seen in normal populations (4,23), the ES measurements of the short axis are not (4). More recently, interest has increased in the TMTMR to more accurately identify those with abnormal trabeculations (12).

Previous studies focused on a threshold point to determine imaging criteria for LVNC either by echocardiography or CMR. Our study demonstrates a linear relationship between the ESNCCR and LVEF, LVEDVi, 3DSi, and MT. ES measures may also provide intrinsic information about the underlying function of the compacted myocardium as assessed by

MT (24–29). We demonstrated a strong statistically significant correlation between greater ESNCCR and worse MT (Fig. 3). Our data suggest that even after adjustment for covariates, the ESNCCR criteria had the greatest OR (OR: 29.4) for identifying a clinical diagnosis of heart failure. Although we cannot conclude that the diagnosis of heart failure equates to the clinical phenotype of LVNC cardiomyopathy, it stands to reason that in the absence of other cardiac disorders, the presence of both a depressed LVEF and NC may be related, especially because the prevalence of those meeting the ESNCCR criteria in this study was 0.6% in our CMR database, comparable to other reported frequencies (30,31).

Our study supports that ED measurements have weaker associations with LV function, but may provide additional information. The median LVEF of those who met ED criteria but not ES criteria was 52%. This means that almost half of those who met ED criteria had essentially normal LV systolic function. Morphologically, both ES and ED measurements had abnormal papillary muscle structure. As such, ED measurements may identify individuals who are at higher risk of the development of subsequent LV dysfunction. Interestingly, those who met the TMTMR criteria were at slightly increased odds of having clinical events historically associated with NC, which suggests that it may have a more emerging role.

Study limitations. There are several limitations inherent in any retrospective database analysis. First, with this being a retrospective analysis, our results are hypothesis generating. Our findings will need to be validated by a more prospective approach, which may be difficult given the rare nature of LVNC. Other relevant limitations to our investigation include referral bias, lack of a previous echocardiogram to establish diagnosis, incomplete clinical variables, and variations in how trabecular mass was assessed. First, we are a large tertiary care referral center for CMR and, as such, may have a greater representation of rare cardiovascular disorders including LVNC. Second, in most situations, participants had nondiagnostic echocardiograms or were referred from an outside institution without available echocardiograms. Third, the reliance of clinical records to establish diagnoses can result in misclassification, but in many instances, we lacked the necessary records to appropriately classify individuals and therefore had to rely on documentation for many of the diagnoses. Fourth, it may be difficult to compare our TMTMRs with those previously published due to a different cutoff. Our concern was that we could not reliably separate trabeculations from papillary muscles, which could introduce a significant amount of bias to our study. Therefore, we elected to measure them together and use previous literature to help us have a higher cutoff. Finally, LVNC appears to be a clinical syndrome characterized with significant variation in presentation.

CONCLUSIONS

ES NC-to-compaction ratios ≥2 are feasible by CMR, have the strongest relationship with LV function, and have the strongest OR for identifying clinical heart failure and clinical events. Future studies in either established LV noncompaction clinical phenotypes or longitudinal investigations of imaging criteria are needed to confirm the clinical significance of these findings.

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