

Does Employing a Flowchart Improve the Diagnostic Performance of Cardiac Magnetic Resonance Imaging in Left Ventricular Noncompaction?

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Background: To test the hypothesis that making a diagnosis of left ventricular noncompaction (LVNC) on cardiac magnetic resonance imaging (CMRI) using a noncompacted-to-compacted (NC/C) myocardium ratio > 2.3 would yield significant errors, and also to test a diagnostic flowchart in patients who undergo CMRI and have clinical and echocardiographic findings suggesting LVNC could improve the diagnosis of LVNC.

Methods: A total of 84 patients with LVNC and 162 controls consisting of patients with other diseases and healthy participants who had CMRI and echocardiograms were selected. The diagnostic flowchart of the study involved the use of CMRI with all available sequences for patients with a high pre-test probability of LVNC. Two blinded independent cardiologists evaluated echocardiograms, and patients with suggestive echocardiographic and clinical findings for LVNC were enrolled in the high pre-test probability of LVNC group. Two independent blinded radiologists established the diagnosis of LVNC based on NC/C ratio > 2.3 on CMRI, and they were allowed to re-assess the patients following the diagnostic flowchart.

Results: An NC/C ratio > 2.3 identified 83 of 84 LVNC patients, yet incorrectly classified 48 of the 162 controls as having LVNC. Radiologists changed their decision in 23 of 48 patients with incorrect diagnoses, resulted in improved specificity (70.4% to 84.6%). The use of the CMRI diagnostic flowchart in the high pre-test probability group yielded a high specificity (97.2%) and accuracy (95.9%).

Conclusions: LVNC diagnosed by CMRI based on the NC/C criterion can lead to overdiagnosis, whereas only using CMRI in patients with a high pre-test probability of LVNC with all available sequences may improve the diagnostic performance.

Key Words: Cardiac image • Echocardiography • Left ventricular function

INTRODUCTION

Isolated left ventricular noncompaction (LVNC) is a disease of the myocardium with unknown etiology and an estimated prevalence reaching up to 1.3%.¹⁻³ The European Society of Cardiology and American Heart Association currently define LVNC as “unclassified cardiomyopathy” and “distinct cardiomyopathy”, respectively.^{4,5} LVNC presents with a wide range of clinical pictures ranging from an asymptomatic course over a lifetime to

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life-threatening complications such as systemic thromboembolism, arrhythmia, and heart failure.⁶ Several genetic and environmental factors have been identified as being potential risk factors for LVNC, however the exact mechanisms leading to LVNC remain unknown.⁶⁻⁸

The hallmark findings of LVNC are increased endocardial trabeculations, deep intertrabecular recesses communicating with the left ventricular cavity, and thin, compacted myocardium.⁹ Imaging modalities, and particularly echocardiography and cardiac magnetic resonance imaging (CMRI), play an important role in the diagnosis of LVNC. Echocardiography is the first-line and most commonly used modality for the diagnosis of LVNC.⁹⁻¹¹ However, echocardiography has several inherent limitations, such as operator dependency and difficulties in the evaluation of cardiac apex. Furthermore, the reproducibility of echocardiographic criteria and over- and underdiagnosis are other areas of concern.¹²⁻¹⁶

CMRI has emerged as a superior method over echocardiography for the diagnosis of LVNC given its better spatial and contrast-resolution, multiplanar imaging capability, and higher inter-observer reliability.^{17,18} Several diagnostic criteria have been proposed for the diagnosis of LVNC on CMRI. The semiquantitative criteria introduced by Petersen et al.¹⁸ including noncompacted-to-compacted (NC/C) myocardium ratio > 2.3 in end-diastole, the visual appearance of two distinct myocardial layers, and the presence of marked trabeculations and deep intertrabecular recesses within the noncompacted layer are the most widely used criteria. However, several authors have questioned the specificity of these criteria and claimed that their use for the diagnosis of LVNC might lead to misdiagnosis or overdiagnosis in a considerable number of patients with other cardiac diseases or in healthy individuals.¹⁹⁻²¹ Recently, several authors have suggested only using CMRI for patients with suggestive clinical or echocardiographic findings, and highlighted the importance of avoiding potential pitfalls before the diagnosis.^{22,23}

The aim of the current study was twofold. First, to test the hypothesis that making a diagnosis of LVNC on CMRI by solely relying on the proposed semiquantitative criterion of an NC/C myocardium threshold ratio > 2.3 would yield significant errors, since many diseases can present with a similar morphological appearance. Sec-

ond, to test the hypothesis that using a diagnostic flow-chart in patients who undergo CMRI and have clinical and echocardiographic findings suggesting LVNC might improve the diagnosis of LVNC on CMRI.

MATERIALS AND METHODS

Patient recruitment

The local ethics committee of our institution approved this retrospective study which was conducted between January 2011 and May 2019. The need for informed consent for the investigation was waived due to the presentation of de-anonymized medical data. A single observer (D.A.), referred to as the first observer in the following sections, retrospectively reviewed the medical database of our hospital and recorded patients with LVNC who underwent CMRI and echocardiography within six months of each other. The diagnosis of LVNC was established by the combination of imaging, clinical, biochemical, electrocardiographic, and genetic findings as recommended by the guidelines.^{4,5}

Patients had to have echocardiography images and cine-loops consisting of apical four-chamber, apical three-chamber, apical two-chamber, mid-papillary parasternal short-axis, and apical parasternal short-axis views with decent image quality. Patients who had incomplete images or cine-loops and those with poor quality echocardiographic or CMRI examinations preventing assessment were excluded from the study.

The control group ($n = 162$) included patients with potential mimickers such as dilated cardiomyopathy (DCM) ($n = 27$), myocarditis ($n = 17$), ischemic cardiomyopathy ($n = 16$), aortic valve stenosis ($n = 15$), restrictive cardiomyopathy ($n = 15$), hypertrophic cardiomyopathy (HCM) ($n = 10$), athlete's heart ($n = 10$), arrhythmogenic right ventricular cardiomyopathy (ARVC) ($n = 9$), postpartum cardiomyopathy ($n = 8$), cardiac amyloidosis ($n = 3$), cardiac sarcoidosis ($n = 2$), and healthy controls ($n = 21$) without any known ischemic, valvular, or autoimmune diseases, or known cardiomyopathy. The diagnoses of the other diseases were made according to relevant guidelines and recommendations.^{4,5,24-27} The CMRI and echocardiography examinations of the patients were retrieved from our picture and archive communication system (Extreme PACS, Ankara, Turkey) and de-anony-

mized by the observer for further evaluations. Figure 1 summarizes the workflow of the present work.

Echocardiography examination

All echocardiograms were performed as recommended by the American Society of Echocardiography. The present study implemented the revised criteria by Stöllberger et al.¹¹ as the fulfillment of all of the following: (1) > 3 prominent trabecular formations at the endocardial side of the left ventricular myocardium visible in end-diastole, distinct from papillary muscles, false tendons, or aberrant bands; (2) 2-layered myocardial structure; (3) NC/C ratio of ≥ 2 at end-systole; and (4) perfusion of the intertrabecular spaces from the ventricular cavity at end-diastole on color-Doppler echocardiography.

Two fully blinded cardiologists (A.A.S. and I.G.) with more than five years of echocardiography experience jointly evaluated the echocardiograms. Patients meeting the criteria as agreed by the two observers were accepted as a highly probable echocardiograms for LVNC. Discordant cases between the observers and patients with an NC/C ratio of ≥ 2 while having fewer than 4

prominent trabecular formations or > 3 prominent trabecular formations but an NC/C ratio of < 2 at end-systole were defined as having suspected LVNC.

CMRI acquisition

All MRI studies were acquired with a 1.5 T scanner (Aera, Siemens Medical Systems, Erlangen, Germany). All CMRI acquisitions were performed using phased-array body coils, and all sequences were acquired using prospective cardiac gating.

The CMRI protocol in the order of first to last consisted of breath-hold black-axial blood fast spin-echo, multiple breath-hold long-axis four-chamber, long-axis two-chamber, and 9-12 stack of short axes cine images breath-hold using balanced steady-state free precession imaging (SSFP), and two-dimensional late gadolinium enhancement (LGE) sequences in four-chamber, two-chamber, and short-axis views covering the entire left ventricle myocardium. The parameters for SSFP cine images were: repetition time (TR)/echo time (TE) = 3.8/1-3 ms, slice thickness = 5 mm with 5 mm interslice gap, temporal resolution = 35 ms. LGE sequences were obtained approximately 12 minutes (range 10-15 minutes)

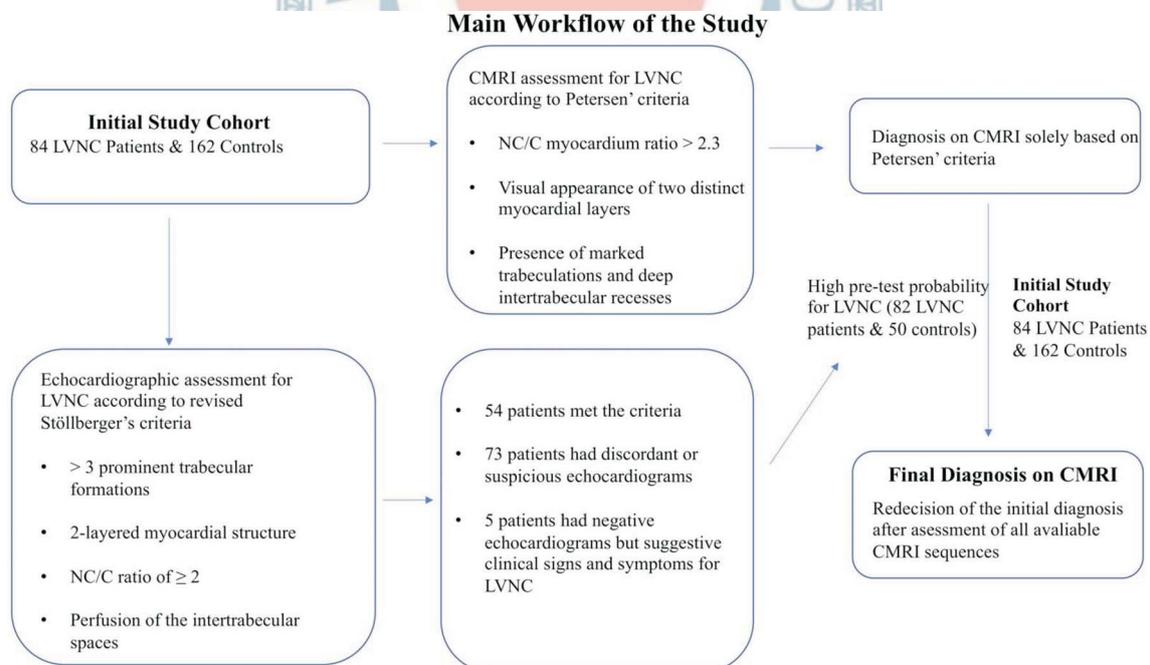


Figure 1. The main workflow of the study. The study cohort composed of 84 patients with LVNC and 162 participants consisted of different cardiac diseases and healthy controls. High pre-test probability group for LVNC that comprised 82 patients with LVNC and 50 controls, for LVNC were selected according to Stöllberger's echocardiographic criteria and clinical findings. CMRI, cardiac magnetic resonance imaging; LVNC, left ventricular noncompaction; NC/C, noncompacted-to-compacted.

after the administration of 0.10-0.12 mmol/kg gadolinium-DTPA (Magnevist, Schering AG[®], Berlin, Germany). The parameters for LGE sequences were TR/TE 9.0/3.0 ms, slice thickness 5 mm, and inversion time adjusted as required for each patient to completely null the normal myocardial signal.

CMRI analysis

Two radiologists (O.A. and C.T.) with over four years of CMRI interpretation experience jointly evaluated all de-anonymized CMRI in random order. For the initial evaluation, the observers were blinded to echocardiographic, clinical, biochemical, and electrocardiographic findings of the patients and were not allowed to evaluate other available CMRI sequences. The left ventricular myocardium was divided into 17 segments as six regions at the basal level, six regions at the midventricular level, four regions at the apical level, and one at the apex according to the American Heart Association segmentation model for the left ventricle.²⁸

The NC/C myocardium was perpendicularly measured on short-axis cine images for segments 1-16 and measured on four-chamber cine images for segment 17, as recommended in a previous study.²⁹ All measurements were performed at end-diastole using digital clip-pers. Patients with an NC/C myocardium ratio > 2.3, marked trabeculations and deep intertrabecular recesses within the noncompacted layer, and distinct 2-layer appearance were defined as being positive for LVNC.¹⁸ Immediately after measuring the NC/C ratio, the observers were allowed to reevaluate their decision based on all available CMRI sequences of each patient in addition to short- and long-axis cine images. The second decision of the observers was noted for each patient.

Statistical analysis

Statistical analyses were performed using SPSS software version 21. The variables were investigated using the Kolmogorov-Smirnov test to determine whether or not they were normally distributed. Descriptive analyses were presented using means and standard deviations for normally distributed variables and median and interquartile ranges for non-normally distributed variables. Sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and diagnostic accuracy were calculated for the CMRI and echocardiographic cri-

teria, and also for the final assessment of available CMRI sequences in the study cohort and high pre-test probability for LVNC patients.

RESULTS

A total of 84 LVNC patients including 47 males (56%) and 37 females (44%) with a median age of 20 years (range 8-63 years), and 162 participants as the control group were enrolled in the study. Detailed clinical and imaging characteristics of the patients with LVNC are depicted in Table 1.

Echocardiographic image analysis

A total of 119 of the 246 (48.4%) participants were categorized as having negative echocardiograms for LVNC, 54 of the 246 participants (22%) met the criteria as agreed by both observers, and 73 of the 246 participants (29.5%) had discordant or suspicious echocardiograms for LVNC. Stöllberger's criteria identified 45 of 84

Table 1. Demographic, clinical, and imaging characteristics of LVNC patients

Variables	Patients (n = 84)
Age (years)	20 (range 8-63)
Gender	
Male	47 (56%)
Female	37 (44%)
Family history	19 (22.6%)
Electrocardiographic findings	
Ventricular arrhythmia	12 (14.2%)
Atrial fibrillation	3 (3.5%)
Wolff-Parkinson-White syndrome	4 (4.7%)
Thromboembolic events	8 (9.5%)
Left ventricular ejection fraction on CMRI	51.42 ± 13.10
Noncompacted layer on CMRI (mm)	12.55 ± 3.67
Compacted layer on CMRI (mm)	3.91 ± 0.8
NC/C ratio on CMRI	3.24 ± 0.85
Left ventricular ejection fraction on echocardiography	54.32 ± 15.12
NC/C ratio on echocardiography	2.44 ± 1.22
Late gadolinium enhancement	2 (2.4%) [#]

CMRI, cardiac magnetic resonance imaging; LVNC, left ventricular noncompaction; NC/C, noncompacted-to-compacted.

* All variables are presented as mean ± standard deviations.

[#] Presented as median (interquartile ranges).

patients with LVNC (sensitivity 53.6%) and incorrectly classified nine of the 162 participants in the control group as having LVNC (specificity 94.4%) (Table 2). Of the 73 participants with discordant or suspicious echocardiograms, 32 had LVNC (43.8%) and 41 had (56.2%) other conditions.

CMRI analysis

The NC/C ratio cut-off threshold value of > 2.3 identified 83 of 84 LVNC patients (sensitivity 98.8%) while incorrectly diagnosed 48 of the 162 participants in the control group as having LVNC (specificity 79.4%) [DCM ($n = 9$), ischemic cardiomyopathy ($n = 8$), healthy controls ($n = 5$), myocarditis ($n = 4$), restrictive cardiomyopathy ($n = 4$), aortic valve stenosis ($n = 4$), athlete's heart

($n = 3$), HCM ($n = 3$), post-partum cardiomyopathy ($n = 3$), amyloidosis ($n = 2$), sarcoidosis ($n = 1$), and ARVC ($n = 2$)] (Table 2).

During the reevaluation after assessing all available CMRI sequences of the patients, the observers changed their decision in 23 of 48 patients with an incorrect diagnosis of LVNC, resulting in improvement in specificity from 70.4% to 84.6% and diagnostic accuracy from 80.1% to 89.4% (Table 2). These patients included three with myocarditis (based on Lake Louise criteria) (Figure 2); three with HCM (based on increased thickness of the interventricular septum) (Figure 3); one with athlete's heart (based on symmetric increased thickness of compacted myocardium wall); one with cardiac sarcoidosis based on typical LGE pattern (Figure 4); two with restric-

Table 2. Performance of imaging modalities and the diagnostic flowchart in discriminating LVNC from other patients and healthy controls

	SEN (%)	SPE (%)	NPV (%)	PPV (%)	ACC (%)
Echocardiographic criteria as identified by both observers*	53.6	94.4	78.1	83.3	80.4
Patients meeting the criteria, discordant cases, and patients with suspicious findings on echocardiography [#]	92.9	69.8	95	61.4	77.6
CMRI criteria [†]	98.8	70.4	99.1	63.4	80.1
CMRI assessment with available sequences [‡]	98.8	84.6	99.3	76.9	89.4
CMRI assessment with available sequences employed in high pre-test probability for LVNC cohort [§]	96.4	97.2	98.1	92	95.9

ACC, accuracy; CMRI, cardiac magnetic resonance imaging; LVNC, left ventricular noncompaction; NPV, negative predictive value; PPV, positive predictive value; SEN, sensitivity; SPE, specificity.

* Revised criteria by Stöllberger et al.¹³ [#] Patients meeting the criteria as agreed by two observers, discordant cases between the observers, and patients with NC/C ratio of ≥ 2 while having less than 4 prominent trabecular formations or having > 3 prominent trabecular formations but NC/C ratio of < 2 . [†] Criteria by Petersen et al.²⁰ [‡] Interpreted by the blinded two observers with evaluating all available sequences of the patients in a consensus. [§] Patients with having a high-probable or suspicious echocardiogram for LVNC and patients with negative echocardiographic findings but with highly suggestive.



Figure 2. (A) An 18-year-old male patient with acute myocarditis. The noncompacted-to-compacted ratio is measured as 2.38 on the short-axis cine image. (B) Late gadolinium enhancement (LGE) image shows increased signal in the anterior and anterolateral wall extending from mid myocardium to subendocardial area and also subepicardial area in the inferolateral wall (arrows). (C) TRIM T2-weighted image of the same patients shows mid myocardial to subendocardial signal increase in the anterior wall (arrows). The cardiac magnetic resonance imaging (CMRI) findings of the patient meet the Lake Louise Consensus criteria, and the observers' final diagnosis was acute myocarditis.

tive cardiomyopathy (based on biatrial enlargement accompanied by restrictive diastolic filling pattern and preserved systolic function); two with cardiac amyloidosis (based on diffuse subendocardial LGE), six with ischemic cardiomyopathy (based on subendocardial or

transmural LGE in coronary artery territories) (Figure 5); two with ARVC (based on right ventricular volumetric measurements, fatty infiltration in the right ventricular wall, and subendocardial LGE in the right ventricular myocardium); and three with aortic stenosis (based on flow measurements with phase-contrast images and planimetry of the annulus) (Figure 6).^{4,5,26-29}

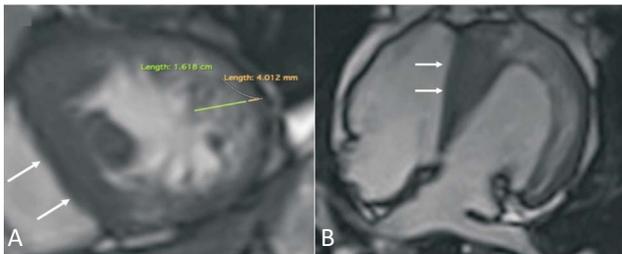


Figure 3. A 33-year-old male patient with hypertrophic cardiomyopathy. (A) The short-axis and (B) four-chamber long-axis cine image show prominent trabeculations in the lateral wall, and the noncompacted-to-compacted ratio is measured as 4. The patient meets the morphological criteria by Petersen et al.; however, the final diagnosis of the observers was hypertrophic cardiomyopathy with diffuse septal involvement (arrows).

CMRI analysis of the patients with high pre-test probability of LVNC

To identify the participants with a high pre-test probability of LVNC, the first observer (D.A.) evaluated the results of echocardiographic image analysis and also the clinical signs and symptoms of the cohort. The clinical findings suggestive of LVNC were defined as the following: symptoms including dyspnea, chest pain, palpitations, or syncope, in addition to an abnormal electrocardiogram (e.g., ventricular tachycardia, atrial fibrillation, bundle blocks) that could not be explained by any



Figure 4. A 42-year-old-female patient with cardiac sarcoidosis. (A) The short-axis cine image shows prominent trabeculations in the lateral wall at the mid-ventricular level, and the noncompacted-to-compacted ratio is measured as 4.3. (B) During the reevaluation, the observers made the diagnosis of cardiac sarcoidosis thanks to typical epicardial and mid-myocardial contrast-enhancement involving the septum, inferior, and anterior myocardium, and also extending to the right ventricle (arrows).

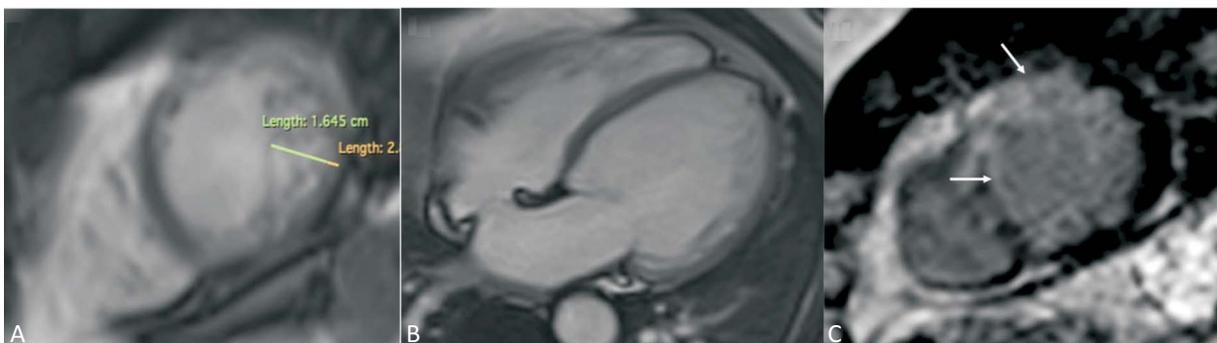


Figure 5. A 62-year-old male patient with ischemic cardiomyopathy. (A) The short-axis and (B) four-chamber long-axis cine image shows prominent trabeculations in the lateral wall and the dilated left ventricular cavity. The noncompacted-to-compacted ratio is measured as 6.1. (C) During the re-assessment, the observers made the diagnosis of ischemic cardiomyopathy because of the transmural and subendocardial late gadolinium enhancement involving the anterior apical wall and septum, respectively, which is consistent with the coronary territories.

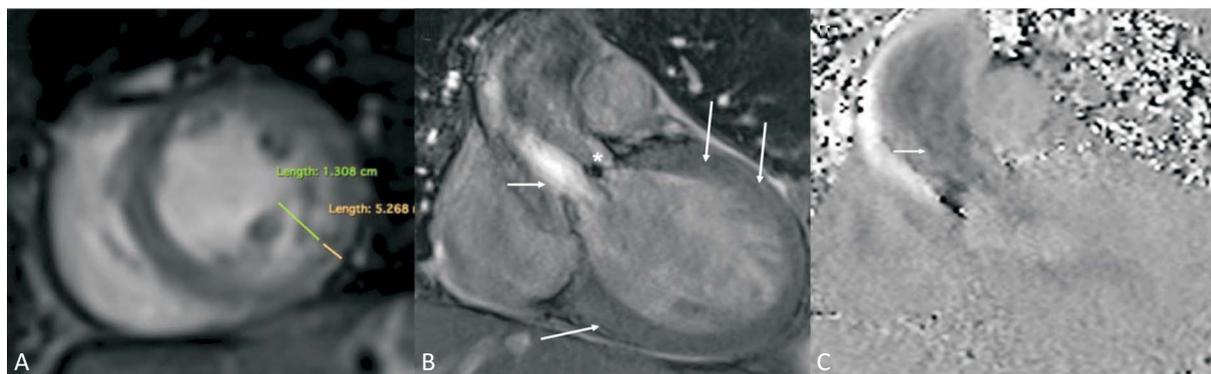


Figure 6. A 55-year-old female patient with degenerative aortic stenosis. (A) The short-axis cine image shows prominent trabeculations in the lateral wall at the mid-ventricular level, and the noncompacted-to-compacted ratio is measured as 2.5. (B) During the reevaluation, the observers exclude the diagnosis of LVNC given to high-velocity jet on cine and (C) phase-contrast images (arrows) and reduced aortic valve area (not shown). Also, note the thickened valve leaflets (asterisk) and hypertrophied left ventricular walls (long arrows).

other disease.²⁹ All patients with highly probable (n = 54) or suspicious echocardiograms with clinically suggestive findings (n = 73) for LVNC were included in the high pre-test probability group for LVNC. Additionally, the first observer included patients with negative echocardiographic findings but with highly suspicious clinical findings for LVNC (five patients, of whom three had a first-degree relative with LVNC and suggestive symptoms and signs for LVNC, and two had Wolff-Parkinson-White syndrome) in the high pre-test probability group. Finally, the high pre-test probability group consisted of 132 patients.

The diagnostic flowchart in which CMRI interpretation of all available CMRI sequences used for the high pre-test probability group identified 81 of 84 LVNC patients, while it incorrectly classified seven of the 162 participants in the control group as having LVNC, resulting in a sensitivity of 96.4% and a specificity of 97.2% (Table 2). In the high pre-test probability group, CMRI correctly confirmed echocardiography in 45 of 54 of the LVNC patients with a highly probable echocardiogram, and correctly discarded an LVNC diagnosis in five of 54 patients with a highly probable echocardiogram. Only four of 56 patients, with both CMRI and echocardiography, were incorrectly diagnosed as having LVNC. In 73 patients with discordant or suspicious echocardiograms for LVNC, CMRI correctly confirmed the diagnosis of LVNC in 31 patients and correctly discarded the diagnosis of LVNC in 38 patients. Only three patients in the control group were incorrectly classified as having LVNC. Figure 7 shows the diagnostic performance of the flowchart.

DISCUSSION

The present study demonstrated that: (1) Petersen's CMRI criteria¹⁸ had excellent sensitivity (98.8%) and low specificity (70.4%) when applied in a heterogeneous cohort; (2) the specificity of CMRI for the diagnosis of LVNC was significantly improved from 70.4% to 84.6% when all available CMRI sequences including LGE were evaluated; (3) employing CMRI for only patients with high pre-test probability as determined by echocardiograms and clinical findings yielded the highest diagnostic performance with a sensitivity of 96.4%, specificity of 97.2%, and accuracy of 95.9%; and (4) evaluation of CMRI including LGE and other available sequences successfully confirmed or discarded a diagnosis of LVNC in patients with suspicious or discordant echocardiographic findings for LVNC.

Petersen et al.¹⁸ were the first to introduce CMRI criteria for the diagnosis of LVNC. They identified that an NC/C ratio of > 2.3 in end-diastole could identify LVNC with a sensitivity of 86% and specificity of 99%, in a study cohort composed of seven patients with LVNC and 170 participants as a control group consisting of patients with different cardiac diseases and healthy controls.¹⁸ However, the authors of the Multi-Ethnic Study of Atherosclerosis (MESA) demonstrated that 140 of 343 participants (43%) without cardiac disease or hypertension had an NC/C ratio of > 2.3 on CMRI.¹⁹ A further study, which extended the analysis of the initial MESA study, showed that 706 of 2,742 participants (25.7%) had at least one cardiac segment, and that 218 of 742 partici-

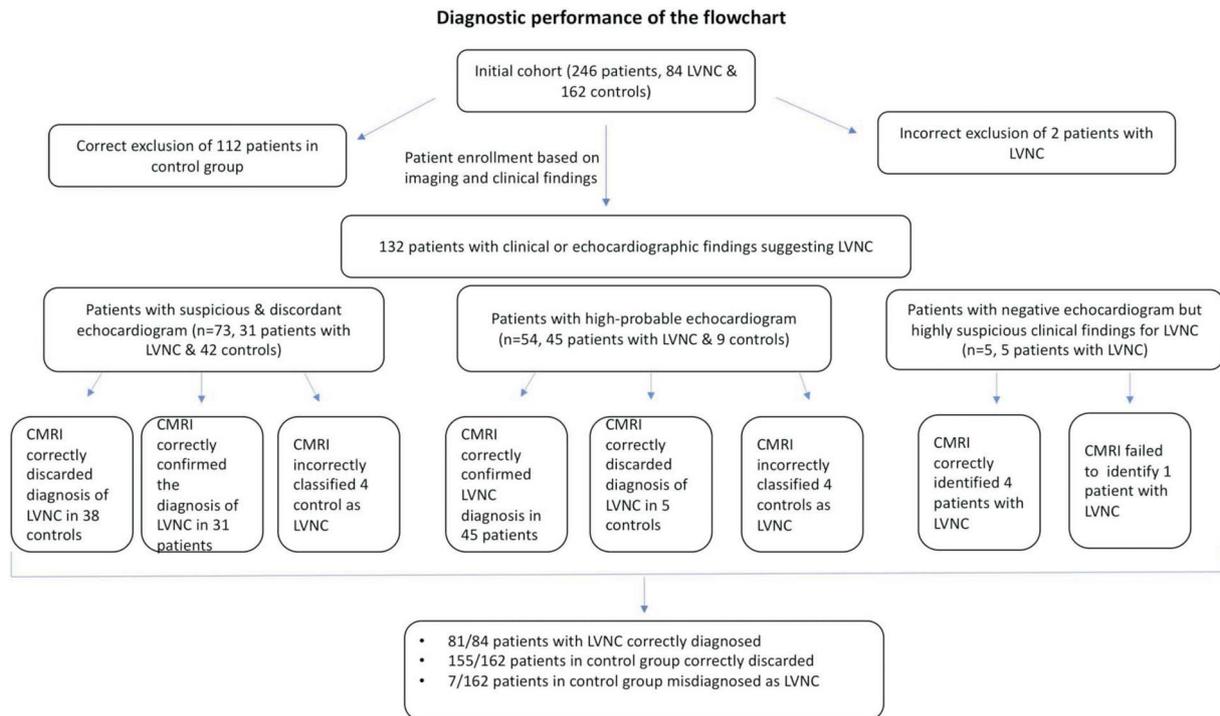


Figure 7. The diagnostic performance of the flowchart is summarized. CMRI, cardiac magnetic resonance imaging; LVNC, left ventricular noncompaction.

pants (8.0%) had at least two segments with an NC/C ratio of > 2.3 on CMRI.²⁰ Other studies have also pointed out that an NC/C ratio of > 2.3 on CMRI might be too sensitive and have voiced concerns regarding the potential over- or misdiagnoses when using the criteria.²¹ In the current study, an NC/C myocardium ratio of > 2.3 also demonstrated low specificity similar to these studies.

Apart from the semiquantitative criteria of Petersen et al.,¹⁸ several other quantitative criteria have been proposed for the diagnosis of LVNC on CMRI. Grothoff et al.,³⁰ Jacquier et al.,³¹ and Choi et al.³² offered absolute CMR quantification of the NC myocardial mass for the diagnosis of LVNC that yielded promising results. However, all authors offered different cut-off values and also used different approaches for the measurements.³⁰⁻³² The reproducibility of these criteria is also questionable.³² Additionally, CMR quantification of the NC myocardial mass is somewhat complex and time-consuming to be integrated into daily practice.

Zuccarino et al.²² and Gati et al.²³ carried out in-depth investigations of the literature on the role of imaging modalities for the diagnosis of LVNC. Both groups of authors suggested that a diagnosis of LVNC could not

be readily achieved by relying solely on current diagnostic criteria of CMRI or echocardiography, and using these criteria, particularly those for CMRI, might lead to the overdiagnosis of LVNC, especially in low-risk populations.^{22,23} In the current study, we implemented a diagnostic workflow mostly stemming from the suggestions of these works, and demonstrated that the diagnosis of LVNC could be more precisely established when CMRI was used in a population with high pre-test probability, suggesting that the diagnosis of LVNC should not be made in every patient with an NC/C myocardium ratio of > 2.3 on CMRI. Our results highlight that all available CMRI sequences should be evaluated in corroboration with clinical and echocardiographic findings to discard potential pitfalls. The diagnostic workflow proposed in this study, which used CMRI only for patients with suggestive clinical or imaging findings for LVNC, might prevent misdiagnosis or overdiagnosis in a significant number of patients.

The present study had several limitations. First, there was an obvious selection bias during the patient recruitment phase, since we only included patients with diseases that might show a similar morphological appear-

ance with LVNC on imaging. Therefore, our findings might not be generalizable beyond the study sample. Second, the observers were blinded to the clinical findings of the patients, and several of the incorrect diagnoses might have been avoided by clinical findings, such as in patients with athlete's heart or post-partum cardiomyopathy. Third, the observers were allowed to investigate all available CMRI sequences of the patients; hence, the presence of several sequences which are only used for particular clinical conditions such as early gadolinium enhancement images for myocarditis or phase-contrast images for aortic stenosis inevitably added bias to their decision. Fourth, we did not assess interobserver variability of echocardiography; however, the interobserver reliability of the method has been widely investigated in previous works,¹²⁻¹⁴ and exploring this metric was beyond the scope of the present study.

Fifth, the cardiologists performing echocardiographic assessment only evaluated the images based on Stöllberger's criteria.¹¹ Hence, the potential exclusion of several diseases such as aortic stenosis that could be readily established on echocardiography was not made. Nevertheless, the aim of the present work was not to compare the diagnostic performance of CMRI and echocardiography, but rather to test the diagnostic performance of a multimodal imaging approach. Finally, we did not evaluate diagnostic performance of several other proposed criteria for the diagnosis of LVNC such as measuring total trabeculated mass and myocardial strain.^{32,33}

CONCLUSIONS

In conclusion, using an NC/C ratio of > 2.3 on CMRI resulted in misdiagnosis or overdiagnosis of LVNC. We suggest only using CMRI in patients with clinical or echocardiographic findings suggesting LVNC, and we also emphasize the importance of excluding all potential mimickers based on imaging and clinical findings before establishing the diagnosis.

ACKNOWLEDGEMENT AND/OR DISCLAIMERS

None.

ETHICAL STATEMENT

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. A local ethics committee approved this retrospective study conducted at our institution between January 2011 and May 2019 and waived the need for informed consent for the investigation and presentation of de-anonymized medical data.

DATA STATEMENT

According to our institute policy, the data of the present work available from the corresponding author on reasonable request.

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