Left Ventricular Non-Compaction: Insights From Cardiovascular Magnetic Resonance Imaging

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Clinical Insights From Cardiac Imaging

Left Ventricular Non-Compaction

Insights From Cardiovascular Magnetic Resonance Imaging

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OBJECTIVES We aimed to test the diagnostic accuracy of cardiovascular magnetic resonance (CMR) imaging in distinguishing pathological left ventricular non-compaction (LVNC) from lesser degrees of trabecular layering seen in healthy volunteers and, in those with cardiomyopathies and concentric left ventricular hypertrophy, potential differential diagnoses. We hypothesized that pathological trabeculation could be distinguished by determining the ratio of non-compacted to compacted myocardium (NC/C ratio).

BACKGROUND Left ventricular non-compaction is characterized by a non-compacted myocardial layer in the left ventricle. Cardiovascular magnetic resonance images this layer with unprecedented quality, particularly in the ventricular apex, where echocardiography has inherent difficulties.

METHODS We analyzed magnetic resonance cine images, using the 17-segment model in 45 healthy volunteers, 25 athletes, 39 patients with hypertrophic cardiomyopathy and 14 with dilated cardiomyopathy, 17 with hypertensive heart disease, and 30 with aortic stenosis, as well as images from 7 patients previously diagnosed with LVNC whose diagnoses were supported by additional features.

RESULTS Areas of non-compaction were common and occurred more frequently in all groups studied in apical and lateral, rather than in basal or septal, segments. A NC/C ratio of >2.3 in diastole distinguished pathological non-compaction, with values for sensitivity, specificity, and positive and negative predictions of 86%, 99%, 75%, and 99%, respectively.

CONCLUSIONS Left ventricular non-compaction is diagnosed accurately with CMR using the NC/C ratio in diastole. (J Am Coll Cardiol 2005;46:101–5) © 2005 by the American College of Cardiology Foundation

Left ventricular non-compaction (LVNC) is characterized by the presence of an extensive non-compacted myocardial layer lining the cavity of the left ventricle (LV) and potentially leads to cardiac failure, thromboembolism, and malignant arrhythmias (1,2). It can be associated with neuromuscular disorders (3) and can co-exist with other cardiac malformations (2). On the basis of echocardiographic studies, its prevalence has been estimated at 0.05% in the general population (1), and the finding of a ratio of >2.0 between the thickness of the non-compacted and compacted myocardial layers in systole is considered diagnostic (4). Echocardiography, however, poses inherent problems in assessing the LV apex, known to be the most commonly non-compacted area (5).

Because high-resolution imaging techniques, such as multi-detector computed tomography, have shown the frequent presence of pronounced trabeculae within healthy myocardium (6), a similar finding may be expected in both healthy and diseased hearts with cardiovascular magnetic resonance (CMR), which is increasingly used in clinical practice. Accordingly, it is necessary to establish specific CMR criteria for the diagnosis of pathological non-compaction. To this end, we examined healthy volunteers as well as patients with potential differential diagnoses for LVNC. Findings from this group were compared with those of unequivocal LVNC cases whose diagnoses were supported by other clinical features.

METHODS

The study was approved by our institutional ethics committee. Each participant gave written informed consent.

Participants. We enrolled seven patients with clinical diagnoses of LVNC on the basis of either echocardiographic or CMR documentation of a distinct two-layered appearance of trabeculated and compacted myocardium. An arbitrary threshold for the degree of non-compaction was not applied so as not to exclude patients with a partial expression of the disease (7). The imaging findings had to be accompanied by one of the following to increase the pre-test probability for this diagnosis: documentation of a similar appearance in first-degree relatives suggestive of autosomal dominant transmission, associated neuromuscular disorders,

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Abbreviations and Acronyms

CMR = cardiovascular magnetic resonance
DCM = dilated cardiomyopathy
LV = left ventricle/ventricular
LVNC = left ventricular non-compaction
NC/C ratio = ratio of non-compacted to compacted myocardium

or complications, such as systemic embolization and regional wall motion abnormalities (Table 1). The remaining subjects were healthy volunteers without a history of cardiovascular symptoms or risk factors or drawn from groups given a potential differential diagnosis for LVNC: 25 competitive athletes, 14 patients with dilated cardiomyopathy (DCM), 39 with hypertrophic cardiomyopathy, 17 with LV hypertrophy secondary to hypertension, and 30 with aortic stenosis.

High-level competitive athletes with an average of 19 ± 7 h of training per week were recruited. Patients with hypertrophic cardiomyopathy were diagnosed on the basis of family history and standard electrocardiographic and echocardiographic criteria in the absence of a secondary cause for cardiac hypertrophy. The diagnosis of DCM was made on the basis of impaired global LV function, with an ejection fraction of <40% on echocardiography, and exclusion of other causes of LV dysfunction. Patients with hypertension and patients with aortic stenosis were enrolled if they showed an end-diastolic wall thickness of >13 mm on echocardiography.

Magnetic resonance imaging. All CMR exams were performed at 1.5-T (Sonata, Siemens Medical Solutions, Erlangen, Germany). Steady-state free precession cine images (echo time/repetition time 1.5/3.0 ms, flip angle 60°) were acquired in three long-axis views (i.e., horizontal and vertical long-axis and LV outflow tract), planned on short-axis pilots at 60° angles to each other to visualize all 17 segments according to the American Heart Association recommendation (8).

Data analysis. Cine images were analyzed with CMR tools (Imperial College, London, United Kingdom); the observer was blinded to the diagnosis. The distribution of non-compaction was assessed by qualitative analysis of all 17 segments for presence or absence of any degree of non-compaction (i.e., for a distinct two-layered appearance of trabeculated and compacted myocardium). A segment was regarded as non-compacted if the visual appearance clearly suggested the presence of two myocardial layers with different degrees of tissue compaction. In each of the three diastolic long-axis views, the segment with the most pronounced trabeculations was chosen for measurement of the thickness of the non-compacted and the compacted myocardium perpendicular to the compacted myocardium. The ratio of non-compacted to compacted myocardium (NC/C ratio) in diastole was calculated for each of the three long-axis views, and only the maximal ratio was then used for analysis. The apex (segment 17) was excluded from the measurements, because the compacted myocardium is generally thinner in this area and inclusion would have led to artificially high ratios.

Statistical analysis. All data are presented as mean ± standard deviation. Nominal data were tested using the chi-square test. Continuous data were analyzed using analysis of variance with post-hoc Bonferroni analysis to establish differences between LVNC and the six remaining groups individually. A p value of <0.05 (after Bonferroni adjustment) was considered statistically significant. We used receiver operating characteristics to generate cut-off values for optimized sensitivity and specificity to distinguish LVNC from all other groups of subjects.

RESULTS

Non-compaction was more common in the apical segments of the healthy volunteers, being found in 91% of subjects, as compared with the mid-cavity levels (78%) and the basal segments (21%) (Fig. 1). Non-compaction was most common in the anterior segment, becoming less frequent in successive segments as viewed in a clockwise direction. Similar patterns of distribution were seen in hearts of the patients with confirmed LVNC and in those of the other groups (Fig. 1). Overall, patients with pathological non-compaction had involvement of significantly ($p < 0.01$) more myocardial segments (10 ± 3 segments) than did healthy volunteers (6 ± 3 segments), athletes (6 ± 4 segments), patients with hypertrophic (5 ± 4 segments) and dilated cardiomyopathy (7 ± 3 segments), and patients with LV hypertrophy secondary to hypertension (4 ± 4 segments), and patients with aortic stenosis (6 ± 4 segments).

Table 1. Characteristics of Patients Diagnosed With LVNC

LVNC Patients	Age (yrs)	Gender	Symptoms	FH	ECG Changes	Regional Wall Motion Abnormality	LVEF (%)	Neuromuscular Findings	NC/C Ratio	No. of Segments With NC
1	14	M	Heart failure as baby	+	+	—	48	—	2.4	12
2	15	F	—	+	+	—	64	—	1.1	9
3	38	M	—	+	—	—	61	—	2.3	8
4	41	M	—	+	—	+	53	—	3.3	12
5	46	M	Systemic embolus	—		+	17	—	6.1	15
6	26	F	—	—	—	+	68	—	2.9	9
7	25	M	Syncope	—	+	+	59	+	2.7	8

FH = family history; ECG = electrocardiographic; LVNC = left ventricular non-compaction; NC = non-compaction; NC/C = non-compacted to compacted myocardium.

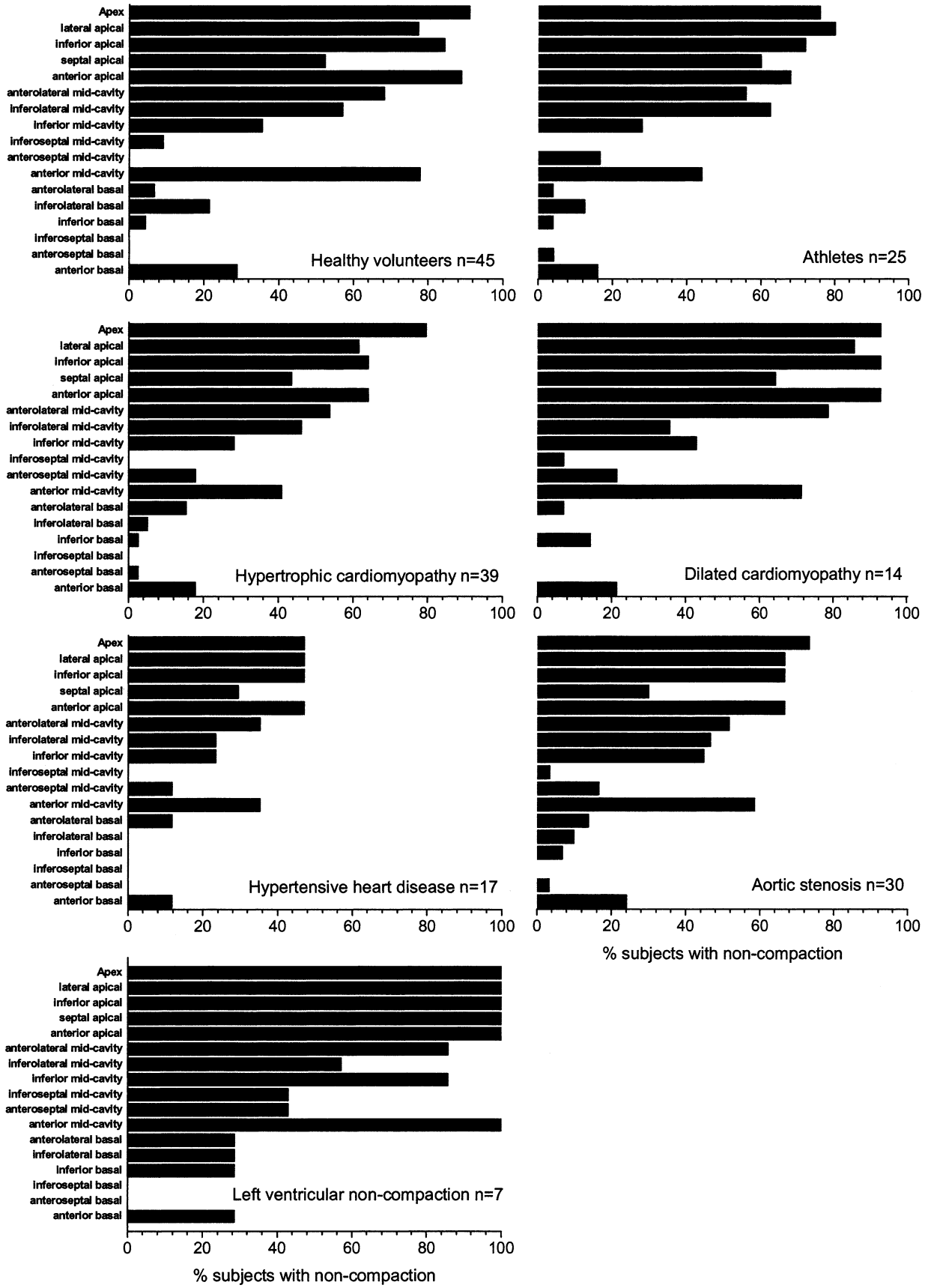

Figure 1. Distribution of non-compaction. The **bars** represent the percentage of subjects in each group with non-compaction in given segments. The pattern of distribution of non-compaction does not separate the groups.

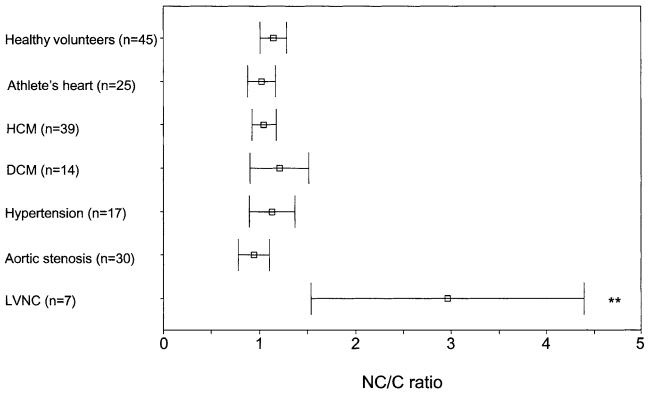

Figure 2. Ratio of the end-diastolic thickness of the non-compacted and compacted layers of the myocardium (NC/C ratio). Data are presented as means **(squares)** and 95% confidence interval **(whiskers)**. $^{**}p < 0.01$. DCM = dilated cardiomyopathy; HCM = hypertrophic cardiomyopathy; LVNC = left ventricular non-compaction.

The end-diastolic NC/C ratio was, on average, at least 60% greater in patients with LVNC (3.0 ± 1.5) compared with all other groups ($p < 0.01$ for all) (Fig. 2). Receiver operating characteristics analysis identified the end-diastolic NC/C ratio as a valuable parameter to distinguish pathological non-compaction from the lesser degrees of non-compaction encountered in healthy, dilated, and hypertrophied hearts. A NC/C ratio of >2.3 in diastole distinguished pathological non-compaction, with values for sensitivity, specificity, positive, and negative predictions of 86%, 99%, 75%, and 99%, respectively.

DISCUSSION

We found that the degree of non-compaction of the LV was far more frequent in healthy, dilated, and hypertrophied hearts than previously reported in cardiac imaging studies; presumably this is a manifestation of the increased sensitivity of CMR. Nevertheless, we have shown that the ratio between the trabecular and compact layers of the myocardium as measured by CMR in diastole is accurate in detecting pathological LVNC.

The segmental distribution of non-compaction in healthy, dilated, and hypertrophied hearts was similar to that found in the patients with confirmed LVNC; however, the ratio between the myocardial thicknesses was at least 60% greater in those with LVNC. Therefore, we are unable to lend support to the recent suggestion that the segmental distribution can be used to clarify the diagnosis of LVNC (2,4).

The trabecular layer of the developing ventricular walls is known to compact during its development from base to apex, from epicardium to endocardium, and from the septal to the lateral wall (9). Although the underlying pathophysiologic mechanisms for lack of such compaction remain unresolved, varying degrees of arrest of this normal embryologic process (4) provide an attractive explanation for the typical pattern of distribution seen in all our subjects. Almost 70% of autopsied healthy hearts are reported to show some degree of non-compaction (10), a finding endorsed by the prevalence observed in our study and

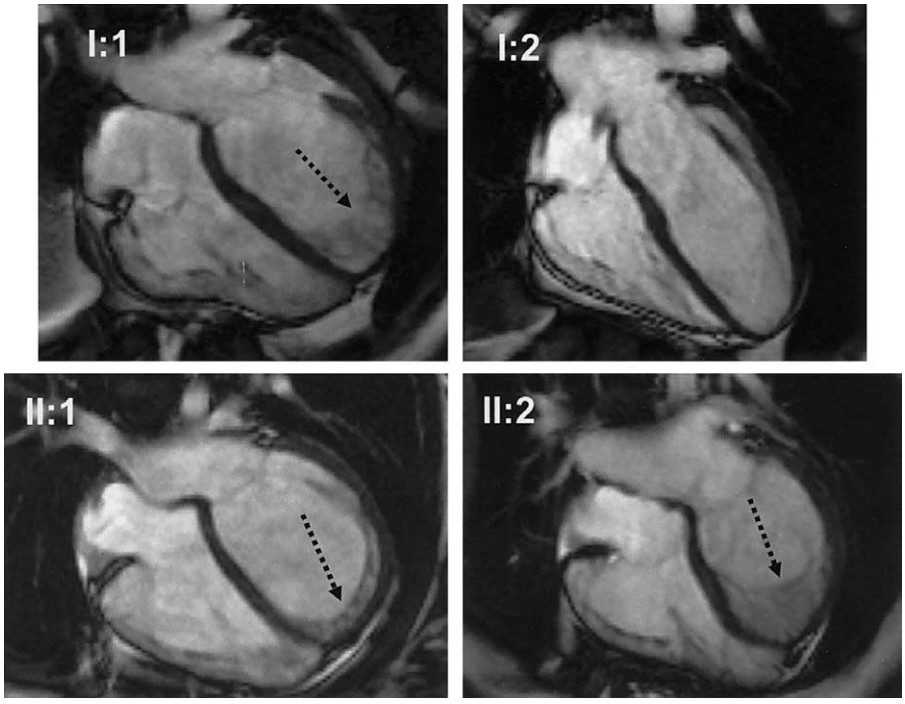

Figure 3. The autosomal dominant pattern of inheritance in a family with pathological left ventricular non-compaction. Diastolic horizontal long-axis views of parents (I:1 father and I:2 mother) and children (II:1, II.2) show variable degrees of non-compaction **(black dotted arrows)** in I:1 (Patient #3; Table 1), II:1 (Patient #2; Table 1), and II:2 (Patient #1; Table 1). Patient II:1 likely illustrates partial expression of pathological non-compaction, because her ratio of end-diastolic thicknesses is <2.3 (1.1).

probably one with no prognostic relevance. Partial expression of pathological LVNC is illustrated by one patient (Patient #2; Table 1, Fig. 3) who has only mild anatomical non-compaction, but supporting evidence for this diagnosis. This phenomenon is typical of autosomal dominant conditions and has recently been reported in large families with autosomal dominant LVNC (7).

Previous case studies using CMR imaging have usually considered echocardiographic criteria to represent the gold standard for diagnosis. One small study, mainly using older gradient echo sequences, suggested echocardiography to be superior to CMR at that time (11). Advances in CMR have resulted in superior image quality. We used diastolic steady-state free precession cine frames to determine the ratio of thickness of the trabecular and compact layers, the trabeculations being more easily identified by CMR in the relaxed heart. The diastolic ratio of >2.3 showed high diagnostic accuracy for distinguishing pathological LVNC from the degrees of non-compaction observed in healthy, dilated, and hypertrophied hearts. This slightly higher cut-off value reflects that the measurement obtained with CMR is taken in diastole, whereas the echocardiographic values are taken in systole (cut-off value of 2.0) (4).

Study limitations. The main limitation of our study is the relatively small number of patients with features of LVNC in whom the diagnosis could be confirmed by the presence of other abnormalities. Isolated echocardiographic or CMR evidence of marked non-compaction was intentionally not considered sufficient for inclusion so as to avoid circular reasoning.

Conclusions. We have shown that, on the basis of the ratio of end-diastolic thickness of the non-compacted and compacted layers of the myocardium, CMR imaging is accurate when diagnosing pathological LVNC. We propose that measurements are best made in diastole and that the cut-off values should be different from those used in echocardiography. Our findings support the clinical use of CMR in diagnosing LVNC, especially for those patients with poor echocardiographic windows.

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REFERENCES

1. Ritter M, Oechslin E, Sutsch G, Attenhofer C, Schneider J, Jenni R. Isolated noncompaction of the myocardium in adults. Mayo Clin Proc 1997;72:26–31.
2. Oechslin EN, Attenhofer Jost CH, Rojas JR, Kaufmann PA, Jenni R. Long-term follow-up of 34 adults with isolated left ventricular noncompaction: a distinct cardiomyopathy with poor prognosis. J Am Coll Cardiol 2000;36:493–500.
3. Stollberger C, Finsterer J, Blazek G. Left ventricular hypertrabeculation/noncompaction and association with additional cardiac abnormalities and neuromuscular disorders. Am J Cardiol 2002;90:899–902.
4. Jenni R, Oechslin E, Schneider J, Jost CA, Kaufmann PA. Echocardiographic and pathoanatomical characteristics of pathological non-compaction, as a distinct cardiomyopathy. Heart 2001;86:666–71.
5. Moon JC, Fisher NG, McKenna WJ, Pennell DJ. Detection of apical hypertrophic cardiomyopathy by cardiovascular magnetic resonance in patients with non-diagnostic echocardiography. Heart 2004;90:645–9.
6. Axel L. Papillary muscles do not attach directly to the solid heart wall. Circulation 2004;109:3145–8.
7. Sasse-Klaassen S, Probst S, Gerull B, et al. Novel gene locus for autosomal dominant left ventricular noncompaction maps to chromosome 11p15. Circulation 2004;109:2720–3.
8. Cerqueira MD, Weissman NJ, Dilsizian V, et al. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: a statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. Circulation 2002;105:539–42.
9. Sedmera D, Pexieder T, Vuillemin M, Thompson RP, Anderson RH. Developmental patterning of the myocardium. Anat Rec 2000;258:319–37.
10. Boyd MT, Seward JB, Tajik AJ, Edwards WD. Frequency and location of prominent left ventricular trabeculations at autopsy in 474 normal human hearts: implications for evaluation of mural thrombi by two-dimensional echocardiography. J Am Coll Cardiol 1987;9:323–6.
11. Weiss F, Habermann CR, Lilje C, et al. [MRI in the diagnosis of non-compacted ventricular myocardium (NCVM) compared to echocardiography]. Rofo Fortschr Geb Rontgenstr Neuen Bildgeb Verfahr 2003;175:1214–9.

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