

# Role of Cardiac Magnetic Resonance in the Diagnosis and Prognosis of Ventricular Noncompaction Cardiomyopathy

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## ABSTRACT

**Objective:** A low left ventricular ejection fraction (LVEF) is the most important marker of a poor clinical prognosis in many heart diseases. This study aimed to determine the cardiac magnetic resonance imaging (MRI) findings most associated with reduced LVEF in left ventricular noncompaction cardiomyopathy (LVNC).

**Methods:** MRI scans of cases of LVNC with isolated left ventricular involvement were reviewed. The number of segments involved by LVNC, LVEF, wall thickness of LVNC-affected segments, cardiac output, and cardiac index were determined. An LVEF value of  $\leq 30\%$  was accepted as a poor prognosis indicator. Low LVEF and morphology were compared by the Pearson correlation method.

**Results:** In total, 31 cases of LVNC were included. The highest correlation was found between EF and the number of segments affected ( $r = -0.6$ ). LVEF was inversely correlated with the number of segments affected. Other factors that were significantly associated with low LVEF were the presence of fibrosis, low cardiac output, and low cardiac index.

**Conclusion:** In conclusion, the number of non-compact segments is the most important morpho-pathological factor in clinical follow-up and treatment planning in LVNC cases due to its effect on EF change.

**Key Words:** Cardiomyopathies; Heart; Magnetic resonance imaging; Myocardium; Prognosis

## 中文摘要

### 心臟磁共振在心室緻密化不全心肌病的診斷和預後的作用

S Altay

**目的：**低左心室射血分數（LVEF）是許多心臟病臨床預後不良的最重要標誌。本研究旨在明確與左心室緻密化不全心肌病（LVNC）中LVEF降低最相關的心臟磁共振成像（MRI）表現。

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**Data Availability:** All data generated or analysed during the present study are available from the corresponding author on reasonable request.

**Ethics Approval:** Izmir Katip Celebi University Non-Interventional Clinical Research Ethics Committee approved this retrospective study and waived the need for informed consent because of the retrospective evaluation of anonymised medical data (Ref: 2020-743).

**方法：**回顧分析孤立左心室受累LVNC病例的MRI掃描。測定LVNC涉及的節段數、LVEF、LVNC受累節段的壁厚、心輸出量和心臟指數。LVEF值30%或以下被認為是預後不良的指標。採用 Pearson 相關分析比較低 LVEF 值和形態學改變。

**結果：**共納入31例 LVNC。在射血分數和受影響的段數之間看到最高相關性 ( $r = -0.6$ )。LVEF與受影響的節段數呈負相關。與低LVEF顯著相關的其他因素包括存在纖維化、低心輸出量和低心指數。

**結論：**非緻密節段的數量是LVNC病例臨床隨訪和治療計劃中最重要形態病理因素，因為它對射血分數變化有影響。

## INTRODUCTION

Left ventricular noncompaction cardiomyopathy (LVNC) is a rare disease that occurs as a result of failure of the process of trabeculation in the left ventricular (LV) wall to proceed after 5 to 8 weeks of foetal development.<sup>1</sup> It is characterised by the presence of a subendocardial non-compacted layer. A non-compacted layer >66% of the entire wall thickness is diagnostic of LVNC.<sup>1,2</sup> The apex and inferolateral wall are the segments most affected in the left and, sometimes, the right ventricle.<sup>1</sup> Resulting heart failure, thromboembolism, arrhythmia, or sudden death can occur.<sup>2</sup> Microvascular dysfunction and ischaemia play a role in the pathogenesis of arrhythmia and/or LV dysfunction.<sup>3</sup> The European Society of Cardiology includes LVNC in the group of unclassified cardiomyopathy as it is unclear whether it is discrete cardiomyopathy or merely a morphological feature shared by many different phenotypic cardiomyopathies, but the American Society of Cardiology considers LVNC primary cardiomyopathy.<sup>3</sup> There are different opinions as to the aetiology. Genetic and sporadic causes are found in the literature.<sup>4,5</sup> Significant genetic heterogeneities have been identified in LVNC, but the familial major genetic cause has not yet been identified.<sup>5</sup>

Data on the pathological findings affecting the clinical course in LVNC cases are insufficient in the literature.<sup>6</sup> In many studies, LVNC cases have been evaluated by echocardiography, but morpho-pathological causes affecting the prognosis of the disease have not been clearly defined.<sup>7</sup> Morphological and functional data may be obtained with cardiac magnetic resonance (CMR) examinations in LVNC cases. We examined the morphological and functional abnormalities of LVNC with CMR.

A lower left ventricular ejection fraction (LVEF) than normal values determine the clinical severity of LVNC heart involvement. Correlations between CMR findings

and LVEF change in LVNC cases were evaluated. This study aimed to find out the effects of morpho-pathological changes on prognosis in LVNC cases.

## METHODS

### Patients

A total of 63 cases diagnosed with LVNC in CMR examination between 2014 and 2019 in our hospital's image archiving system were retrospectively re-evaluated. For the diagnosis of LVNC, the Petersen diagnostic criteria were used in cases with uncompressed tissue thickness  $\geq 66\%$  of the total wall thickness.<sup>8,9</sup> Measurements were made on 2- and 4-chamber images in the end-diastolic phase. Three cases with isolated right ventricular involvement, 10 cases with coronary artery disease, seven cases with right and left ventricular involvement, five cases with dilated cardiomyopathy, and seven cases with a history of cardiac surgery were excluded from the study.

The remaining 31 cases with isolated LV involvement and no known disease were included in the study. Cases were included in the examination regardless of clinical symptoms. Ejection fraction (EF), cardiac output (CO), cardiac index (CI) values, and wall involvement rate (%) as were calculated. The number of segments affected by LVNC was calculated with the American Heart Association's 17-segment model. The data of the patients were evaluated statistically independent of age.

### Cardiac Magnetic Resonance Protocols

CMR studies were performed on a 1.5 Tesla scanner (Aera®; Siemens Healthineers, Erlangen, Germany). Patients were scanned with 16-channel surface phased array body coils. Cine images were acquired in the 2-chamber and 4-chamber views for the heart. Balanced steady-state free precession cine imaging (time of repetition/time of echo, 2.7-3.1/1.4-1.5; flip angle, 65°; temporal resolution, 25-39 ms; in-plane resolution, 1.9 × 1.9 to 2.6 × 2.7 mm; mean ( $\pm$  standard deviation)

value,  $2.2 \pm 0.2 \times 2.2 \pm 0.2$  mm; breath-hold duration, 10 to 12 heartbeats per section acquired. The section thickness was 8 mm with a gap of 2 mm) was performed in long-axis 2- and 4-chamber views for biplanar assessment of LV end-diastolic volume, LV mass, and LVEF. Contours were drawn automatically, and if needed, manually corrected. Biplanar anatomical and functional parameters were calculated automatically by post-processing on a workstation (Syngo; Siemens).

We administered 0.2 mmol/kg intravenous gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) via the antecubital vein for late gadolinium enhancement imaging. A flow rate of 2 mL/sec was used. A minimum of 10 minutes after contrast administration, and inversion-recovery steady-state free precession inversion time (TI) short-axis scouting sequence was acquired at the mid-ventricular level to determine optimal TI. TI was calculated for optimal suppression of myocardial signal. Short- and long-axis late gadolinium enhancement images including LV myocardium were acquired using the FLASH-PSIR sequence.

### Imaging Analysis

CMR examinations were evaluated by a radiologist who has a cardiac imaging certificate with extensive CMR experience (>9 years). EF, stroke volume, CI, CO,

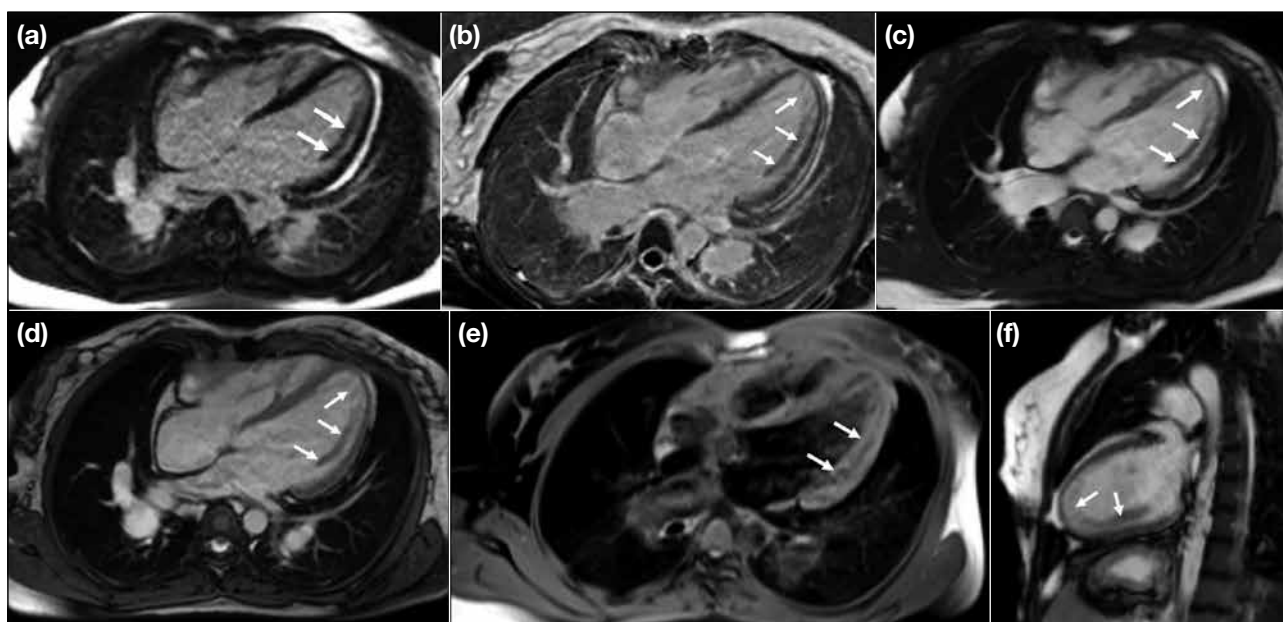
heart muscle weight, and LV peak ejection values were calculated automatically over functional sequences in the workstation. In 2- and 4-chamber images the end-diastolic wall thicknesses were measured manually as a full layer and a non-compacted layer. The presence of myocardial fibrosis was analysed as present or absent regardless of segment size.

### Statistical Analysis

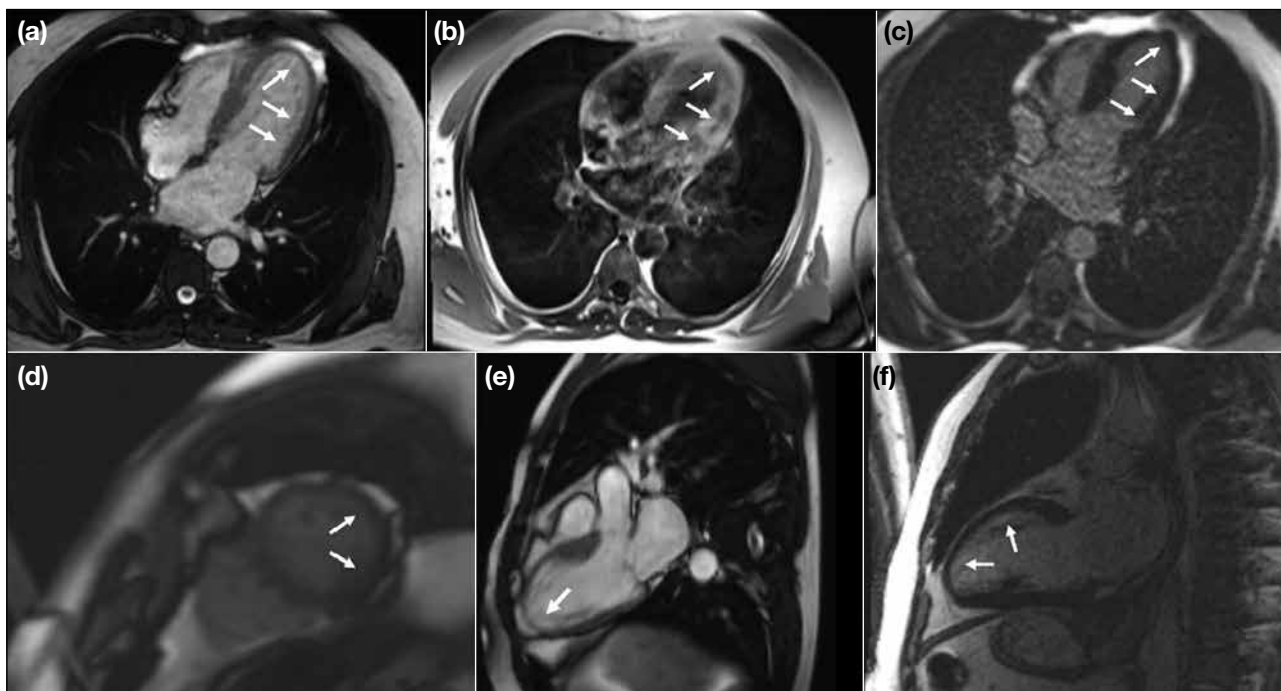
Consequently, the independent variable with a  $p$  value < 0.05 will remain in the final model. The existence of a dependent variable (EF) was investigated. Pearson correlation evaluation was performed to determine the linear relationship between the two continuous variables with EF and LVNC involved wall ratio, CO, and CI change. If the found  $r$  value was -1, it was interpreted as a fully negative linear relationship, while +1 was a fully positive linear relationship. An  $r = 0$  meant no linear relationship between the two variables. The closer the absolute value of the correlation coefficient was to the value of 1, the stronger was the linear association.

### RESULTS

The age range of the 31 cases was between 15 and 56 years (mean =  $45 \pm 20$ ). A total of 25 patients had a known diagnosis of LVNC and six patients presented with increased trabeculation (Figures 1 and 2).



**Figure 1.** Cardiac magnetic resonance in a 54-year-old man with left ventricular noncompaction. Four-chamber magnetic resonance (MR) images (a-e) show the non-compaction. Phase-sensitive inversion-recovery (a, b), cine steady-state free precession (SSFP) 4-chamber planes (c and d), T1-weighted fat-saturation fast spin echo (e) MR images showing left ventricular noncompaction. Vertical long-axis SSFP MR image (f) showing the non-compaction (arrows).



**Figure 2.** A 39-year-old man with left ventricular noncompaction. (a-c) Four-chamber magnetic resonance (MR) images, (d) 2-chamber late gadolinium enhancement (LGE), and (e) vertical-long-axis steady-state free precession (SSFP) and (f) LGE images showing a non-compacted layer of the myocardium (arrows).

### Cardiac Magnetic Resonance Findings

The mean LVEF was  $45.3\% \pm 35\%$ , the number of LVNC affected segments was 10 (range, 3-17), CO was 5.7, and CI was 2.9. The mean stroke volume was 64.2 mL and heart muscle weight was  $132.9 \pm 35.23$  g. Segment involvement was the highest in segment 17 with the apex involved in 29 cases (Figures 3 and 4). The involvement of apical segments 13 to 16, medial segments 7 to 12, and basal segments 1 to 6 are shown in Figures 5 and 6. Fibrosis in myocardial tissue was detected in five cases. Additional LV findings in CMR were a sigmoid septum in two cases, atrial septal defect in one case, the false tendon anatomic variant in two cases, LV lateral wall systolic hypokinesia in five cases, first-degree mitral valve insufficiency in 10 cases, and first-degree mitral valve stenosis in nine cases. Cor triatriatum was observed in the right ventricle in one case.

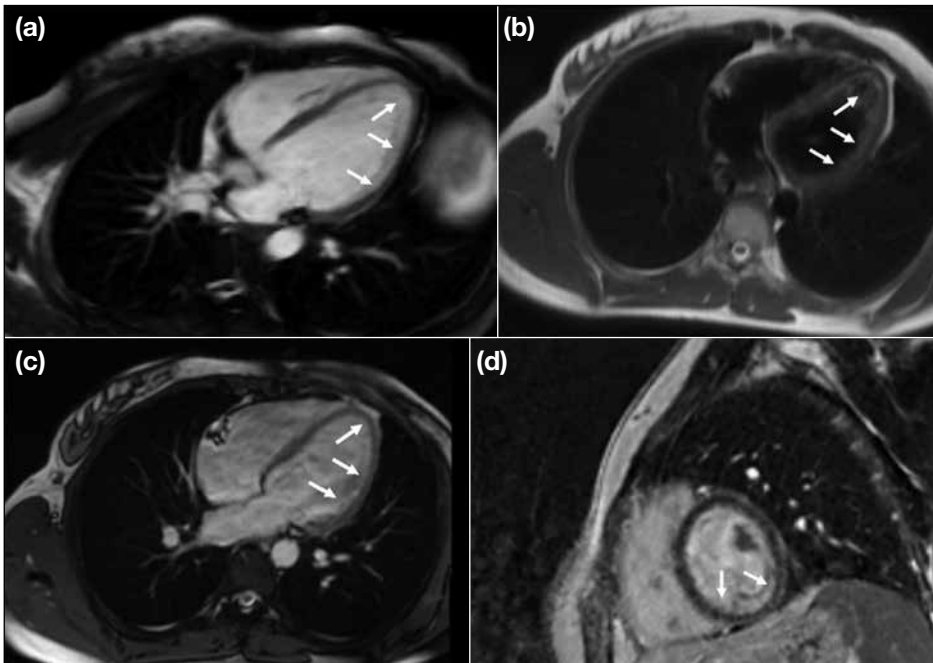
### Correlation between Ejection Fraction and Other Cardiac Magnetic Resonance Findings

Correlation coefficients between EF and the following findings are as follows: the number of affected segments ( $r = -0.613$ ), fibrosis ( $r = 0.217$ ), CO ( $r = -0.112$ ),

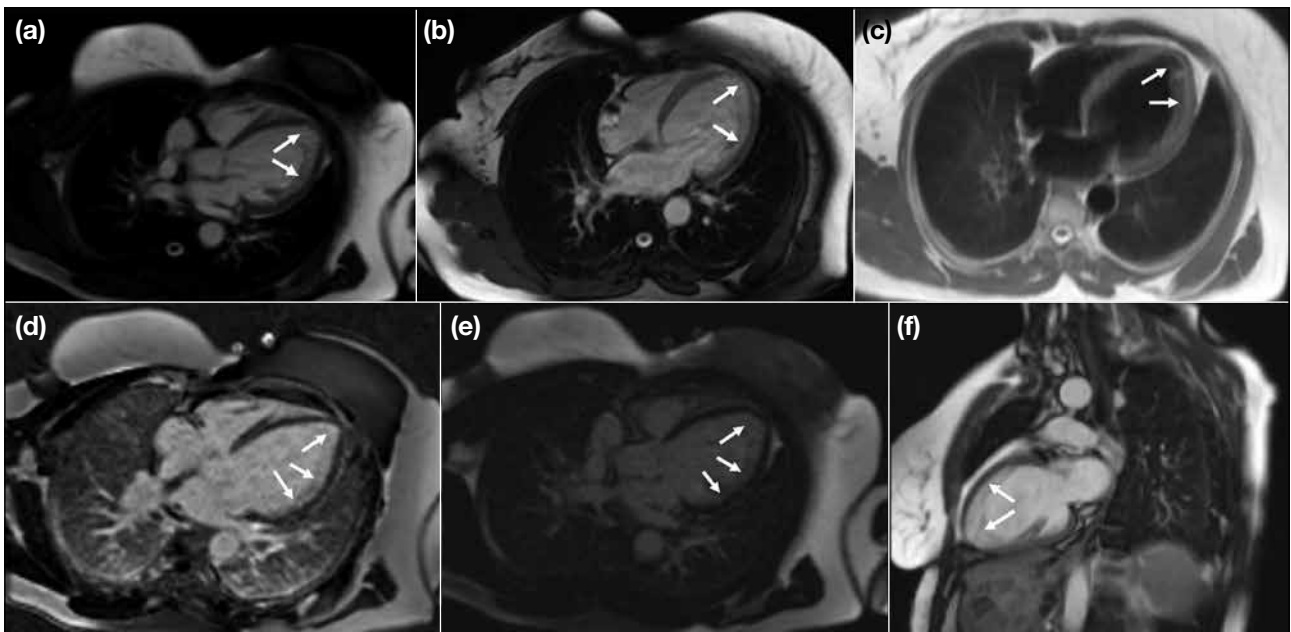
CI ( $r = -0.079$ ), and the percentage of non-compaction in the wall ( $r = -0.043$ ) (Table 1 and Figure 7). The most consistent factor affecting the EF was the number of segments affected by LVNC (Table 2). There is no multiple dependency variable in our variables. In the evaluation made in terms of the statistical value of the EF and Pearson correlation, the statistical value in the number of segments held was found as  $p < 0.001$ , in the presence of fibrosis as  $p = 0.240$ , with CO as  $p = 0.549$ , with CI as  $p = 0.672$  and the percentage of non-compaction in the wall was found to be as  $p = 0.816$ . Pearson correlation coefficient ( $r$ ) value explanations are made as there is no correlation if  $r < 0.2$ , a weak correlation from 0.2 to 0.4, moderate correlation from 0.4 to 0.6, a high correlation from 0.6 to 0.8, and a very high correlation from 0.8 to 1 (Tables 1 and 3). Statistically, the finding affecting clinical severity in patients with LVNC and highly correlated with prognosis was the number of segments affected by the disease.

### DISCUSSION

This study aimed to define the morphological pathology most closely linked to the prognosis in LVNC. Knowledge regarding diagnosis, morbidity, and



**Figure 3.** Cardiac magnetic resonance (CMR) in a 35-year-old woman, with an ejection fraction of 50%. Four-chamber CMR images cine steady-state free precession (a), T1-weighted fat-saturation fast spin echo (b), and 4-chamber plane (c) showing ventricular noncompaction. Two-chamber late-gadolinium-enhanced image (d) showing papillary muscle and right ventricle.

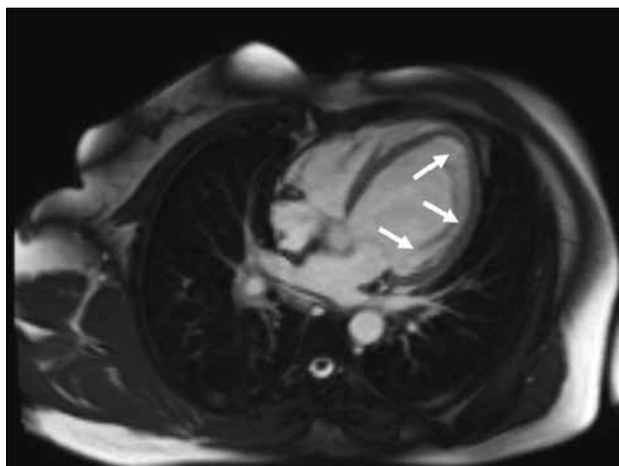


**Figure 4.** Left ventricular noncompaction. A 59-year-old woman with an ejection fraction of 45%. Images including 4-chamber view cine steady-state free precession (a, b), T2-weighted fast spin echo (c), 4-chamber late gadolinium enhancement (LGE) (d, e), and 2-chamber LGE (f) showing apical, mid and basal ventricular noncompaction.

prognosis in this disease is limited.<sup>8</sup> CMR is recognised as the gold standard for measuring the volume, mass, and ejection fraction of both ventricles.<sup>10</sup> EF value is an

important indicator of prognosis in coronary pathologies. A low EF is a predictor of poor prognosis, except in cases with preserved ejection fraction and heart failure.<sup>7</sup>

In this study, the morphological finding showing the highest correlation with EF change was investigated. In LVNC cases, the highest correlation was found between low EF and the number of segments involved. In the study, a high inverse correlation was observed between the number of affected segments in LVNC and EF. In conclusion, the number of affected segments in LVNC

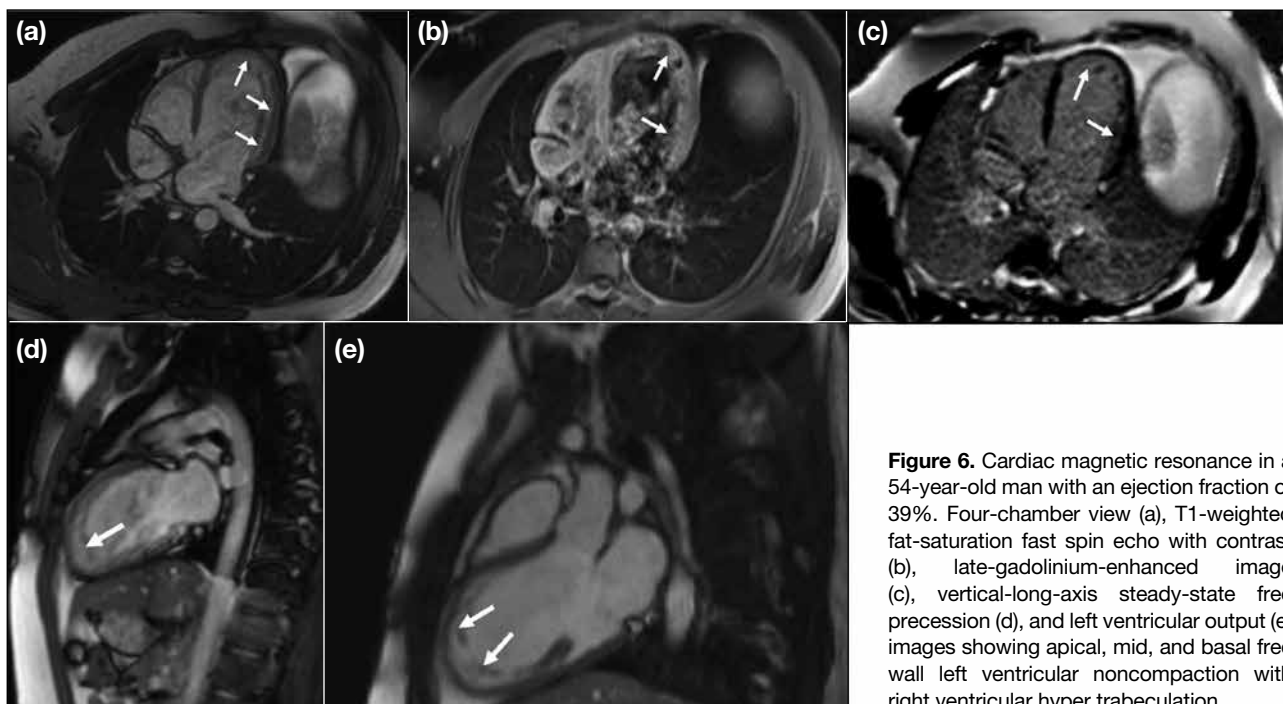


**Figure 5.** Left ventricular noncompaction. A 55-year-old woman with an ejection fraction of 46%. The 4-chamber view shows apical, mid, and basal free wall noncompaction.

cases is the most influential factor in clinical follow-up and treatment planning due to EF effects.

Low LVEF in LVNC cases is an important indicator of a negative prognosis. Dodd et al<sup>4</sup> evaluated the relationship between prognosis in myocardial fibrosis and LVNC.<sup>3</sup> Negri et al<sup>1</sup> evaluated multiple studies reporting associations between LVNC and ventricular tachycardia. The prognosis was evaluated in LVNC with a single variable in the studies the literature; this study evaluated many morphological and functional factors and consequently found the increase in the number of affected segments corresponds most closely to low EF in LVNC.

The 2016 European Society of Cardiology guidelines for the diagnosis and treatment of heart failure defined heart failure based on LVEF. The decrease in EF may manifest itself as heart failure. Heart failure can develop in LVNC cases.<sup>10</sup> Morpho-pathological factors affecting this process have not been defined as multivariate in the literature before. This study showed the highest correlation with the decreasing LVEF in the LVNC cases the number of involved segments. The number of affected segments must be the most important factor for clinical follow-up and treatment planning in LVNC cases after these results.

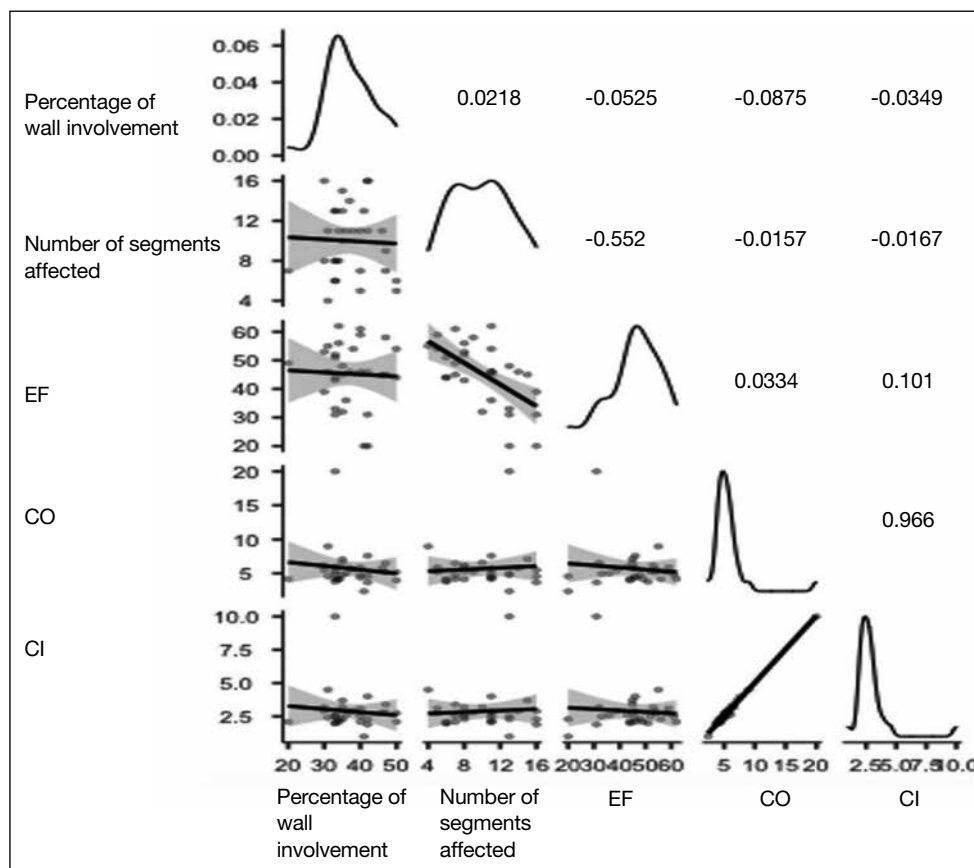


**Figure 6.** Cardiac magnetic resonance in a 54-year-old man with an ejection fraction of 39%. Four-chamber view (a), T1-weighted fat-saturation fast spin echo with contrast (b), late-gadolinium-enhanced image (c), vertical-long-axis steady-state free precession (d), and left ventricular output (e) images showing apical, mid, and basal free wall left ventricular noncompaction with right ventricular hypertrabeculation.

**Table 1.** Ejection fraction (EF) Pearson correlation (r) values with the percentage of wall involvement, number of segments affected, cardiac output (CO), cardiac index (CI), and fibrosis.

	EF	Wall involvement	Number of segments affected	CO	CI	Fibrosis
<b>EF</b>						
Pearson correlation	1	-0.043	-0.613*	-0.112	-0.079	0.217
p Value (2-tailed)		0.816	<0.001	0.549	0.672	0.240
No.	31	31	31	31	31	31
<b>Wall involvement</b>						
Pearson correlation	-0.043	1	-0.040	-0.124	-0.104	-0.066
p Value (2-tailed)	0.816		0.831	0.505	0.579	0.724
No.	31	31	31	31	31	31
<b>Number of segments affected</b>						
Pearson correlation	-0.613*	-0.040	1	0.073	0.066	-0.111
p Value (2-tailed)	<0.001	0.831		0.694	0.724	0.551
No.	31	31	31	31	31	31
<b>CO</b>						
Pearson correlation	-0.112	-0.124	0.073	1	0.996*	0.078
p Value (2-tailed)	0.549	0.505	0.694		<0.001	0.676
No.	31	31	31	31	31	31
<b>CI</b>						
Pearson correlation	-0.079	-0.104	0.066	0.996*	1	0.069
p Value (2-tailed)	0.672	0.579	0.724	<0.001		0.714
No.	31	31	31	31	31	31
<b>Fibrosis</b>						
Pearson correlation	0.217	-0.066	-0.111	0.078	0.069	1
p Value (2-tailed)	0.240	0.724	0.551	0.676	0.714	
No.	31	31	31	31	31	31

\* Correlation is significant at the 0.01 level (2-tailed).



**Figure 7.** Correlations of cardiac magnetic resonance morphologic findings in PLOT Graphic, including percentage of wall involvement, number of segments affected, cardiac output (CO), cardiac index (CI), ejection fraction (EF).

**Table 2.** The dependent variable was ejection fraction (EF). The linear relationship between the two continuous variables with EF decrease and left ventricular noncompaction the percentage of wall involvement, number of segments affected, cardiac output, and cardiac index change.

Model		Unstandardised coefficients		Standardised coefficients	t	p Value	95% confidence interval for B	Correlations		
		B	Standard error	Beta				Zero-order	Partial	Part
1	(Constant)	61.849	13.730		4.505	0.000	33.571-90.127			
	Wall involvement	-0.238	0.232	-0.145	-1.024	0.316	-0.715 to 0.240	-0.043	-0.201	-0.140
	Number of segments affected	-1.742	0.430	-0.563	-4.048	0.000	-2.628 to -0.855	-0.613	-0.629	-0.555
	Cardiac output	-14.763	5.705	-4.002	-2.588	0.016	-26.513 to -3.012	-0.112	-0.460	-0.355
	Cardiac index change	28.674	11.288	3.915	2.540	0.018	5.427-51.922	-0.079	0.453	0.348
	Fibrosis	6.035	4.448	0.189	1.357	0.187	-3.125 to 15.195	0.217	0.262	0.186

**Table 3.** Summary of results according to subgroups.

Model			Fibrosis	Wall involvement	Cardiac index	Number of segments affected	Cardiac output
1	Correlations	Fibrosis	1.000	0.038	0.100	0.127	-0.106
		Wall involvement	0.038	1.000	-0.214	0.019	0.223
		Cardiac index	0.100	-0.214	1.000	0.083	-0.996
		Number of segments affected	0.127	0.019	0.083	1.000	-0.090
	Covariances	Cardiac output	-0.106	0.223	-0.996	-0.090	1.000
		Fibrosis	19.782	0.039	5.001	0.243	-2.697
		Wall involvement	0.039	0.054	-0.561	0.002	0.296
		Cardiac index	5.001	-0.561	127.414	0.403	-64.140
		Number of segments affected	0.243	0.002	0.403	0.185	-0.220
	Cardiac output	-2.697	0.296	-64.140	-0.220	32.551	

\* Ejection fraction being the dependent variable.

## Limitations of the Study

Our study design had a few limitations. First, there were no histologically confirmed cases of LVNC. Another limitation of our study was that it was performed with a small number of patients. Furthermore, because this review was retrospective, the clinical information was incomplete. LVNC is rare cardiomyopathy that is not fully classified.<sup>11</sup> Involvement is not homogeneous throughout the heart. The patient group was heterogeneous in terms of the diagnostic methodology. Long-term follow-up is required to determine the prognosis in LVNC cases. Long-term follow-up was not possible in the study. No age grouping was made since our cases were few. Another limitation was that the study was a single-centre study and all CMR examinations were interpreted by a single radiologist. Current criteria for the diagnosis of LVNC lead to highly variable disease prevalence in patients referred for CMR. Petersen criteria were used in this study.<sup>1,9,12,13</sup>

## CONCLUSION

A high correlation was found between the number of segments involved and a poor prognosis in LVNC cases. The number of preserved segments correlates positively with LVEF and is the most influential anatomical factor in the clinical severity of the cases in the clinical prognosis and treatment planning of LVNC cases. In the CMR examination by radiologists, reporting the number of preserved segments in LVNC patients will be a guide to determining the appropriate treatment choice. Prospective studies with larger patient series are needed to determine the factors that play a role in the prognosis of this disease.

## REFERENCES

1. Negri F, De Luca A, Fabris E, Korcova R, Cernetti C, Grigoratos C, et al. Left ventricular noncompaction, morphological, and clinical features for an integrated diagnosis. *Heart Fail Rev.* 2019;24:315-23.
2. Peters F, Khandheria BK, dos Santos C, Matioda H, Maharaj N,



- Libhaber E, et al. Isolated left ventricular noncompaction in sub-Saharan Africa: a clinical and echocardiographic perspective. *Circ Cardiovasc Imaging*. 2012;5:187-93.
3. Mihailovici AR, Padureanu V, Albu CV, Dinescu VC, Pirlog MC, Dinescu SN, et al. Myocardial noncompaction. *Rev Chim*. 2018;69:2209-12.
  4. Dodd JD, Holmvang G, Hoffmann U, Ferencik M, Abbara S, Brady TJ, et al. Quantification of left ventricular noncompaction and trabecular delayed hyperenhancement with cardiac MRI: correlation with clinical severity. *AJR Am J Roentgenol*. 2007;189:974-80.
  5. Hussein A, Karimianpour A, Collier P, Krasuski R. Isolated noncompaction of the left ventricle in adults. *J Am Coll Cardiol*. 2015;66:578-85.
  6. Finsterer J, Stöllberger C, Towbin JA. Left ventricular noncompaction cardiomyopathy: cardiac, neuromuscular, and genetic factors. *Nat Rev Cardiol*. 2017;14:224-37.
  7. 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.
  8. Jefferies JL, Chang AC, Rossano JW, Shaddy RE, Towbin JA, editors. *Heart Failure in the Child and Young Adult from Bench to Bedside Memphis*: Elsevier; 2018. p 269-90.
  9. Petersen SE, Selvanayagam JB, Wiesmann F, Robson MD, Francis JM, Anderson RH, et al. Left ventricular non-compaction: insights from cardiovascular magnetic resonance imaging. *J Am Coll Cardiol*. 2005;46:101-5.
  10. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the task force for the diagnosis and treatment of acute and chronic heart failure of the European society of cardiology (ESC). Developed with the special contribution of the heart failure association (HFA) of the ESC. *Eur Heart J*. 2016;37:2129-200.
  11. Dreisbach JG, Mathur S, Houbois CP, Oechslin E, Ross H, Hanneman K, et al. Cardiovascular magnetic resonance-based diagnosis of left ventricular non-compaction cardiomyopathy: impact of cine bSSFP strain analysis. *J Cardiovasc Magn Reson*. 2020;22:9.
  12. Captur G, Muthurangu V, Cook C, Flett AS, Wilson R, Barinson A, et al. Quantification of left ventricular trabeculae using fractal analysis. *J Cardiovasc Magn Reson*. 2013;15:36.
  13. Ivanov A, Dabiesingh DS, Bhumireddy GP, Mohamed A, Asfour A, Briggs WM, et al. Prevalence and prognostic significance of left ventricular noncompaction in patients referred for cardiac magnetic resonance imaging. *Circ Cardiovasc Imaging*. 2017;10:e006174.