Left ventricular characteristics of noncompaction phenotype patients with good ejection fraction measured with cardiac magnetic resonance

Anna Reka Kiss, Zsófia Gregor, Adam Furak, Attila Tóth, Márton Horváth, Liliana Szabo, Csilla Czimbalmos, Zsofia Dohy, Bela Merkely, Hajnalka Vago, Andrea Szucs

Semmelweis University Heart and Vascular Center; Budapest-*Hungary*

Abstract

Objective: We describe left ventricular (LV) volumes, myocardial and trabeculated muscle mass and strains with Cardiac magnetic resonance of a large cohort (n=81) who fulfilled the morphologic criteria of left ventricular noncompaction (LVNC) and had good ejection fraction (EF >55%) and compare them with healthy controls (n=81). Male and female patients were compared to matched controls and to each other. We also investigated the LV trabeculated muscle mass cutoff in male and female patients with LVNC.

Methods: 81 participants with LVNC and 81 healthy controls were included. Male and female patients were compared to matched controls and to each other. We also investigated the left ventricular trabeculated muscle mass cut-off in male and female LVNC patients.

Results: The LV parameters of the LVNC population were normal, but they had significantly higher volumes, myocardial and trabeculated muscle mass, and a significantly smaller EF than the controls. Similar differences were observed after stratifying by sex. The optimal LV trabeculated muscle mass cutoffs were 25.8 g/m^2 in men (area under the curve: 0.81) and 19.0 g/m^2 in women (area under the curve: 0.87). The patients had normal global strains but a significantly worse global circumferential strain (patients vs controls: –29.9±4.9 vs. –35.8±4.7%, p<0.05) and significantly higher circumferential mechanical dispersion than the controls (patients vs. controls: 7.6±4.2 vs. 6.1±2.8%; p<0.05). No disease-related strain differences were noted between men and women.

Conclusion: The LV functional and strain characteristics of the LVNC cohort differed significantly from those of healthy participants; this might be caused by increased LV trabeculation, and its clinical relevance might be questionable. The LV trabeculated muscle mass was very different between men and women; thus, the use of sex-specific morphologic diagnostic criteria should be considered.

Keywords: left ventricular noncompaction, cardiac magnetic resonance, feature-tracking, trabecular mass quantification

Cite this article as: *Kiss AR, Gregor Z, Furak A, Tóth A, Horváth M, Szabo L, et al. Left ventricular characteristics of noncompaction phenotype patients with good ejection fraction measured with cardiac magnetic resonance. Anatol J Cardiol 2021; 25: 565-71.*

Introduction

Left ventricular noncompaction (LVNC) is a rare disease with excessive endomyocardial trabeculation in the apical part of the heart. In many cases, LVNC is an incidental finding in asymptomatic patients with good left ventricular (LV) ejection fraction (EF); however, LVNC can manifest as severe heart failure and dilated cardiomyopathy (1). Cardiac magnetic resonance (CMR) imaging has become the number one diagnostic modality due to its superior signal-to-noise ratio compared to echocardiography, thereby allowing better visualization of the endocardial borders and ease in differentiating between noncompacted and compacted myocardium (2). Several morphological criteria for LVNC have been published, and the criterion given by Petersen et al. (3, 4) is most commonly applied: the ratio of noncompacted/compacted myocardial layers >2.3 measured in end-diastole, Zemrak et al. (5) demonstrated in the Multi-Ethnic Study of Atherosclerosis that 27.5% of the 2742 volunteers free of clinically recognized cardiovascular disease had a higher noncompacted/compacted ratio than the diagnostic cutoff value. These data suggest that the lack of accepted diagnostic standards might result in overdiagnosis (6). Moreover, we have inconsistent information about normal LV trabeculation in men and women, and the importance of sex regarding the diagnostic criteria

Address for Correspondence: Andrea Szucs, MD, Semmelweis University Heart and Vascular Center; Városmajor u 68 1122, Budapest-*Hungary*
Phone: 0036208258055 E-mail: szucsand@gmail.com
Accepted Date: 11.03.2021 **Available Online Date:** 27.04.2021

DOI:10.5152/AnatolJCardiol.2021.25905

Anatol J Cardiol 2021; 25: 565-71
DOI:10.5152/AnatolJCardiol.2021.25905

HIGHLIGHTS

- Left ventricular noncompaction (LVNC) morphology is associated with higher volumes and lower ejection fraction.
- LV alterations might be caused by excessive trabeculation.
- The optimal trabecular mass index cutoff value for LVNC should be sex-specific.
- LVNC morphology is associated with lower global circumferential and radial strain.
- The decreased strain values can be caused by excessive trabeculation.

of LVNC is (7, 8). These observations highlight the need for additional diagnostic criteria for a morphologic-only analysis (9).

For this cardiac imaging focused study, we recruited a large cohort who fulfilled the morphological criteria of LVNC and had good EF and no comorbidities, aiming to describe the LV volumetric parameters and the myocardial and trabeculated muscle mass of this population, as measured with threshold-based papillary and trabeculated muscle quantification software, and to study the LV strain characteristics with CMR feature-tracking. Male and female patients were compared with each other to describe the differences between sexes. Moreover, we investigated the different cutoff points of LV trabeculated muscle mass for male and female patients with LVNC to differentiate them from healthy subjects.

Methods

Patient characteristics

Between October 2007 and February 2019, a total of 351 patients fulfilled the two most often used morphologic criteria of LVNC set by Petersen et al. (3) (noncompacted/compacted ratio >2.3, Fig. 1) and Jacquier et al. (10) (trabeculated LV mass >20% of the total LV mass, Fig. 1). A total of 81 patients with good LV ejection fraction (>55%) and no known cardiovascular or other comorbidities were included in this retrospective study (age: 35.6±14.7 year, male: n=44) (11). The exclusion criteria were reduced LV EF (<55%, n=180), presence of ischemic, valvular or congenital heart disease (n=57), presence of significant comorbidities (e.g., diabetes, hypertension, chronic kidney disease, chronic liver failure, n=9), and technical reasons (artifacts, short-axis cine images performed after the injection of contrast agent, n=49) (12, 13). We selected 81 sex-matched healthy volunteers from similar age groups who did not have any cardiovascular or other systemic diseases and who did not have excessive endocardial trabeculation (noncompacted/compacted >2.3 or trabeculated LV mass >20% of the total LV mass) measured on the short axis cine images (age: 38.2±12.8 year, male: n=44). All procedures performed in this study were in accordance with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Ethical approval was obtained from the Central Ethics Committee of Hungary, and all participants provided informed consent.

Image acquisition and analysis

The cardiac magnetic resonance (CMR) examinations were performed with a 1.5 T MR scanner (Achieva, Philips Medical System, Eindhoven, the Netherlands) and a 5-channel cardiac coil. Retrospectively gated, balanced, steady-state free precession cine images in 2-, 3-, and 4-chamber long-axis views and breath-hold short-axis cine images were acquired from base to apex with a temporal resolution of 25 phases per cardiac cycle. The slice thickness was 8 mm with no interslice gap, and the field of view was 350 mm on the average, adapted to body size.

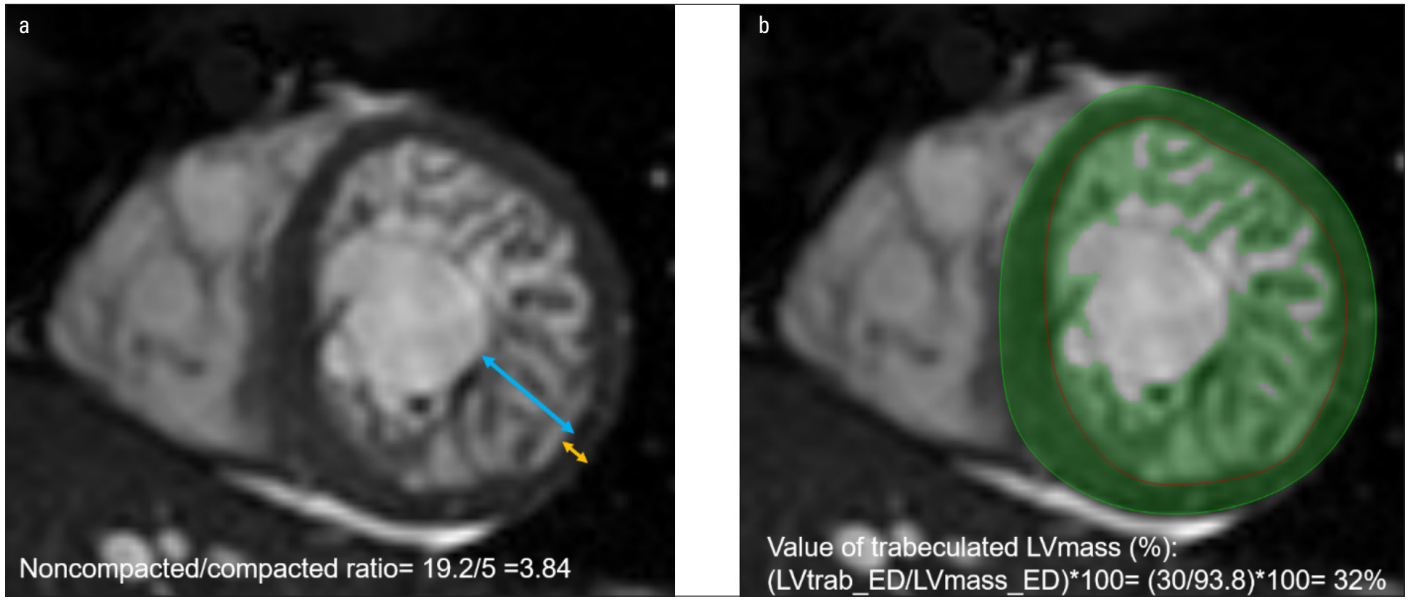

Figure 1. Short-axis image of a participant who fulfilled the Petersen (a) and Jacquier (b) morphologic criteria of left ventricular noncompaction. The orange line represents the compacted myocardial layer, the blue line represents the noncompacted layer (a), the green area represents the compacted and noncompacted myocardium while the red line borders the endocardial trabeculation (b).

Table 1. Comparison of left ventricular functional parameters between left ventricular noncompaction patients and healthy control groups, and between sexes

	Total			LVNC			Control			Male			Female		
	LVNC	Control	*P*	Male	Female	*P*	Male	Female	*P*	LVNC	Control	*P*	LVNC	Control	*P*
Number of participants (n)	81	81	-	44	37	-	44	37	-	44	44	-	37	37	-
Age (year)	35.6±14.7	38.2±12.8	0.153	34.3±14.6	37.0±14.8	0.288	38.4±10.4	37.9±15.2	0.618	34.3±14.6	38.4±10.4	0.042*	37.0±14.8	37.9±15.2	0.867
EDVi (ml/m^2)	77.4±14.5	69.0±11.8	<0.001*	83.1±14.3	70.8±11.8	<0.001*	73.2±12.2	64.0±9.2	<0.001*	83.1±14.3	73.2±12.2	0.001*	70.8±11.8	64.0±9.2	0.008*
ESVi (ml/m^2)	26.6±7.4	20.6±5.4	<0.001*	29.7±7.4	22.9±5.6	<0.001*	22.6±5.7	18.2±4.0	<0.001*	29.7±7.4	22.6±5.7	<0.001*	22.9±5.6	18.2±4.0	<0.001*
SVi (ml/m^2)	50.8±9.3	48.8±8.7	0.146	53.4±9.5	47.8±8.1	0.006*	50.6±8.7	46.6±8.3	0.037*	53.4±9.5	50.6±8.7	0.157	47.8±8.1	46.6±8.3	0.522
EF (%)	65.9±5.2	70.2±5.0	<0.001*	64.4±5.1	67.7±4.8	0.004*	69.2±5.2	71.5±4.4	0.037*	64.4±5.1	69.2±5.2	<0.001*	67.7±4.8	71.5±4.4	0.001*
LVmass-ED (g/m^2)	76.3±17.0	69.7±13.3	0.013*	86.8±13.6	64.0±11.5	<0.001*	79.3±9.3	58.1±6.4	<0.001*	86.8±13.6	79.3±9.3	0.004*	64.0±11.5	58.1±6.4	0.016*
LVtrab-ED (g/m^2)	26.0±7.5	19.4±4.1	<0.001*	29.0±7.4	22.4±6.0	<0.001*	22.0±3.3	16.4±2.5	<0.001*	29.0±7.4	22.0±3.3	<0.001*	22.4±6.0	16.4±2.5	<0.001*

EDVi - end-diastolic volume index, EF - ejection fraction, ESVi - end-systolic volume index, LVmass-EDi - end-diastolic myocardial mass index, LVNC - left ventricular noncompaction, LVtrab-EDi - end-diastolic papillary and trabecular mass index, SVi - stroke-volume index

When the contrast agent was given, the cine images were acquired before its injection.

Endo-and epicardial borders were manually traced on the short-axis images in end-systolic and end-diastolic phases by two observers (A.S.Z. with 7 years of experience and A.R.K. with 2 years of experience). A threshold-based papillary and trabeculated muscle quantification analysis software (the MassK module of Medis Suite, version 3.0, Medis Medical Imaging Systems, Leiden, the Netherlands) was used to calculate the following LV parameters from the short-axis images: end-systolic volume, end-diastolic volume, stroke-volume, EF, end-diastolic myocardial mass, and end-diastolic papillary and trabecular mass. This semiautomatic software differentiates muscle from the blood pool based on their different signal intensities; thus, each voxel is classified as either blood or myocardium according to the chosen threshold, which was set to the default value (50%) (14). Endocardial borders included the trabeculated muscle, and papillary muscles were excluded from the trabeculation unless they were indistinguishable. All the measured parameters were indexed to body surface area. We used the normal values reported by Alfakih et al. (11) as this is the setup reference value of the postprocessing software. We tested the inter-observer agreement on 10 randomly selected patients and controls with the interclass correlation coefficient (ICC). Global ICC, which represents the inter-observer agreement of all measured LV parameters, was 0.92 (interpreted as: 0.4-0.75 - fair to good, greater than 0.75 - excellent).

Feature-tracking analysis

Commercially available software was used for the feature-tracking strain analysis (QStrain, Medis Suite, version 3.0, Medis Medical Imaging Systems, Leiden, the Netherlands). The endocardial contours of the left ventricle were manually traced in the 2-, 3-, 4- chamber long-axis and the short-axis views, excluding the endocardial trabeculation and papillary muscles. Global longitudinal strain (GLS), global radial strain (GRS), global circumferential strain (GCS), and rotation (ROT) were measured as described elsewhere (15). The standard deviation of the time-to-peak strains between segments was analyzed in both the long-axis and short-axis views to determine the degrees of intraventricular synchronous contraction in the longitudinal and circumferential directions [longitudinal mechanical dispersion (SD-TTP-LS) and circumferential mechanical dispersion (SD-TTP-CS)].

We used the CMR-FT normal values presented by Peng et al. (16). The inter-observer agreements of the measured global strain parameters were good-to-excellent [ICC (95% confidence interval): GLS: 0.96 (0.89–0.98), GRS: 0.99 (0.96–0.99), GCS: 0.96 (0.89–0.98), ROT: 0.68 (0.19-0.87), SD-TTP-*LS:* 0.87 (0.68-0.95), SD-TTP-*CS:* 0.75 (0.38–0.90)].

Statistical analysis

Continuous variables are presented as the mean and standard deviation. The Shapiro-Wilk test was used to assess whether the data fitted a normal distribution. An independent-sample *t*-test was used to compare parameters that fitted a normal distribution; otherwise a Mann-Whitney test was applied. Receiver operating characteristic curves and optimal cutoff values for the LV trabecular mass index were calculated. MedCalc Statistical Software version 17.9.5 (MedCalc Software, Ostend, Belgium) was used for statistical calculations.

Results

First, we compared the LV functional parameters, calculated with the threshold-based software, between the LVNC and control groups. The measured functional parameters in the patients were in the normal range; however, compared with the controls, the LVNC group had significantly higher end-diastolic and end-systolic volumes and LV myocardial and trabecular mass values and a significantly lower EF (Table 1).

We segregated the LVNC and control groups by sex and found similar results in both sexes. The stroke-volume did not

Anatol J Cardiol 2021; 25: 565-71
DOI:10.5152/AnatolJCardiol.2021.25905

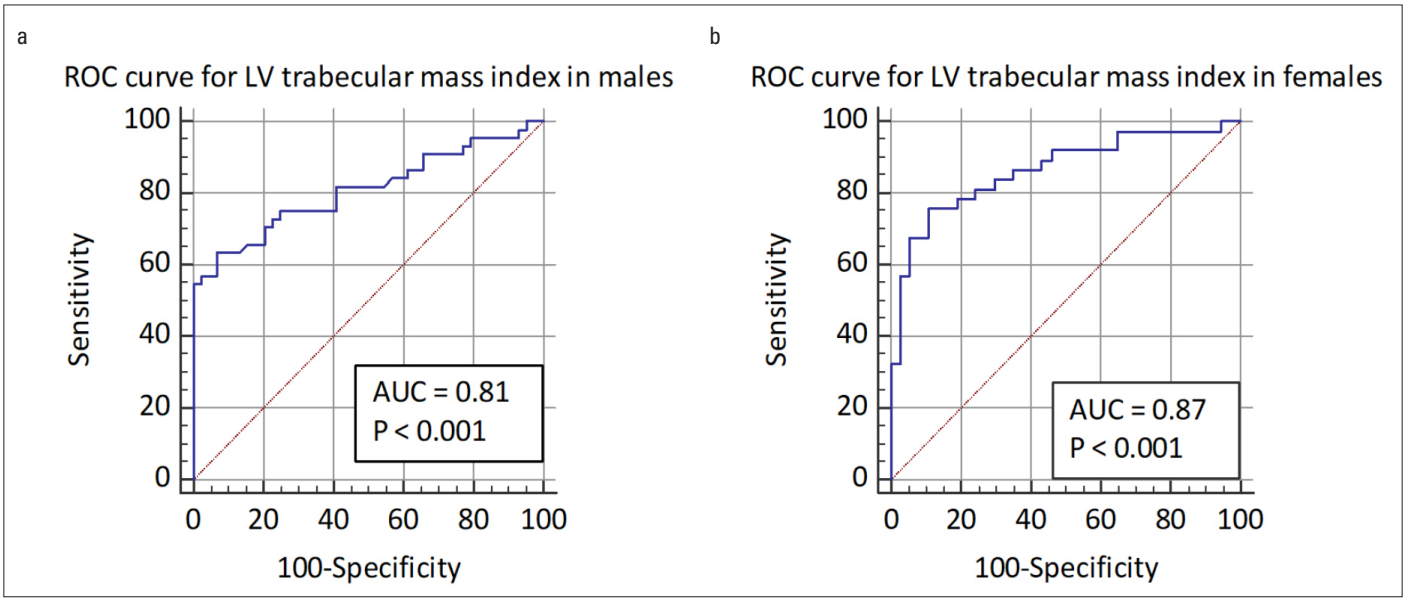

Figure 2. Receiver operating characteristic curves for the trabeculated muscle mass cutoff values in male (a) and female (b) left ventricular noncompaction groups.

Table 2. Comparison of global strain values between left ventricular noncompaction patients and healthy control groups, and between sexes

	Total			LVNC			Control			Male			Female		
	LVNC	Control	*P*	Male	Female	*P*	Male	Female	*P*	LVNC	Control	*P*	LVNC	Control	*P*
GLS (%)	-22.2±2.6	-23.3±3.5	0.155	-21.7±2.7	-22.9±2.4	0.027*	-22.7±3.5	-24.0±3.3	0.046*	-21.7±2.7	-22.7±3.5	0.125	-22.9±2.4	-24.0±3.3	0.119
GRS (%)	55.6±8.2	64.3±13.2	<0.001*	53.8±7.7	57.8±8.4	0.028*	63.3±14.2	65.6±12.0	0.276	53.8±7.7	63.3±14.2	0.001*	57.8±8.4	65.6±12.0	0.004*
GCS (%)	-29.9±4.9	-35.6±4.8	<0.001*	-30.3±5.1	-29.5±4.7	0.467	-35.0±4.6	-36.2±5.0	0.29	-30.3±5.1	-35.0±4.6	<0.001*	-29.5±4.7	-36.2±5.0	<0.001*
ROT (°)	10.1±12.3	7.9±13.4	0.185	12.1±12.1	7.7±13.5	0.127	6.8±15.5	9.2±10.3	0.355	12.1±12.1	6.8±15.5	0.078	7.7±13.5	10.1±30.5	0.589
SD-TTP-LS (%)	10.2±3.9	11.0±3.9	0.178	10.2±4.2	10.3±3.6	0.925	10.9±4.1	11.2±3.7	0.771	10.2±4.2	10.9±4.1	0.398	10.3±3.6	11.2±3.7	0.279
SD-TTP-CS (%)	7.6±4.2	6.1±2.8	0.046*	6.8±3.8	8.5±4.6	0.079	5.6±2.7	6.6±2.8	0.075	6.8±3.8	5.6±2.7	0.152	8.5±4.6	6.6±2.8	0.147

GCS - global circumferential strain, GLS - global longitudinal strain, GRS - global radial strain, LVNC - left ventricular noncompaction, ROT - rotation, SD-TTP-CS - standard deviation of time-to-peak circumferential strains, SD-TTP-LS - standard deviation of time-to-peak longitudinal strains.

differ between the patients and controls or between men and women (Table 1).

Finally, we compared the LV parameters of men and women in both the patient and control groups and found that all the parameters, except the EF, were significantly higher in men than in women (Table 1).

By studying the optimal LV trabecular mass index cutoff values to differentiate between patients with LVNC and healthy controls, we found that the optimal cutoffs were 25.8 g/m^2 in men (area under the curve: 0.81, 95% confidence interval: 0.71–0.88, sensitivity: 63.6%, specificity: 93.2%) and 19.0 g/m^2 in women (area under the curve: 0.87, 95% confidence interval: 0.77-0.93, sensitivity: 75.7%. specificity: 89.2%, Fig. 2). Patients with a higher LV trabecular mass index value than the proposed cutoffs are more likely to have LVNC than those who are below the described cutoffs.

GCS and GRS in the patient group were significantly worse, but still in the normal range, compared to those in the healthy controls, while GLS and rotation were not significantly different between the 2 groups. The circumferential mechanical dispersion was significantly higher in patients than in the controls, while the longitudinal mechanical dispersion was almost equal in the 2 groups (Table 2).

By comparing male and female patients with LVNC to controls, we found that the GCS and GRS were lower in patients with LVNC of both sexes than in male and female healthy controls (Table 2).

Furthermore, we compared the strain parameters of men and women in the LVNC and control groups and found that GLS was significantly lower for men in both groups compared to women. GRS was also significantly lower in male patients compared to female patients (Table 2).

Discussion

In this retrospective study, we describe the LV myocardial mechanics of a large cohort who fulfilled the morphological criteria of LVNC and had good LV EF and evaluate the differences between male and female patients.

The volumetric and myocardial mass values were in the normal range; however, the LVNC group had significantly larger end-systolic and end-diastolic volumes, and a significantly smaller EF, than the control group. These results correlate with those presented by Zemrak et al. (5) who state that higher LV trabeculated muscle/total myocardial mass ratio is associated with lower LV EF and higher LV volumes in a population free of clinically recognized cardiovascular disease. However, no association was found between increased LV trabeculation and increase in LV volumes or decrease in LV function during the 9.5-year follow-up of the same study population (5). Another study also revealed that the morphological diagnosis of LVNC was not associated with adverse clinical events during the almost 7 years of follow-up (17). The diagnosis of LVNC based on morphological criteria exclusively might be insufficient, and an integrated diagnostic algorithm with additional anamnestic and clinical information should be used to avoid overdiagnosis (1).

Well-known biometric alterations between sexes were present in our male and female control groups, and these alterations could be the cause of significant differences between the functional parameters of male and female patients with LVNC (8). Previous studies with other techniques have described the different trabeculated volumes and different thickness but not the differing trabeculated muscle mass of noncompacted and compacted myocardium between healthy men and women (8). Gender-related differences were also present in our study in the trabeculated muscle mass values of both patients and controls. As a novelty, our results show that the optimal trabecular mass index cutoff value for LVNC was very different for men and women, suggesting that the diagnostic cutoffs should be sex-specific. We did not find any information about the trabeculated muscle mass value of male and female patients with LVNC or its diagnostic cutoff values. The LV trabecular mass index might be a useful parameter, but further studies are required, as the sensitivities of the proposed cutoff values were quite low in our study. Grothoff et al. (18) previously proposed a cutoff value for noncompacted myocardial mass index regardless of gender of 15 g/m^2, although their study included a smaller LVNC population, and they used a different method to measure trabeculated myocardium mass.

Of the studied feature-tracking strain parameters, GLS was not different between the LVNC group and the controls in our study. The normal GLS value, in addition to the good EF, suggest normal LV function and no presence of subtle LV dysfunction in this patient cohort. According to the literature, normal GLS values are associated with good prognosis in different patient populations with preserved EF. Furthermore, Andreini et al. (19) have described that LVNC patients with good LV EF, good stroke volume, and without LV dilatation have less cardiac events and excellent outcome and survival rate (20-22). In contrast to our results, a recent publication described decreased GLS in patients with LVNC with a median LV EF of 54%, which is lower than the mean EF of our LVNC group (23). We know from mathematical and echocardiographic studies that for patients with higher than 50% LV EF, GLS can vary more with less effect on the EF than in patients with decreased LV function, which can explain these diverse results (24). The GLS values in male patients and male controls were significantly reduced (but still in the normal range) compared to those in female patients and controls, which seems to be a sex-related difference rather than an LVNC-related phenomenon (25, 26).

In contrast to GLS, GCS and GRS in patients with LVNC were significantly reduced compared to controls, and this significance did not change after we divided the groups by sex. These results correlate with the findings of a recent study of a pediatric LVNC population with good EF, although this was performed with speckle tracking echocardiography (27). CMR studies on healthy populations have revealed that increased LV trabeculation is associated with impaired circumferential strain, even after adjustments for age, sex and body mass index; however, the relationship between LV hypertrabeculation and decreased circumferential strain in unclear (28, 29). In addition to decreased GCS, the circumferential mechanical dispersion, which describes the interventricular dissynchrony, was higher in patients than in controls. We do not have enough information yet to evaluate the clinical relevance of this statistically significant result because the feature-tracking normal values for the standard deviation of time-to-peak circumferential strain (%) are not available. Previous studies conducted on healthy populations have revealed that mechanical dispersion is higher in participants with longer QTc time and mechanical dispersion is also predictive of arrhythmic risk in different diseases (30-33). Further follow-up studies are necessary to investigate the possible prognostic role of these parameters in this patient population.

Regarding the changes in GRS, radial thickening arises from both longitudinal and circumferential shortening; thus, compared to that in controls, the significantly decreased GRS value in patients may be due to the significantly decreased GCS. The difference in GRS between male and female patients may be due to the small number of patients when the groups were separated by sex. GRS is less reproducible than the other two global strain parameters and shows large differences between studies regarding a normal range; thus, the importance of GRS needs further evaluation (25, 34, 35).

Study limitations

The main limitation is that we needed to exclude patients who received contrast agents prior to SA cine imaging (n=26) because both the functional parameters and strain values are altered when measured on postcontrast SA cine images (10, 11).

Conclusion

The functional parameters of this large cohort, which fulfilled the morphologic criteria for LVNC, were in the normal range but differed significantly from those of healthy controls, which might be caused by the increased amount of LV trabeculation. The decreased GCS and GRS values and increased circumferential mechanical dispersion can also be related to excessive trabeculation. The LV trabeculated muscle mass is

very different between men and women; thus, the use of sex-specific morphologic diagnostic criteria should be considered.

Acknowledgments: We thank the technicians who helped performing the cardiac magnetic resonance imaging examinations.

Funding: The research was financed by the Thematic Excellence Programme (Tématerületi Kiválósági Program, 2020-4.1.1.-TKP2020) of the Ministry for Innovation and Technology in Hungary, within the framework of the Therapeutic Development and Bioimaging programmes of the Semmelweis University. The research was supported by the Ministry of Innovation and Technology NRDI Office within the framework of the Artificial Intelligence National Laboratory Program.

Conflict of interest: None declared.

Peer-review: Externally peer-reviewed.

Author contributions: Concept – A.R.K., Z.G., A.S.; Design – A.R.K., M.H., A.S.; Supervision – H.V., A.S.; Fundings – B.M.; Materials – L.S., C.C., Z.D., B.M., H.V.; Data collection &/or processing – A.R.K., A.F., A.T., C.C., Z.D.; Analysis &/or interpretation – A.R.K., A.F., A.T., L.S., A.S.; Literature search – A.R.K., Z.G.; Writing – A.R.K., A.S.; Critical review – Z.G., A.F., A.T., M.H., L.S., C.C., Z.D., B.M., H.V., A.S.

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. [Crossref]
2. Bennett CE, Freudenberger R. The Current Approach to Diagnosis and Management of Left Ventricular Noncompaction Cardiomyopathy: Review of the Literature. Cardiol Res Pract 2016; 2016: 5172308. [Crossref]
3. 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. [Crossref]
4. Zuccarino F, Vollmer I, Sanchez G, Navallas M, Pugliese F, Gayete A. Left ventricular noncompaction: imaging findings and diagnostic criteria. AJR Am J Roentgenol 2015; 204: W519-30. [Crossref]
5. Zemrak F, Ahlman MA, Captur G, Mohiddin SA, Kawel-Boehm N, Prince MR, et al. The relationship of left ventricular trabeculation to ventricular function and structure over a 9.5-year follow-up: the MESA study. J Am Coll Cardiol 2014; 64: 1971-80. [Crossref]
6. Ross SB, Jones K, Blanch B, Puranik R, McGeechan K, Barratt A, et al. A systematic review and meta-analysis of the prevalence of left ventricular non-compaction in adults. Eur Heart J 2020; 41: 1428-36. [Crossref]
7. Dawson DK, Maceira AM, Raj VJ, Graham C, Pennell DJ, Kilner PJ. Regional thicknesses and thickening of compacted and trabeculated myocardial layers of the normal left ventricle studied by cardiovascular magnetic resonance. Circ Cardiovasc Imaging 2011; 4: 139-46. [Crossref]
8. André F, Burger A, Lossnitzer D, Buss SJ, Abdel-Aty H, Gianntisis E, et al. Reference values for left and right ventricular trabeculation and non-compacted myocardium. Int J Cardiol 2015; 185: 240-7. [Crossref]
9. Kawel N, Nacif M, Arai AE, Gomes AS, Hundley WG, Johnson WC, et al. Trabeculated (noncompacted) and compact myocardium in adults: the multi-ethnic study of atherosclerosis. Circ Cardiovasc Imaging 2012; 5: 357-66. [Crossref]
10. Jacquier A, Thuny F, Jop B, Giorgi R, Cohen F, Gaubert JY, et al. Measurement of trabeculated left ventricular mass using cardiac magnetic resonance imaging in the diagnosis of left ventricular non-compaction. Eur Heart J 2010; 31: 1098-104. [Crossref]
11. Alfakih K, Plein S, Thiele H, Jones T, Ridgway JP, Sivananthan MU. Normal human left and right ventricular dimensions for MRI as assessed by turbo gradient echo and steady-state free precession imaging sequences. J Magn Reson Imaging 2003; 17: 323-9. [Crossref]
12. Kuetting DL, Dabir D, Homsi R, Sprinkart AM, Luetkens J, Schild HH, et al. The effects of extracellular contrast agent (Gadobutrol) on the precision and reproducibility of cardiovascular magnetic resonance feature tracking. J Cardiovasc Magn Reson 2016; 18: 30. [Crossref]
13. Szűcs A, Kiss AR, Suhai FI, Tóth A, Gregor Z, Horváth M, et al. The effect of contrast agents on left ventricular parameters calculated by a threshold-based software module: does it truly matter? Int J Cardiovasc Imaging 2019; 35: 1683-9. [Crossref]
14. Jaspers K, Freling HG, van Wijk K, Romijn EI, Greuter MJ, Willems TP. Improving the reproducibility of MR-derived left ventricular volume and function measurements with a semi-automatic threshold-based segmentation algorithm. Int J Cardiovasc Imaging 2013; 29: 617-23. [Crossref]
15. Schuster A, Hor KN, Kowallick JT, Beerbaum P, Kutty S. Cardiovascular Magnetic Resonance Myocardial Feature Tracking: Concepts and Clinical Applications. Circ Cardiovasc Imaging 2016; 9: e004077. [Crossref]
16. Peng J, Zhao X, Zhao L, Fan Z, Wang Z, Chen H, et al. Normal Values of Myocardial Deformation Assessed by Cardiovascular Magnetic Resonance Feature Tracking in a Healthy Chinese Population: A Multicenter Study. Front Physiol 2018; 9 :1181. [Crossref]
17. 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. [Crossref]
18. Grothoff M, Pachowsky M, Hoffmann J, Posch M, Klaassen S, Lehmkuhl L, et al. Value of cardiovascular MR in diagnosing left ventricular non-compaction cardiomyopathy and in discriminating between other cardiomyopathies. Eur Radiol 2012; 22: 2699-709. [Crossref]
19. Andreini D, Pontone G, Bogaert J, Roghi A, Barison A, Schwitter J, et al. Long-Term Prognostic Value of Cardiac Magnetic Resonance in Left Ventricle Noncompaction: A Prospective Multicenter Study. J Am Coll Cardiol 2016; 68: 2166-81. [Crossref]
20. Tops LF, Delgado V, Marsan NA, Bax JJ. Myocardial strain to detect subtle left ventricular systolic dysfunction. Eur J Heart Fail 2017; 19: 307-13. [Crossref]
21. Romano S, Judd RM, Kim RJ, Heitner JF, Shah DJ, Shenoy C, et al. Feature-Tracking Global Longitudinal Strain Predicts Mortality in Patients With Preserved Ejection Fraction: A Multicenter Study. JACC Cardiovasc Imaging 2020; 13: 940-7. [Crossref]
22. Fischer K, Obrist SJ, Erne SA, Stark AW, Marggraf M, Kaneko K, et al. Feature Tracking Myocardial Strain Incrementally Improves Prognostication in Myocarditis Beyond Traditional CMR Imaging Features. JACC Cardiovasc Imaging 2020; 13: 1891-901. [Crossref]
23. 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. [Crossref]

24. Stokke TM, Hasselberg NE, Smedsrud MK, Sarvari SI, Haugaa KH, Smiseth OA, et al. Geometry as a Confounder When Assessing Ventricular Systolic Function: Comparison Between Ejection Fraction and Strain. J Am Coll Cardiol 2017; 70: 942-54. [Crossref]
25. Andre F, Steen H, Matheis P, Westkott M, Breuninger K, Sander Y, et al. Age- and gender-related normal left ventricular deformation assessed by cardiovascular magnetic resonance feature tracking. J Cardiovasc Magn Reson 2015; 17: 25. [Crossref]
26. Menting ME, McGhie JS, Koopman LP, Vletter WB, Helbing WA, van den Bosch AE, et al. Normal myocardial strain values using 2D speckle tracking echocardiography in healthy adults aged 20 to 72 years. Echocardiography 2016; 33: 1665-75. [Crossref]
27. Yubbu P, Nawaytou HM, Calderon-Anyosa R, Banerjee A. Diagnostic value of myocardial deformation pattern in children with noncompaction cardiomyopathy. Int J Cardiovasc Imaging 2018; 34: 1529-39. [Crossref]
28. Cai J, Bryant JA, Le TT, Su B, de Marvao A, O'Regan DP, et al. Fractal analysis of left ventricular trabeculations is associated with impaired myocardial deformation in healthy Chinese. J Cardiovasc Magn Reson 2017; 19: 102. [Crossref]
29. Kawel-Boehm N, McClelland RL, Zemrak F, Captur G, Hundley WG, Liu CY, et al. Hypertrabeculated Left Ventricular Myocardium in Relationship to Myocardial Function and Fibrosis: The Multi-Ethnic Study of Atherosclerosis. Radiology 2017; 284: 667-75. [Crossref]
30. Verdugo-Marchese M, Coiro S, Selton-Suty C, Kobayashi M, Bozec E, Lamiral Z, et al. Left ventricular myocardial deformation pattern, mechanical dispersion, and their relation with electrocardiogram markers in the large population-based STANISLAS cohort: insights into electromechanical coupling. Eur Heart J Cardiovasc Imaging 2020; 21: 1237-45. [Crossref]
31. Jalanko M, Tarkiainen M, Sipola P, Jääskeläinen P, Lauerma K, Laine M, et al. Left ventricular mechanical dispersion is associated with nonsustained ventricular tachycardia in hypertrophic cardiomyopathy. Ann Med 2016; 48: 417-27. [Crossref]
32. Ermakov S, Gulhar R, Lim L, Bibby D, Fang Q, Nah G, et al. Left ventricular mechanical dispersion predicts arrhythmic risk in mitral valve prolapse. Heart 2019; 105: 1063-9. [Crossref]
33. Åström Aneq M, Maret E, Brudin L, Svensson A, Engvall J. Right ventricular systolic function and mechanical dispersion identify patients with arrhythmogenic right ventricular cardiomyopathy. Clin Physiol Funct Imaging 2018; 38: 779-87. [Crossref]
34. Claus P, Omar AMS, Pedrizzetti G, Sengupta PP, Nagel E. Tissue Tracking Technology for Assessing Cardiac Mechanics: Principles, Normal Values, and Clinical Applications. JACC Cardiovasc Imaging 2015; 8: 1444-60. [Crossref]
35. Kutty S, Rangamani S, Venkataraman J, Li L, Schuster A, Fletcher SE, et al. Reduced global longitudinal and radial strain with normal left ventricular ejection fraction late after effective repair of aortic coarctation: a CMR feature tracking study. Int J Cardiovasc Imaging 2013; 29: 141-50. [Crossref]