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Highlights of right ventricular characteristics of left ventricular noncompaction using 3D echocardiography

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A R T I C L E I N F O

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A B S T R A C T

Highlights of right ventricular characteristics of left ventricular noncompaction using 3D echocardiography.

The aspects of right ventricular volumes and function investigated with 3D echocardiography in a large cohort of left ventricular noncompaction morphology (LVNC) population remains unclear.

The objective of our research was to study the left (LV) and right (RV) ventricular parameters using 3D echocardiography and analyze the clinical features of a LVNC population with preserved LV ejection fraction (EF > 50 %) in comparison with healthy controls (HC).

We selected 41 LVNC subjects with preserved LV function (EF: 52.91 ± 3 %, male n = 26) and without any comorbidities and compared them with an age and sex-matched HC. Three dimensional endocardial contours were evaluated to determine the following LV and RV parameters: end-diastolic (EDV) and end-systolic (ESV) volumes, stroke volume, EF, LV global longitudinal and circumferential strain and RV septal and free wall longitudinal strain.

Regarding the clinical characteristics, the family involvement had a notable proportion, accounting for 51%. The EF and strain values of the LVNC population were significantly decreased in both RV and LV compared to HC. Although the LV volumes of the LVNC group were significantly elevated, the RV volumetric parameters did not differ significantly compared to controls. We found significant correlations between LV and RV volumetric and functional parameters and linear regression models showed that LV EDV and LV ESV determined the RV volumetric values.

While the alteration and relationship of the RV parameters may represent the potential of biventricular involvement, clinical characteristics of the LVNC group underlines the necessity of monitoring this population, even with preserved EF.

1. Introduction

Growing literature investigating the left ventricular noncompaction morphology (LVNC) with detailed diagnostic criteria and risk stratification methods is now available [1–3]. As hypertrabeculation can occur in up to 20 % of the general population, according to recent guidelines, individuals without any symptoms and history of any cardiac diseases may defined as healthy subjects with excessive trabeculation [4]. Apart from adaptive forms caused by volume overload, there are less individuals who are diagnosed with primary, asymptomatic LVNC with preserved left ventricular (LV) ejection fraction (EF) [5]. Moreover, novel recommendations agree that in some of them, definitive cardiomyopathy may evolve leading to heart failure, arrhythmias, and thromboembolic events.

The role of biventricular involvement of LVNC remains unclear, as few studies have been conducted to examine this relationship. However, right ventricular noncompaction is difficult to assess because of the complex morphology and the physiologically greater trabeculation of the right ventricle (RV) [6].

Although cardiac magnetic resonance imaging (CMR) is considered the gold-standard diagnostic tool for LVNC, echocardiography is a more accessible imaging modality in the everyday practice [7], as cardiac ultrasound-based monitoring of functional and volumetric changes can be valuable for patient follow-up and may also have prognostic

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significance [8].

2D speckle-tracking echocardiography has a long-standing application in deformation analysis and detects subclinical changes in cardiac function; however, it has some limitations regarding the RV due to the complex three-dimensional (3D) motion of this chamber [9]. A 3D version of speckle tracking echocardiography is now available which is able to examine the complex morphology and function of the RV by quantifying the RV volumes, ejection fraction, and longitudinal strain within the actual cardiac cycle. This method is advantageous compared to other techniques because it provides a more comprehensive assessment of the RV.

Apart from few case reports, only cardiac MR studies of RV involvement in LVNC are available and the usefulness of 3D echocardiography highlighting on right ventricular involvement in LVNC is not well established.

Therefore, we aimed to use 3D echocardiography to investigate the RV and the LV and the relationship of these ventricles in LVNC subjects with preserved LV function and to compare them with healthy controls (HC). Furthermore, we also investigated the clinical characteristics of the LVNC group.

2. Study population

From our LVNC register, we enrolled 41 randomly selected patients (male n = 26, avg. age: 39.58 ± 15 years) with preserved left ventricular function (EF > 50 %) who underwent 3D echocardiography examination. In addition to this hypertrabeculated population, we included 41 age- and sex-matched healthy volunteers without underlying cardiac or systemic disorders (male n = 26, avg. age: 39.64 ± 15 years).

Patients were included in the study if they were diagnosed with LVNC, confirmed by cardiac MR, which satisfied both the Petersen (ratio of noncompacted to compacted myocardial layer exceeding 2.3 at end-diastole) [10] and the Jacquier criteria (trabecular mass greater than 20 % of total myocardial mass at end-diastole) [11].

We excluded patients with reduced EF (<50 %), coronary artery disease, congenital heart disease, other cardiomyopathies, or other significant comorbidities (e.g., diabetes, untreated hypertension), individuals engaged in physical training > 6 h a week, and those with images that could not be reliably processed for technical reasons.

All examinations performed in this study were in accordance with the Helsinki Declaration (1964) and its subsequent modifications. Ethical approval was obtained from the Central Ethics Committee of Hungary, and all participants provided informed consent.

3. Image acquisition and analysis

3D echocardiography examinations were performed with a GE Vivid E95 system with a 4Vc-D phased-array transducer (GE Vingmed Ultrasound, Horten, Norway). LV- and RV-focused, ECG-gated full-volume 3D datasets were obtained from the apical four-chamber view using multibeat reconstruction from 4 cardiac cycles. Offline analyses of these datasets focusing on the LV and RV were performed after selecting the optimal heart cycle using commercially available software (4D LV Analysis 3 and 4D RV Function 2, TOMTEC Imaging Systems GmbH, Unterschleissheim, Germany). The algorithm automatically generated the endocardial contours of the cavities, which were manually corrected on multiple short- and long-axis planes throughout the entire cardiac cycle. During the analysis, the endocardial contour in both ventricles was at the boundary of the compact-noncompact muscle layer, so that the trabecular layer was located in the ventricular cavity. Speckle tracking technique was used for the deformation analysis. Then, the aforementioned software was used to calculate volumetric parameters, such as end-diastolic volume (EDV), end-systolic volume (ESV), and stroke volume (SV), and functional data, such as EF, global longitudinal strain (GLS) and global circumferential strain (GCS) in the case of the LV and septal longitudinal strain (SLS) and free wall longitudinal strain (FWLS) in the case of the RV. The volumetric parameters were indexed to the body surface area, while the measured strain values are reported as absolute values to allow an easier comparison, as interpreted in the Discussion session.

4. Statistics

The Shapiro–Wilk test was used to assess the normality of data distributions. For normally distributed data, an unpaired two-sided Student's *t* test was used to compare continuous variables between groups, and a Mann–Whitney *U* test was used in the case of data that were not normally distributed.

Pearson correlation was used to examine relationships between variables, and multiple linear regression analysis was applied to determine independent predictors for RV volumetric parameters.

Correlations were evaluated as follows: they were rated as weak when below 0.3, moderately good when between 0.3 and 0.6, and excellent when above 0.6.

Interobserver agreement was tested and presented using the interclass correlation coefficient (ICC) and 95 % confidence intervals. A p value of < 0.05 was used as the criterion for statistical significance. Bland–Altman analysis was used to determine intramodality agreement [12].

Statistical analyses were performed using SPSS (IBM, New York, USA) and Microsoft Excel (Microsoft, Redmond, USA) software.

5. Results

The interobserver agreement of the LV and RV, as assessed by the ICC was analyzed in ten randomly selected patients and ten healthy subjects. The results of the interobserver variability test can be found in the supplementary material.

The investigation of the clinical characteristics of the LVNC cohort found that over half of the participants (51 %) had a family history of cardiac complications. Specifically, more than half of the first-degree relatives were diagnosed with a hereditary myocardial disease, and 90 % had a documented arrhythmia. Approximately 12 % of patients experienced at least one unexplained syncope event during their lifetime, for which no other etiology was found. Nearly 40 % of the patients had documented arrhythmia, two-thirds of which originated in the ventricles. Two individuals in the study population had to be resuscitated, and one suffered from a thromboembolic event (Table 1).Studying the left ventricular volumetric and functional parameters, LVNC patients were within the normal range; however, the volumes were significantly higher, and the EF and strain values were significantly lower than those of healthy individuals (Fig. 1.A).Fig. 2

Table 1
Clinical characteristics of the LVNC population.

Clinical characteristics	Prevalence
Positive family history	51,2%
• Hereditary heart muscle disease	66,7%
• Sudden cardiac death	23,8%
• Arrhythmia	90,5%
• PM / ICD implantation	19,0%
Syncope	12,2%
Arrhythmia confirmed by ECG	39,0%
• Atrial	50,0%
• Ventricular	68,8%
VES	90,9%
NSVT	9,1%
PM implantation	2,4%
Reanimation	4,9%
TIA/Stroke	2,4%

LVNC: left ventricular noncompaction; PM: pacemaker; ICD: implantable cardioverter defibrillator; VES: ventricular extrasystole; NSVT: non-sustained ventricular tachycardia; TIA: transient ischemic attack.

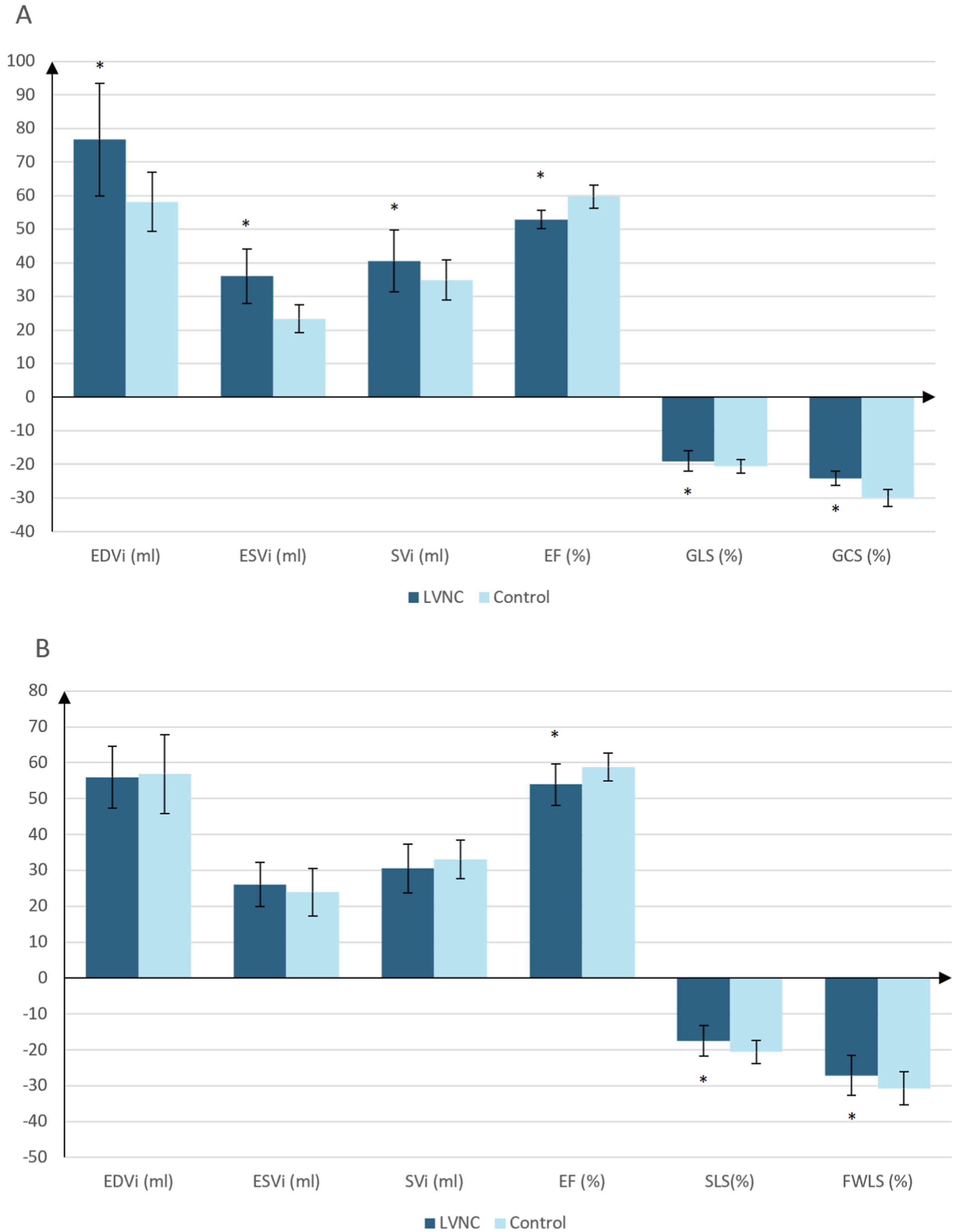

Fig. 1. Comparison of volumetric and functional parameters of LVNC and controls groups using 3D echocardiography. (A: left ventricle, B: right ventricle). LVNC: left ventricular noncompaction, EDV: end-diastolic volume, ESV: end-systolic volume, SV: stroke volume, i: indexed to body surface area; EF: ejection fraction, GLS: global longitudinal strain, GCS: global circumferential strain; SLS: septal longitudinal strain, FWLS: free-wall longitudinal strain; *: $p < 0.05$.

In the RV, the volumetric parameters of the LVNC population and HC group were comparable, while the EF and strain parameters were significantly lower in the LVNC subjects (Table 2) (Fig. 1.B).

Further analysis of the right ventricular parameters revealed a significant association between RV EDV and RV SV and volumetric parameters of the LV. RV EF strongly correlated with LV EF and LV GLS, while RV SLS and RV FWLS were correlated with LV EF (Table 3).

Linear regression was conducted to identify independent predictors

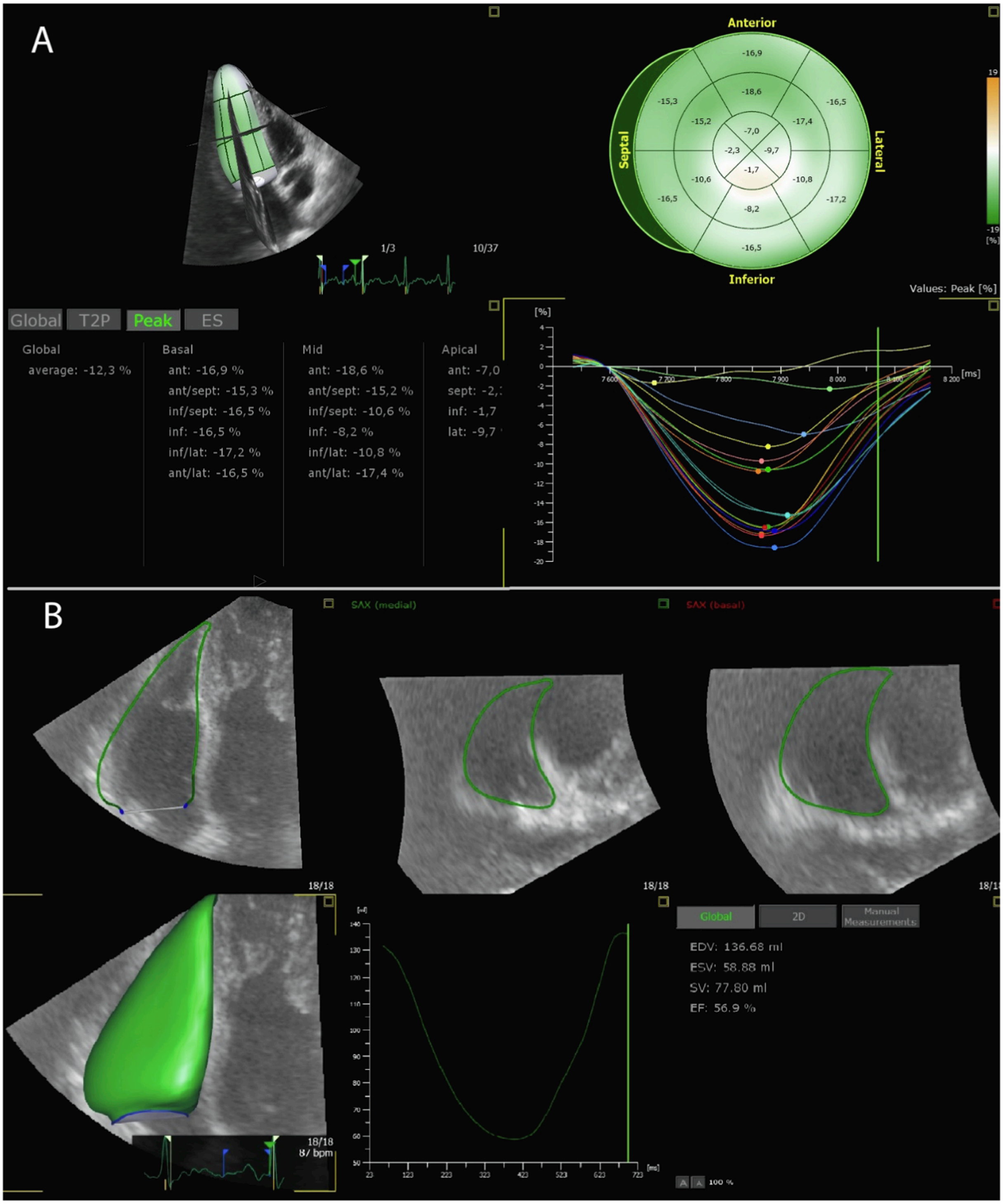

Fig. 2. Speckle tracking analysis using 3D echocardiography. A: Left ventricle, B: right ventricle.

of right ventricular volumes, which demonstrated that the left ventricular EDV and ESV predicted the right ventricular volumetric values (Table 4).

6. Discussion

This study used 3D echocardiography to investigate the characteristics of the left and right ventricle and the relationship between them in both subjects with LVNC and preserved LV EF and HC group; furthermore, we examined the clinical characteristics of the patient population.

It's worth mentioning that the presents of family involvement had a notable proportion among the clinical features, however the clinical characteristics of our patients represents benign conditions. Studying the LVNC group, although the LV volumes were significantly elevated, the RV volumetric parameters did not differ significantly compared to HC The EF and strain values of the LVNC population were significantly decreased in both ventricles compared to HC group. We found significant correlations between LV and RV volumetric and functional parameters and linear regression showed that LV EDV and ESV determined the RV volumetric values [13,14].

Table 2
Comparison of left and right ventricular volumetric and functional parameters.

LV	LVNC	Control	p
EDVi (ml)	76.65 ± 16.6	58.13 ± 9.79	<0.001
ESVi (ml)	36.05 ± 7.95	23.39 ± 4.63	<0.001
SVi (ml)	40.59 ± 9.13	34.93 ± 5.95	<0.001
EF (%)	52.91 ± 2.76	59.75 ± 3.41	<0.001
GLS (%)	−19.01 ± 2.99	−20.60 ± 1.99	<0.001
GCS (%)	−24.12 ± 2.48	−29.92 ± 2.75	<0.001
RV			
EDVi (ml)	56.01 ± 12.03	56.79 ± 12.37	0.854
ESVi (ml)	26.06 ± 6.57	23.89 ± 6.55	0.147
SVi (ml)	30.58 ± 7.33	33.04 ± 6.70	0.095
EF (%)	53.97 ± 5.71	58.83 ± 4.20	<0.001
SLS(%)	−17.46 ± 4.15	−20.57 ± 3.97	<0.001
FWLS (%)	−27.09 ± 5.58	−30.74 ± 5.11	0.006

LVNC: left ventricular noncompaction, LV: left ventricular, RV: right ventricular, EDV: end-diastolic volume, ESV: end-systolic volume, SV: stroke volume, EF: ejection fraction, GLS: global longitudinal strain, GCS: global circumferential strain, SLS: septal longitudinal strain, FWLS: free-wall longitudinal strain

Regarding the LV parameters, our findings agree with MRI studies conducted with a large cohort of LVNC participants with preserved or preserved-to-moderately reduced EF, which observed that these participants had larger LV volumes and lower LV ejection fraction and strain values compared to healthy individuals [15–17]. Similar results were obtained in studies employing 3D echocardiography, but these were mainly case reports or were performed on small cohorts [18]. However, no studies using 3D echocardiography have been conducted to examine either the RV or the LV in a large population.

All parameters of the RV in the LVNC population were within the normal range, and the volumetric parameters were comparable with the HC group; however, the patient population demonstrated significantly lower EF and strain parameters [19]. Similar finding was reported by Sarnecki et al., who examined 16 children diagnosed with LVNC using MR tissue tracking [20]. Another CMR study observed elevated volumetric and decreased functional parameters of the RV when comparing 81 LVNC patients with a control group [16]. However, our study did not show volumetric differences, which might be due to the smaller patient population. Moreover, a novel study of 117 noncompacted participants using 2D STE demonstrated that decreased conventional parameters for right ventricular function (tricuspid annular systolic excursions, tricuspid S′ velocity, and RV fractional area change and reduced right ventricular strain values) were all independent predictors of mortality, regardless of the left ventricular EF [21,22].

The notable differences between the LV and RV paramters in the LVNC group and the HC group raises the question of whether there is a correlation between left ventricular parameters and right ventricular volumes. The phenomenon of ventricular interdependency has been highlighted in several studies, indicating that 20–40 % of right ventricular function can be supported by the LV [23,24]. Our previous studies performed by CMR also showed a relationship between left and right ventricular function in LVNC population both with preserved and reduced LV EF [25,26]. These findings are corroborated with our 3D echo study, which revealed a relationship between the left and right volumetric parameters. Furthermore, we also observed a strong correlation between RV EF and LV EF and LV GLS, which raises the possibility of right ventricular involvement.

Based on these findings, we created regression models to identify the predictors of the RV parameters in the LVNC group. According to this, the LV volumes predicted the RV volumetric and functional parameters, indicating the possibility that the RV volumetric parameters might also increase in connection with the disease progression.

The MESA study, which followed a large number of hypertrabeculated subjects with preserved LV EF found that there was no significant deterioration in volumetric and functional parameters during 9.5 years of follow-up [27].

However, over a period of 16 years, Vaidya et al. monitored 339 LVNC group with mixed EF. In contrast to LVNC subjects with a preserved LV EF, they observed that the primary endpoint (the survival rate) of the total LVNC cohort was inferior to that of the control group [8].As 3D LV GLS which was slightly decreased in our study can be an early indicator of reduced LV function, this may also affect the RV due to the ventricular interdependence and support our investigation [28,29].

In summary, based on clinical characteristics and the above mentioned subclinical volumetric and functional changes regular follow-up may recommended to patients with LVNC and preserved LV function, for which 3D echocardiography may be a suitable modality.

Table 4
Correlation of left and right ventricular parameters in the LVNC group.

	RV_EDV	RV_ESV		
Covariate	**β**	**p**	**β**	**p**
LV_EDVi	3,855	**0,034**	2,614	**0,036**
LV_ESVi	−7,701	**0,043**	−5,285	**0,044**
LV_EF	−5,075	0,057	−4,006	**0,030**
LV_GLS	−0,661	0,241	−0,624	0,111
LV_GCS	−0,893	0,368	−0,580	0,394
Cumulative r	0,522		0,554	
Standard error	7,805		5,372	
Cumulative p	**0,025**		**0,014**	

LVNC: left ventricular noncompaction, LV: left ventricular, RV: right ventricular, EDV: end-diastolic volume, ESV: end-systolic volume, SV: stroke volume, EF: ejection fraction, GLS: global longitudinal strain, GCS: global circumferential strain, SLS: septal longitudinal strain, FWLS: free-wall longitudinal strain, r: correlation coefficient, *: $p < 0.05$; **: $p < 0.01$.

Table 3
Regression analysis of right ventricular volumetric parameters.

		LV_EDVi	LV_ESVi	LV_SVi	LV_EF	LV_GLS	LV_GCS
RV_EDVi	r	0.40*	0.38*	0.40*	0.01	−0.07	−0.05
	p	0.01	0.02	0.01	0.99	0.69	0.79
RV_ESVi	r	0.28	0.34*	0.21	−0.31	−0.32	−0.26
	p	0.09	0.04	0.21	0.06	0.05	0.12
RV_SVi	r	0.42**	0.34*	0.47**	0.26	0.18	0.09
	p	0.01	0.04	0.01	0.12	0.27	0.57
RV_EF	r	016	0.03	0.27	0.55**	0.52**	0.32
	p	0.34	0.89	0.10	0.00	0.01	0.05
RV_SLS	r	−0.05	−0.15	0.04	0.41**	0.22	0.26
	p	0.77	0.37	0.80	0.01	0.18	0.12
RV_FWLS	r	−0.06	−0.19	0.07	0.55**	0.23	0.28
	p	0.74	0.25	0.69	0.000	0.16	0.08

LV: left ventricular, RV: right ventricular, EDV: end-diastolic volume, ESV: end-systolic volume, EF: ejection fraction, GLS: global longitudinal strain, GCS: global circumferential strain

7. Conclusions

This study investigated left and right ventricular volumetric and functional parameters in subjects with LVNC and preserved LV function using 3D echocardiography, compared them with HC and investigated the clinical characteristics of this LVNC population.

The analysis of clinical characteristics of LVNC cohort revealed strong familial involvement; however, the this population presented only minor symptoms.

All the measured parameters of the LV and RV were within the normal range, however, the LV volumes were significantly higher, and the LV EF and strain values were significantly lower in LVNC subject than in HC individuals. Regarding the RV, volumetric parameters of the LVNC and HC population were comparable, and the EF and strain values were significantly lower in the LVNC group.

Further analysis identified significant correlations between LV and RV, and our linear regression models showed that LV EDV and ESV determined RV volumetric values.

The subclinical alterations of RV and LV parameters the potential involvement of the r RV and the clinical characteristics suggest the necessity for monitoring LVNC morphology individuals using 3D echocardiography, even with preserved LV EF.

8. Limitations

Limitation of our research is the relatively small number of patients, namely primary LVNC is a rather rare disease. Our registry is constantly expanding; however, prospective, multimodal analysis of this geographically dispersed population is not easily performed.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2023.101289.

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