

Original Research

Left Atrial Volumetric and Strain Analysis by Three-Dimensional Speckle-Tracking Echocardiography in Noncompaction Cardiomyopathy: Results from the MAGYAR-Path Study

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Introduction: Noncompaction cardiomyopathy (NCCM) is a rare congenital cardiomyopathy characterised by a distinctive 2-layered appearance of the myocardium due to hypertrabecularisation and deep intertrabecular recesses. The present study was designed to assess left atrial (LA) volumes and volumetric and strain-based functional properties by three-dimensional speckle-tracking echocardiography (3DSTE) in NCCM.

Methods: The study included 12 consecutive NCCM patients. Their results were compared to 20 age- and sex-matched healthy controls. Complete two-dimensional Doppler echocardiography and 3DSTE were performed in all cases.

Results: Calculated LA maximum (76.5 ± 26.8 mL vs. 45.3 ± 15.1 mL, $p=0.0002$) and minimum (56.9 ± 27.3 mL vs. 25.3 ± 15.2 mL, $p=0.0002$) volumes and LA volume before atrial contraction (67.1 ± 28.2 mL vs. 35.7 ± 16.4 mL, $p=0.0004$) were significantly greater in NCCM patients. Total, active, and passive LA emptying fractions proved to be smaller in NCCM. Peak global radial ($-9.3 \pm 7.8\%$ vs. $-16.8 \pm 10.2\%$, $p=0.05$), circumferential ($12.8 \pm 8.4\%$ vs. $26.2 \pm 9.2\%$, $p=0.0003$), longitudinal ($12.8 \pm 8.2\%$ vs. $22.5 \pm 8.5\%$, $p=0.004$), and area ($26.7 \pm 18.5\%$ vs. $51.6 \pm 20.3\%$, $p=0.001$) strains were significantly smaller in NCCM patients as compared to matched controls.

Conclusions: Significantly greater LA volumes and compromised LA functional properties could be demonstrated by 3DSTE in patients with NCCM.

Noncompaction of the left ventricular (LV) myocardium is a rare congenital cardiomyopathy characterised by a distinctive 2-layered appearance of the myocardium due to hypertrabecularisation and deep intertrabecular recesses.¹ It usually presents with ventricular dysfunction, thromboembolic events and arrhythmias. However, little is known about the behaviour of the left atrium (LA) in noncompaction cardiomyopathy (NCCM) at this time.² Several non-invasive clinical tools, including three-di-

mensional (3D) speckle-tracking echocardiography (STE), have been demonstrated to be useful for the assessment of LA function.³ The present study was designed to assess LA volumes and volume- and strain-based functional properties by 3DSTE in NCCM.

Methods

Patient population

The present study included 12 patients

with typical features of NCCM. The diagnosis of NCCM was confirmed in all patients according to Jeni's criteria.¹ Their results were compared to 20 age- and sex-matched healthy controls. Complete two-dimensional (2D) Doppler echocardiography and 3DSTE were performed in all NCCM cases and controls. Diabetes mellitus (DM) was defined in accordance with the criteria of the American Diabetes Association⁴ and World Health Organisation.⁵ Hypertension was defined as either a systolic or a diastolic elevation of the blood pressure (>140/90 mmHg), or ongoing antihypertensive therapy. Hypercholesterolemia was defined as a total cholesterol level >5.0 mmol/L or current treatment with lipid-lowering medications. All subjects were enrolled in the MAGYAR-Path Study (Motion Analysis of the heart and Great vessels by three-dimensional speckle-tracking echocardiography in Pathological cases). This was organised at the Cardiology Centre of the University of Szeged to evaluate the usefulness, diagnostic and prognostic value of 3DSTE-derived volumetric, strain, rotational, dyssynchrony, etc., parameters in pathological cases ("Magyar" means "Hungarian" in the Hungarian language). Informed consent was obtained from each patient and control subject and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki, as reflected in *a priori* approval by the institution's human research committee.

Two-dimensional echocardiography

Complete Doppler 2D echocardiographic examinations were performed in all cases. Standard 2D echocardiographic studies were carried out using commercially available Toshiba Artida™ echocardiography equipment (Toshiba Medical Systems, Tokyo, Japan) with a PST-30SBP (1-5 MHz) phased-array transducer. Left ventricular (LV) and LA dimensions, volumes and LV ejection fraction (EF) were calculated in accordance with the guidelines.⁶ Colour Doppler echocardiography was used to visually quantify the degree of mitral regurgitation.

Three-dimensional speckle-tracking echocardiography

All patients underwent 3D echocardiographic acquisitions immediately after a 2D echocardiographic study, using the same Toshiba Artida™ echocardiography equipment and a commercially available PST-25SX matrix-array transducer with 3DSTE capability.^{3,7} Within a single breath-hold and during a constant RR interval, 6 wedge-shaped subvolumes were acquired from an apical window to create full-volume 3D datasets. The sector width was decreased as much as possible to improve the temporal and spatial resolution of the image in order to obtain a 3D full-volume dataset of the LA with optimal border delineation. LA chamber quantification was performed offline using 3D Wall Motion Tracking software version 2.5 (Toshiba Medical Systems, Tokyo, Japan). Three-dimensional echocardiographic datasets were displayed in apical 4-chamber (AP4CH) and 2-chamber (AP2CH) views and 3 short-axis views in basal, mid-atrial, and superior LA regions (Figure 1). In the AP4CH and AP2CH views, the endocardial border was traced by the user, who set multiple reference points starting at the base of the LA at mitral valve level, progressing toward the LA apex, and excluding the LA appendage and pulmonary veins from the LA cavity. The epicardial border was adjusted manually or by setting a default thickness for the myocardium. After detection of the LA borders on the end-diastolic reference frame, 3D wall motion tracking, which is based on a 3D block-matching algorithm, was automatically performed by the software. The user could correct the shape of the LA if needed throughout the entire cardiac cycle.

3DSTE-derived volumetric measurements

The following volumetric calculations were performed:^{3,7}

1. maximum LA volume (V_{\max}) at end-systole, the time at which LA volume was largest just before mitral valve opening,
2. minimum LA volume (V_{\min}) at end-diastole, the

Table 1. The way of calculating left atrial stroke volumes and emptying fractions in each phase of left atrial motion.

| | Reservoir | Conduit function | Active contraction |
|------------------------|----------------------------------|---|--|
| Stroke volumes (mL) | Total SV = $V_{\max} - V_{\min}$ | Passive SV = $V_{\max} - V_{\text{preA}}$ | Active SV = $V_{\text{preA}} - V_{\min}$ |
| Emptying fractions (%) | Total EF = Total SV/ V_{\max} | Passive EF = Passive SV/ V_{\max} | Active EF = Active SV/ V_{preA} |

EF – ejection fraction; LV – left ventricular; SV – stroke volume; V_{\max} – maximum left atrial volume; V_{\min} – minimum left atrial volume; V_{preA} – left atrial volume before left atrial contraction.

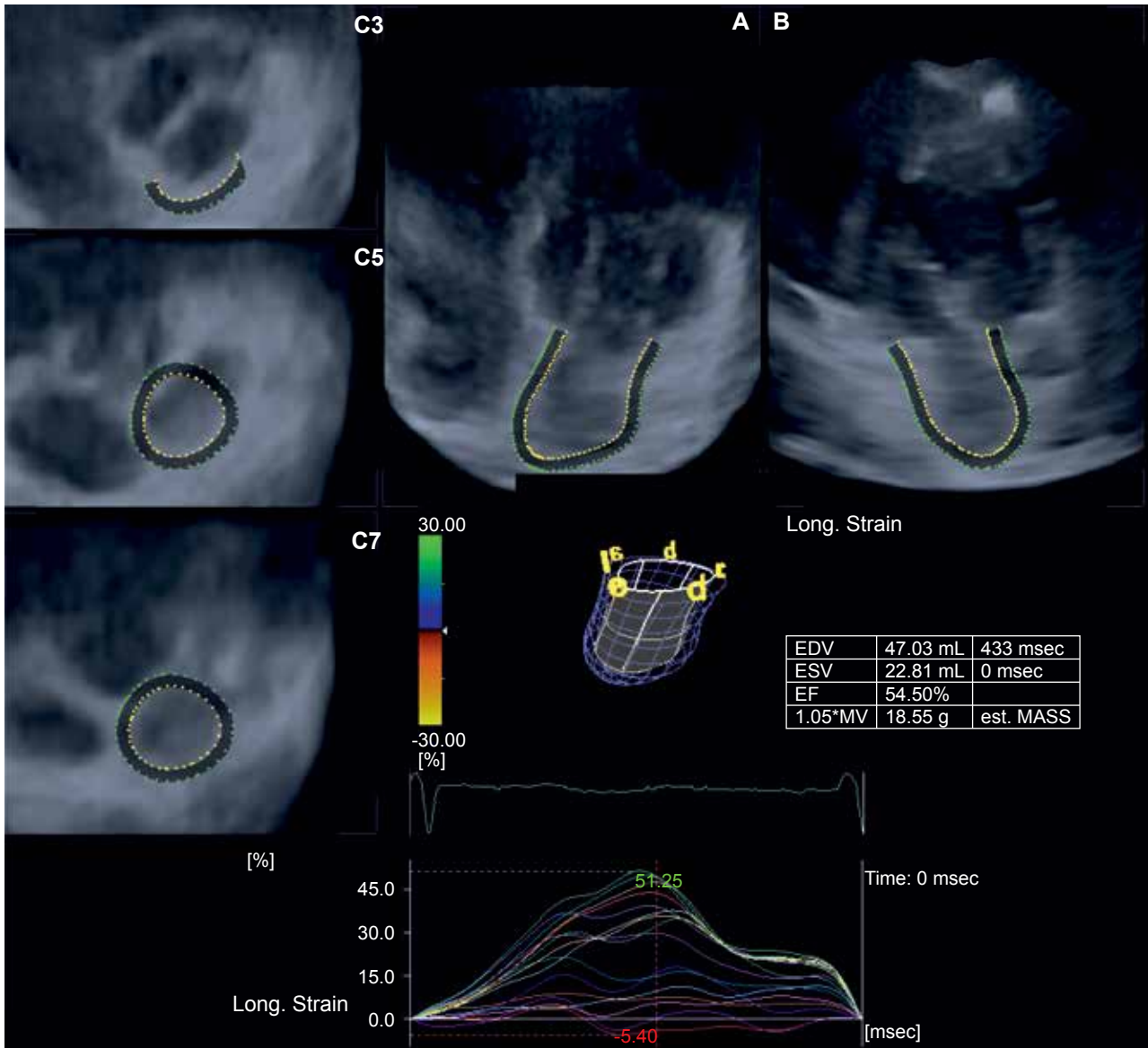


Figure 1. Images from three-dimensional full-volume dataset showing left atrium: (A) apical four-chamber view, (B) apical two-chamber view, (C3) parasternal short-axis view at basal, (C5) mid- and (C7) superior left atrial level. The semi-automated left atrial border definition, left atrial volumetric data and three-dimensional “wire” reconstruction of the left atrium based on three-dimensional speckle tracking echocardiographic analysis, together with time-segmental longitudinal strain curves are also presented.

time at which LA volume reaches its nadir before mitral valve closure,

3. LA volume before atrial contraction (V_{preA}), the last frame before mitral valve reopening or at the time of the P wave on the ECG.

From these three volumes, several parameters characterising all phases of LA function (reservoir, conduit and active contraction) including total, active and passive LA stroke volumes and emptying fractions, were derived (Table 1).

3DSTE-derived strain measurements

The following peak strain parameters were routinely measured by the software in a semi-automatic fashion from the 3D echocardiographic datasets to characterise LA reservoir function:^{3,7-9} longitudinal strain (LS) in the direction tangential to the endocardial contour, circumferential strain (CS) in a circumferential direction, and radial strain (RS) in a perpendicular direction to the endocardial contour. Besides these “unidimensional” parameters, novel strain parameters were

also recorded, such as 3D strain (3DS), defined as strain in the wall-thickening direction, and area strain (AS), as a ratio of endocardial area change during the cardiac cycle.

Statistical analysis

All data are reported as mean \pm standard deviation. A value of $p < 0.05$ was considered to be statistically significant. For comparing variables, Student's t-test, chi-square analysis, and Fisher's exact test were used. MedCalc software was used for the statistical calculations (MedCalc, Mariakerke, Belgium).

Results

Clinical characteristics of patients

Cardiovascular risk factors and medications of NCCM patients and controls are presented in Table 2.

Two-dimensional echocardiographic data

Standard 2D echocardiographic data are summarised in Table 2. Significant ($>$ grade 2) mitral regurgitation could be detected in 4 patients with NCCMP (33%) and in none of the controls. Increased LV di-

ameters and volumes, and decreased LV-EF could be confirmed in NCCM patients (Table 2).

Three-dimensional speckle-tracking echocardiographic data

Significantly increased LA maximum and minimum volumes and LA volume before atrial contraction could be detected in NCCM patients. Total, passive and active LA emptying fractions were significantly decreased in patients with NCCM (Table 3). Peak global and mean LA segmental strains proved to be lower in NCCM patients as compared to controls (Table 4). Alterations in segmental LA strain parameters in NCCM patients are summarised in Table 5. The number of noncompacted segments (extent of noncompaction) did not correlate with atrial functional properties.

Follow up

The success rate of follow up proved to be 100%. During a mean follow up of 27 ± 1 months, cardiovascular events were found in the anamnesis of 5 NCCM patients, including coronary angiographically-proven multi-vessel disease requiring coronary artery bypass grafting in 2 cases, resynchronisation treat-

Table 2. Clinical and two-dimensional echocardiographic characteristics of patients with noncompaction cardiomyopathy and of controls

| | NCCM patients (n=12) | Controls (n=20) | p |
|-----------------------------------|-------------------------|--------------------|---------|
| Risk factors: | | | |
| Age (years) | 54.2 \pm 15.0 | 51.9 \pm 12.7 | 0.65 |
| Male sex (%) | 5 (42) | 12 (60) | 0.47 |
| Diabetes mellitus (%) | 0 (0) | 0 (0) | 1.00 |
| Hypertension (%) | 5 (42) | 0 (0) | 0.004 |
| Hypercholesterolaemia (%) | 3 (25) | 0 (0) | 0.04 |
| Medications: | | | |
| β -blockers (%) | 10 (83) | 0 (0) | <0.0001 |
| ACE-inhibitors (%) | 10 (83) | 0 (0) | <0.0001 |
| Diuretics (%) | 9 (75) | 0 (0) | <0.0001 |
| Two-dimensional echocardiography: | | | |
| LA diameter (mm) | 49.4 \pm 8.7 | 33.0 \pm 2.0 | <0.0001 |
| LV end-diastolic diameter (mm) | 62.7 \pm 13.2 | 47.4 \pm 4.3 | <0.0001 |
| LV end-diastolic volume (mL) | 198.8 \pm 89.5 | 104.6 \pm 21.1 | 0.0001 |
| LV end-systolic diameter (mm) | 47.7 \pm 15.4 | 31.0 \pm 4.3 | 0.0001 |
| LV end-systolic volume (mL) | 116.2 \pm 76.5 | 37.5 \pm 10.3 | 0.0001 |
| Interventricular septum (mm) | 10.1 \pm 1.8 | 9.1 \pm 2.0 | 0.17 |
| LV posterior wall (mm) | 9.8 \pm 1.4 | 9.8 \pm 2.1 | 1.00 |
| LV ejection fraction (%) | 41.5 \pm 17.7 | 64.0 \pm 6.1 | <0.0001 |
| E/A | 1.6 \pm 0.7 | 1.2 \pm 0.1 | 0.02 |
| Number of noncompacted segments | 6.5 \pm 1.7 | 0 | - |

ACE – angiotensin-converting enzyme; LA – left atrium; LV – left ventricular; NCCM – noncompaction cardiomyopathy.

Table 3. Comparison of three-dimensional speckle-tracking echocardiography-derived left atrial volumetric parameters in patients with noncompaction cardiomyopathy and in controls.

| | NCCM patients (n=12) | Controls (n=20) | p |
|------------------------|-------------------------|--------------------|--------|
| Frame rate (vps) | 23.2 ± 3.6 | 19.8 ± 0.8 | 0.0003 |
| Calculated volumes: | | | |
| V _{max} (mL) | 76.5 ± 26.8 | 45.3 ± 15.1 | 0.0002 |
| V _{min} (mL) | 56.9 ± 27.3 | 25.3 ± 15.2 | 0.0002 |
| V _{preA} (mL) | 67.1 ± 28.2 | 35.7 ± 16.4 | 0.0004 |
| Stroke volumes: | | | |
| TASV (mL) | 19.6 ± 4.8 | 19.9 ± 6.4 | 0.89 |
| PASV (mL) | 9.5 ± 2.8 | 9.5 ± 5.3 | 1.00 |
| AASV (mL) | 10.1 ± 5.4 | 10.3 ± 4.0 | 0.91 |
| Emptying fractions: | | | |
| TAEF (%) | 29.3 ± 13.1 | 46.0 ± 13.3 | 0.002 |
| PAEF (%) | 15.1 ± 9.7 | 22.6 ± 9.0 | 0.05 |
| AAEF (%) | 17.1 ± 8.8 | 30.7 ± 9.2 | 0.0003 |

AAEF – active atrial emptying fraction; AASV – active atrial stroke volume; PSV – passive stroke volume; PAEF – passive atrial emptying fraction; TAEF – total atrial emptying fraction; TASV – total atrial stroke volume; V_{max} – maximum left atrial volume; V_{min} – minimum left atrial volume; V_{preA} – volume before atrial contraction.

Table 4. Comparison of three-dimensional speckle-tracking echocardiography-derived peak global and mean segmental strain parameters in patients with noncompaction cardiomyopathy and in controls.

| | NCCM patients (n=12) | Controls (n=20) | p |
|----------------------|-------------------------|--------------------|--------|
| Peak global: | | | |
| RS (%) | -9.3 ± 7.8 | -16.8 ± 10.2 | 0.05 |
| CS (%) | 12.8 ± 8.4 | 26.2 ± 9.2 | 0.0003 |
| LS (%) | 12.8 ± 8.2 | 22.5 ± 8.5 | 0.004 |
| 3DS (%) | -6.4 ± 5.8 | -7.3 ± 12.3 | 0.81 |
| AS (%) | 26.7 ± 18.5 | 51.6 ± 20.3 | 0.001 |
| Peak mean segmental: | | | |
| RS (%) | -12.7 ± 6.9 | -19.8 ± 8.0 | 0.02 |
| CS (%) | 16.2 ± 9.1 | 30.9 ± 11.8 | 0.0009 |
| LS (%) | 15.9 ± 8.9 | 26.1 ± 7.7 | 0.002 |
| 3DS (%) | -9.3 ± 5.3 | -13.7 ± 9.1 | 0.32 |
| AS (%) | 32.4 ± 20.1 | 58.9 ± 21.3 | 0.002 |

3DS – three-dimensional strain; AS – area strain; CS – circumferential strain; LS – longitudinal strain; NCCM – noncompaction cardiomyopathy; RS – radial strain.

Table 5. Comparison of three-dimensional speckle-tracking echocardiography-derived peak segmental strain parameters in patients with noncompaction cardiomyopathy and in controls.

| | NCCM patients (n=12) | Controls (n=20) | p |
|---------------------------|-------------------------|--------------------|---------|
| RS _{basal} (%) | -9.3 ± 6.7 | -23.3 ± 11.4 | 0.0006 |
| RS _{mid} (%) | -12.8 ± 6.6 | -20.6 ± 11.6 | 0.04 |
| RS _{apical} (%) | -17.9 ± 14.1 | -18.8 ± 13.0 | 0.96 |
| CS _{basal} (%) | 16.4 ± 12.3 | 40.6 ± 14.5 | <0.0001 |
| CS _{mid} (%) | 14.6 ± 9.2 | 28.8 ± 12.3 | 0.002 |
| CS _{apical} (%) | 19.1 ± 13.8 | 25.9 ± 16.7 | 0.24 |
| LS _{basal} (%) | 13.0 ± 5.7 | 19.6 ± 10.8 | 0.06 |
| LS _{mid} (%) | 21.9 ± 14.2 | 35.4 ± 10.2 | 0.004 |
| LS _{apical} (%) | 11.6 ± 8.6 | 20.9 ± 10.9 | 0.02 |
| 3DS _{basal} (%) | -6.5 ± 4.3 | -17.7 ± 10.9 | 0.002 |
| 3DS _{mid} (%) | -9.2 ± 5.2 | -13.3 ± 9.7 | 0.19 |
| 3DS _{apical} (%) | -13.4 ± 10.2 | -12.4 ± 9.0 | 0.77 |
| AS _{basal} (%) | 27.6 ± 19.0 | 58.9 ± 26.7 | 0.001 |
| AS _{mid} (%) | 37.4 ± 26.8 | 69.1 ± 27.8 | 0.004 |
| AS _{apical} (%) | 32.7 ± 23.0 | 54.5 ± 37.5 | 0.08 |

Abbreviations as in Table 4.

ment in 1 case, cardiac decompensation and new-onset atrial fibrillation in 1 case, and prosthetic valve implantation for significant aortic regurgitation and pacemaker implantation for ventricular arrhythmias in 1 case. 3DSTE-derived atrial volumetric and functional properties in NCCM patients with and without events are given in Table 6.

Discussion

3DSTE allows a detailed evaluation of LA function

through volumetric measurements and strain analysis.^{3,7} To the best of the authors' knowledge, this is the first study in which LA function was assessed by 3DSTE in a series of patients with NCCM and compared to matched controls. Increased LA volumes, reduced LA emptying fractions and peak LA strain parameters could be demonstrated in patients with NCCM.

The LA serves multiple functions, acting as a reservoir during LV systole, a conduit for blood transiting from the pulmonary veins to the LV during early

Table 6. Comparison of three-dimensional speckle-tracking echocardiography-derived peak global and mean segmental strain parameters in noncompaction cardiomyopathy patients with versus without events during follow up.

| NCCM patients | With events (n=5) | Without events (n=7) | P |
|-------------------------|----------------------|-------------------------|------|
| Calculated volumes: | | | |
| V _{max} (mL) | 92.0 ± 15.0 | 65.6 ± 28.6 | 0.09 |
| V _{min} (mL) | 73.7 ± 16.2 | 44.9 ± 28.1 | 0.07 |
| V _{preA} (mL) | 84.7 ± 16.5 | 54.5 ± 28.9 | 0.06 |
| Stroke volumes: | | | |
| TASV (mL) | 18.4 ± 5.7 | 20.5 ± 4.2 | 0.47 |
| PASV (mL) | 7.3 ± 2.8 | 11.0 ± 1.5 | 0.01 |
| AASV (mL) | 11.0 ± 6.4 | 9.5 ± 5.0 | 0.65 |
| Emptying fractions: | | | |
| TAEF (%) | 20.3 ± 6.3 | 35.7 ± 13.0 | 0.04 |
| PAEF (%) | 8.3 ± 4.0 | 20.0 ± 9.7 | 0.03 |
| AAEF (%) | 13.0 ± 6.9 | 20.1 ± 9.3 | 0.18 |
| Peak global strains: | | | |
| RS (%) | 5.8 ± 3.9 | 11.9 ± 9.1 | 0.19 |
| LS (%) | 7.1 ± 3.9 | 16.9 ± 8.2 | 0.03 |
| CS (%) | 9.3 ± 8.6 | 15.3 ± 8.0 | 0.24 |
| 3DS (%) | 4.6 ± 3.2 | 7.7 ± 7.0 | 0.38 |
| AS (%) | 15.2 ± 13.8 | 34.9 ± 17.6 | 0.06 |
| Mean segmental strains: | | | |
| RS (%) | 9.5 ± 2.8 | 15.1 ± 8.2 | 0.18 |
| LS (%) | 9.1 ± 3.3 | 20.8 ± 8.4 | 0.01 |
| CS (%) | 11.3 ± 8.1 | 19.8 ± 8.6 | 0.12 |
| 3DS (%) | 7.3 ± 3.2 | 10.7 ± 6.2 | 0.29 |
| AS (%) | 19.3 ± 13.6 | 41.8 ± 19.2 | 0.05 |

AAEF – active atrial emptying fraction; AASV – active atrial stroke volume; AS – area strain; CS – circumferential strain; LS – longitudinal strain; NCCM – noncompaction cardiomyopathy; PAEF – passive atrial emptying fraction; PASV – passive stroke volume; RS – radial strain; TAEF – total atrial emptying fraction; TASV – total atrial stroke volume; V_{max} – maximum left atrial volume; V_{min} – minimum left atrial volume; V_{preA} – volume before atrial contraction; 3DS – three-dimensional strain.

diastole, and an active contractile chamber that augments LV filling in late diastole.¹⁰ Nowadays, there are several imaging methodologies that appear to make the accurate evaluation of LA volumes and functional parameters feasible, including 3DSTE.^{3,8,9} 3DSTE is based on block matching of the myocardial speckles of the endocardial border during their motion from frame to frame.¹¹ Although volumetric real-time three-dimensional echocardiography (RT3DE) and strain-based 3DSTE are different 3D echocardiographic techniques using different algorithms during their evaluations, RT3DE and 3DSTE were found to give comparable and reproducible quantification of LV and LA volumes and function, making interchangeable application a viable option in daily clinical practice.¹²

There are several ways in which 3DSTE could characterise LA function:

1. measuring LA volumes with respect to the heart cycle and calculating parameters characterising all the phases of LA motion detailed above (see Table 1);¹²⁻¹⁴
2. calculating different LA strain parameters from the same 3D cast, including RS, LS, CS, 3DS and AS;^{7,15,16}
3. measuring LA ejection force from planimetry-derived mitral annulus data and mitral inflow A-wave velocity measured by Doppler echocardiography characterising LA systolic function.¹⁷

Cardiomyopathies are frequently associated with volumetric and functional deterioration of different heart chambers.¹⁸⁻²⁰ However, relatively few studies are available in which LA (dys)function was investigated in NCCM. In a recent RT3DE study, LA ejection force was found to be greater in NCCM as compared to controls.^{2,17} In the present study, a significantly reduced active atrial emptying fraction could be demonstrated during LA contraction. Moreover, all calculated LA volumes proved to be increased, while LA emptying fractions with respect to the cardiac cycle were decreased in NCCM, demonstrating significant alterations in all aspects of LA function. During strain analysis, certain peak global and mean segmental strain parameters showed reductions in NCCM patients, confirming changes in LA reservoir function.

Limitations

The following important limitations should be taken into consideration:

1. The LA appendage and pulmonary veins were not considered during LA volumetric and strain assessments.
2. 3DSTE-derived image quality is worse than for 2D echocardiography, because of low temporal and spatial image resolution.
3. The results of a relatively small number of NCCM patients were analysed. However, it should be considered that this was a single-centre experience and NCCM is a relatively rare disorder.
4. Some NCCM patients showed higher-grade mitral regurgitation. This could have affected our results.

Conclusions

Significantly increased LA volumes and reduced LA functional properties could be demonstrated in NCCM by 3DSTE.

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