2nd Department of Medicine and Cardiology Center, Medical Faculty,
Albert Szent-Györgyi Clinical Center,
University of Szeged

Advances in the assessment of left atrial function by three-dimensional speckle tracking echocardiography

Péter Domsik MD

PhD thesis

Tutors:

Attila Nemes MD, PhD, DSc
Prof. Tamás Forster MD, PhD, DSc

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Relevant publications

Full papers

I. Nemes A, Domsik P, Kalapos A, Lengyel C, Orosz A, Forster T. Comparison of Three-Dimensional Speckle Tracking Echocardiography and Two-Dimensional Echocardiography for Evaluation of Left Atrial Size and Function in Healthy Volunteers (Results from the MAGYAR-Healthy Study). *Echocardiography* 2014; 31: 865–871. (Impact factor: 1.254)

II. Domsik P, Kalapos A, Lengyel Cs, Orosz A, Forster T, Nemes A. Relationship between mitral annular and left atrial function as assessed by three-dimensional speckle-tracking echocardiography in healthy volunteers Results from the MAGYAR-Healthy Study. *Orv Hetil* 2014; 155: 1517–1523.

III. Nemes A, Hausinger P, Kalapos A, Domsik P, Forster T. Alternative ways to assess left atrial function in noncompaction cardiomyopathy by three-dimensional speckle-tracking echocardiography (A case from the MAGYAR-Path Study). *Int J Cardiol* 2012; 158: 105-107. (Impact factor: 7.078)

IV. Domsik P, Kalapos A, Chadaide S, Sepp R, Hausinger P, Forster T, Nemes A. Three-Dimensional Speckle Tracking Echocardiography Allows Detailed Evaluation of Left Atrial Function in Hypertrophic Cardiomyopathy – Insights from the MAGYAR-Path Study. *Echocardiography* 2014; 31: 1245-1252. (Impact factor: 1.254)

V. Nemes A, Domsik P, Kalapos A, Forster T. Visualization of left atrial appendage by three-dimensional speckle-tracking echocardiography (A case from the MAGYAR-Path Study). *Herz* 2014; 39: 832-833. (Impact factor: 0.912)

Abstracts

I. Domsik P, Kalapos A, Chadaide S, Forster T, Sepp R, Nemes A. Evaluation of left atrial function in hypertrophic cardiomyopathy by volumetric and strain analysis –

Results from the three-dimensional speckle-tracking echocardiographic MAGYAR-Path Study. *Cardiol Hung* 2013; 43: B48.

II. Nemes A, Domsik P, Kalapos A, Orosz A, Lengyel C, Forster T. Comparison of three-dimensional speckle-tracking echocardiography and two-dimensional echocardiography for evaluation of left atrial size and function in healthy volunteers. *Eur Heart J Cardiovasc Imaging* 2013; 43 (Suppl 2): ii68.

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Abbreviations

2D	two-dimensional
3D	three-dimensional
3DS	three-dimensional strain
3DSTE	three-dimensional speckle-tracking echocardiography
AAEF	active atrial emptying fraction
AASV	active atrial stroke volume
AP2CH	apical 2-chamber view
AP4CH	apical 4-chamber view
AS	area strain
CMR	cardiovascular magnetic resonance
CT	computed tomography
CS	circumferential strain
DM	diabetes mellitus
EDV	end-diastolic volume
EF	ejection fraction
EFO	ejection force
ESV	end-systolic volume
HCM	hypertrophic cardiomyopathy
L	left atrial long axis
LA	left atrial
LAA	left atrial appendage
LA-EFO	left atrial ejection force
LS	longitudinal strain
LV	left ventricular
LVOT	left ventricular outflow tract
MA	mitral annulus
MAA-D	end-diastolic mitral annular area
MAAI-D	end-diastolic mitral annular area index
MAAI-S	end-systolic mitral annular area index
MAA-S	end-systolic mitral annular area
MAD-D	end-diastolic MA diameter

MADI-D	end-diastolic mitral annular diameter index
MADI-S	end-systolic mitral annular diameter index
MAD-S	end-systolic mitral annular diameter
MAFAC	mitral annular fractional area change
MAFS	mitral annular fractional shortening
'MAGYAR'	'**M**otion **A**nalysis of the heart and **G**reat vessels b**Y** three-dimension**A**l speckle-t**R**acking echocardiography'
MAP-D	end-diastolic mitral annular perimeter
MAPI-D	end-diastolic MA perimeter index
MAP-S	end-systolic MA perimeter
MAPI-S	end-systolic MA perimeter index
MR	mitral regurgitation
MRI	magnetic resonance imaging
NCCM	noncompaction cardiomyopathy
PAEF	passive atrial emptying fraction
PASV	passive atrial stroke volume
RS	radial strain
RT3DE	real-time three-dimensional echocardiography
STE	speckle-tracking echocardiography
SV	stroke volume
TAEF	total atrial emptying fraction
TASV	total atrial stroke volume
TDI	tissue doppler imaging
Vmax	maximum left atrial volume
Vmin	minimum left atrial volume
VpreA	left atrial volume before atrial contraction

1. Introduction

Noninvasive accurate assessment of left atrial (LA) size and function is an essential requirement in daily clinical practice (1). LA is a dynamically moving cardiac chamber, which acts as a reservoir during the cardiac cycle, receiving pulmonary venous return in left ventricular (LV) systole, works as a conduit, passively transferring blood to the LV during early diastole and have a booster pump function in late diastole (2). To perform these complicated cardiac motions, condition and function of both the pulmonary veins and the mitral valve have an essential role.

Two-dimensional (2D) echocardiography is one of the most widely used standardized imaging tool for the evaluation of LA dimensions in the real clinical practice (3). Today, different kinds of 3D echocardiographic methods are available based on different algorithms: besides the volumetric real-time 3D echocardiography (RT3DE) (4), 3D speckle-tracking echocardiography (STE) has been introduced in the latter years (5). Early results have already raised confirming that RT3DE seems to be a proper solution to assess the LA and mitral annular (MA) periodic functions respecting cardiac cycle (6-10). RT3DE with direct volumetric assessment has been found to be a highly accurate and reproducible non-invasive tool for the evaluation of LA dimensions and functional properties (6,7). 3DSTE uses different, as called „block-matching" algorithm by strain analyis during evaluations. It has been validated mostly for LV volumetric measurements (5). This methodology tries to merge advantages of 3D echocardiography and STE: while heart could be examined according to its nature in 3D, segmental motions could be quantified by strain analysis with STE, as well (5). In a recent study, RT3DE and 3DSTE methods for quantification of LV and LA volumes and functional properties were found to be comparable, reproducible and interchangeable (11).

However, there is limited information on the *validity of 3DSTE*-derived LA dimensions and functional data. Moreover, the *relationship between LA and MA data* as assessed simultaneously by 3DSTE has also not been confirmed even in healthy subjects. There was no information on the usefulness of 3DSTE in the *evaluation of LA appendage*, as well.

Noncompaction cardiomyopathy (NCCM) is a rare congenital disease, which is likely to develop in the embryonic period and is characterized by prominent myocardial trabeculations and deep intertrabecular recesses (12). NCCM is caused by the intrauterine arrest of the myocardial compaction process in the beginning of the fetal development. NCCM is frequently associated with arrhythmias, thrombembolic events and heart failure. Due to guidelines for treatment of arrhythmias, the accurate evaluation of LA size and function would be essential in this disease.

Hypertrophic cardiomyopathy (HCM) is a complex, relatively common genetic cardiac disease, that is heterogeneous with respect to gene mutations, clinical symptoms, prognosis, and treatment strategies (13). HCM represents a generalized myopathic process affecting both ventricular and atrial myocardium (14). Most of the patients are in steady condition, although HCM is known as one of the most common cause of sudden death in juvenile patients (13). HCM is characterised by excessive asymmetric LV hypertrophy involving primarily the interventricular septum (13). It is known, that diastolic LV dysfunction is more common in HCM than systolic dysfunction. Due to reduced ventricular compliance and impaired relaxation, elevated LA and pulmonary vascular pressures are known complications in HCM (15). Due to sensitivity of thin-walled LA to volume and pressure changes, increased LV load pressure could lead to LA dilation which is known to be associated with increased morbidity and mortality in HCM (16). Enlarged LA volume was found to be associated with impaired functional NYHA class and shows inverse correlation with treadmill exercise capacity in HCM (17). P-wave duration combined with LA antero-posterior diameter and myocardial deformation indices resulted in a higher power for discriminating HCM patients with paroxysmal atrial fibrillation. All these studies should draw our attention to the importance of accurate evaluation of LA volumes and function respecting cardiac cycle in HCM (18,19).

2. Aims

To compare 2D echocardiography with 3DSTE for calculation of LA volumes and assessment of LA functional properties in healthy subjects.

To evaluate the relationship between 3DSTE-derived LA and MA morphologic and functional parameters in healthy volunteers.

To demonstrate alternative ways in assessing LA (dys)function in NCCM by 3DSTE.

To measure and compare 3DSTE-derived LA volumetric and strain parameters in HCM and healthy matched controls.

To demonstrate the usefulness of 3DSTE in the visualisation and evaluation of the LA appendage.

3. Methods

Patient population (general considerations). All healthy subjects and patients have been included in the **MAGYAR-Healthy Study** and **MAGYAR-Path Study** (**M**otion **A**nalysis of the heart and **G**reat vessels b**Y** three-dimension**A**l speckle-t**R**acking echocardiography in **Healthy** subjects and in **Path**ological cases). These have been organized at the Cardiology Center of the University of Szeged, Hungary to evaluate usefulness, diagnostic and prognostic value of 3DSTE-derived volumetric, strain, rotational etc. parameters in healthy volunteers as well as in pathological cases ('magyar' means 'Hungarian' in Hungarian language). In all patients complete 2D Doppler echocardiography study was performed extended with 3DSTE measurements. In healthy volunteers there was no any disease or other condition, which could influence results. Informed consent was obtained from each patient 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 (20).

Two-dimensional echocardiography. Complete 2-dimensional (2D) Doppler echocardiographic examinations were performed in all cases. Standard 2D echocardiographic studies were carried out with a commercially available Toshiba Artida^{TM} echocardiography equipment (Toshiba Medical Systems, Tokyo, Japan) with a PST-30SBP (1-5 MHz) phased-array transducer. LV dimensions, volumes and ejection fraction and LA dimensions were measured in parasternal long-axis view by Teichholz method. Colour Doppler echocardiography was used to visually quantify degree of mitral regurgitation (MR).

In some studies, for evaluation of LA size and function, the following parameters were measured on 2D images (Figure 1):

1) LA area at apical 4-chamber view (AP4CH) (A1) by manual tracing of LA endocardial border. The superior border of atrial outline was a straight line connecting both sides of the mitral leaflet base attachment points. Both LA appendage and pulmonary veins were excluded when visualized, and
2) LA area at apical 2-chamber (AP2CH) (A2) with same tracing, and LA long axis (L) defined as the distance of the perpendicular line measured from the middle of the plane of mitral annulus to the superior aspect of LA in both apical 4CH and 2CH views and the shortest of both lines was used.

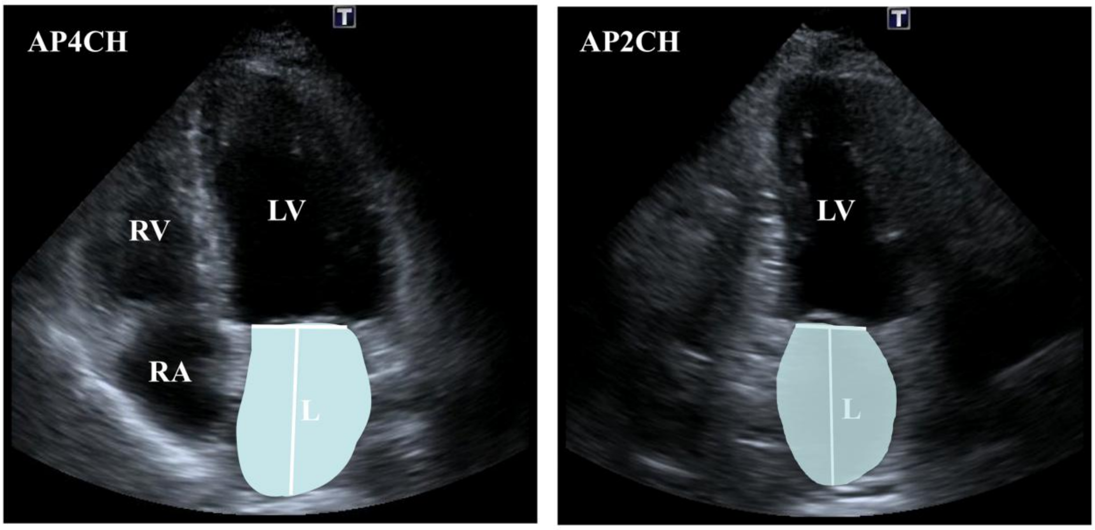

Figure 1. Calculation of left atrial (LA) volume using 2-dimensional echocardiography by manual tracing of LA endocardial border at apical 4-chamber (AP4CH) and 2-chamber views (AP2CH). L is the long axis, then apply the formula.

Abbreviations: LV: left ventricle, RA: right atrium, RV: right ventricle

3DSTE volumetric measurements. All patients underwent 3D echocardiographic acquisitions immediately following 2D echocardiographic study using a commercially available 1-4 MHz matrix-array PST-25SX transducer (Toshiba Medical Systems, Tokyo, Japan) with 3DSTE capability (11,21-23). 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 including LA. The sector width was decreased as much as possible to improve temporal and spatial resolution of the image in order to obtain a full-volume dataset of LA with optimal border delineation. Chamber quantification by 3DSTE was performed off-line using 3D Wall Motion Tracking software version 2.7 (Toshiba Medical Systems, Tokyo, Japan). 3D echocardiographic datasets were displayed in AP4CH and AP2CH views and 3 short-axis views in basal, midatrial, and superior LA regions, respectively (Figure 2). In the AP4CH and AP2CH views, the endocardial border was traced by setting multiple reference points by the user starting at base of the LA at mitral valve level on the septal side, where anterior mitral leaflet origins going toward the apex on counterclockwise direction to the origin of the mitral posterior leaflet excluding the LA appendage and the pulmonary veins from the LA cavity. Measurements were performed firstly on AP4CH view, and later on AP 2CH view. After detection of the myocardial borders at the end-diastolic reference frame, the user could correct the LA shape, if necessary. The 3D wall motion tracking was then automatically performed through the entire cardiac cycle. 3D cast and volumetric data of LA at different moments of cardiac cycle were generated by the software (Figure 2).

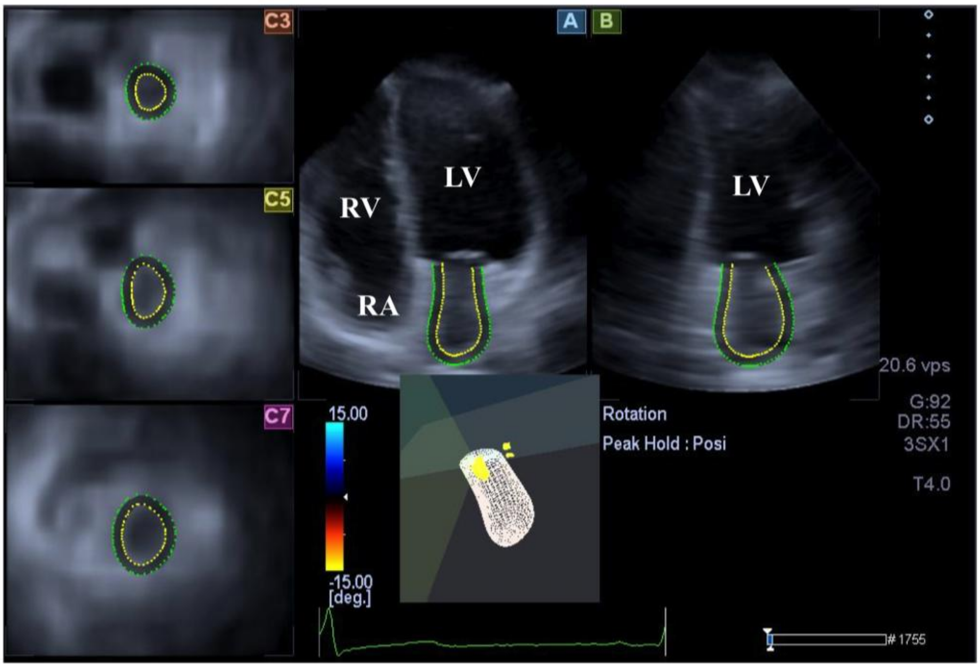

Figure 2. Three-dimensional echocardiographic dataset is displayed in apical 4-chamber (A) and 2-chamber views (B) and 3 short-axis views in the basal (C3), midatrial (C5), and apical (C7) regions, respectively. Three-dimensional LA cast is also presented.

Abbreviations: LV: left ventricle, RA: right atrium, RV: right ventricle

The epicardial border was adjusted manually or by setting a default thickness for the myocardium. After detection of the LA borders at the end-diastolic reference frame 3D wall motion tracking, which is based on 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.

The following volumetric calculations have been performed (Figure 3) (6):

[1] maximum volume (Vmax) at end-systole, the time at which atrial volume was largest just before mitral valve opening,

[2] minimum volume (Vmin): at end-diastole, the time at which atrial volume is at its nadir before mitral valve closure,

[3] volume before atrial contraction (VpreA): the last frame before mitral valve reopening or at the time of P wave on ECG.

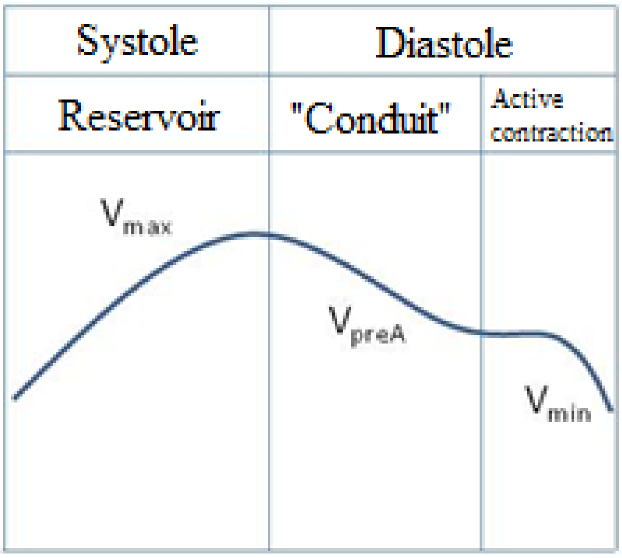

Figure 3. Volume changes in the LA during heart cycle

From the three volumes several parameters characterizing each phasis of LA function were assessed (Table 1).

Table 1. The way to calculate left atrial stroke volumes and emptying fractions in each phasis of left atrial motion.

Functions	**Stroke volumes (ml)**	**Emptying fractions (%)**
Reservoir	**Total atrial SV (TASV) = Vmax-Vmin**	**Total atrial EF (TAEF) = Total SV/Vmax**
Conduit function	**Passive atrial SV (PASV) = Vmax-VpreA**	**Passive atrial EF (PAEF) = Passive SV/Vmax**
Active contraction	**Active atrial SV (AASV) = VpreA-Vmin**	**Active atrial EF (AAEF) = Active SV/VpreA**

Abbreviations: EF: emptying fraction, SV: stroke volume, Vmax: maximum left atrial volume, Vmin: minimum left atrial volume, VpreA: left atrial volume before left atrial contraction

3DSTE strain measurements. The following strain parameters were routinely measured by the software in a semi-automatic fashion from the 3D echocardiographic dataset in some studies: longitudinal strain (LS) in the direction tangential to the endocardial contour, circumferential strain (CS) in circumferential direction and radial strain (RS) in perpendicular direction to the endocardial contour. Besides these ’unidimensional’ parameters, novel strain parameters using 3D wall motion tracking were also recorded, such as 3D strain (3DS) defined as strain in the direction of wall thickening and area strain (AS) as a ratio of endocardial area change during the cardiac cycle (21,22). Examples of time-strain curves generated by the software are given in Figure 4.

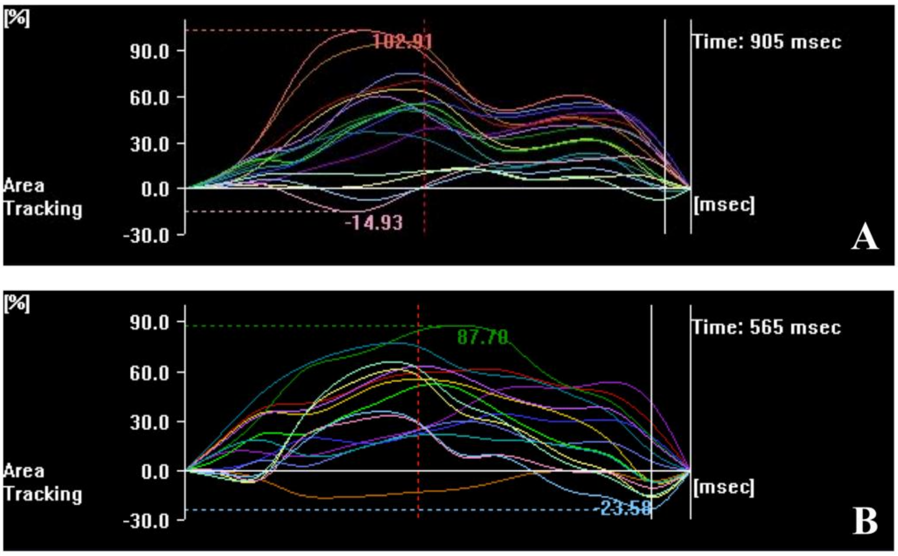

Figure 4. Examples of time-strain curves of 16 left atrial segments in a healthy control subject (A) and in a patient with hypertrophic cardiomyopathy (B).

3DSTE for the measurement of MA. MA diameter could be easily measured from the digitally collected 3D echocardiographic database by the special software. Longitudinal planes were optimized to the LV longitudinal axis in AP4CH and AP2CH views, then we set optional cross-sectional plain (the lowest, C7 is the practical) to the endpoints of MA in both views. In this case MA front-wise (“en-face”) could be visualized on the cross-sectional plain (e.g. C7), where the MA area could be measured by planimetry and the largest MA (cross-) diameter could be selected. The measurements were performed in systole and in diastole, as well (Figure 5). The following measurements have been performed:

- end-diastolic and end-systolic MA diameters (MAD)
- end-diastolic and end-systolic MA diameter indices (MADI) = MAD/BSA
- end-diastolic and end-systolic MA areas (MAA)
- end-diastolic and end-systolic MA area indices (MAAI) = MAA/BSA
- end-diastolic and end-systolic MA perimeter (MAP)
- end-diastolic and end-systolic MA perimeter index (MAPI) = MAP/BSA

From the above detailed morphologic data the following MA functional parameters have been calculated (8-10):

- MA fractional shortening (MAFS) = (end-diastolic MAD – end-systolic MAD) / end-diastolic MAD x 100 (%)
- MA fractional area change (MAFAC) = (end-diastolic MAA – end-systolic MAA) / end-diastolic MAA x 100 (%)

Figure 5 Evaluation of the mitral annulus (MA) by three-dimensional speckle-tracking echocardiography. Longitudinal planes were optimalized to the left atrial longitudinal axis in apical four-chamber (A) and two chamber (B) views created from the three-dimensional "echo-cloud" by the software, then an optional cross-sectional image (e.g. C7) has been inserted to the endpoints of the mitral annulus in both views. In the cross-sectional (C7) image the MA is visualized front-wise ("en-face"), where the MA area and perimeter can be measured with planimetry, and the largest MA (cross-) diameter can be selected.

Abbreviations: Area: mitral annulus area, Circ: mitral annulus perimeter, Dist: mitral annulus diameter

Stastical analysis. Data are reported as mean ± standard deviation. A value of $p < 0.05$ was considered to be statistically significant. MedCalc software was used for statistical calculations (MedCalc, Mariakerke, Belgium). Paired sample *t*-test and Chi-square test were used for comparisons. Pearson's coefficient was used for interobserver and intraobserver and other correlations. Intra- and interobserver agreements were studied according to Bland and Altman method (24).

4. Results

4.1. Comparison of three-dimensional speckle-tracking echocardiography and two-dimensional echocardiography for evaluation of left atrial size and function in healthy volunteers

Study population. The present work comprised randomly selected 35 healthy subjects (mean age: 40.9 ± 10.9 years, 20 men) in sinus rhythm, they all had undergone standard transthoracic Doppler 2D echocardiographic study extended with 3DSTE.

Volumetric 3DSTE and 2D echocardiographic data. Volumetric data and functional parameters of LA are presented in Table 2.

Table 2. Left atrial dimensions and functional parameters using two-dimensional echocardiography and three-dimensional speckle-tracking echocardiography in healthy controls

	2D echocardiography	3DSTE	p
Calculated LA volumes			
Vmax (ml)	35.5 ± 0.7	36.6 ± 6.5	NS
Vmin (ml)	14.9 ± 0.4	16.5 ± 5.0	NS
VpreA (ml)	23.8 ± 4.8	24.0 ± 6.1	NS
LA stroke volumes			
TASV (ml)	20.6 ± 5.9	20.1 ± 5.0	NS
PASV (ml)	12.1 ± 4.3	12.3 ± 5.0	NS
AASV (ml)	8.8 ± 3.8	7.5 ± 2.9	NS
LA emptying fractions			
TAEF (%)	57.6 ± 10.0	55.2 ± 10.7	NS
PAEF (%)	32.0 ± 11.9	34.6 ± 11.3	NS
AAEF (%)	37.0 ± 13.8	31.5 ± 9.5	< 0.05

Abbreviations: AAEF: Active Atrial Emptying Fraction, AASV: Active Atrial Stroke Volume, PAEF: Passive Atrial Emptying Fraction, PASV: Passive Atrial Stroke Volume, TAEF: Total Atrial Emptying Fraction, TASV: Total Atrial Stroke Volume, Vmax: maximum volume at end-systole, Vmin: minimum volume at end-diastole, VpreA: volume before atrial contraction, 2D: 2-dimensional, 3DSTE: three-dimensional speckle-tracking echocardiography

Correlations between 3DSTE-derived and 2D echocardiographic data. A good correlation was found between both techniques for Vmax (r =0.93, p <0.0001), Vmin (r =0.62, p <0.0001) and VpreA (r =0.74, p <0.0001). Similar correlations were found between TASV (r =0.85, p <0.0001), TAEF (r =0.81, p <0.0001), PASV (r =0.67, p <0.0001), PAEF (r =0.74, p <0.0001), AASV (r =0.71, p <0.0001) and AAEF (r =0.69, p <0.0001).

Reproducibility of measurements. The mean ± standard deviation difference in values obtained by 2 mesurements of the same observer for the measurements of 3DSTE-derived Vmax, Vmin and VpreA was –0.8 ± 9.3 ml, -0.5 ± 6.6 ml, -1.5 ± 8.0 ml, respectively. Correlation coefficients between measurements of 2 observers were 0.76, 0.79 and 0.82 (p <0.0001), respectively (Figures 3-5) (intraobserver agreement). The mean ± standard deviation difference in values obtained by two observers for 3DSTE-derived Vmax, Vmin and VpreA was 0.9 ± 9.3 ml, -0.3 ± 7.4 ml, -0.5 ± 7.3 ml, respectively. Correlation coefficient between these independent measurements of the same observer were 0.75, 0.77 and 0.82 (p <0.0001), respectively (Figures 6-8) (interobserver agreement).

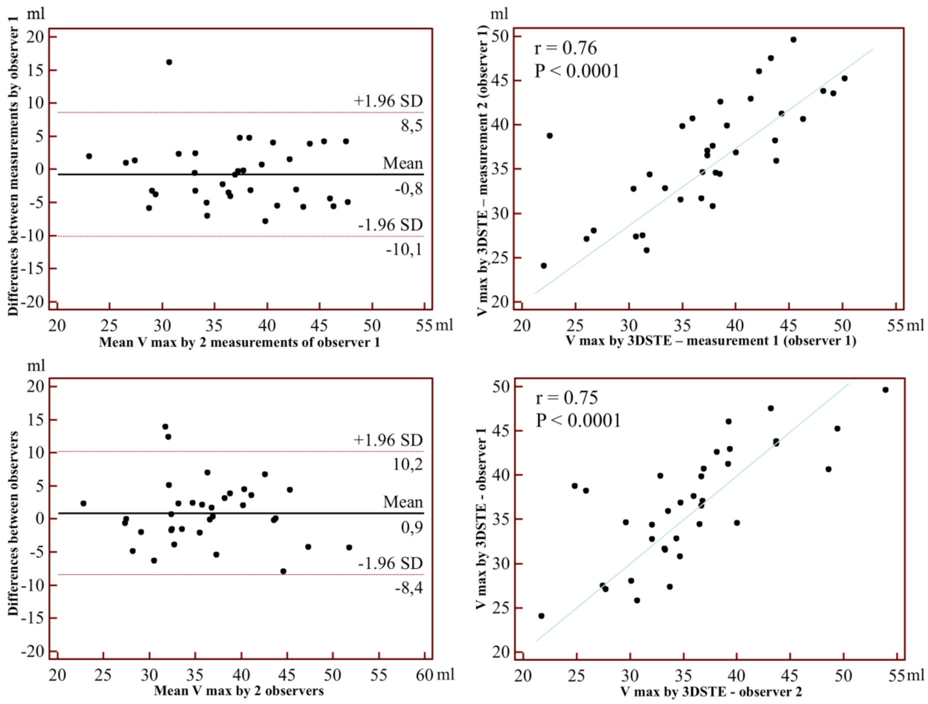

Figure 6. Intraobserver (upper graphs) and interobserver (lower graphs) agreements and correlations for measuring Vmax by three-dimensional speckle-tracking echocardiography are presented.

Abbreviations: Vmax: maximum left atrial volume, 3DSTE: three-dimensional speckle-tracking echocardiography

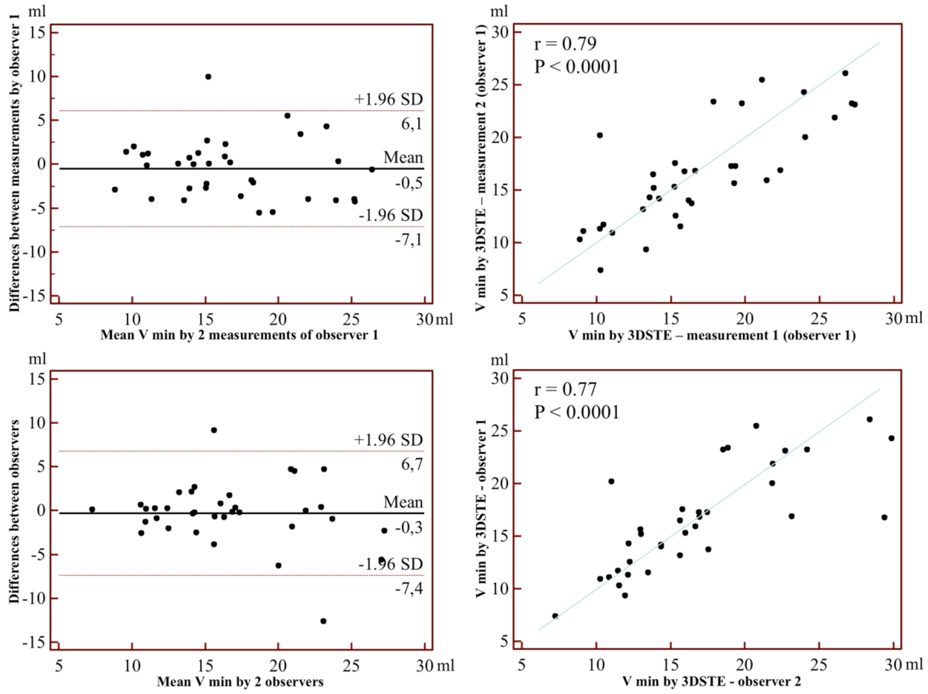

Figure 7. Intraobserver (upper graphs) and interobserver (lower graphs) agreements and correlations for measuring Vmin by three-dimensional speckle-tracking echocardiography are presented.

Abbreviations: Vmax: minimum left atrial volume, 3DSTE: three-dimensional speckle-tracking echocardiography

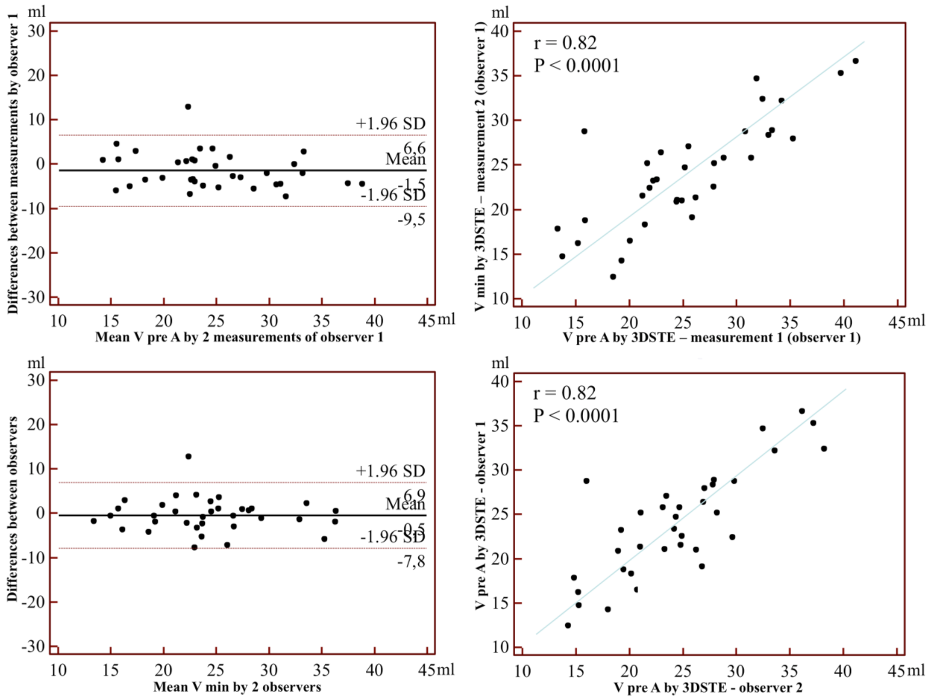

Figure 8. Intraobserver (upper graphs) and interobserver (lower graphs) agreements and correlations for measuring VpreA by three-dimensional speckle-tracking echocardiography are presented.

Abbreviations: VpreA: volume before atrial contraction, 3DSTE: three-dimensional speckle-tracking echocardiography

4.2. Relationship between mitral annular and left atrial function as assessed by three-dimensional speckle-tracking echocardiography in healthy volunteers

Study population. The present study comprised 35 randomly selected healthy individuals (mean age: 35.9 ± 11.1 years, 20 men).

Clinical and routine 2D echocardiographic data are showen in the Table 3.

Table 3. Clinical and echocardiographic data

	values
n	35
Age (years)	35.9 ± 11.1
Male gender (%)	20 (57)
BSA (m^2)	1.93 ± 0.19
Two-dimensional echocardiography	
LA diameter (in parasternal long axis view) (mm)	33.6 ± 3.6
LV end-diastolic diameter (mm)	46.9 ± 6.4
LV end-diastolic volume (ml)	98.9 ± 24.3
LV end-systolic diameter (mm)	30.3 ± 4.5
LV end-systolic volume (ml)	36.0 ± 13.2
Interventricular septum (mm)	9.7 ± 1.9
LV posterior wall (mm)	10.1 ± 2.1
LV ejection fraction (%)	63.7 ± 8.1

Abbreviations: LV: left ventricle, LA: left atrium, BSA: body surface area

3DSTE-derived LA and MA parameters. Volumetric LA parameters are demonstrated in Table 4.

Table 4. Left atrial dimensions and calculated volumetric functional parameters using three-dimensional speckle-tracking echocardiography

	values
Calculated LA volumes	
Vmax (ml)	36.6 ± 6.5
Vmin (ml)	16.5 ± 5.0
VpreA (ml)	24.0 ± 6.1
Stroke volumes	
TASV (ml)	20.1 ± 5.0
PASV (ml)	12.7 ± 4.7
AASV (ml)	7.5 ± 2.9
Emptying fractions	
TAEF (%)	55.2 ± 10.7
PAEF (%)	34.6 ± 11.3
AAEF (%)	31.5 ± 9.5

Abbreviations: AAEF: active atrial emptying fraction, AASV: active atrial stroke volume, PAEF: passive atrial emptying fraction, PASV: passive atrial stroke volume, TAEF: total atrila emptying fraction, TASV: total atrial stroke volume, Vmax: maximal left atrial volume, Vmin: minimal left atrial volume, VpreA: volume before atrial contraction

The parameters measured with 3DSTE, which describes morphology and function of the MA are shown in Table 5.

Relationships between LA volumes and MA data as assessed by 3DSTE. The Vmax correlated with diastolic MAA (R =0.43, p =0.01), MAP (R =0.53, p =0.01), as well as with systolic MAA (R =0.49, p =0.003), MAAI (R =0.37, p =0.03) and MAP (R =0.52, p =0.001). The Vmin showed correlations with systolic MAA (R =0.43, p =0.01) and MAP (R =0.35, p =0.04). The VpreA showed similar correlations with systolic MAA (R =0.47, p =0.004), MAAI (R =0.33, p =0.05) and MAP (R =0.41, p =0.01). MAFAC and MAFS did not correlated with any of LA volumes.

Table 5. Morphologic and functional parameters of the mitral annulus as assessed by three-dimensional speckle-tracking echocardiography

	values
Morphologic parameters – diastole	
end-diastolic MA diameter (MAD-D) (mm)	2.72 ± 0.36
end-diastolic MA diameter index (MADI-D) (mm/m^2)	1.42 ± 0.23
end-diastolic MA area (MAA-D)	8.36 ± 1.96
end-diastolic MA area index (MAAI-D) (mm/m^2)	4.36 ± 0.98
end-diastolic MA perimeter (MAP-D)	10.72 ± 1.25
end-diastolic MA perimeter index (MAPI-D) (mm/m^2)	5.61 ± 0.73
Morphologic parameters –systole	
end-systolic MA diameter (MAD-S) (mm)	2.07 ± 0.31
end-systolic MA diameter index (MADI-S) (mm/m^2)	1.08 ± 0.17
end-systolic MA area (MAA-S) (mm)	4.71 ± 1.01
end-systolic MA area index (MAAI-S) (mm/m^2)	2.45 ± 0.49
end-systolic MA perimeter (MAP-S) (mm)	8.07 ± 0.88
end-systolic MA perimeter index (MAPI-S) (mm/m^2)	4.22 ± 0.51
Functional parameters	
MAFAC (%)	42.7 ± 11.3
MAFS (%)	24.5 ± 13.4

Abbreviations: MA: mitral annulus, MAFAC: mitral annulus fractional area change, MAFS: mitral annulus fractional shortening

Relationships between LA volumetric functional parameters and MA data as assessed by 3DSTE. Only TASV and PASV showed correlations with MA parameters. TASV correlated with diastolic MAA (R =0.39, p =0.03), MAAI (R =0.38, p =0.02), MAP (R =0.42, p =0.01), and MAPI (R =0.40, p =0.02), and systolic MAP (R=0.32, p=0.05), MAPI (R =0.32, p =0.05), and MAFS (R =0.43, p=0.02). The PASV showed correlations with diastolic MAA (R =0.31, p =0.07), MAAI (R =0.34, p =0.05), MAP (R =0.40, p =0.02), MAPI (R =0.38, p =0.03) and MAFS (R =0.33, p =0.07). AASV and emptying fractions did not show any correlations with the above mentioned parameters.

4.3. Alternative ways to assess left atrial function in noncompaction cardiomyopathy by three-dimensional speckle-tracking echocardiography

Case study. A 60 year-old patient with typical features of NCCM is demonstrated (Figure 9).

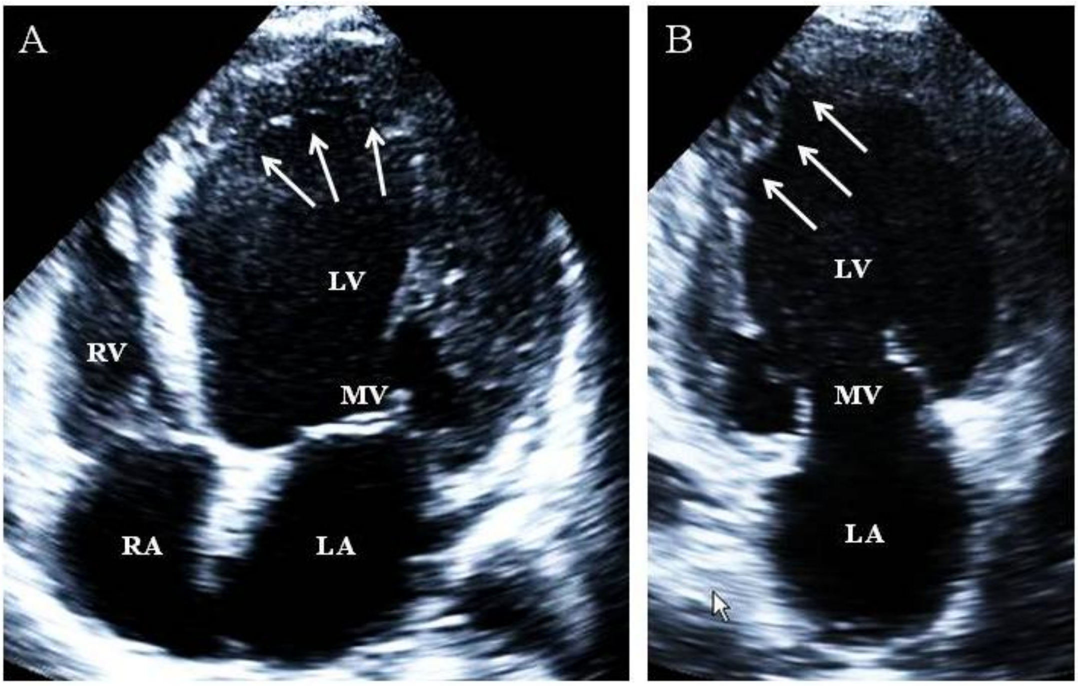

Figure 9. Two-dimensional echocardiographic images with four-chamber (A) and two-chamber views (B). Noncompaction cardiomyopathy is characterized by prominent myocardial trabeculations and deep intertrabecular recesses (see white arrows).

Abbreviations: LA: left atrium, LV: left ventricle, MV: mitral valve, RA: right atrium, RV: right ventricle.

3DSTE has been performed to analyse LA morphology and function as described previously in the Methods section (Figure 10).

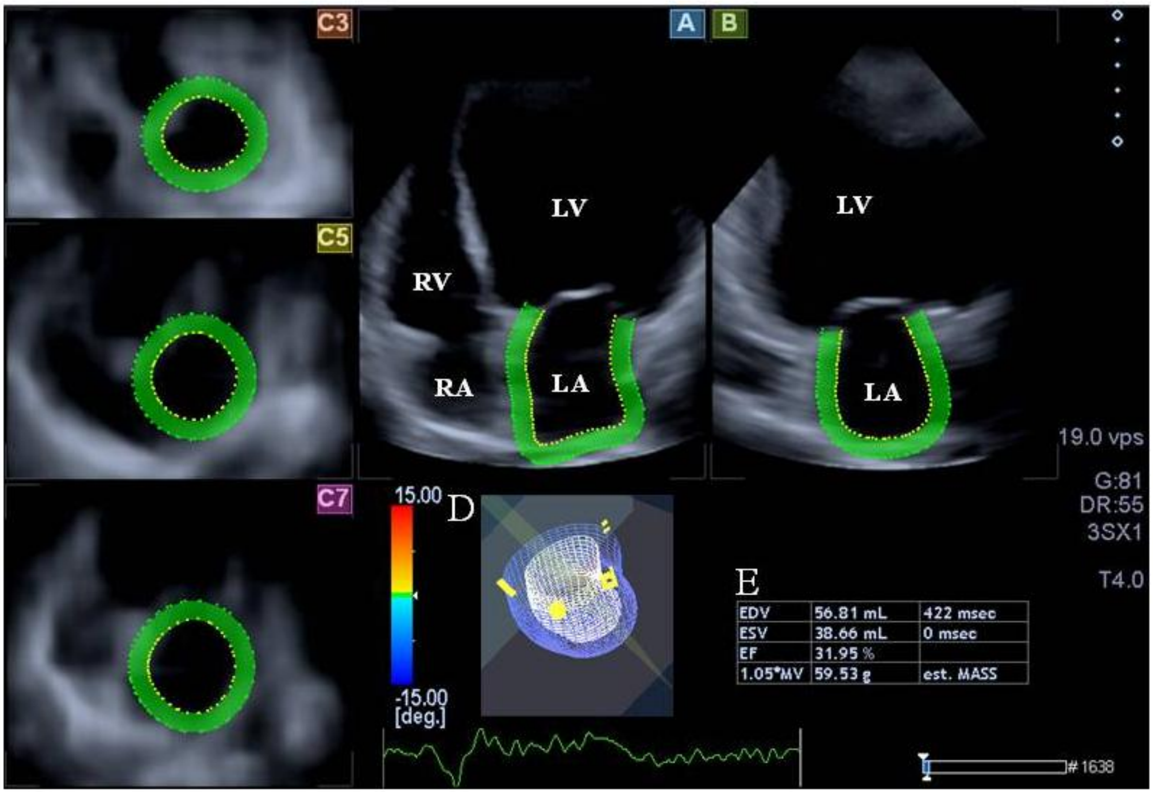

Figure 10. Three-dimensional echocardiographic dataset is displayed in apical 4-chamber (A) and 2-chamber views (B) and 3 short-axis views in the basal (C3), midatrial (C5), and apical (C7) regions, respectively. Three-dimensional cast (D) and calculated characteristics of left atrium are also presented (E).

Abbreviations: LA: left atrium, LV: left ventricle, RA: right atrium, RV: right ventricle.

LA functional parameters based on volumetric data could have been calculated as described previously (3). From 3D echocardiographic datasets, the MA could also be obtained by optimizing cross-sectional planes on the apical AP4CH and AP2CH views and therefore demonstrating the optimal image at the level of MA as already shown (Figure 11).

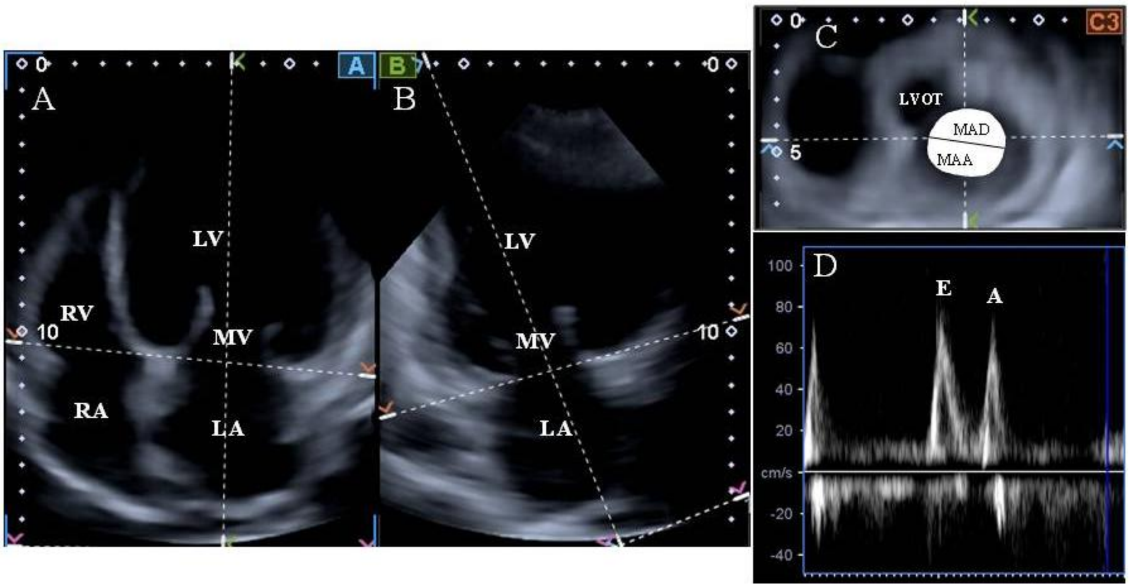

Figure 11. From 3D echocardiographic dataset, the mitral annulus (MA) could be obtained by optimizing cross-sectional planes on the apical 4-chamber (A) and 2-chamber (B) views and therefore demonstrating the optimal MA image (C). Using Doppler-derived mitral inflow peak A wave velocity, the left atrial ejection force (LA-EFO), a characteristic of left atrial systolic function, were calculated.

Abbreviations: LA: left atrium, LV: left ventricle, LVOT: left ventricular outflow tract, MV: mitral valve, RA: right atrium, RV: right ventricle, E and A: Doppler-derived mitral inflow velocities.

According to the Newton's second law of motion, the force generated by the LA in pushing blood forward into the LV during LA systole, is defined as the product of the mass and acceleration of blood ejected from the LA during the accelerative phase of LA systole (25). Mass may be further defined as the product of the blood density (1.06 g/cm^3) and the volume of blood passing through the MA. This volume may be evaluated as the product of the MA area and the area under the transmitral Doppler A wave from onset of the A wave to peak A wave velocity (V) (25). The area under the accelerative portion of the A wave may be approximated as one-half the product of the peak A wave velocity and the time to peak A wave velocity. Because A wave acceleration is relatively constant, it can be approximated as the peak A velocity divided by the time to peak A velocity (25). Using MAD and MAA data, LA-EFO$_{3D\text{-}MAD}$ and LA-EFO$_{3D\text{-}MAA}$ were calculated using the following equation: LAEFO= $0.5 \times 1.06 \times (MAD_{3D}$ or $MAA_{3D}) \times V^2$ (25, 26), where 0.5 is a coefficient factor. LA-EFO$_{3D\text{-}MAD}$ and LAEFO$_{3D\text{-}MAA}$ were 3.8 kdyne and 13.5 kdyne in this case.

4.4. Three-dimensional speckle-tracking echocardiography allows detailed evaluation of left atrial function in hypertrophic cardiomyopathy

Patient population. A total of 23 patients with typical features of HCM were included in the present study. The diagnosis of HCM was confirmed in all patients according to the guidelines (27). In all cases, hypertrophy was asymmetrical and had septal localization. HCM was known for several years in these patients, and 75% of the cases were genetically analysed with genotype/mutation analysis. Their results were compared to 23 age- and gender-matched healthy controls. Diabetes mellitus (DM) was defined in accordance with the American Diabetes Association and World Health Organization criteria. 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.

Clinical characteristics are presented in Table 2. Eleven out of 23 HCM patients had significant (>30 mmHg) resting peak LV outflow tract gradient (mean: 69.5 ± 30.1 mmHg), while 15 HCM patients had systolic anterior motion of the anterior leaflet of the mitral valve. Other 3 HCM patients had implantable cardiac defibrillator due to prophylaxis of malignant arrhythmia and 1 HCM patient had biological prosthetic valve in aortic position. One HCM patient had former percutaneous transluminal septal myocardial ablation.

Two-dimensional echocardiographic data. Standard 2D echocardiographic data are summarized in Table 2. Significant (≥grade 2) MR could be detected in 7 HCM patients (30%). LV end-systolic diameter was significantly decreased, while interventricular septum was significantly increased in HCM patients (Table 6).

3DSTE data. Significantly increased LA volumes respecting heart cycle could be detected in HCM patients. TASV and AASV were significantly increased, while TAEF and PAEF were significantly decreased in patients with HCM (Table 7). Global and mean segmental peak strain parameters proved to be reduced in HCM patients as compared to controls (Table 8). There were no differences between HCM patients with vs. without hypertension and/or DM in this patient population in both LA volumetric and strain functional properties. Calculated LA volumes were significantly larger in HCM patients with MR ≥2 vs. cases with MR <2, only TAEF showed significant difference from calculated parameters. There were no differences between HCM patients with MR ≥2 vs. MR <2 in strain parameters.

Table 6. Clinical and two-dimensional echocardiographic characteristics of hypertrophic cardiomyopathy patients and controls

	HCM patients (n = 23)	Controls (n = 23)
Risk factors		
Age (years)	48.5 ± 15.1	41.0 ± 11.8
Male gender (%)	14 (61)	13 (57)
Body mass index (kg/m^2)	27.4 ± 5.0	25.3 ± 3.5
Diabetes mellitus (%)	10 (44)*	0 (0)
Hypertension (%)	11 (48)*	0 (0)
Hypercholesterolaemia (%)	2 (9)*	0 (0)
Medications		
β-blockers (%)	20 (87)*	0 (0)
ACE-inhibitors (%)	8 (35)*	0 (0)
Diuretics (%)	8 (35)*	0 (0)
Two-dimensional echocardiography		
LA diameter (mm)	46.2 ± 5.2†	33.8 ± 3.9
LV end-diastolic diameter (mm)	45.1 ± 3.9	46.3 ± 5.1
LV end-diastolic volume (ml)	95.5 ± 23.4	100.2 ± 26.8
LV end-systolic diameter (mm)	27.3 ± 4.8*	31.2 ± 4.9
LV end-systolic volume (ml)	29.9 ± 13.1	37.9 ± 15.2
Interventricular septum (mm)	22.8 ± 5.6†	9.2 ± 2.1
LV posterior wall (mm)	12.1 ± 4.2	10.6 ± 2.2
LV ejection fraction (%)	68.4 ± 7.6	68.6 ± 7.7
E/A	1.04 ± 0.53	1.21 ± 0.30

Abbreviations: ACE: angiotensin-converting enzyme, LA: left atrial, LV : left ventricular, HCM: hypertrophic cardiomyopathy

*p =0.02 vs. Controls, †p =0.0001 vs. Controls

Table 7. Comparison of 3DSTE-derived volumetric left atrial parameters of patients with hypertrophic cardiomyopathy and controls

	Controls (n=23)	HCM patients (n=23)	HCM patients with hypertension and/or DM (n=10)	HCM patients without hypertension and/or DM (n=13)	HCM patients with MR ≥2 (n=9)	HCM patients with MR <2 (n=14)
Calculated Volumes						
V_{max} (ml)	36.0 ± 6.1	66.4 ± 20.4*	65.2 ±10.7*	67.2 ± 26.0*	76.2 ± 26.0*‡	59.0 ± 13.3*
V_{min} (ml)	16.0 ± 4.6	39.2 ± 19.1*	38.9 ± 14.1*	39.4 ± 22.7*	46.6 ± 23.8*‡	32.7 ± 13.3*
V_{pre}A (ml)	24.0 ± 6.2	53.6 ± 19.9*	54.0 ± 12.6*	53.3 ± 24.5*	64.1 ± 22.4*‡	45.3 ± 14.7*
Stroke Volumes						
TASV (ml)	20.0 ± 4.6	27.2 ± 9.7†	26.3 ± 11.4†	27.8 ± 8.5†	26.6 ± 10.0†	26.3 ± 9.5†
PSV (ml)	12.0 ± 4.6	12.8 ± 8.6	11.2 ± 10.8	13.9 ± 6.6	12.1 ± 7.3	14.3 ± 9.1
AASV (ml)	8.0 ± 3.2	14.4 ± 8.1†	15. 0± 10.5†	13.9 ± 6.0†	17.4 ± 9.4†	12.6 ± 6.8†
Emptying fractions						
TAEF (%)	55.3 ± 9.8	42.8 ± 15.5†	40.8 ± 16.9†	44.3 ± 14.8†	41.1 ± 14.9†‡	45.6 ± 15.6†
PAEF (%)	33.5 ± 11.6	19.9 ± 14.5†	16.8 ± 16.1†	22.2 ± 13.1†	15.7 ± 9.3†	23.6 ± 16.9†
AAEF (%)	33.3 ± 9.5	28.6 ± 14.3	27.8 ± 17.6	29.3 ± 11.9	29.4 ± 17.3	29.0 ± 12.5

*p <0.0001 vs. Controls; †p <0.05 vs. Controls; ‡p <0.05 vs. HCM patients with MR <2

Abbreviations: Vmax: maximal left atrial volume, Vmin: minimal left atrial volume, VpreA: volume before atrial contraction, TASV: total atrial stroke volume, TAEF: total atrial emptying fraction, AASV: active atrial stroke volume, AAEF: active atrial emptying fraction, PSV: passive stroke volume, PAEF: passive atrial emptying fraction, DM: diabetes mellitus, HCM: hypertrophic cardiomyopathy, MR: mitral regurgitation

Table 8. Comparison of 3DSTE-derived left atrial strain parameters of patients with hypertrophic cardiomyopathy and controls

	Controls (n=23)	HCM patients (n=23)	HCM patients with hypertension and/or DM (n=10)	HCM patients without hypertension and/or DM (n=13)	HCM patients with MR ≥2 (n=9)	HCM patients with MR <2 (n=14)
Global strains						
Radial strain (%)	-19.6 ± 11.7	-12.2 ± 6.7*	-14.5 ± 8.5	-10.4 ± 4.4*	-12.1 ± 5.8	-12.3 ± 7.4†
Circumferential strain (%)	29.8 ± 12.1	26.5 ± 16.5	26.4 ± 19.1	26.6 ± 15.0	25.3 ± 15.9	27.2 ± 17.4
Longitudinal strain (%)	23.9 ± 6.3	18.0 ± 7.4*	18.0 ± 6.8†	18.0 ± 8.1†	15.8 ± 6.4*	19.4 ± 7.9
3-dimensional strain (%)	-12.5 ± 10.2	-6.1 ± 4.4*	-7.9 ± 5.1	-4.7 ± 3.3*	-6.6 ± 4.8	-5.8 ± 4.2†
Area strain (%)	59.0 ± 19.1	49.3 ± 27.8	51.0 ± 31.2	48.0 ± 26.2	44.4 ± 27.3	52.3 ± 28.7
Mean segmental strains						
Radial strain (%)	-23.7 ± 11.5	-16.3 ± 10.7†	-18.6 ± 8.6	-14.6±3.2*	-16.2 ± 5.7	-16.4 ± 6.9†
Circumferential strain (%)	38.6 ± 23.5	29.9 ± 18.2	31.3 ± 17.9	28.8 ± 15.1	26.8 ± 17.1	31.9 ± 15.6
Longitudinal strain (%)	30.6 ± 17.7	20.1 ± 12.4†	20.5 ± 6.1	19.7±7.9†	17.9±5.9†	21.4 ± 7.6
3-dimensional strain (%)	-17.0 ± 9.5	-10.7 ± 8.3†	-12.3 ± 5.8	-9.4 ± 2.5*	-11.0 ± 4.3	-10.5 ± 4.6†
Area strain (%)	75.9 ± 41.7	54.1 ± 33.2†	56.4 ± 32.2	52.4 ± 26.3	49.4 ± 29.5	57.1 ± 28.3

*p <0.01 vs. Controls; †p <0.05 vs. Controls; ‡p <0.05 vs. HCM patients with MR <2

Abbreviations: DM=diabetes mellitus, HCM=hypertrophic cardiomyopathy, MR=mitral regurgitation

4.5. Visualisation of left atrial appendage by three-dimensional speckle-tracking echocardiography

Case study. We present a 48-year male patient with hypertrophic cardiomyopathy who was examined by 3DSTE. First, LA was looked for in apical 4-chamber and 2-chamber views. Later on, longitudinal sectional planes were optimalized to the LA appendage (LAA) in perpendicular planes (Figures 12A and 12B). Then cross-sectional views were chosen just above the ostium of the LAA (Figure 12C7), at the middle of the LAA (Figure 12C5) and just below the apex of the LAA (Figure 12C3). Following manual corrections, a 3D cast of the LAA has been created (Figure 12D). Maximum (EDV), minimum (ESV) LAA volumes, ejection fraction and mass of the LAA are also presented (Figure 12E). Moreover, rotational characteristics of this LAA could also be demonstrated (Figure 12F).

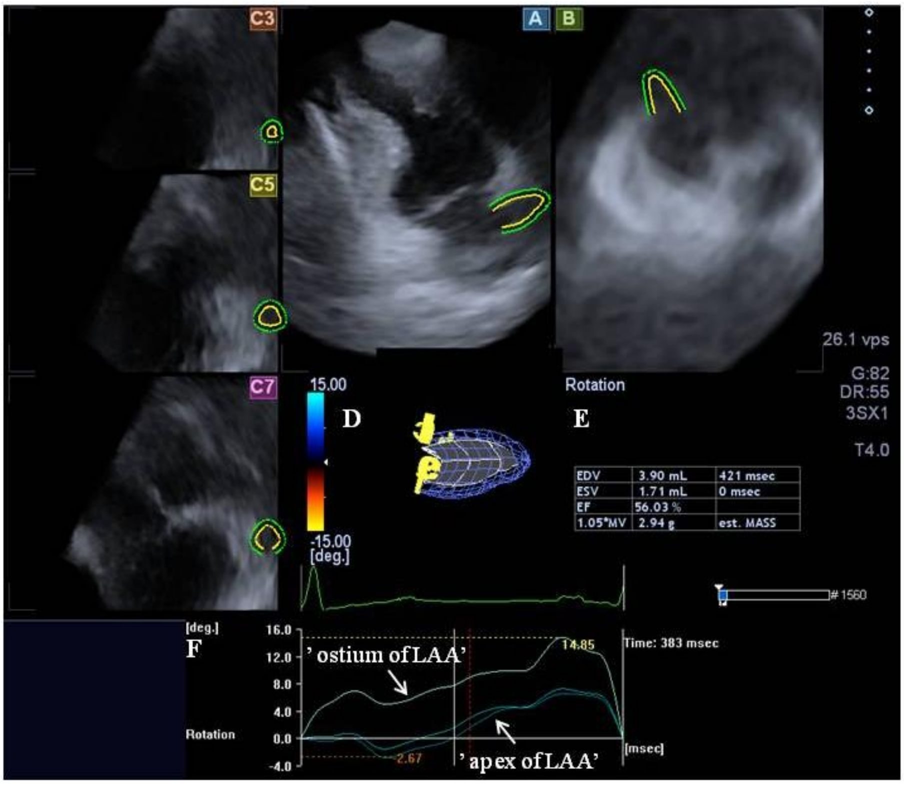

Figure 12. Visualisation of the left atrial appendage (LAA) by three-dimensional speckle-tracking echocardiography. Following optimalization of longitudinal sectional planes to the LAA in perpendicular planes (*A and B*), cross-sectional views were chosen at the ostium of the LAA (*C7*), at the middle of the LAA (*C5*) and just before the apex of the LAA (*C3*). Following manual corrections, a 3D cast of the LAA has also been created (*D*). Maximum (EDV), minimum (ESV) LAA volumes, ejection fraction and mass of the LAA are also presented (*E*) together with its rotational characteristics (*F*).

5. Discussion

5.1. Comparison of three-dimensional speckle-tracking echocardiography and two-dimensional echocardiography for evaluation of left atrial size and function in healthy volunteers

Results of the present study could suggest feasibility of 3DSTE in detection of cyclic changes in LA volumes and calculation of its functional properties. To the best of authors' knowledge this is the first study to directly compare 3DSTE with 2D echocardiography for the evaluation of volumetric and functional LA parameters.

LA volume has been identified as a potential biomarker for different cardiovascular diseases (2). However, during evaluation of volumes phasic function of the LA should be respected including:

1) a reservoir during LV systole („Reservoir function")
2) a conduit for blood transiting from the pulmonary veins to the LV during early diastole („Conduit function")
3) an active contractile chamber that augments LV ventricular filling in late diastole („Active contraction")

These phases of the LA function could be characterized by several parameters based on accurate measurement of maximum and minimum LA volumes (Vmax and Vmin) and LA volume before atrial contraction (VpreA) (6,7). 2D echocardiographic evaluation of LA is standardized for a decade and provides reasonable assessment of LA volumes (3), although all measurement methods underestimate LA volumes with 14-37% as compared to computed tomography (CT) (28) and magnetic resonance imaging (MRI) (29). A minor non-significant improvement in the evaluation of LA could be obtained by the early generation multiplane 3D echocardiographic method based on 90 images acquired by apical probe rotation (29). Anwar *et al.* demonstrated the feasibility and reproducibility of direct volumetric RT3DE in the detection of cyclic changes in LA volumes and calculation of its function as compared to 2D echocardiography (6,7).

Recently, 3DSTE has been introduced, firstly to provide a comprehensive assessment of LV function through strain analysis in four dimensions (11,30-32). 3DSTE uses different algorithm as compared to RT3DE which is based on block matching of the myocardial speckles of the endocardial border during their motion from frame-to-frame (33). This new

3DSTE technique for LV volume measurements has been validated and its superior accuracy and reproducibility over previously used 2DSTE have even been demonstrated by MRI (30). Good intra-observer, inter-observer, and test-retest reliability were found supporting the use of 3DSTE for routine evaluation of LV volumes and ejection fraction (32). Kleijn *et al.* were the first to demonstrate that 3D echocardiography with direct volumetric (RT3DE) and speckle-tracking methods (3DSTE) give comparable and reproducible quantification of LV and LA volumes and function, making interchangable application a viable option in daily clinical practice (11). Nagaya *et al.* aimed to validate the accuracy of 3DSTE and 2DSTE for the assessment of LA volume and function by comparison with 3D-CT (34). 3DSTE allowed more accurate measurement of LA volume and function than 2DSTE and had high reproducibility (34). Results of the present study are in agreement with these findings demonstrating feasibility and reproducibility of 3DSTE in the evaluation of LA volumes and functional properties. Good correlations were found between measured volumetric and calculated functional properties between 2D echocardiography and 3DSTE. Despite image quality for 3DSTE is worse due to low temporal and spatial image resolutions than 2D echocardiography, but 3D echo visualizes LA as it truly is: 3D organ. This advantage of 3DSTE (and RT3DE) could highlight our attention on this new technology which probably will be a milestone in the echocardiographic evaluation of LA volumes and functional properties.

Study limitations. However, some important limitations should be taken into consideration analyzing our results:

- **(1)** LA appendage for calculation of LA volume and function was not included due to its variability in shape and lack of standard figures (6).
- **(2)** The current image quality obtained by 3DSTE is worse than for 2D echocardiography due to low temporal and spatial image resolutions.
- **(3)** This was a single-centre experience and limited by a relatively small number of healthy volunteers. The study would have been statistically stronger, if larger number of subjects had been evaluated. Caution should be taken when interpreting the results observed.
- **(4)** Although 3DSTE seems to be feasible for the assessment of strain, rotational, synchronicity characteristics of LA, the present study did not aimed to evaluate and validate these parameters (23).

5.2. Relationship between mitral annular and left atrial function as assessed by three-dimensional speckle-tracking echocardiography in healthy volunteers

To the best of the authors' knowledge, this is the first study, which examines the relationship between 3DSTE-derived LA and MA morphological and functional parameters in healthy volunteers. While (systolic) maximal LA volume (Vmax) correlated with both the systolic and diastolic MA parameters, (diastolic) minimal LA volume (Vmin) and LA volume before atrial contraction (VpreA) correlated only with systolic MA parameters. Systolic TASV showed correlated with both systolic and diastolic MA characteristics, diastolic PASV correlated only with diastolic MA parameters. Nor the AASV neither any of emptying fractions showed correlations with MA morphological and functional parameters. LA volumes did not show correlations with MA functional characteristics, while the (systolic) TASV and (diastolic) PASV correlated with MA fractional shortening.

The saddle–shaped two-leaflet (bicuspid) mitral valve situates between the LA and LV, regulating the blood flow between these chambers by the help of papillary muscles and tendon-chords (35). During diastole the normal mitral valve opens by the effect of the elevated LA pressure and the blood flows into the LV. In the initial phase of diastole LA works like a "conduit" (channel), i.e. it provides the bloodstream from the pulmonary veins into the LV. Diastole ends with LA contraction, which is responsible for the 20% of the total streaming blood (36,37). Normally in systole with the closure of the mitral valve the blood does not flow back from the LV to the LA, but it flows via the aortic valve to the aorta. Simultaneously the LA is filled back from the pulmonary veins and reaches the maximal capacity volume (reservoir function). The above-mentioned mechanism opens the door to maintain the normal cardiac pump function, in which the mitral valve and its annulus (MA) have an important role. The change of the function and size of the MA can be associated with several diseases (cardiomyopathies, myocardial infarction, etc.), which can affect the LA and LV functions with feedback mechanism (e.g. effects of consequential mitral regurgitation, etc.) (35). In the present study we have found the above-mentioned relationships between the morphological and functional MA and LA parameters even in healthy volunteers by 3DSTE.

As mentioned previously, both early 3D echocardiographic methods (38), and RT3DE are proved to be suitable for the measurement of LA volumes (4,6,7). 3DSTE is a new clinical method, which is a suitable procedure for describing the volumes and functions of the chambers with the help of 3D strain analysis (5,30). 3DSTE was found to be an accurate and reproducible method for assessment of LA volumes and volume-based functional and strain functional properties when it was compared to 2D echocardiography, 2DSTE, RT3DE and CT (5,11,23,34). 3DSTE-derived LA strain values showed alterations in atrial fibrillation (21,22) and in HCM (39).

During 3D echocardiography not only LA volumes and functional properties, but the mitral valve and its annulus (MA) could be described simultaneously, as well (4). Its reason could be found in the method giving opportunity to the “en-face”, i.e. front-wise examination of the valves (4). RT3DE was found to be a suitable method for the measurement of MA diameter (MAD) and area (MAA), and it was confirmed that 2D echocardiography underestimates these morphological parameters (8). RT3DE-derived MAD and MAA proved to be larger in case of cardiomyopathy, while it was associated with more significant MA function in HCM, MA function proved to be reduced in dilated and noncompaction cardiomyopathy (9,10). Up to the present the available literature dealing with 3DSTE is limited, but it seems to be a suitable procedure for calculation of MA morphological and functional parameters (40).

Study limitations. During the analysis of our data, the following important limiting factors occurred over that ones previously mentioned:

(1) The aim of our present study was the evaluate LA and MA by 3DSTE. The assessment of LV and other heart chambers by 3DSTE was not the subject of this study.

(2) Further studies are warranted in connection with validity of 3DSTE-derived MA or other valvular data.

5.3. Alternative ways to assess left atrial function in noncompaction cardiomyopathy by three-dimensional speckle-tracking echocardiography

To the best of authors’ knowledge this is the first report to demonstrate the clinical usefulness of 3DSTE in the evaluation LA function in NCCM. Recently, direct volumetric RT3DE was found to be useful to assess isolated LV-NCCM alone (41–48), or in combination with Ebstein’s anomaly (49) or double-orifice mitral valve (50). Moreover, isolated right ventricular (51) and biventricular forms were also evaluated by RT3DE (52). In a larger series of NCCM patients, noncompacted and compacted LV segments had comparable increased 3D regional volumes and reduced systolic function suggesting that systolic LV dysfunction is not confined to noncompacted LV segments (53). In a RT3DE study, both LV trabecular mass as well as the total number of trabeculations in NCCM patients were significantly underestimated by 2D echocardiography as compared to RT3DE (54). MA could be also assessed ’en-face’ by RT3DE and was found to be enlarged and functionally impaired in NCCM patients, with a higher incidence and severity of MR (10). LA-EFO was increased in NCCM patients compared to normal individuals suggesting compensating LA work against the dysfunctional LV in NCCM patients (26). 3D-STE-derived LA-EFO of the present NCCM case was in the range previously given by RT3DE (26).

STE is a promising new echocardiographic method, with which LV strain, rotational and twist parameters can be non-invasively assessed. Van Dalen *et al.* were the first to demonstrate that 2DSTE-derived 'LV solid/rigid body rotation', with near absent LV twist, may be a new sensitive and specific, objective and quantitative, functional diagnostic criterion and have good predictive value for the diagnosis of NCCM (55,56). LV myocardial deformation was also found to be reduced in the longitudinal and circumferential dimensions and manifested tight systolic-diastolic coupling in children with NCCM (57).

As demonstrated in this report, 3DSTE could help in the evaluation of LA function in 3D space. However, due to limited number of NCCM reports, further clinical studies with 3DSTE in series of NCCM patients are warranted, especially focusing on assessment of regional LA and LV strain, rotational and twist parameters.

5.4. Three-dimensional speckle-tracking echocardiography allows detailed evaluation of left atrial function in hypertrophic cardiomyopathy

To the best of authors’ knowledge this is the first study in which increased LA volumes and TASV and AASV could be demonstrated in patients with HCM by 3DSTE. Moreover, TAEF and PAEF proved to be significantly decreased. 3DSTE-derived strain parameters were also reduced in HCM patients as compared to matched controls. These data could draw our attention to the fact that 3DSTE enables more detailed evaluation of LA dysfunction including detection of volumetric changes respecting its motion during heart cycle, even in HCM. Moreover, evaluation of different strains at the same time seems to be a quantitative way to demonstrate LA functional abnormalities.

As already mentioned, several non-invasive imaging methods including M-mode and 2D Doppler echocardiography (3,58), 2DSTE (59), tissue-Doppler imaging (TDI) (59), RT3DE (11, 60), cine CT (61), cardiac MRI (62) etc. have been used for evaluation of LA dimensions, volumes and function. As mentioned in the previous chapters, 3DSTE has just been introduced, which encompasses benefits of STE and 3D echocardiography. Over assessment of LA volumetric and functional properties, 3DSTE seems to be reliable method for the accurate measurement of LV volumes respecting cardiac cycle (30,63,64). 3DSTE is also able to quantify regional and global LV myocardial deformation by strain analysis from a single data aquisition (31,65,66). 3DSTE is a non-invasive tool for quantification of rotational and twist LV mechanics, as well (67-69). Several calculated dyssynchrony parameters of the LV have been demonstrated by different authors (70-72). Some specific case report suggested its role in the evaluation of LA appendage (73) and quantification of right ventricular volumes (74) and aortic root rotation (75), etc. However, its clinical utility in the evaluation of the heart and large vessels is not fully described in the literature.

Increased volumes and impaired LA myocardial deformation are known features in HCM (76). Moreover, occurrence of myocardial fibrosis in HCM was found to be associated with LA dysfunction (77). Abnormalities in strain theoretically could be due to chronically high LA pressures from diastolic dysfunction, LV outflow tract obstruction or higher grade MR, but intrinsic abnormalities including fibrosis of the LA wall should also be considered. However, further studies are warranted to examine whether relationship exists between dynamic obstruction and LA functional parameters detailed above. Moreover, the effect of alcohol septal ablation on these parameters could be also a subject of research.

Limitation section. Over the previously mentioned limitations the following important ones should be taken into consideration:

(1) 3DSTE seems to be a feasible method for volumetric (11,23) and strain (21,22) assessment of the LA. Despite several non-invasive tools (TDI, RT3DE, 2DSTE, CMR, CT, etc.) could be used to quantify LA volumes and function (6,7,11,58-62), only limited number of studies are available, in which 3DSTE was compared to these widely used and accepted methodologies (11,23). Therefore, more comparative studies with other methods are warranted especially focusing on the limitations of 3DSTE.

(2) 3DSTE-derived strain parameters of healthy subjects were somewhat different from the results of previous studies (21,22). It could be explained by the fact, that these parameters depend on the place of measurement (basal-mid-superior regions etc.), even in healthy subjects. Moreover, the values are affected by the age, and other factors, as well (78).

(3) Despite the fact that LA appendage could be analysed by modern transthoracic echocardiographic methodologies including TDI (79,80), 3DSTE (73) etc, LA appendage and pulmonary veins were excluded from evaluations.

(4) There are several aspects of HCM including genetic background, history of embolism, development of arrhythmias, etc., their relationship to the LA dysfunction was not examined in the present study.

(5) The effects of dynamic obstructions on LA functional parameters were not examined in this study.

(6) LA function deteriorated in patients with sick sinus syndrome and in those with paroxysmal atrial fibrillation (22). However, all of our patients and controls were in sinus rhythm.

5.5. Visualisation of left atrial appendage by three-dimensional speckle-tracking echocardiography

To the best of authors' knowledge this is the first case, in which usefulness of 3DSTE is presented for the volumetric and functional evaluation of LAA. The presented method seems to be easy to perform, but highly depends on the image quality (worse than 2D echocardiography), extent and complexity of LAA (large one-lobe LAA could be assessed as the presented case), etc. Therefore, further comparative studies with larger number of healthy subjects and pathological cases are warranted to demonstrate feasibility of 3DSTE in the assessment of LAA.

6. Conclusions (new observations)

Three-dimensional speckle-tracking echocardiography is feasible in the detection of cyclic changes in left atrial volumes and calculation of its functional properties is comparable to two-dimensional echocardiography.

Three-dimensional speckle-tracking echocardiography is a proper method for the simultaneous evaluation of left atrial and mitral annular morphological and functional characteristics. Correlations exist between left atrial and mitral annular morphological and functional parameters in healthy subjects.

Three-dimensional speckle-tracking echocardiography could help in the detailed evaluation of left atrial dysunction in noncompaction cardiomyopathy by several ways.

Three-dimensional speckle-tracking echocardiography allows evaluation of LA dysfunction by volumetric and strain analysis in hypertrophic cardiomyopathy.

In special cases three-dimensional speckle-tracking echocardiography allows volumetric and functional assessment of a left atrial appendage by a simple non-invasive way.

7. References

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Photocopies of essential publications