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Correlations between three-dimensional speckle-tracking echocardiography-derived left atrial functional parameters and aortic stiffness in healthy subjects – Results from the MAGYAR-Healthy Study

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Left atrial (LA) distension has been demonstrated to be linked with aortic stiffness in different patient populations. Three-dimensional (3D) speckle-tracking echocardiography (STE) seems to be a promising tool for volumetric and functional evaluation of the LA. The aim of the present study was to determine whether correlations exist between 3DSTE-derived LA volume-based and strain parameters characterizing all phasic functions of the LA and echocardiographic aortic elastic properties in healthy subjects. The study included 19 healthy volunteers (mean age: 37.9 ± 11.4 years, 11 men) who had undergone complete two-dimensional (2D) Doppler transthoracic echocardiography extended with the assessment of aortic elastic properties and 3DSTE. *Results:* None of LA volumes correlated with echocardiographic aortic elastic properties. Active atrial stroke volume correlated with aortic stiffness index (ASI, $r = 0.45$, $p = 0.05$). None of other volume-based functional properties significantly correlated with aortic stiffness parameters. Global peak 3D strain correlated with aortic strain ($r = -0.46$, $p = 0.05$). Global radial pre-atrial contraction strain correlated with ASI ($r = -0.49$, $p = 0.04$) and AS ($r = -0.50$, $p = 0.04$). *Conclusions:* Correlations exist between 3DSTE-derived LA functional parameters and eschocardiographic aortic elastic properties in healthy subjects.

Keywords: aortic, distensibility, echocardiography, function, left atrium, speckle-tracking, stiffness, three-dimensional

There is a strong interplay between vascular and cardiac mechanics including arterial-ventricular coupling. Left ventricular (LV) remodeling is a powerful determinant of left atrial (LA) size, therefore arterial stiffness could influence LA dimensions, as well (5, 6, 12). Arterial stiffness was found to be associated with LA size in different patient populations (12). Three-dimensional (3D) speckle-tracking echocardiography (STE) seems to be an optimal choice for non-invasive quantification of LV and LA volumes and deformation parameters by 3D volumetric and strain analysis (1, 4, 7, 8, 11, 13, 15, 17–19, 22). The aim of the present study was to determine whether correlations exist between 3DSTE-derived LA volume-based and strain parameters characterizing all phasic functions of the LA and echocardiographic aortic elastic properties in healthy subjects.

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Materials and Methods

Patient population

The study included 19 healthy volunteers (mean age: 37.9 ± 11.4 years, 11 men) who had undergone complete two-dimensional (2D) Doppler transthoracic echocardiography extended with echocardiographic aortic elastic properties assessments. 3DSTE has also been performed following 2D echocardiography in all cases. None of the subjects had any known disease which could have affected results. All subjects have been included in the MAGYAR- Healthy Study (Motion Analysis of the heart and Great vessels bY three-dimensionAl speckle-tRacking echocardiography in Healthy subjects). The study aimed to evaluate diagnostic and prognostic significance of 3DSTE-derived volumetric, strain, rotational, dyssynchrony, etc. parameters in healthy cases (‘magyar’ means ‘Hungarian’ in the Hungarian language). 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 (23).

Two-dimensional echocardiography

Standard 2D echocardiographic imaging was performed with the patient in the left lateral decubitus position using a commercially available Toshiba Artida™ echocardiography equipment (Toshiba Medical Systems, Tokyo, Japan) in the tissue harmonic mode. 2D echocardiographic images were obtained using the PST-30SBP (1–5 MHz) phased-array transducer in parasternal and apical 4-chamber (AP4CH) and 2-chamber (AP2CH) views. Special care was taken to avoid foreshortening during measurements. LV dimensions, volumes, ejection fraction and LA dimension were measured, while presence of valvular regurgitations and stenoses were excluded by Doppler echocardiography in all cases (21). All echocardiographic measurements were averaged from 3 beats.

Measurement of blood pressure values

Systolic (SBP) and diastolic blood pressure (DBP) values were estimated by a mercury cuff sphygmomanometer following 10 min of rest on the right arm in the supine position (16). The first Korotkoff sound for at least two consecutive heart beats was considered the SBP, while disappearance of fifth Korotkoff sound proved to be the DBP. Coffeinated drinks like coffee, tea, or other types of beverages, and cigarettes were not used or ingested from half and hour before the blood pressure measurements. Data were taken as the average of three consecutive measurements.

Evaluation of aortic stiffness parameters

Systolic and diastolic ascending aortic diameters (SD and DD, respectively) were recorded in M-mode echocardiography at a level of 3–4 cm above the aortic valve from a parasternal long-axis view as described in more details in the literature (16, 20) (Fig. 1). The SD and DD were considered at the time out of maximum aortic anterior motion and at the peak of QRS complex, respectively. All measurements were repeated 3 times, and average data have been given. Echocardiographic aortic elastic properties were calculated using the following equations:

[1] Aortic strain [AS] = (SD – DD) / DD

[2] Aortic stiffness index [ASI] = ln (SBP / DBP) / [(SD – DD) / DD], where ‘ln’ is the natural logarithm

[3] Aortic distensibility [AD] = 2 × (SD – DD) / [(SBP – DBP) × DD]

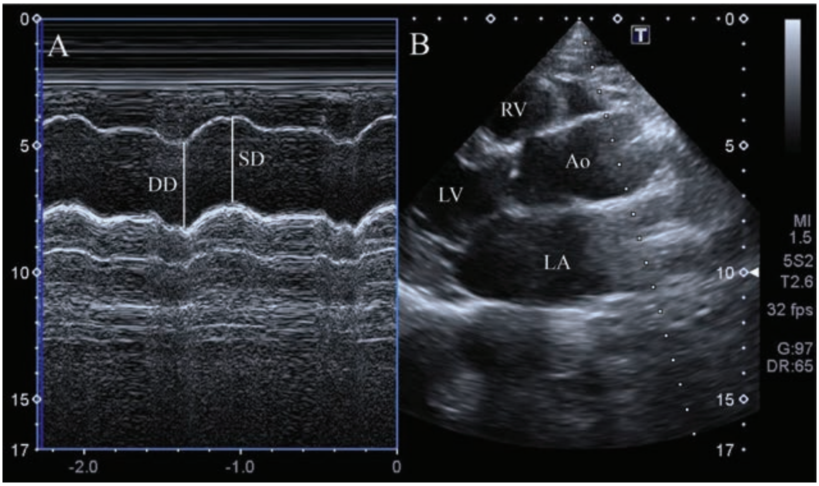

Fig. 1. Measurements of systolic (SD) and diastolic (DD) diameters of the ascending aorta (A) are shown on the M-mode tracing obtained at a level 3 cm above the aortic valve (B) at parasternal long-axis view.

Abbreviations: LV = left ventricle, RV = right ventricle, LA = left atrium, Ao = ascending aorta

3DSTE-derived volumetric measurements

All patients underwent 3D echocardiographic acquisitions immediately after 2D echocardiographic study from the same apical window using the fully sampled PST-25SX matrix-array transducer (Toshiba Medical Systems, Tokyo, Japan) with 3DSTE capability (19). During acquisitions full volume mode was used in which six wedge-shaped subvolumes were acquired over six consecutive cardiac cycles during a single breath-hold. If there was an opportunity the sector width was decreased as much as possible to improve temporal and spatial image resolutions. Pyramid-shape 3D datasets were analysed using 3D Wall Motion Tracking software version 2.5 (Toshiba Medical Systems, Tokyo, Japan) by experienced investigators (AN, PD). AP4CH, AP2CH and 3 short-axis views at different levels of the LA (basal, midatrial, and superior LA regions) were automatically selected from the 3D pyramidal dataset (Fig. 2). In the AP4CH and AP2CH views, the LA endocardial boundaries were manually traced by setting multiple reference points starting at the mitral valve level going toward the LA apex. Regarding to the literature LA appendage and pulmonary veins were not considered as the part of the LA cavity during 3DSTE assessments (7, 18). 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 endocardial surface was automatically reconstructed and tracked in 3D throughout the cardiac cycle. The user could manually adjust endocardial and epicardial LA surface when it was necessary. The following volumes have been calculated (7, 8, 11, 15, 18):

[1] maximum LA volume (V_{max}) defined as the largest LA volume at end-systole just before mitral valve opening,

[2] minimum LA volume (V_{min}) defined as the smallest LA volume at end-diastole before mitral valve closure,

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

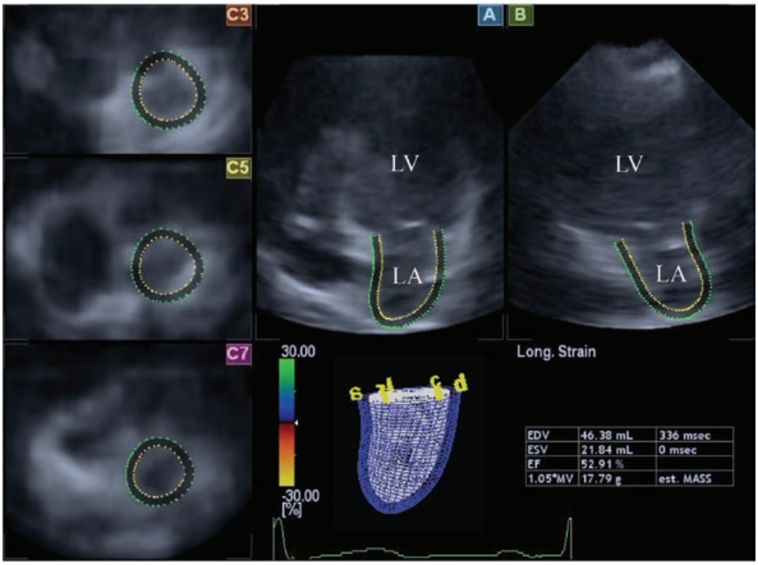

Fig. 2. Images from three-dimensional full-volume dataset showing left atrium in a patient with type 1 diabetes mellitus: (A) apical four-chamber view, (B) apical two-chamber view, (C3) parasternal short-axis view at basal, (C5) mid- and (C7) superior left atrial level. The semi-automated left atrial border definition and three-dimensional "wire" reconstruction of the left atrium based on three-dimensional speckle tracking echocardiographic analysis are also presented.

Abbreviations: LA = left atrium, LV = left ventricle

Several LA volume-based parameters characterizing each phasis of LA function were calculated from these volumes as demonstrated in Table I.

Table I. Calculation of left atrial stroke volumes and emptying fractions in different phasis of left atrial motion respecting cardiac cycle is presented

Functions	**Stroke volumes (ml)**	**Emptying fractions (%)**
Reservoir (Systole)	Total atrial SV = $V_{max}–V_{min}$	Total atrial EF = Total atrial SV/ V_{max}
Conduit function (Diastole)	Passive atrial SV = $V_{max}–V_{preA}$	Passive atrial EF = Passive atrial SV/ V_{max}
Active contraction (Diastole)	Active atrial SV = $V_{preA}–V_{min}$	Active atrial EF = Active atrial SV/V_{preA}

Abbreviations: EF = emptying fraction, SV = stroke volume, V_{max} = maximum left atrial volume, V_{min} = minimum left atrial volume, V_{preA} = left atrial volume before atrial contraction

3DSTE-derived strain measurements

From the same 3D echocardiographic dataset the following LA deformation parameters were calculated (4, 7, 13, 14) (Fig. 2):

[1] Longitudinal strain (strain in the direction parallel to the endocardial contour),

[2] Circumferential strain (fiber shortening along the circular perimeter, strain in the circumferential direction),

[3] Radial strain (radially directed deformation, strain in the perpendicular direction),
[4] 3D strain (strain in the wall thickening direction, combination of radial, circumferential and longitudinal strains), and
[5] Area strain (ratio of endocardial area change during the cardiac cycle, percentage change in area).

Global and mean segmental peak and pre-atrial contraction LA strain parameters were calculated in each patient.

Stastical analysis

Statistical analyses were performed using the MedCalc software (MedCalc, Mariakerke, Belgium). All continuous variables are expressed as mean ± standard deviation. Statistical significance was determined as a P value of less than 0.05 for all tests. To compare continuous variables independent samples Student's t-test were used. Chi-square tests were used for comparison of categorical variables.

Results

Two-dimensional echocardiographic data

Routine 2D echocardiographic LV and LA data and aortic elastic properties are summarized in Table II.

Table II. Two-dimensional echocardiographic data and aortic elastic properties of subjects

	Data
Left ventricular diastolic diameter (mm)	48.0 ± 6.8
Left ventricular systolic diameter (mm)	30.1 ± 4.2
Left ventricular diastolic volume (ml)	100.7 ± 20.2
Left ventricular systolic volume (ml)	34.8 ± 11.0
Interventricular septum (mm)	9.5 ± 2.0
Left ventricular posterior wall (mm)	9.5 ± 2.3
Left ventricular ejection fraction (%)	65.7 ± 7.0
Systolic aortic diameter (mm)	30.3 ± 3.6
Diastolic aortic diameter (mm)	26.8 ± 3.8
Systolic minus diastolic aortic diameter (mm)	3.50 ± 2.28
Aortic strain	0.13 ± 0.09
Aortic distensibility (cm^2/dynes 10^{-6})	4.58 ± 3.21
Aortic stiffness index	5.17 ± 3.45

Three-dimensional speckle-tracking echocardiographic data

3DSTE-derived LA volumes, volume-based functional properties and strain parameters are summarized in Tables III and IV.

Correlations (volumetric data vs. aortic elastic properties)

None of LA volumes correlated with echocardiographic aortic elastic properties. Active atrial stroke volume correlated with ASI ($r = 0.45$, $p = 0.05$), while passive atrial stroke volume tended to be correlated with ASI ($r = –0.42$, $p = 0.09$). None of other volume-based functional properties correlated with any of aortic stiffness parameters.

Table III. Comparison of 3DSTE-derived volumetric and volume-based functional left atrial parameters in patients with type 1 diabetes mellitus and controls

	Data
Calculated volumes (ml)	
Maximum left atrial volume (V_{max})	35.6 ± 6.4
Minimum left atrial volume (V_{min})	16.3 ± 4.9
Left atrial volume before atrial contraction (V_{preA})	23.8 ± 6.7
Stroke volumes (ml)	
Total atrial stroke volume	19.3 ± 4.5
Passive atrial stroke volume	11.8 ± 4.7
Active stroke volume	7.5 ± 3.2
Emptying fractions (%)	
Total atrial emptying fraction	54.5 ± 10.2
Passive atrial emptying fraction	33.5 ± 12.3
Active atrial emptying fraction	31.4 ± 9.2

Table IV. Comparison of 3DSTE-derived global and mean segmental peak and pre-atrial contraction left atrial strain parameters in healthy subjects

	Peak	Pre-atrial contraction
Global strain parameters		
Radial strain (%)	–21.8 ± 11.8	–8.5 ± 8.3
Circumferential strain (%)	28.7 ± 10.0	10.7 ± 11.4
Longitudinal strain (%)	24.2 ± 6.6	9.0 ± 9.4
Area strain (%)	57.7 ± 17.6	16.5 ± 16.5
3D strain (%)	–13.9 ± 10.8	–5.3 ± 5.4
Mean segmental strain parameters		
Radial strain (%)	–23.1 ± 9.0	–8.6 ± 5.5
Circumferential strain (%)	36.6 ± 12.4	13.3 ± 10.0
Longitudinal strain (%)	31.6 ± 6.7	9.2 ± 6.2
Area strain (%)	74.5 ± 23.2	21.2 ± 15.1
3D strain (%)	–16.4 ± 6.8	–6.7 ± 5.0

Abbreviation: 3D = three-dimensional

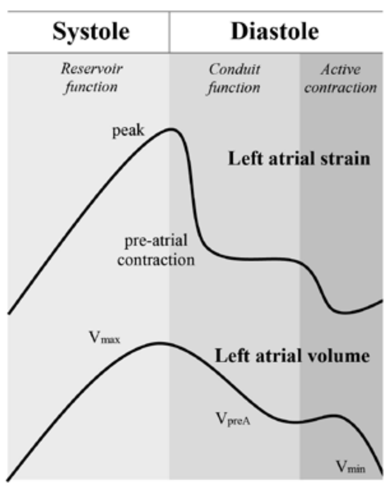

Fig. 3. Schematic figure demonstrating volumetric and strain changes during all the three functions of the left atrium and their relation to the cardiac cyle

Correlations (peak strains vs. aortic elastic properties)
Global peak 3D strain correlated with aortic strain (r = –0.46, p = 0.05). Only tendentious correlations could be demonstrated between global radial peak strain and ASI (r = –0.39, p = 0.08) and AS (r = –0.41, p = 0.07) and between mean longitudinal peak strain and AS (r = 0.41, p = 0.08).

Correlations (pre-atrial contraction strains vs. aortic elastic properties)
Global radial pre-atrial contraction strain correlated with ASI (r = –0.49, p = 0.04) and AS (r = –0.50, p = 0.04) and tended to be correlated with AD (r = 0.43, p = 0.07).

Discussion

To the best of authors' knowledge this is the first study in which correlations could be demonstrated between echocardiographic aortic elastic properties and 3DSTE-derived LA functional parameters in healthy subjects. 3DSTE is a new non-invasive clinical tool based on frame-by-frame tracking of speckle patterns created by interference of the ultrasound beam within the myocardial tissue in the 3D space (1, 22). 3DSTE has been found to be feasible for non-invasive quantification of LA volumes and functional properties allowing complex evaluation of LA phasic function during cardiac cycle which includes (2, 9) (Fig. 3):

[1] Reservoir function (LA inflow during LA systole),
[2] Conduit function (LA passive emptying during LV relaxation and diastasis, when blood transiting from the pulmonary veins to the LV during early diastole),
[3] Active contraction or booster pump function (LA active emptying, when LA works like an active contractile chamber that augments LV filling in late diastole).

There are several ways for functional assessment of LA including calculation of volume-based and strain parameters by 3DSTE as demonstrated before (4, 7, 8, 11, 13, 15, 18). With these parameters detailed characterization of all three LA functions possible:

[1] *Reservoir function* by total atrial SV and total atrial EF together with global and mean segmental peak strain parameters,
[2] *Conduit function* by passive atrial SV and passive atrial EF, and
[3] *Active contraction (booster pump)* by active atrial SV and active atrial EF together with global and mean segmental pre-atrial contraction strain parameters.

It is known that due to large number of collagens and filaments, the normal aorta is working as an elastic artery. As a physiologic consequence of the reduction of aortic buffering (Windkessel) function, SBP increases and DBP decreases leading to increased LV afterload and impaired LV relaxation (3). In the present study most of functional LA parameters showing correlations with aortic elastic properties are characteristics of atrial booster pump function reflecting magnitude and timing of atrial contractility but is dependent on the degree of venous return, LV end-diastolic pressures and LV systolic reserve (9). Moreover, correlations were found between aortic elasticity and characteristics of LA reservoir and conduit functions, as well. Because of the close interplay between LA, LV remodeling and diastolic function, the relationship is not suprising. However, in the present study detailed analysis could be demonstrated between echocardiographic aortic elastic properties and all the LA phasic functions by 3DSTE-derived volume-based and strain parameters even in healthy subjects.

Limitation section

The following important limitations should be mentioned when interpreting results:

[1] Due to lower temporal and spatial image resolutions the 3DSTE-derived image quality is mostly worse than that of 2D echocardiography.

[2] Despite 3DSTE seems to be an applicable technique for non-invasive estimation of LA volumes and functional properties, more comparative and validation studies with other methodologies are warranted (11, 15, 18).

[3] At this moment 3DSTE-derived normal strain reference values has not been described and the results of the present study were somewhat different as compared to that of previous findings. It could be explained by methodological differences, but the effect of the age and other factors could also not be excluded (4, 7, 13).

[4] LA appendage and pulmonary veins were excluded from evaluations.

[5] It is known that LA function could be deteriorated in different arrhytmologic disorders like in atrial fibrillation. However, all of the studied healthy subjects were in sinus rhythm.

[6] Theoretically higher grade of MR could affect LA function. However, none of the healthy subjects had $\geq$ grade 1 MR.

[7] Quantification of LV strains and rotational parameters by 3DSTE was not aimed in the present study.

[8] The blood pressure in the brachial artery and ascending aorta may be different which could theoretically affect our results. However, the presented non-invasive imaging technique has been validated against invasive methods in the evaluation of aortic stiffness parameters (3, 20).

[9] 3DSTE was performed in only a small population of healthy subjects.

Conclusions

Correlations exist between 3DSTE-derived functional LA parameters and echocardiographic aortic elastic properties in healthy subjects.

Conflict of Interest

None declared.

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