Left Atrial Strain Measured by Two-Dimensional Speckle Tracking Represents a New Tool to Evaluate Left Atrial Function

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Background: Left atrial (LA) strain (ϵ) and ϵ rate (SR) analysis by two-dimensional speckle tracking can represent a new tool to evaluate LA function. To assess its potential value, the authors addressed whether LA ϵ and SR measured in normal subjects correlates with other Doppler echocardiographic parameters that evaluate LA function and left ventricular function.

Methods: Sixty-four healthy subjects were studied. LA ϵ and SR were calculated with the reference point set at the P wave, which enabled the recognition of peak negative ϵ ($\epsilon_{neg\ peak}$), peak positive ϵ ($\epsilon_{pos\ peak}$), and the sum of those values, total LA ϵ (ϵ_{tot}), corresponding to LA contractile, conduit, and reservoir function, respectively. Similarly, peak negative SR (LA $SR_{late\ neg\ peak}$) during LA contraction, peak positive SR (LA $SR_{pos\ peak}$) at the beginning of LV systole, and peak negative SR (LA $SR_{early\ neg\ peak}$) at the beginning of LV diastole were identified.

Results: Global LA $\epsilon_{pos\ peak}$, $\epsilon_{neg\ peak}$, and ϵ_{tot} were 23.2 ± 6.7%, −14.6 ± 3.5%, and 37.9 ± 7.6%, respectively. Global LA $SR_{pos\ peak}$, $SR_{early\ neg\ peak}$, and $SR_{late\ neg\ peak}$ were 2.0 ± 0.6 s^{-1}, −2.0 ± 0.6 s^{-1}, and −2.3 ± 0.5 s^{-1}, respectively. The above-described variables derived from analysis of global LA ϵ and LA SR correlated significantly with Doppler echocardiographic indexes that evaluated the same phase of the cardiac cycle or the same component of the LA function, including indexes derived from mitral inflow, pulmonary vein velocities, tissue Doppler, and LA volumes. Global LA $\epsilon_{pos\ peak}$, LA ϵ_{tot}, and LA $SR_{early\ neg\ peak}$ also correlated significantly with age or body mass index. Global LA $SR_{late\ neg\ peak}$ also correlated significantly with age.

Conclusions: LA ϵ analysis is a new tool that can be used to evaluate LA function. Further studies are warranted to determine the utility of LA ϵ in disease states. (J Am Soc Echocardiogr 2010;23:172-80.)

Keywords: Two-dimensional strain, Left atrial function, Reference values

The left atrial (LA) volume index is a recognized prognostic marker in diverse conditions, such as heart failure,[1] myocardial infarction,[2] and atrial fibrillation.[3] Moreover, LA function has also been described as a prognostic indicator.[4] As we improve the evaluation of LA function, it may emerge as an important component in the evaluation of a number of diseases, such as atrial arrhythmias, heart failure, and mitral valve disease.

Invasive measurements of LA function are not feasible in most patients. Therefore, the components of LA function (contractile, conduit, and reservoir function) are traditionally estimated using two-dimensional (2D) echocardiography and Doppler analysis of transmitral and pulmonary vein flows. However, the evaluation of LA function is still challenging. The evaluation of LA volumes by 2D echocardiography is limited by the use of geometric models to determine the volume of a nonsymmetric chamber and by errors due to foreshortening. Thus, 2D echocardiography may underestimate LA volumes compared with three-dimensional methods.[5,6] The evaluation of LA function by Doppler analysis of transmitral and pulmonary vein flows is indirect and therefore also limited.

Two-dimensional speckle tracking is a new echocardiographic tool that tracks the speckle pattern frame by frame in standard B-mode images to calculate left ventricular (LV) strain (ϵ).[7,8] This analysis may allow a more direct assessment of LA endocardial contractility and passive deformation and has been recently proposed,[9] but data on normal values for LA ϵ and ϵ rate (SR) are still scarce,[10-12] and the values found have not been correlated with traditional 2D Doppler echocardiographic parameters.

Therefore, our aims were to evaluate the components of LA function by 2D speckle tracking in normal subjects and to correlate the values found with traditional 2D Doppler echocardiographic measurements of LA function and LV function.

METHODS

Patients

We retrospectively examined images from healthy volunteers who were examined in our echocardiographic laboratory from 2005 to

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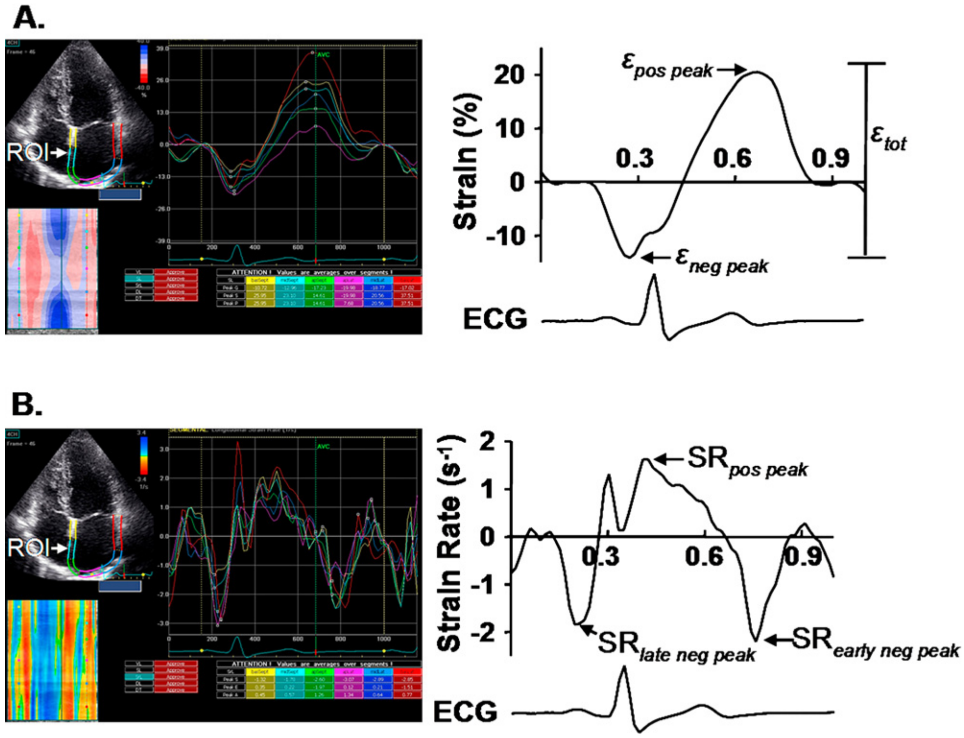

Figure 1 Two-dimensional LA speckle tracking. *(Left)* Four-chamber views depicting the region of interest (ROI) created by the speckle-tracking software and the corresponding LA ϵ curves **(A)** and LA SR curves **(B)** for each of 6 segments analyzed in each view. *(Right)* Average LA ϵ **(A)** and SR **(B)** curves obtained after averaging the 6 curves *(left)*. The reference point was placed at the onset of the P wave, which allowed the measurement of peak negative strain ($\epsilon_{neg\ peak}$), corresponding to LA contractile function, and peak positive strain ($\epsilon_{pos\ peak}$), corresponding to LA conduit function. The sum of the peak positive and negative strains was considered to be total LA strain (ϵ_{tot}), corresponding to LA reservoir function. Similarly, peak negative global LA SR ($SR_{late\ neg\ peak}$) during LA contraction, peak positive global LA SR ($SR_{pos\ peak}$) at the beginning of LV systole, and peak negative global LA SR ($SR_{early\ neg\ peak}$) at the beginning of LV diastole can be identified. *ECG*, Electrocardiogram.

2006. Subjects were declared healthy after undergoing thorough medical histories and physical examinations. All subjects had normal findings on resting electrocardiography and baseline echocardiography. All subjects gave written informed consent before their participation. A previous work describing LV ϵ using this same database was recently published.[13]

We identified 97 normal subjects in our database. Of these, 33 subjects were excluded from analysis for inadequate electrocardiograms ($n = 6$) or inadequate imaging quality due to acquisition with low frame rates ($n = 13$), LA foreshortening ($n = 7$), or inadequate acoustic windows ($n = 7$). The final study population consisted of 64 individuals. Among them, 10 patients did not have adequate 3-chamber views for analysis and had only 4-chamber and 2-chamber views analyzed.

Echocardiography

Studies were performed using phased-array ultrasound systems (Vivid 7; GE Medical Systems, Milwaukee, WI) equipped with 3S phased-array transducers. Cardiac dimensions were measured in accordance with the recommendations of the American Society of Echocardiography.[14] Echocardiograms were stored digitally and reviewed offline with software (ProSolv Cardiovascular Analyzer; Problem Solving Concepts, Indianapolis, IN). The values for 2D echocardiographic parameters were obtained after averaging 3 consecutive cycles.

M-mode echocardiography was used to measure LA diameter and LV end-diastolic and end-systolic diameters. LV and LA volumes were determined using the modified Simpson's rule with images obtained from apical 4-chamber and 2-chamber views. Pulsed-wave Doppler was obtained in the apical 4-chamber view. From transmitral recordings, the peak early (E) and late (A) diastolic filling velocities, E/A ratio, E-wave deceleration time, E-wave velocity-time integral (VTI_E), A-wave VTI (VTI_A), and LA filling fraction ($[(VTI_A/(VTI_E + VTI_A)] \times 100$) were obtained. From pulmonary vein velocities obtained at the right upper pulmonary vein, the following measurements were taken: peak S-wave inflow velocity during ventricular systole, peak D-wave inflow velocity during the early phase of ventricular diastole and the corresponding S/D ratio, peak reversed atrial wave (Ar) velocity during LA contraction, S-wave VTI, D-wave VTI, and Ar-wave VTI.

Doppler tissue imaging of the mitral annular level was obtained at the septal and lateral positions. Values shown for peak early (E′) and late (A′) diastolic annular velocities are averages of the values obtained at septal and lateral positions.

The following indexes of LA function were calculated according to previous study.[15] Total LA stroke volume was calculated as maximum LA volume − minimum LA volume. Active LA stroke volume was calculated as precontraction LA volume − minimum LA volume. Passive LA stroke volume was calculated as maximum LA volume − precontraction LA volume. The total LA emptying fraction was calculated as (total LA stroke volume/maximum LA volume) × 100. The active LA emptying fraction was calculated as (active LA stroke volume/precontraction LA volume) × 100. The passive LA

Table 1 Clinical and 2D echocardiographic characteristics of subjects (n = 64)

Variable	Value
Clinical	
Age (y)	40.2 ± 13.6
Body mass index (kg/m^2)	25.6 ± 4.4
Women	44 (69%)
Arterial systolic blood pressure (mm Hg)	118 ± 12
Arterial diastolic blood pressure (mm Hg)	69 ± 8
Heart rate (beats/min)	69.4 ± 9.7
Echocardiographic	
LA diameter (cm)	3.47 ± 0.45
LA area (cm^2)	15.9 ± 3.3
LV end-diastolic diameter (cm)	4.72 ± 0.48
LV end-systolic diameter (cm)	2.86 ± 0.39
LV fractional shortening (%)	39.3 ± 6.6
LV end-diastolic volume (mL/m^2)	54.7 ± 11.8
LV end-systolic volume (mL/m^2)	14.3 ± 4.6
LV ejection fraction (%)	73.8 ± 6.6
LV longitudinal ϵ (%)	−19.8 ± 2.4
E (cm/s)	82.0 ± 20.1
A (cm/s)	58.6 ± 13.7
E/A ratio	1.47 ± 0.50
LA filling fraction (%)	30.8 ± 7.0
E-wave deceleration time (ms)	176 ± 42
E′ average (cm/s)	13.2 ± 2.8
E/E′ ratio average	6.4 ± 1.6
A′ average (cm/s)	9.7 ± 2.1
Ar (cm/s)	28.3 ± 6.3
S (cm/s)	58.9 ± 12.4
D (cm/s)	53.0 ± 10.4
S/D ratio	1.15 ± 0.31

Data are expressed as mean ± SD or as number (percentage).

Table 2 Two-dimensional echocardiographic LA volume and function (n = 64)

Variable	Value
Maximum LA volume index (mL/m^2)	21.9 ± 5.1
Minimum LA volume index (mL/m^2)	7.3 ± 5.0
Precontraction LA volume index (mL/m^2)	12.1 ± 4.4
Total LA stroke volume (mL)	28.0 ± 7.7
Total LA emptying fraction (%)	70.3 ± 9.2
Active LA stroke volume (mL)	10.6 ± 5.0
Active LA emptying fraction (%)	46.6 ± 11.7
Passive LA stroke volume (mL)	17.5 ± 6.0
Passive LA emptying fraction (%)	44.3 ± 12.1
LA expansion index (%)	271.5 ± 126.4

Data are expressed as mean ± SD.

emptying fraction was calculated as (passive LA stroke volume/maximum LA volume) × 100. The LA expansion index was calculated as (total LA stroke volume/minimum LA volume) × 100.

Longitudinal ϵ Analysis

The images used for LV ϵ analysis were acquired focusing the LV by adjusting the depth and frame rate. LV longitudinal ϵ was calculated as previously described.[13]

The clips used for LA ϵ and SR analysis were different from those used for LV ϵ analysis but were acquired during the same exam. Only clips with good quality images, enough depth to include the whole LA and acquired with high frame rates were used for analysis. The average frame rate of the clips used for LA ϵ analysis was 64.1 ± 6.6 frames/s.

In contrast to the assessment of LV ϵ, in which the R-wave onset of the electrocardiogram is used as a reference point, we used the onset of the P wave as the reference point for the calculation of LA ϵ and SR, as previously proposed.[11] We used this point because it most relevantly represents the LA cavity just prior to its contraction. The use of the P wave as the reference point enabled the recognition of peak positive global LA ϵ ($\epsilon_{pos\ peak}$), which corresponded to LA conduit function; peak negative global LA ϵ ($\epsilon_{neg\ peak}$), which corresponded to LA contractile function; and the sum of these values (total global LA ϵ [ϵ_{tot}]), which corresponded to LA reservoir function (Figure 1). Similarly, we identified peak negative global LA SR (LA $SR_{late\ neg\ peak}$) during LA contraction, peak positive global LA SR (LA $SR_{pos\ peak}$) at the beginning of LV systole, and peak negative global LA SR (LA $SR_{early\ neg\ peak}$) at the beginning of LV diastole.

To calculate LA ϵ and SR, we used 2D speckle-tracking software (EchoPAC; GE Medical Systems), as previously described,[11] using images obtained in apical 4-chamber, 2-chamber, and 3-chamber views. Regarding the 3-chamber view, we included only the inferoposterior wall, as the opposing wall includes the ascending aorta.[11] This software was previously validated for the measurement of LV ϵ[8,16] and detects and tracks the ultrasonic interference pattern (speckle) inherent to standard 2D echocardiography. This software has been previously used for measuring LA ϵ with high feasibility and good agreement.[10-12] Briefly, 2D images at one specific cardiac cycle were selected, and the LA endocardial surface was manually traced by a point-and-click approach. An epicardial surface tracing was automatically generated by the system, creating a region of interest, which was manually adjusted to cover the full thickness of the myocardium. Before processing, a cine loop preview was used to confirm if the internal line of the region of interest followed the LA endocardial border throughout the cardiac cycle. The software divided the LA endocardium into 6 segments, resembling the approach used when studying LV ϵ. Segments in which no adequate image quality could be obtained were rejected by the software and excluded from the analysis. Last, the software calculated average ϵ for 6 LA segments for each apical view, and the LA ϵ and SR values for each view were the averages of the values obtained for the LA segments at each view, excluding the 3 LA segments of the anteroseptal wall of the 3-chamber view. The final LA ϵ and SR values were the averages of the values obtained for each apical view.

Statistical Analysis

Calculations were done using commercially available statistical software (GraphPad Prism 3.02 [GraphPad Software Inc, La Jolla, CA] and MedCalc 9.2.0.2 [MedCalc Software, Mariakerke, Belgium]). Continuous variables are expressed as mean ± SD and discrete variables as percentages. All echocardiographic variables passed standard tests of normality (Kolmogorov-Smirnov test), allowing the use of parametric tests. Correlations between variables were tested by simple linear regression analysis (Pearson's correlation). Data between age subgroups were compared using one-way analysis of variance followed by Student-Newman-Keuls post hoc analysis. Intraobserver and interobserver reproducibility were assessed using Bland-Altman analysis.[17] P values ≤ .05 were considered significant.

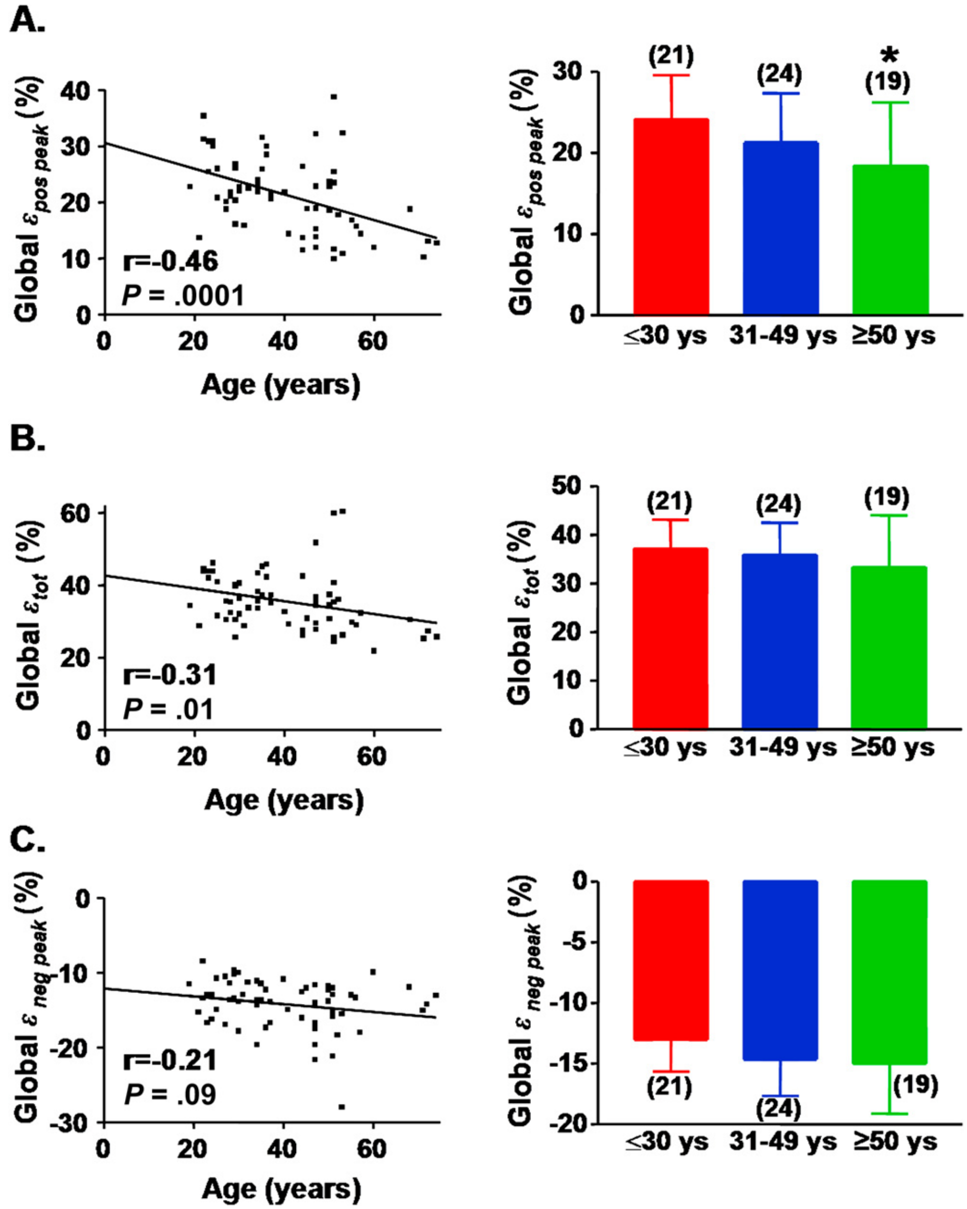

Figure 2 Correlations between global LA ϵ and age. Global LA peak positive ϵ ($\epsilon_{pos\ peak}$) **(A)** and global LA total ϵ (ϵ_{tot}) **(B)** displayed negative correlations with age. The bar graphs *(right)* also demonstrate that global LA $\epsilon_{pos\ peak}$ was lower in subjects aged >50 years. On the other hand, global LA peak negative strain ($\epsilon_{neg\ peak}$) **(C)** did not present significant variation with age. **P* < .05 versus age < 30 years.

RESULTS

Subject Characteristics

Population characteristics are summarized in Table 1. Subjects presented with normal blood pressures and heart rates. The 2D echocardiographic characteristics are depicted in Table 1, including chamber dimensions and measurements of LV diastolic and systolic function. All were within normal reference values. LA volumes and indexes of LA function are described in Table 2.

LA ϵ and SR Values and Correlations With Age

Adequate tracking of LA wall was possible in 872 of 930 analyzed segments (93.8%). Global LA $\epsilon_{pos\ peak}$ was 21.4 ± 6.7% and presented significant negative correlations with both age (Figure 2) and body mass index ($r = -0.40$, $P = .001$). Global LA ϵ_{tot} was 35.6 ± 7.9% and presented significant negative correlations with both age (Figure 2) and body mass index ($r = -0.32$, $P = .01$). Global LA $\epsilon_{neg\ peak}$ was −14.2 ± 3.3% and did not present a significant correlation with age (Figure 2) or body mass index. Global LA $SR_{pos\ peak}$ was 2.0 ± 0.6 s^{-1} and correlated negatively with body mass index ($r = -0.28$, $P = .03$) but not with age. Global LA $SR_{early\ neg\ peak}$ was −2.0 ± 0.6 s^{-1} and correlated significantly with both age ($r = 0.45$, $P = .0002$) and body mass index ($r = 0.40$, $P = .001$). Global LA $SR_{late\ neg\ peak}$ was −2.3 ± 0.5 s^{-1} and correlated significantly with age ($r = -0.28$, $P = .02$) but not with body mass index.

The interobserver and intraobserver agreement for global LA ϵ and SR were determined after offline reanalysis of recorded clips of 12

Table 3 Univariate regression analysis: global LA $\epsilon_{pos\ peak}$ and global LA $SR_{pos\ peak}$ versus 2D Doppler echocardiographic parameters of LA conduit function and LV diastolic function

	Global LA $\epsilon_{pos\ peak}$		Global LA $SR_{pos\ peak}$	
Variable	*r*	*P*	*r*	*P*
E	0.47	<.0001	−0.04	NS
E/A ratio	0.54	<.0001	−0.09	NS
E-wave deceleration time	−0.17	NS	−0.01	NS
VTI_E	0.30	.02	0.03	NS
E′ average	0.55	<.0001	0.07	NS
E/E′ ratio	−0.06	NS	−0.14	NS
S	−0.06	NS	0.21	NS
D	0.30	.01	0.01	NS
S/D ratio	−0.33	.008	0.13	NS
Maximum LA volume index	−0.26	.04	−0.47	<.0001
Passive LA stroke volume	0.18	.14	−0.11	NS
Passive LA emptying fraction	0.54	<.0001	0.36	.003
LA expansion index	0.32	.009	0.21	.09

randomly selected subjects. The mean differences for intraobserver agreement for LA ϵ were −0.6 % (95% confidence interval [CI], −1.9% to 0.7%), 0.5% (95% CI, −0.3% to 1.2%), and −1.1 % (95% CI, −3.1% to 0.9%) for global LA $\epsilon_{pos\ peak}$, LA $\epsilon_{neg\ peak}$, and LA ϵ_{tot}, respectively. The mean differences for interobserver agreement for LA ϵ were 1.8% (95% CI, 0.04% to 3.5%), −0.7% (95% CI, −1.8% to 0.4%), and 2.8% (95% CI, 0.3% to 5.3%) for global LA $\epsilon_{pos\ peak}$, LA $\epsilon_{neg\ peak}$, and LA ϵ_{tot}, respectively. The mean differences for intraobserver agreement for LA SR were 0.07 s^{-1} (95% CI, −0.06 to 0.20 s^{-1}), −0.03 (95% CI, −0.24 to 0.18 s^{-1}), and −0.06 s^{-1} (95% CI, −0.14 to 0.02 s^{-1}) for global LA $SR_{pos\ peak}$, $SR_{late\ neg\ peak}$, and $SRearly_{neg\ peak}$, respectively. The mean differences for interobserver agreement for LA SR were 0.18 s^{-1} (95% CI, 0.09 to 0.28 s^{-1}), −0.21 (95% CI, −0.42 to −0.01 s^{-1}), and −0.23 s^{-1} (−0.38 to −0.09 s^{-1}) for global LA $SR_{pos\ peak}$, $SR_{late\ neg\ peak}$, and $SR_{early\ neg\ peak}$, respectively.

Global LA $\epsilon_{pos\ peak}$ and LA $SR_{pos\ peak}$ Versus 2D Doppler Echocardiographic Parameters of LA Conduit Function and LV Function

Global LA $\epsilon_{pos\ peak}$ correlated significantly with parameters of LV diastolic function and LA indexes of conduit function. Global LA $\epsilon_{pos\ peak}$ presented positive correlations with E-wave velocity, E/A ratio, VTI_E, E′ velocity, and D-wave velocity and a negative correlation with S/D ratio (Table 3, Figures 3A and 3B). Global LA $\epsilon_{pos\ peak}$ also correlated positively with the passive LA emptying fraction and the LA expansion index and negatively with maximum LA volume index (Table 3, Figure 3C). Global LA $\epsilon_{pos\ peak}$ did not correlate with LV systolic parameters, including LV ϵ. Global LA $SR_{pos\ peak}$ did not correlate with LV diastolic parameters but correlated negatively with maximum LA volume index and positively with the passive LA emptying fraction (Table 3). Global LA $SR_{pos\ peak}$ correlated negatively with LV end-systolic diameter (r = −0.34, P = .006) but did not correlate with other LV systolic parameters.

Therefore, subjects with higher E/A ratios (Figure 3D) or higher E′ velocities (Figure 4D) displayed higher values of global LA $\epsilon_{pos\ peak}$, whereas subjects with lower E/A ratios (Figure 3E) or lower E′ velocities (Figure 4E) displayed lower values of global LA $\epsilon_{pos\ peak}$.

Global LA ϵ_{tot} Versus 2D Doppler Echocardiographic Parameters of LA Reservoir Function and LV Diastolic Function

Global LA ϵ_{tot} correlated significantly with parameters of LV diastolic function and LA indexes of reservoir function. There were positive correlations with E-wave velocity, E/A ratio, and E′ velocity and a negative correlation with maximum LA volume index. Global LA ϵ_{tot} also significantly correlated with the total LA emptying fraction and the LA expansion index (Table 4, Figures 4A-4C). Therefore, subjects with higher E/A ratios (Figure 3D) or higher E′ velocities (Figure 4D) displayed higher values of global LA ϵ_{tot}, whereas subjects with lower E/A ratios (Figure 3E) or lower E′ velocities (Figure 4E) displayed lower values of global LA ϵ_{tot}.

Global LA $SR_{early\ neg\ peak}$ Versus Echocardiographic Parameters of LV Diastolic Function

Global LA $SR_{early\ neg\ peak}$ correlated significantly with parameters of LV diastolic function and LA indexes of conduit function. There were negative correlations with E-wave velocity (r = −0.35, P = .005), E/A ratio (r = −0.37, P = .003), E′ velocity (r = −0.49, P < .0001), passive LA emptying fraction (r = −0.53, P < .0001), and LA expansion index (r = −0.36, P = .004) and positive correlations with E-wave deceleration time (r = 0.25, P = .04) and maximum LA volume index (r = 0.41, P = .0009).

Global LA $\epsilon_{neg\ peak}$ and $SR_{late\ neg\ peak}$ Versus 2D Doppler Echocardiographic Parameters of LA Contractile Function

There were significant correlations between both global LA $\epsilon_{neg\ peak}$ and $SR_{late\ neg\ peak}$ and parameters derived from Doppler analysis of LA contractile function. Global LA $\epsilon_{neg\ peak}$ and $SR_{late\ neg\ peak}$ showed negative correlations with A-wave velocity, VTI_A, LA filling fraction, A′ velocity, and Ar velocity (Table 5). However, both global LA $\epsilon_{neg\ peak}$ and $SR_{late\ neg\ peak}$ did not correlate with parameters derived from 2D LA volume estimates (Table 5). Therefore, subjects with higher A velocities (Figure 3E) or higher A′ velocities (Figure 4E) displayed higher values of global LA $\epsilon_{neg\ peak}$, whereas subjects with lower A velocities (Figure 3D) or lower A′ velocities (Figure 4D) displayed lower values of global LA $\epsilon_{neg\ peak}$.

DISCUSSION

This study demonstrated the feasibility of performing LA ϵ analysis, which derived 3 different parameters (global LA $\epsilon_{neg\ peak}$, LA $\epsilon_{pos\ peak}$, and LA ϵ_{tot}) that may be used to evaluate the contractile, conduit, and reservoir components of LA function. Similarly, we also described 3 components of LA SR (global LA $SR_{late\ neg\ peak}$, $SR_{early\ neg\ peak}$, and $SR_{pos\ peak}$) that may also be useful to analyze LA function. We also demonstrated that each of these parameters correlated with Doppler-derived and/or 2D volume–derived parameters used to evaluate LA function or LV diastolic function, thus corroborating the potential clinical value of LA ϵ analysis.

Parameters that evaluate LA function may have prognostic potential. LA reservoir function may predict the first atrial fibrillation or flutter episode in elderly subjects,[4] and LA systolic force may predict cardiovascular events in a population with high prevalence of hypertension and diabetes.[18] However, all these echocardiographic parameters and others that evaluate LA function are influenced by LV dynamics and geometry[18] and/or rely on measurements that are subjected to error.[5,6] Therefore, new methodologies that can evaluate LA

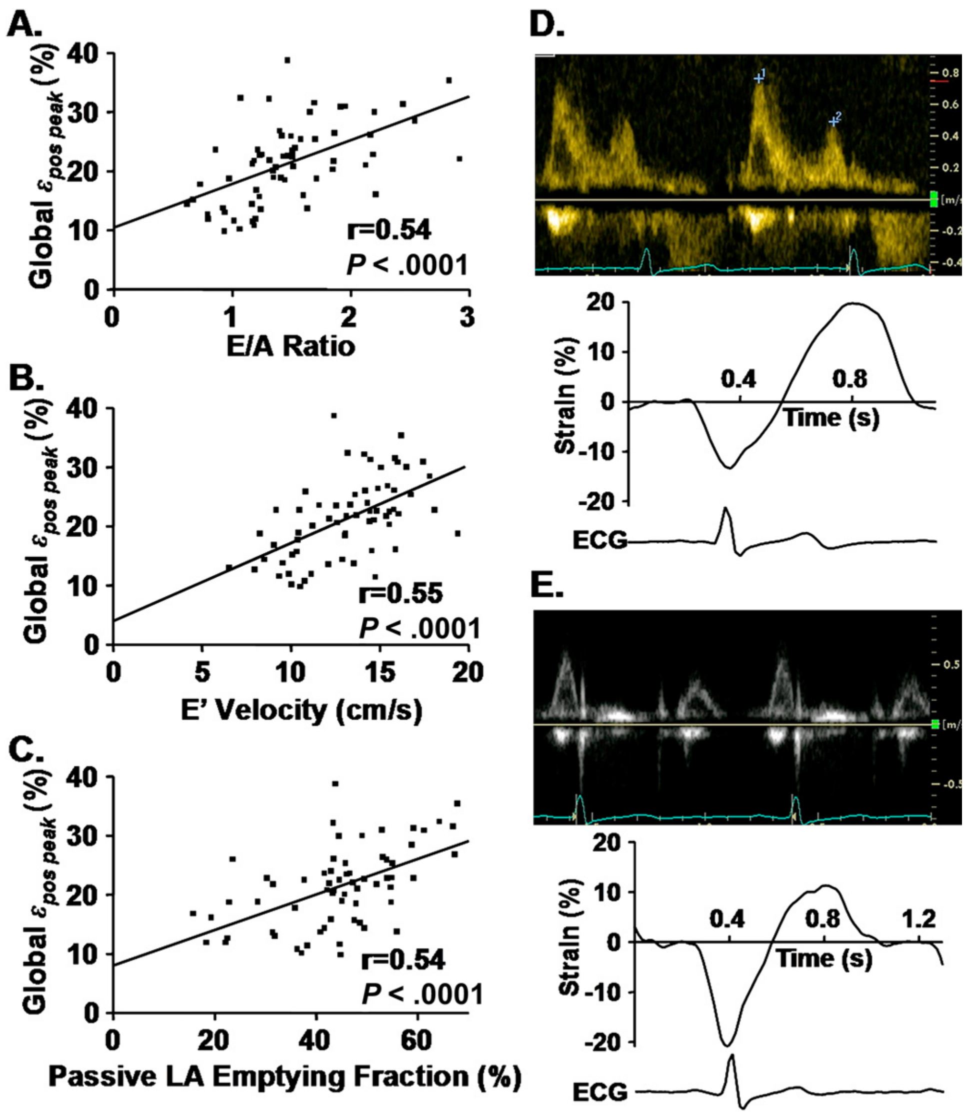

Figure 3 Correlations between global LA peak positive strain ($\epsilon_{pos\ peak}$) and echocardiographic parameters. Global LA $\epsilon_{pos\ peak}$ displayed positive correlations with LV diastolic parameters, E/A ratio **(A)**, parameters of the early phase of LV relaxation, E′ velocity **(B)**, and volumetric parameters of LA conduit function, passive LA emptying fraction **(C)**. Note on the *right* an example from a subject with a higher E/A ratio **(D)** displaying a more prominent positive component of LA ϵ and a less prominent negative component of LA ϵ, whereas a subject with a lower E/A ratio **(E)** displayed a less prominent positive component of LA ϵ and a more prominent negative component of LA ϵ.

function by analysis of LA myocardial deformation may be of potential clinical interest.

LA ϵ and SR were the focus of studies that analyzed LA ϵ derived from tissue Doppler.[19-21] However, 2D speckle-tracking analysis is angle independent, which is an advantage over ϵ derived from tissue Doppler velocities and also allows the measurement of LA ϵ in all segments of the LA, whereas previous studies based on tissue Doppler limited the analysis to specific segments of the LA wall. Therefore, recent studies have concentrated on the description of LA ϵ using 2D speckle tracking in normal subjects and described the feasibility of this approach with good reproducibility.[10-12] Vianna-Pinton et al[11] also focused on the ϵ of LA specific segments and showed that regional differences in LA $\epsilon_{neg\ peak}$ and LA $\epsilon_{pos\ peak}$ were consistently present. We built on these findings by analyzing global LA ϵ and SR, deriving parameters that can be used to evaluate the contractile, conduit, and reservoir components of LA function.

The global LA $\epsilon_{pos\ peak}$ and $SR_{pos\ peak}$ values and the global LA $\epsilon_{neg\ peak}$ and $SR_{neg\ peak}$ values we have described are within the range of the values recently described in another normal population.[12] The global LA ϵ_{tot} values we have described are within the range of those in recent studies that analyzed LA ϵ using the R wave as the reference point.[10,12]

Global LA $\epsilon_{neg\ peak}$ and $SR_{late\ neg\ peak}$ displayed significant correlations with parameters derived from Doppler analysis of LA contractile function. However, we and others[12] did not find correlation between LA active emptying fraction and global LA $\epsilon_{neg\ peak}$ or $SR_{late\ neg\ peak}$. It is possible that 2D echocardiography underestimates LA volumes, thus contributing for the described discrepancy.[5,6] Moreover, LA contractile function is dependent not only on preload stretch (precontraction LA volume) but also on afterload, represented by LV end-diastolic pressure. In fact, LA ϵ during LA contraction was shown to have a significant correlation with LV end-diastolic pressure.[22] Therefore, global

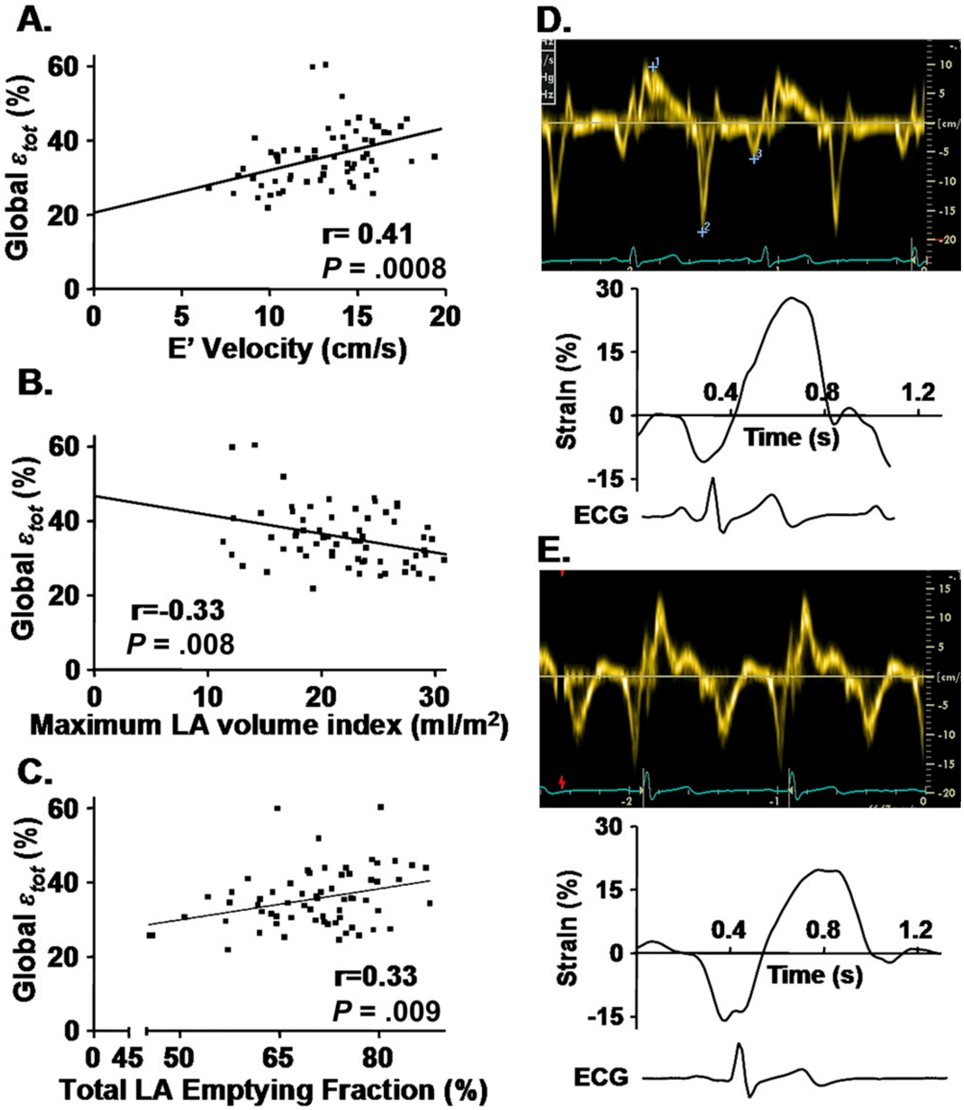

Figure 4 Correlations between global LA total strain (ϵ_{tot}) and echocardiographic parameters. Global LA ϵ_{tot} displayed positive correlations with parameters of the early phase of LV relaxation, E′ velocity **(A)**. Global LA ϵ_{tot} also correlated with volumetric indexes of LA function presenting inverse relationship with maximum LA volume index **(B)** and a positive correlation with total LA emptying fraction, an index of LA reservoir function **(C)**. Note on the *right* an example from a subject with higher E′ velocity **(D)** displaying a more prominent positive component of LA ϵ, whereas a subject with lower E′ velocity **(E)** displayed a less prominent positive component of LA ϵ.

LA $\epsilon_{neg\ peak}$ and $SR_{late\ neg\ peak}$ may represent new indexes of LA contractile function that deserve further assessment.

Global LA $\epsilon_{pos\ peak}$ and ϵ_{tot} are considered to be determined by LA relaxation and the LV base descent during LV systole, expressed by the longitudinal LV ϵ.[23,24] When the LA is well stretched longitudinally, and consequently a high LA $\epsilon_{pos\ peak}$ is present, the LV then relaxes rapidly, generating high E wave and E′, as blood rushes into the LV, generating a high passive LA emptying fraction. Therefore, global LA $\epsilon_{pos\ peak}$ and/or ϵ_{tot} correlated with parameters of LV diastolic function, the maximum LA volume, and LA volumetric indexes of conduit and reservoir function. However, in our study, we did not find significant correlations between LV systolic parameters, including LV longitudinal ϵ, and global LA $\epsilon_{pos\ peak}$, ϵ_{tot}, or $SR_{pos\ peak}$. In contrast, Wakami et al[22] found a significant relation between peak LA wall ϵ during LV systole, which would correspond to LA ϵ_{tot} measured by us, and LV hemodynamic measurements. In Wakami et al's[22] study, peak LA ϵ during LV systole correlated inversely with LV end-diastolic pressure and LV end-systolic volume and positively with the LV ejection fraction. However, their population included patients with LV systolic dysfunction, whereas our study included only subjects with normal systolic function and, therefore, narrower variation in LV ejection fraction and LV longitudinal ϵ. Interestingly, they also found significant correlation between LA ϵ during LV systole and LV end-diastolic pressure, indicating a possible interaction of LV diastolic dysfunction and LA filling during LV systole.[22]

We also showed that global LA $\epsilon_{pos\ peak}$, LA ϵ_{tot}, and absolute values of LA $SR_{early\ neg\ peak}$ decreased with age, while the absolute values of LA $SR_{late\ neg\ peak}$ increased with age. This may be explained at least in part by the known effect of age on LV diastolic function. In fact, in our population, E wave, E/A ratio, and A wave all correlated

Table 4 Univariate regression analysis: global LA ϵ_{tot} versus 2D Doppler echocardiographic parameters of LA reservoir function and LV diastolic function

Variable	*r*	*P*
E	0.29	.02
E/A ratio	0.31	.01
E-wave deceleration time	−0.01	NS
VTI_E	0.21	NS
E′ average	0.41	.0008
E/E′ ratio	−0.12	NS
S	0.04	NS
D	0.13	NS
S/D ratio	−0.11	NS
Maximum LA volume index	−0.33	.008
Total LA stroke volume	−0.22	NS
Total LA emptying fraction	0.33	.009
LA expansion index	0.30	.01

Table 5 Univariate regression analysis: global LA $\epsilon_{neg\ peak}$ and global LA $SR_{late\ neg\ peak}$ versus 2D Doppler echocardiographic parameters of LA contractile function

	Global LA $\epsilon_{neg\ peak}$		Global LA $SR_{late\ neg\ peak}$	
Variable	*r*	*P*	*r*	*P*
A	−0.26	.04	−0.27	.03
VTI_A	−0.33	.007	−0.28	.02
LA filling fraction	−0.38	.002	−0.41	.0008
A′ average	−0.36	.004	−0.32	.009
Ar	−0.37	.002	−0.52	<.0001
Precontraction LA volume index	0.20	NS	0.23	.07
Active LA stroke volume	0.10	NS	0.20	NS
Active LA emptying fraction	−0.05	NS	−0.07	NS

with age (data not shown). Other work that analyzed LA function using speckle tracking also demonstrated the age dependence of LA function.[25] However, in this last work, speckle tracking was used as a tool to estimate LA volume,[25] whereas in our study, we used 2D speckle tracking to measure LA ϵ.

Global LA $\epsilon_{pos\ peak}$ and global LA ϵ_{tot} also decreased with higher body mass index. Although our study did not focus on obese patients, body mass index is a known independent determinant of LA size,[26] and LA emptying index was described to be reduced in obese patients.[27] Therefore, body mass index may negatively influence LA function measured by 2D speckle tracking. This may be a focus of further research.

Clinical Implications

There is great potential clinical use of these new LA functional parameters derived from 2D speckle tracking. The value of LA ϵ derived from tissue Doppler analysis has been the subject of several recent studies focusing on conditions such as atrial fibrillation[19,21] and hypertrophic cardiomyopathy.[20] However, all these previous studies analyzed LA ϵ only at specific segments of the LA, whereas 2D speckle tracking can analyze global LA ϵ and therefore may become a better surrogate for LA function. It is also important to recognize the significant relationship we found between global LA ϵ_{tot} and LA $SR_{pos\ peak}$ and maximal LA volume index, a recognized predictor index in different conditions. LA ϵ may become a tool for analyzing LA function in clinical trials evaluating the prediction of developing arrhythmias or the success of drugs or radiofrequency ablation to treat arrhythmias.

Strengths and Limitations

Our population consisted of healthy volunteers, and our high feasibility rate may not be reproduced in patients with difficult acoustic windows. Additionally, the mean age of our studied population was 40 years, with a paucity of elderly patients, limiting the comparison of our findings to disease states seen in the age group we studied. Further studies are necessary to address the value of LA ϵ in the elderly population. Another limitation of our study population was the higher proportion of women in relation to men. Another limitation was the lack of studies in which LA ϵ obtained by 2D speckle tracking was compared with sonomicrometry or tagged magnetic resonance imaging. However, LV ϵ obtained by 2D speckle tracking has good agreement with that obtained by sonomicrometry[28] and by tagged magnetic resonance imaging.[8] Test-retest variability was not addressed in this study. Additionally, although intraobserver and interobserver agreement in our study were similar to the data of Kim et al,[12] interobserver variability still may represent a limitation to this method. We and others[11,12] used small numbers of subjects to assess variability in LA ϵ and SR, and the use of a larger number of subjects may help clarify this issue. The lack of correlation between global LA $\epsilon_{neg\ peak}$ and $SR_{late\ neg\ peak}$ and LA volumes is a limitation that needs further study.

Our study showed the strength of using the current speckle-tracking software to analyze LA ϵ, as we described a high feasibility rate. Future studies comparing LA ϵ with invasive hemodynamic parameters can further increase the value of this new approach to evaluate LA function.

CONCLUSIONS

The measurement of LA ϵ is feasible, and reference values are provided. It was possible to evaluate the 3 components of LA function using this new technology, and the values provided correlated with traditional echocardiographic indexes used to evaluate LA conduit, contractile, and reservoir function. Further studies are warranted to determine the value of this new tool to evaluate LA function in disease states and its potential value to identify patients at risk for LA failure or arrhythmias.

REFERENCES

1. Rossi A, Cicoira M, Zanolla L, Sandrini R, Golia G, Zardini P, et al. Determinants and prognostic value of left atrial volume in patients with dilated cardiomyopathy. J Am Coll Cardiol 2002;40:1425-30.
2. Moller JE, Hillis GS, Oh JK, Seward JB, Reeder GS, Wright RS, et al. Left atrial volume: a powerful predictor of survival after acute myocardial infarction. Circulation 2003;107:2207-12.
3. Osranek M, Bursi F, Bailey KR, Grossardt BR, Brown RD Jr., Kopecky SL, et al. Left atrial volume predicts cardiovascular events in patients originally diagnosed with lone atrial fibrillation: three-decade follow-up. Eur Heart J 2005;26:2556-61.
4. Abhayaratna WP, Fatema K, Barnes ME, Seward JB, Gersh BJ, Bailey KR, et al. Left atrial reservoir function as a potent marker for first atrial fibrillation or flutter in persons > or = 65 years of age. Am J Cardiol 2008;101:1626-9.

5. Suh IW, Song JM, Lee EY, Kang SH, Kim MJ, Kim JJ, et al. Left atrial volume measured by real-time 3-dimensional echocardiography predicts clinical outcomes in patients with severe left ventricular dysfunction and in sinus rhythm. J Am Soc Echocardiogr 2008;21:439-45.
6. Maddukuri PV, Vieira ML, DeCastro S, Maron MS, Kuvin JT, Patel AR, et al. What is the best approach for the assessment of left atrial size? Comparison of various unidimensional and two-dimensional parameters with three-dimensional echocardiographically determined left atrial volume. J Am Soc Echocardiogr 2006;19:1026-32.
7. Notomi Y, Lysyansky P, Setser RM, Shiota T, Popovic ZB, Martin-Miklovic MG, et al. Measurement of ventricular torsion by two-dimensional ultrasound speckle tracking imaging. J Am Coll Cardiol 2005;45:2034-41.
8. Cho GY, Chan J, Leano R, Strudwick M, Marwick TH. Comparison of two-dimensional speckle and tissue velocity based strain and validation with harmonic phase magnetic resonance imaging. Am J Cardiol 2006;97:1661-6.
9. D'Andrea A, Caso P, Romano S, Scarafile R, Riegler L, Salerno G, et al. Different effects of cardiac resynchronization therapy on left atrial function in patients with either idiopathic or ischaemic dilated cardiomyopathy: a two-dimensional speckle strain study. Eur Heart J 2007;28:2738-48.
10. Cameli M, Caputo M, Mondillo S, Ballo P, Palmerini E, Lisi M, et al. Feasibility and reference values of left atrial longitudinal strain imaging by two-dimensional speckle tracking. Cardiovasc Ultrasound 2009;7:6.
11. Vianna-Pinton R, Moreno CA, Baxter CM, Lee KS, Tsang TS, Appleton CP. Two-dimensional speckle-tracking echocardiography of the left atrium: feasibility and regional contraction and relaxation differences in normal subjects. J Am Soc Echocardiogr 2009;22:299-305.
12. Kim DG, Lee KJ, Lee S, Jeong SY, Lee YS, Choi YJ, et al. Feasibility of two-dimensional global longitudinal strain and strain rate imaging for the assessment of left atrial function: a study in subjects with a low probability of cardiovascular disease and normal exercise capacity. Echocardiography. In press.
13. Marwick TH, Leano RL, Brown J, Sun JP, Hoffmann R, Lysyansky P, et al. Myocardial strain measurement with 2-dimensional speckle-tracking echocardiography: definition of normal range. JACC Cardiovasc Imaging 2009;2:80-4.
14. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440-63.
15. Anwar AM, Soliman OI, Geleijnse ML, Nemes A, Vletter WB, ten Cate FJ. Assessment of left atrial volume and function by real-time three-dimensional echocardiography. Int J Cardiol 2008;123:155-61.
16. Helle-Valle T, Crosby J, Edvardsen T, Lyseggen E, Amundsen BH, Smith HJ, et al. New noninvasive method for assessment of left ventricular rotation: speckle tracking echocardiography. Circulation 2005;112:3149-56.
17. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986;327:307-10.
18. Chinali M, de Simone G, Roman MJ, Bella JN, Liu JE, Lee ET, et al. Left atrial systolic force and cardiovascular outcome. The Strong Heart Study. Am J Hypertens 2005;18:1570-6.
19. Thomas L, McKay T, Byth K, Marwick TH. Abnormalities of left atrial function after cardioversion: an atrial strain rate study. Heart 2007;93:89-95.
20. Telagh R, Hui W, Abd El Rahman M, Berger F, Lange PE, Abdul-Khaliq H. Assessment of regional atrial function in patients with hypertrophic cardiomyopathies using tissue Doppler imaging. Pediatr Cardiol 2008;29:301-8.
21. Wang T, Wang M, Fung JW, Yip GW, Zhang Y, Ho PP, et al. Atrial strain rate echocardiography can predict success or failure of cardioversion for atrial fibrillation: a combined transthoracic tissue Doppler and transoesophageal imaging study. Int J Cardiol 2007;114:202-9.
22. Wakami K, Ohte N, Asada K, Fukuta H, Goto T, Mukai S, et al. Correlation between left ventricular end-diastolic pressure and peak left atrial wall strain during left ventricular systole. J Am Soc Echocardiogr 2009;22:847-51.
23. Barbier P, Solomon SB, Schiller NB, Glantz SA. Left atrial relaxation and left ventricular systolic function determine left atrial reservoir function. Circulation 1999;100:427-36.
24. Appleton CP, Kovács SJ. The role of left atrial function in diastolic heart failure. Circ Cardiovasc Imaging 2009;2:6-8.
25. Okamatsu K, Takeuchi M, Nakai H, Nishikage T, Salgo IS, Husson S, et al. Effects of aging on left atrial function assessed by two-dimensional speckle tracking echocardiography. J Am Soc Echocardiogr 2009;22:70-5.
26. Ayer JG, Almafragy HS, Patel AA, Hellyer RL, Celermajer DS. Body mass index is an independent determinant of left atrial size. Heart Lung Circ 2008;17:19-24.
27. Lavie CJ, Amodeo C, Ventura HO, Messerli FH. Left atrial abnormalities indicating diastolic ventricular dysfunction in cardiopathy of obesity. Chest 1987;92:1042-6.
28. Korinek J, Wang J, Sengupta PP, Miyazaki C, Kjaergaard J, McMahon E, et al. Two-dimensional strain—a Doppler-independent ultrasound method for quantitation of regional deformation: validation in vitro and in vivo. J Am Soc Echocardiogr 2005;18:1247-53.