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Evaluation of Left Atrial Two-Dimensional Strain in Patients with Systolic Heart Failure using Velocity Vector Imaging

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Background: Two-dimensional (2D) Strain is a new reproducible technique for assessing regional myocardial function; however, its application for evaluation of left atrium (LA) function is less studied.
Objectives: We sought to assess LA function in heart failure patients using velocity vector imaging (VVI).
Patients and Methods: Thirty five patients (mean age: 43.34 ± 18.1 years, 59.3% male) with systolic dysfunction [left ventricle ejection fraction (LVEF) < 35%] enrolled. Standard Doppler echocardiography and 2D strain were performed on all subjects. Strain measurements were obtained from apical views.
Results: A significant differences in LA volume index (LAVI) and strain were found in patients with systolic heart failure (SHF) versus normal subjects (23.8 ± 4.1 versus 57.8 ± 19.7 ml/m^2, P < 0.001 and 39.6 ± 10.6 versus 8.2 ± 5.3%, P < 0.001). Multivariate analysis of separate walls revealed significant inverse relationship between LA size and volume with total and regional (2-ch view) 2D strains of LA. Significant inverse relationship were also detected between pulmonary artery systolic pressure and both total LA strain (22 ± 8 versus 42 ± 10 mmHg, r = -0.4, P < 0.001) and LA strain in 2-chamber (r = -0.5, P < 0.001). A cutoff value of total average LA strain (≥ 23.28%) can differentiate normal and abnormal LA function with a sensitivity of 93% and specificity of 100% and a cutoff value of total LA strain (in average) of 17.2% can differentiate mild and moderate and severe diastolic dysfunction with a sensitivity of 100% and a specificity of 97%.
Conclusions: LA strain seems to be a better determinant for diagnosis of abnormal LA function and the degree of diastolic dysfunction in SHF.

Keywords: Systolic Heart Failure; Speckle Tracking Echocardiography; Velocity Vector Imaging; Left Atrium

1. Background

Heart failure is a major and growing public health problem because of aging of the population and improved survival of patients. Systolic heart failure is known as impaired organ perfusion due to inefficient cardiovascular pump function. LA plays an important role in the overall cardiovascular performance (1). The enlargement of LA diameter is associated with left ventricle (LV) remodeling, diastolic dysfunction and is a risk factor for cardiovascular events and death. LA function reliably predicts exercise capacity in patients with ischemic or non-ischemic dilated cardiomyopathy (DCM) and differs in these groups of patients. Traditionally, LA function has been mainly evaluated using LA volumetric parameters, such as LA area, LA volume, and LA emptying fraction (EF) by two-dimensional echocardiography (2-8). An alternative method has been incorporated since several years ago using tissue Doppler-derived strain and strain rate measures to evaluate atrial myocardial deformation (9-15). Strain rate imaging allows the non-invasive functional quantification of the LA function analyzing the deformation properties independent of cardiac rotational motion and the tethering effect (16). However, there are several limitations of Doppler-derived strains, such as angle-dependency, suboptimal reproducibility, and inability to assess the curved atrial roof. 2D strain overcomes these limitations in the quantification of atrial function (17-19), 2D strain allows angle-independent assessment of regional and global strain and strain rate from 2D echocardiographic images and has been validated for the LV and right ventricle (20-22). However, only a few studies

Implication for health policy/practice/research/medical education:
Our study, entitled “Evaluation of Left Atrial Two Dimensional Strain in Patients with Systolic Heart Failure using Velocity Vector Imaging” showed feasibility of measuring the regional longitudinal strain of the left atrium to quantify LA function in patients with systolic heart failure. On the other hand, the results revealed that 2D strain seems to be a better determinant for diagnosis of abnormal LA function and the degree of diastolic dysfunction in systolic heart failure (SHF).

have applied 2D strain for the assessment of atrial mechanic.

2. Objectives

The purpose of this study was to assess LA strain by velocity vector imaging in SHF patients, compare with control group and evaluate its relation to LA size and volume and diastolic parameters.

3. Patients and Methods

3.1. Patients' Population

This single center case series randomly enrolled thirty five SHF patients with an LVEF less than 35 % and normal sinus rhythm referring to the heart failure clinic of our institution. For all the patients, a thorough history taking was followed by a complete physical examination. The exclusion criteria comprised congenital heart disease, significant valvular heart disease, atrial fibrillation, acute ischemia, pericardial diseases, hypertrophic and restrictive cardiomyopathy, arrhythmias, and pulmonary arterial hypertension. Twenty five controls were enrolled from the referrals for a routine check-up who had non-anginal chest pain and normal echocardiography [(LVEF > 55% and normal LV diastolic function with no valvular disease and normal pulmonary artery pressure (PAP)].

3.2. Echocardiographic Study

Echocardiography examinations were performed with the subjects lying in the left lateral decubitus position using a 3.5-MHz transducer on Dimension ultrasound equipment MyLab 60, Esaote, S.P, A-Italy. Two-dimensional gray scale images were acquired in the standard parasternal and apical (apical 4, apical 2, and apical long) views, and three cardiac cycles were recorded. Left ventricular and left atrial dimensions were measured and LV ejection fraction was used as a standard index of global LV systolic function using Simpson's method. Mitral inflow velocities were recorded by standard pulse wave Doppler at the tips of the mitral valve leaflets at end expiration in an apical four-chamber view at a sweep speed of 100 mm/s allowed us to measure early diastolic filling (E) and late diastolic filling (A) velocities, the ratio of early diastolic filling to late diastolic filling (E/A ratio), and E wave deceleration time (DT) using as standard indices of LV diastolic function. LV longitudinal function was explored by pulsed Tissue Doppler imaging, placing the sample volume at the level of mitral lateral and septal annulus from the apical four-chamber view. Mean peak systolic (Sa), early diastolic (Ea), and late diastolic (Aa) annular velocities were obtained by averaging respective values measured at the septal and lateral sides of the mitral annulus. The ratio of early mitral diastolic velocity to early mitral annular diastolic velocity (E/Ea) ratio was also calculated. The maximal LA volume (LAV) was also measured by biplane area-length method [0.85(area 1 × area 2 /the shortest length)] indexed to body surface area as left atrium volume index (LAVI). LA superior-inferior diameter was measured from the mitral annular plane to the posterior wall of the LA in the apical 4-chamber view.

3.3. Velocity Vector Imaging

Apical four and two-chamber views images were obtained using conventional two- dimensional gray scale echocardiography during breath hold and a suitable electrocardiographic recording. Care was taken to obtain true apical images using standard anatomic landmarks in each view and not foreshorten the left atrium, allowing a more reliable delineation of the atrial endocardial border. We also avoided visualization of the LA appendage in the apical 2-chamber view to minimize its effect on LA strain measurements. Three consecutive heart cycles were recorded and the mean value considered. The frame rate was set between 60 and 80 per second. LA endocardial border is manually traced in four, two and three chamber views, thus delineating a region of interest, composed by eight segments, placing the sample in the mid septal and mid lateral LA walls and the roof in the same cardiac cycle. In the mid septal wall, the sample was placed 1cm proximal to the medial mitral annulus, and the fossa ovalis was avoided for optimal tracking of the endocardium. In the lateral wall, the sample was placed 1 cm proximal to the lateral mitral annulus, and the point of entry of the pulmonary veins was avoided. Offline analyses of the gray scale images obtained by 2D echocardiography were done by using Velocity Vector Imaging (VVI) X Strain software, Esaote.S.P, Italy. Thus, strain and strain rate curves were generated from these regions of interest. Peak atrial strain was measured at the end of the systole before MV opening, by separately values observed in 4, 2 and 3- chamber views (Figure 1). Also the average values in 4, 2 and 3- chamber views and total strain of LA was considered.

3.4. Statistical Analysis

Data were described as mean ± standard deviation for normal distribution and as frequencies and percentages for categorical variables. Baseline characteristics were compared between the groups by Student's t or Pearson's chi square tests. Correlations between interval variables were assessed by Person correlation coefficient (r). Statistical analyses were performed using SPSS 15 for Windows (SPSS Inc., Chicago, Illinois). To find a diagnostic accuracy and sensitivity and specificity of the best cutoff value for LA strain in SHF patients, a nonparametric receiver-operating characteristics (ROC) curve analysis was constructed, area under the curve (AUC) which shows the discriminatory ability of the variable cutoff was reported. A value of $P < 0.05$ was considered statistically significant.

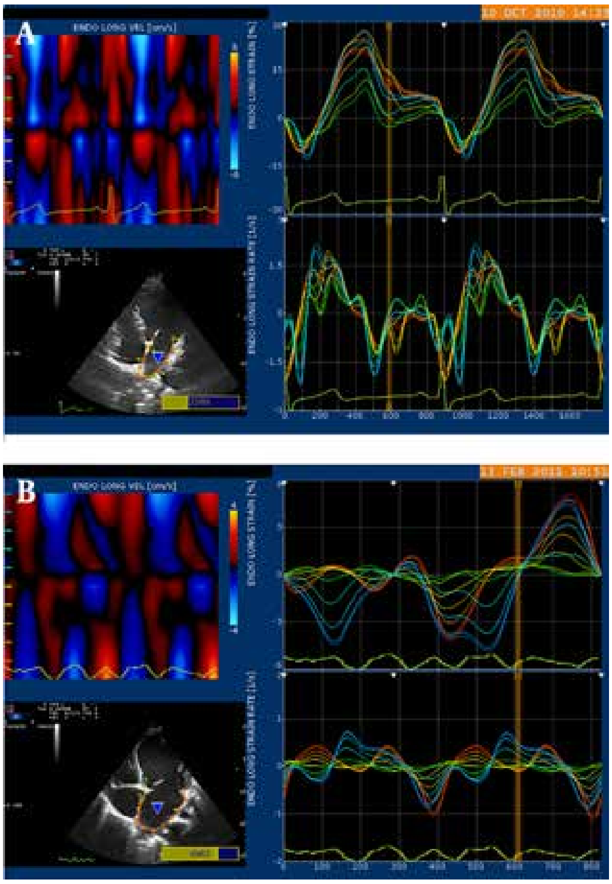

Figure 1. (A) LA 2D Strain curve in a Normal Subject; (B) a Patient with Systolic Heart Failure

3.5. Reproducibility

Interobserver variability expressed as a coefficient of variation was assessed by analyzing 10 regions in different, randomly chosen subjects by two independent investigators. For intraobserver variability, 10 longitudinal regions were analyzed by one investigator for two times within four weeks. The second round of intraobserver measures was blinded to results from initial measures.

4. Results

Baseline characteristics of the patient and control subjects as well as echocardiography data are shown in Table 1 and 2. Two third of patients (59.3%) were male and 75% of the patients were diagnosed to have DCM with a mean LVEF of 19 ± 6.5%. Mean LA diameter, area and volume index were significantly larger in patients than control group ($P < 0.000$). In addition, total LA strain was substantially lower in SHF patients in comparison with normal subjects (39.6 ± 10.6 versus 8.2 ± 5.3%, $P < 0.000$). Multivariate analysis of separate walls revealed significant inverse relationship between LA size, area and LAVI with total and regional (2-ch view) 2D strains of LA (Table 3). Analysis of the diastolic parameters and LA strain also showed significant relationship between total and regional (2-ch view) LA 2D strain with systolic PAP, A wave velocity and degree of diastolic dysfunction, but not with either mitral E and Ea velocities, and or E/Ea (Table 3). Using ROC curve analysis, we could be able to suggest cutoff values of LA size and function to distinguish abnormal atrial function in SHF patients. A cutoff value of total average LA strain (≥ 23.28%) can differentiate normal and abnormal LA function with a sensitivity of 93% and specificity of 100%. Additionally, our results showed a cutoff value of total LA strain (in average) of 17.2% can differentiate mild and moderate and severe diastolic dysfunction with a sensitivity of 100% and a specificity of 97% (Table 4). The estimated sensitivity and specificity of suggested LA dimension, area and volume along with total and regional LA strains for differentiation between mild and moderate and severe diastolic dysfunction were shown in Table 4.

Table 1. Baseline Characteristics in Normal and Patients Group

Baseline characteristics	Control (n=25)	Patients (n=35)	P value
Age, y, mean (SD)	34 (9.6)[a]	43 (18.1)	0.231
Sex, No. (%)			0.448
Female	12 (48)	14 (40)	
Male	13 (52)	21 (60)	
BSA[a], mean (SD)	1.77 (0.13)	1.69 (0.17)	
4-ch LAA, cm^2, mean (SD)	14.2 (1.49)	26.2 (6.1)	< 0.001
2-ch LAA, cm^2, mean (SD)	14.08 (1.6)	24.3 (5.3)	< 0.001
LA size, cm, mean (SD)	3.9 (0.44)	5.7 (0.78)	< 0.001
LAVI, ml/m^2, mean (SD)	23.8 (4.14)	57.83 (19.7)	< 0.001

[a] Abbreviations: 4-ch LAA, left atrial area in 4 chamber view; 2-ch LAA, left atrial area in 2 chamber view; BSA, body surface area ; LA, left atrium; LAVI, left atrial volume index

Table 2. Left Atrial Strain Values (%) in Different Sites as mean (SD) in Patients and Normal Control Group

Left Atrial Wall	Control, mean (SD) (n=25)	Patients, mean (SD) (n=35)	P value
Septum	66.8 (42)	7.8 (6.13)	< 0.001
Lateral	44.9 (19.7)	11.2 (8.4)	< 0.001
Anterior	43.2 (25.4)	10.3 (8)	< 0.001
Inferior	54.7 (25.9)	9.2 (11.4)	< 0.001
Posterior	36.7 (22.5)	9.2 (6.5)	< 0.001
Roof,4-ch	25.04 (16.2)	6.5 (6.2)	< 0.001
Roof,2-ch	22.6 (11.4)	6.4 (7.3)	< 0.001
Roof,3-ch	27.08 (19.9)	5.9 (7.9)	< 0.001
Average,4-ch[a]	45.6 (22)	8.5 (5.6)	< 0.001
Average,2-ch	40.2 (14.3)	8.7 (8.2)	< 0.001
Average,3-ch	31.9 (17.4)	7.6 (6.5)	< 0.001
Average, total	39.6 (10.6)	8.2 (5.3)	< 0.001

[a] Abbreviations: 4-ch,4 chamber view; 2-ch, 2 chamber view; 3-ch, 3 chamber view

Table 3. Correlations Between LA Size, Area, Volume and LV Diastolic Parameters, and LA Strain Values in Systolic Heart Failure Patients

	E[a], r/P value	A, r/P value	Ea, r/P value	E/Ea, r/P value	DT, r/P value	SPAP, r/P value	LA dimension, r/P value	2ch LAA, r/P value	4ch LAA, r/P value	LAVI, r/P value
Septum,4-ch	-0.08/0.6	0.3/0.06	0.2/0.09	-0.2/0.09	0.1/0.4	-0.4/0.007	-0.3/0.06	-0.2/0.08	-0.3/0.05	-0.3/0.02
Lateral, 4-ch	-0.01/0.9	0.2/0.2	0.09/0.6	-0.1/0.53	0.04/0.7	-0.1/0.42	-0.1/0.28	-0.2/0.18	-0.3/0.03	-0.2/0.08
Anterior, 2-ch	-0.2/0.2	0.5/0.000	0.2/0.2	-0.2/0.1	0.3/0.02	-0.4/0.004	-0.4/0.01	-0.2/0.01	-0.4/0.004	-0.3/0.02
Inferior, 2-ch	-0.1/0.5	0.5/0.000	0.04/0.04	-0.02/0.09	0.2/0.12	-0.5/0.000	-0.4/0.004	-0.3/0.06	-0.5/0.002	-0.4/0.01
Posterior, 3-ch	-0.2/0.2	0.1/0.3	0.2/0.4	-0.3/0.08	0.07/0.6	-0.08/0.6	-0.2/0.14	-0.1/0.5	-0.05/0.76	-0.04/0.79
Roof, 4-ch	-0.2/0.1	0.1/0.4	0.06/0.7	-0.2/0.2	0.3/0.09	-0.3/0.02	-0.4/0.006	-0.2/0.1	-0.4/0.01	-0.3/0.03
Roof, 2-ch	-0.1/0.4	0.5/0.000	0.09/0.09	-0.2/0.12	0.4/0.003	-0.4/0.01	-0.5/0.001	-0.4/0.01	-0.5/0.001	-0.4/0.008
Roof, 3-ch	-0.2/0.2	0.1/0.57	0.1/0.2	-0.2/0.19	0.02/0.8	-0.1/0.3	-0.3/0.08	-0.07/0.7	-0.2/0.17	-0.1/0.5
Average, 4-ch	-0.1/0.46	0.2/0.12	0.1/0.3	-0.2/0.16	0.1/0.2	-0.3/0.02	-0.3/0.02	-0.3/0.05	-0.4/0.005	-0.4/0.01
Average, 2-ch	-0.1/0.3	0.6/0.000	0.3/0.06	-0.3/0.07	0.3/0.01	-0.5/0.001	-0.5/0.001	-0.3/0.03	-0.5/0.001	-0.4/0.007
Average, 3-ch	-0.2/0.1	0.1/0.3	0.1/0.2	-0.2/0.09	0.05/0.7	-0.1/0.4	-0.3/0.07	-0.1/0.5	-0.1/0.3	-0.04/0.7
Average, total	-0.2/0.1	0.4/0.004	0.2/0.08	-0.03/0.04	0.2/0.09	-0.4/0.004	-0.5/0.002	-0.3/0.05	-0.5/0.002	-0.3/0.01

[a] Abbreviations: E, early diastolic mitral inflow velocity, A late diastolic mitral inflow velocity; Ea, mitral annular early diastolic velocity; E/Ea, the ratio of early diastolic mitral inflow velocity to mitral annular early diastolic velocity; DT, E wave deceleration time, SPAP, systolic pulmonary artery pressure; LAA, left atrial area; LAVI, left atrial volume index; 4-ch,4 chamber view; 2-ch, 2 chamber view; 3-ch, 3 chamber view

Table 4. Sensitivity and Specificity of Suggested Cut Points According to ROC Curve to Differentiate Mild From Moderate to Severe LV Diastolic Dysfunction in Heart Failure Patients

	Suggestive cut point	Sensitivity, %	Specificity, %
LA[a]diameter, cm	4.7	90	100
LAVI, ml/m^2	30.3	97	100
2-ch 2DS, (average), %	24	95	94
Total LA 2DS, (average),%	17.2	100	97

[a] Abbreviations: LA, Left atrium; LAVI, left atrial volume index; 2-ch, 2-chamber; 2DS, 2-dimensional strain

5. Discussion

The left atrium plays an important role in the overall cardiovascular performance. This is accomplished through its action as a contractile chamber during late ventricular diastole, as a reservoir distended by the inflow volume from pulmonary veins during ventricular contraction and isovolumic relaxation and a conduit during the early ventricular diastole and diastases (23). Through these varying mechanical functions, the LA modulates LV filling. In addition, the LA also acts as a volume sensor with the atrial wall releasing natriuretic peptides in response to stretch, generating natriuresis, vasodilatation, and inhibition of the sympathetic nervous system and renin-angiotensin-aldosterone system. LA enlargement is often asymmetrical and may occur in the medial-lateral as well as the superior-inferior axes because the enlargement in the antero-posterior axis may be limited by the thoracic cavity. Thus left atrial volume is superior to LA diameter as a measure of LA size (24). Kuppahally et al. (25) mentioned that the relationship between LA size and burden of cardiovascular disease and its outcome is stronger for LA volume than LA dimension. The prognostic implications of LA volume have been more extensively studied in high-risk subgroups. In patients with dilated cardiomyopathy, increased LA volume was associated with poorer survival incremental to LV end-systolic volume, diastolic dysfunction, and mitral regurgitation. It has been reported that an LAVI of >32 mL/m^2 is a powerful marker for increased all-cause mortality, independent of other measures of LV systolic and diastolic function (26). Recently, increased LA volume has been reported as a predictor of diminished exercise capacity in patients with heart failure (27). In patients with DCM, atrial enlargement may also be due to concomitant atrial muscle myopathy caused by a more widespread primary pathologic process (28). Heart failure is associated with the progressive conversion of the LA from a storage and contractile chamber to a more passive simple conduit chamber (29). It is likely that intrinsic alterations of LA myocardial contractility play an important role. However, it is not clear that these myopathic changes happen firstly or occur lately as a consequence of LA dilatation and myofibrils stretching. Few studies have evaluated atrial function using myocardial strain in SHF patients (30). Schneider and colleagues (16) measured tissue Doppler-based strain and strain rate (measures of the degree and rate of LA deformation), in patients with either persistent or paroxysmal atrial fibrillation (AF). Mustafa Kurt et al. (5) evaluated LA strain in diastolic heart failure patients and showed that LA systolic strain and strain rate were significantly lower than those in patients with just diastolic dysfunction. Christina Janet et al. evaluated LA strain by VVI in patients with type 2 diabetes mellitus and mild or moderate LV diastolic dysfunction, and showed that LA strain seems value in distinguishing normal from abnormal diastolic function in diabetic patients (31). But the relation between LA volume, diastolic parameters and the degree of diastolic dysfunction with total and regional LA strains has not been evaluated before. In our study, LA strain was significantly lower in patients with SHF compared to normal subjects (39.6 ± 10.6 versus 8.2 ± 5.3%, P < 0.000). Mi-Sung Shin et al. mentioned that the maximal LA volumes were negatively correlated with the posterior wall longitudinal peak systolic strain and strain rate and posterior wall tissue velocity is an important factor of LA contractility (32) but we couldn't find any significant relationship between posterior LA wall strain and either LAVI and or diastolic parameters. In contrast, we found a significant negative relation between LAVI and LA regional strain in 2-ch view and total LA strain. Kuppahally et al. showed that reduction in atrial strain did not appear to be caused by elevation of filling pressure as assessed by E/Ea (7). In our study, multivariate analysis of diastolic parameters showed a significant inverse relationship between A velocity and systolic PAP with total and most regional LA strain. The relationship between LA strain, as a marker of atrial mechanics and A velocity could be expected but the relationship between LA strain and systolic PAP in SHF patients may be due to advanced LA contractile dysfunction and more prominent passive conduit function in these patients resulting in post capillary pulmonary hypertension. According to our study, we should rely on LA 2D strain in 2-ch view (anterior and inferior walls and specially LA roof) as a valuable marker of LA function. It seems that the above mentioned portions are less influenced by aorta, inter-atrial and inter-ventricular septum and even pericardium, so they are more reliable for evaluation of LA mechanics by 2D strain. Several limitations should be mentioned. Individuals with normal diastolic function were relatively younger than patients' group. Because diastolic function changes with age, this point affects the results of this study. Mitral inflow profiles are affected by loading conditions. However, we used standards for the classification of LV diastolic dysfunction using Doppler echocardiography that are widely accepted and used in clinical practice. We excluded patients with significant MR but LA strain and diastolic parameters might have been affected because of some degree of MR in our patients. Left atrial 2D strain in control subjects are significantly higher than those with SHF. In patients with systolic heart failure, LA strain seems to be a better surrogate than LA size and volume for diagnosing abnormal LA function and diastolic dysfunction.

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Authors' Contributions

Maryam Esmaeilzadeh: Associate Professor of Cardiology, Fellowship in Echocardiography, designing the study, interpreting the data, writing, revising and submitting the manuscript. Farveh Vakilian: Assistant Professor of Cardiology Fellowship in Heart Failure and Transplantation, concept and design of the study; data collection, analysis, and interpretation; and drafting of the manuscript. Majid Maleki: Professor of Cardiology, interpreting the data, revising the manuscript. Ahmad Amin: Assistant Professor of Cardiology Fellowship in Heart Failure and transplantation, interpretation of the data and manuscript. Sepideh Taghavi: Assistant Professor of Cardiology Fellowship in Heart Failure and Transplantation, interpretation of the manuscript. Hooman Bakhshandeh Abkenar: Assistant Professor of Epidemiology, doing statistics and data analysis.

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