Evaluation of Left Atrial Functions in Patients with Dilated Cardiomyopathy Using Conventional echocardiography and Strain Imaging

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Abstract

background

Dilated cardiomyopathy (DCM) is characterized by a dilated left ventricle with systolic dysfunction that is not caused by ischemic or valvular heart disease.

Left atrial (LA) size is a predictor of adverse cardiovascular outcome both in the general population and in selected clinical conditions. The left atrium modulates left ventricular filling through three components: a reservoir phase during systole, a conduit phase during diastole and an active contractile component during late diastole. During diastole the LA is directly exposed to the left ventricular (LV) cavity pressure. With progressive impairment of LV diastolic function, and the consequent increase in LV end-diastolic pressure, the LA increases in size with a reduction of both the LA passive emptying and conduit functions, with a compensatory increase of the active LA emptying, at least in the first stages of LV diastolic dysfunction.

Methods

The study included 50 patients with the diagnosis of DCM (NYHA class I to IV and normal sinus rhythm) and 10 healthy control subjects. Two-dimensional (2D) conventional echocardiography was performed to assess LV dimensions, volumes, ejection fraction (EF), fractional shortening (FS), wall thickness, LA diameter, LA area, Mitral annular plane systolic excursion (MAPSE). Mitral E-wave (E) and A-wave (A) velocities, as well as their ratio (E/A), E' wave and E/E' ratio were measured. LA volumes including maximum (at the end of systole), minimum (at the end of diastole) and pre A LA volumes (before atrial contraction) were measured using the modified Simpson method. LA emptying volume (LAEV) and emptying fraction (LAEF), passive emptying volume (LAPEV) and passive emptying fraction (LAPEF) and active emptying volume (LAAEV) and active emptying fraction (LAAEF) were calculated in apical four-chamber view. We measured the peak LA strain, and strain rate during systole and late diastole using speckle tracking echocardiography in both apical four-chamber and apical two-chamber views.

Results

Patients with DCM showed a significant increase in LA volumes (Maximum, Minimum and Pre-A volumes) compared with the control group. LAEV and LAEF (reservoir function), LAPEV and LAPEF (conduit function) were significantly lower in patients with DCM compared to normal subjects. No significant difference was observed in LAAEV and LAAEF (pump function) between patients and controls. LA strain and LA strain rate and late diastolic strain rate values were decreased in patients with DCM. A negative correlation between LA strain measured in septal, lateral, anterior, and inferior walls and NYH class was observed. Only LAEV and LAEF (reservoir function) was correlated with NYHA class.

Conclusion

In patients with DCM, LA volumes, LA reservoir, Conduit, and pump functions were significantly reduced. Atrial myocardial deformation properties, assessed by strain and strain rate imaging, are abnormal in patients with DCM. The severity of
HF symptoms correlated positively with the LA reservoir function and negatively with the LA strain parameters. These findings suggest that LA systolic and diastolic dysfunction assessed either by conventional echocardiography or speckle tracking imaging could be related to reduced functional capacity in patients with DCM.
Keywords: Dilated cardiomyopathy; Left Atrial Functions; NYHA class; Speckle-tracking echocardiography.

Introduction

Dilated cardiomyopathy (DCM) is a myocardial disease characterized by dilation and impaired contraction of one or both ventricles. DCM is the most common type of cardiomyopathy (1). In patients with DCM, a wide range of LA sizes has been observed. Patients with a reduced left ventricular (LV) ejection fraction (EF) had an increased risk proportional to the increase in the size of the LA, which was independent of EF, age, or symptomatic status. However, it is unclear whether the prognostic power of the enlarged LA might be the result of LV diastolic dysfunction or the presence of mitral regurgitation (MR) or atrial fibrillation (AF) (2, 3).

The LA is directly exposed to LV cavity pressure during diastole, thus an enlarged LA is a robust marker of increased LV filling pressure in absence of LA volume overload, which provides a causal link between LA dilatation and poor outcome (4). Quantifying LA size is difficult, in part because of the left atrium's complex geometry and intricate fiber orientation and the variable contributions of its appendage and pulmonary veins (5). The antero-posterior diameter, calculated with M-mode or 2D echocardiography, is no longer considered as adequately representative of the true LA dimension. For these reasons, the American Society of Echocardiography, in conjunction with the European Association of Echocardiography, recommends the measurement of LA volumes with either an ellipsoid model or the Simpson's method in four- and two- chamber apical views (6). The LA size is measured at the ventricular end-systole when the LA chamber is at its greatest dimension. It is imperative to avoid foreshortening of the LA for computing LA volume. The confluence of the pulmonary veins and LA appendage should be excluded, when performing planimetry. Real-time 3-dimensional (3D) echocardiography has been shown to accurately and reproducibly estimate LA volume compared with cardiac magnetic resonance (CMR) (7).

LA volumes can be accurately measured using cardiac computed tomography (CCT). However, the radiation exposure and need for iodinated contrast medium relegate CCT largely to an important adjunctive role in LA ablation procedures; moreover, the relatively poor temporal resolution of CCT may preclude accurate measurements of phasic LA volumes and atrial function. CMR (considered the "gold standard") provides accurate measurements of LA volume with acceptable temporal resolution but is limited by increased costs, decreased availability, an inability to measure phasic volumes with gated 3D sequences, and problems related to gadolinium contrast and an inability to scan patients with intracardiac devices (8,9).

The principal role of the LA is to modulate LV filling and cardiovascular performance by functioning as a reservoir for pulmonary venous return during ventricular systole, a conduit for pulmonary venous return during early ventricular diastole, and a booster pump that augments ventricular filling during late

ventricular diastole. LA contributes up to 30% of LV output (10). LA function plays a central role in maintaining optimal cardiac output despite impaired LV relaxation and reduced LV compliance. Increased LA volume may be accompanied by a progressive impairment in LA function, and both may precede symptom development and adversely affect prognosis (11). 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 (12).

LV functions influence LA function throughout the cardiac cycle. LA maximum volume is influenced by the mechanical traction of the LV longitudinal fibers, which causes the systolic descent towards the apex of the mitral valve plane and the subsequent stretching of the LA resulting in an active suction of blood in the atrium from the pulmonary veins. Hence, the LV longitudinal systolic function might have an impact on the LA reservoir function and be a determinant of the LA end-systolic dimension (13). Conduit function is influenced by atrial compliance and is reciprocally related to reservoir function but by necessity is closely related to LV relaxation and compliance. Atrial booster pump function reflects the magnitude and timing of atrial contractility but is dependent on the degree of venous return (atrial pre-load), LV end-diastolic pressures (atrial afterload), and LV systolic reserve (14). During diastole, the LA is directly exposed to LV pressure that increases with worsening LV diastolic dysfunction. Consequently, LA pressure increases in order to maintain adequate LV filling. This results in increased LA wall tension and dilatation of the LA (15).

Increased reservoir function may play an important role in accelerating LV filling by helping to maintain an enhanced atrioventricular pressure gradient during diastole and also by increasing LA booster function through increased preload. This is supported by the LA reservoir and booster functions when augmented during exercise, whereas conduit function is not (16). A volumetric assessment of LA reservoir, conduit, and booster pump functions can be obtained from LA volumes at their maximums (at end-systole, just before mitral valve opening) and minimums (at end-diastole, when the mitral valve closes) and immediately before atrial systole (before the electrocardiographic P-wave). From these volumes, total, passive, and active ejection (or emptying) fractions can be calculated (figure 1). Conventional echocardiography allows measurement of all LA volumes:

- Pre-atrial contraction volume (LA preA), measured at the onset of the P-wave on an ECG;
- Minimal LA volume (LA min), measured at the closure of the mitral valve in end-diastole; and
- Maximal LA volume (LA max), measured just before the opening of the mitral valve in end-systole.

The following formulae are used for volumetric assessment of LA function:

LA reservoir function includes:

- LA total emptying volume (LAEV): LA max ─ LA min
- LA total emptying fraction (LAEF): LA max ─ LA min /LA max

LA conduit function includes:

- LA passive emptying volume (LAPEV): LA max ─ LA preA
- LA passive emptying fraction (LAPEF): LA max ─ LA preA /LA max

LA booster pump function includes:

- LA active emptying volume (LAAEV): LA preA ─ LA min
- LA active emptying fraction (LAAEF): LA preA ─ LA min /LA preA

The normal pulmonary venous flow pattern (figure 2) reflects flow from the pulmonary veins to the LA during early ventricular systole, late ventricular systole and isovolumic relaxation (S2 wave), early ventricular diastole (D wave), and reversal of flow from the LA to

pulmonary veins during atrial systole (PVar) (17). The magnitude and VTI of the S waves reflect LA reservoir function and are determined by LV systolic function and LA relaxation (S1 wave), LA compliance (S1 and S2 waves), and right ventricular stroke volume (S2 wave). Peak velocity and VTI of D wave is an index of LA conduit function (18) and is dependent on factors that influence LA afterload: LV relaxation and early filling and mechanical obstruction from the mitral valve apparatus (19).

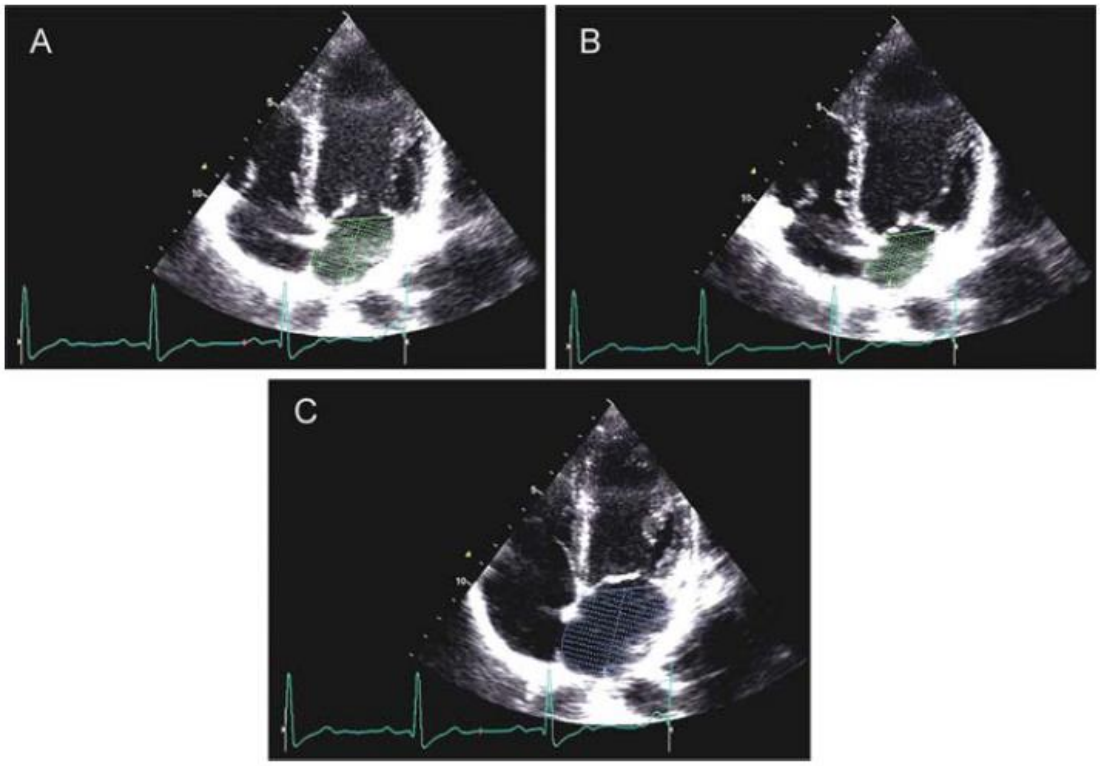


Figure 1: LA volumes measured in the apical 4-chamber views by means of 2-dimensional echocardiography. Preatrial contraction volume (LA preA), measured at the onset of the P-wave on an ECG (A); minimal LA volume (LA min), measured at the closure of the mitral valve in end diastole (B); and maximal LA volume (LA max), measured just before the opening of the mitral valve in end-systole (C).

During LA contraction, blood is ejected from the LA into the LV and the pulmonary veins. Thus, assessment of transmitral (peak A-wave velocity and A-wave VTI) and pulmonary venous blood flow (PVar) provides additive information for the evaluation of LA booster pump function (20). Pulsed-wave and color tissue Doppler of atrial contraction (A') provide regional and global (when several sites are averaged) snapshots of atrial systolic function (figure 3). Tissue velocities during ventricular systole (S') and early diastole (E') correspond to reservoir and conduit function, respectively. However, tissue Doppler velocities are subject to error because of angle dependency and the effects of cardiac motion and tethering and have been superseded by deformation analysis (21).

Strain is a measure of deformation and strain rate is a rate of such deformation. Strain echocardiography has been the most widely used tool to evaluate the ventricular myocardial

mechanics in the field of echocardiography during the last decade (22). Recent studies have suggested that LA strain or strain rate can be measured either by a Tissue Doppler image (TDI) or 2D speckle tracking image based echocardiography and these measurements are useful tools to evaluate the global or regional LA function (23). Although temporal resolution is excellent and ideal 2D image quality is not necessary, TDI is highly angle dependent, and signal-to-noise ratios may be problematic. In contrast, 2D STE analyzes myocardial motion by frame-by-frame tracking of natural acoustic markers that are generated from interactions between ultrasound and myocardial tissue within a user-defined region of interest, without angle dependency. For both modalities, strain imaging of the LA is more difficult and time-consuming than for the LV. Moreover, the far-field location of the atrium, reduced signal-to-noise ratio, the thin atrial wall, and the presence of the appendage and pulmonary vein are challenges in applying deformation analysis to the LA (24).

Figure 2: pattern of Pulmonary vein filling.

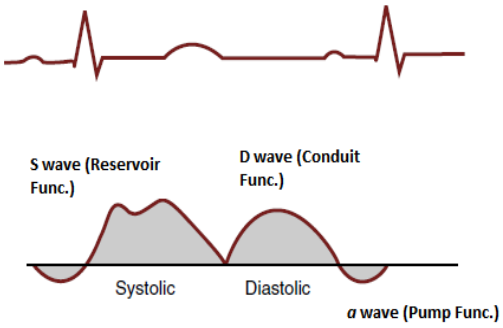
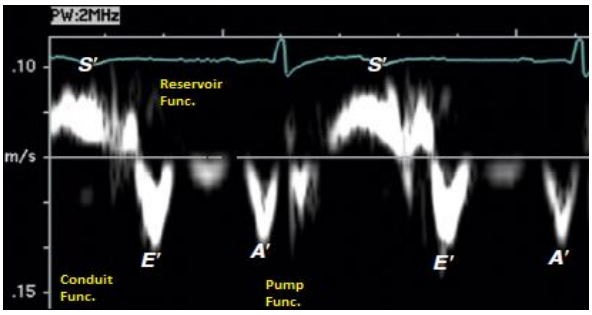


Figure 3: Tissue Doppler Imaging at the mitral annulus shows early diastolic (E') wave, atrial contraction (A') wave & systolic (S') wave



Patients and Methods

A total of 50 patients routinely referred to the Outpatient Clinic of Ibn Albitar Center for Cardiac Surgery with a diagnosis of DCM were studied and 25 volunteers who were age and sex matched to patient group with no history of cardiac disease and with entirely normal echocardiographic findings were enrolled in the study between October and December 2015. Patients and controls with a history of coronary artery disease, hypertension, LV wall motion abnormality, valvular heart disease, any rhythm other than sinus rhythm, congenital heart disease, hypertension, bundle branch block, atrioventricular (AV) conduction abnormalities on ECG, and poor quality echocardiographic and electrocardiographic imaging were excluded from the study.

In all subjects, 2D, M-mode, pulsed, and tissue Doppler echocardiographic examinations were performed using a transducer connected to a commercially available ultrasound machine (S5-1 probe, iE33). During echocardiography, one lead electrocardiography was recorded continuously. M-mode measurements and conventional Doppler echocardiographic examinations were performed according to the criteria of the American Society of Echocardiography guidelines (25). From the apical four-chamber and two-chamber views, LV end-diastolic and end-systolic volumes and ejection fraction were calculated using the biplane Simpson's method. Each subject underwent pulsed-wave Doppler examination

of mitral inflow obtained in the apical four-chamber view. Doppler tissue imaging, used to measure lateral mitral annular velocity, was performed by placing the sample volume in the lateral corner of the mitral annulus in the apical four-chamber view. The ratio of E/E', an index of LV filling pressure, was calculated. LV outflow tract (LVOT) velocities and diameter were obtained from the apical four-chamber view and parasternal long-axis view respectively. Mitral annular plane systolic excursion (MAPSE, a parameter for the assessment of LV longitudinal function and correlates with global systolic function of the LV) was measured by the use of M-mode echocardiography in an apical four-chamber view.

LA longitudinal systolic and diastolic functions were analyzed in the apical four-chamber and two-chamber views using two-dimensional speckle-tracking echocardiography (using QLAB version 7, CMQ; Philips Medical Systems) at frame rate ≥70 fps. The LA endocardial border was traced manually and adjusted to cover the thickness of the LA walls. LA systolic strain (LA-Strain) and LA systolic strain rate (LA-SR) (parameters of the relaxation or diastolic function of the LA) were derived as the average values of peak systolic strain and strain rate of all LA segments obtained in the four-chamber and two-chamber views during LV systole. LA late-diastolic strain rate (LA-SRa) (a parameter of the contraction or systolic function of the LA) was calculated as the average value of peak late diastolic strain rate of all LA segments obtained in the four-chamber and two-chamber views during LV late-diastole or atrial contraction (26). The criteria of LA systolic and diastolic dysfunction were based on previously validated studies. LA dysfunction was defined as LA diastolic dysfunction = LA-SR < 0.82 s_1, and LA systolic dysfunction (by Simpson's method) = LA total emptying fraction < 50% or LA active emptying fraction < 35% (27).

LA volumes were calculated using the modified Simpson's method at 3 distinct points during the cardiac cycle: (1) maximum volume before MV opening (LA max), (2) minimum volume before MV closing (LA min), and (3) volume before LA contraction at the onset of the P-wave (LA preA). From these volumes, the volumetric indices of the LA mentioned above were calculated (LA reservoir function, LA conduit function and LA booster pump function).

Statistical analysis

Data are presented as means ± SD. Comparisons of all measurements between normal subjects and patients with DCM were made using the unpaired t test. Correlations between variables were assessed by correlation coefficient (r). For all statistical analyses, a two-tailed p value <0.05 was considered significant. Statistical analyses were performed using Excel 2010.

Results

A total of 50 patients diagnosed with DCM (35 men and 15 women; age 51.3±7.6 years) formed the study population. The mean EF is 40±7.2% and NYHA class ranging from I to IV. All patients with DCM included in the study underwent coronary angiography which reported normal coronary arteries. The patient group was compared with 25 apparently healthy individuals (control group) with no history of cardiac disease and with entirely normal echocardiographic findings. Baseline characteristics of the patient and control subjects are shown in Table 1. Sixteen patients were asymptomatic (NYHA class I), and 34 patients were symptomatic (NYHA class II in 21, class III in 7, and class IV in 6).

Table 2 showed echocardiographic data of patient and control groups. There was a significant increase in LA diameter, LA area, LV end diastolic diameter (LVEDD), LV end systolic diameter (LVESD), end diastolic

volume (EDV), and end systolic volume (ESV) in patients with DCM compared with the corresponding values of the control group. Also, there was a significant decrease in LV fractional shortening (FS), ejection fraction (EF), E and A wave velocities, E/A ratio, E' and Mitral annular plane systolic excursion (MAPSE) values in patient group compared with the controls, MAPSE measured at the lateral mitral annulus in apical four-chamber view by M-mode echocardiography, the systolic excursion of mitral annulus should be measured from the lowest point at end-diastole, The average normal value of MAPSE ranged between 12 and 15 mm. A mean value for MAPSE of ,7 mm could be used to detect an EF <30% with a sensitivity of 92% and a specificity of 67% in dilated cardiomyopathy patients with severe congestive heart failure (28). The E/E' ratio increased with the severity of diastolic dysfunction. Patients with DCM showed a larger LA diameter, LA area and LA volumes (Maximum LA, minimum LA and pre A volumes) compared with normal control subjects (table 3).

LAEV and LAEF (reservoir function), LAPEV and LAPEF (conduit function) were significantly lower in patients with DCM compared to normal subjects. There was significant reduction in the LAAEF in DCM patients while no significant difference was observed in the LAAEV (pump function) between patients and controls. Adequate speckle tracking of the LA wall was obtained in all subjects (Figure 4 and 5). LA strain (at septal, lateral, anterior and inferior walls) and LA strain rate and late diastolic strain rate values were decreased in patients with DCM (table 4 and 5). There was a negative correlation between LA strain measured in septal, lateral, anterior, and inferior walls and NYH class (table 7). The correlates of symptomatic status (NYHA class) with the LA function (reservoir, conduit and pump functions) are displayed in Table 6. Only LAEV and LAEF (reservoir function) assessed by conventional echocardiography was correlated with NYHA class. We found that patients in NYHA functional classes II, III, and IV had significantly lower values of LA systolic and diastolic function than patients in NYHA functional class I (Table 8 and 9) as reflected by LAEV, LAEF, LAAEV, LAAEF and LA late diastolic strain rate (LA systolic function) or LA strain and strain rate (LA diastolic function).

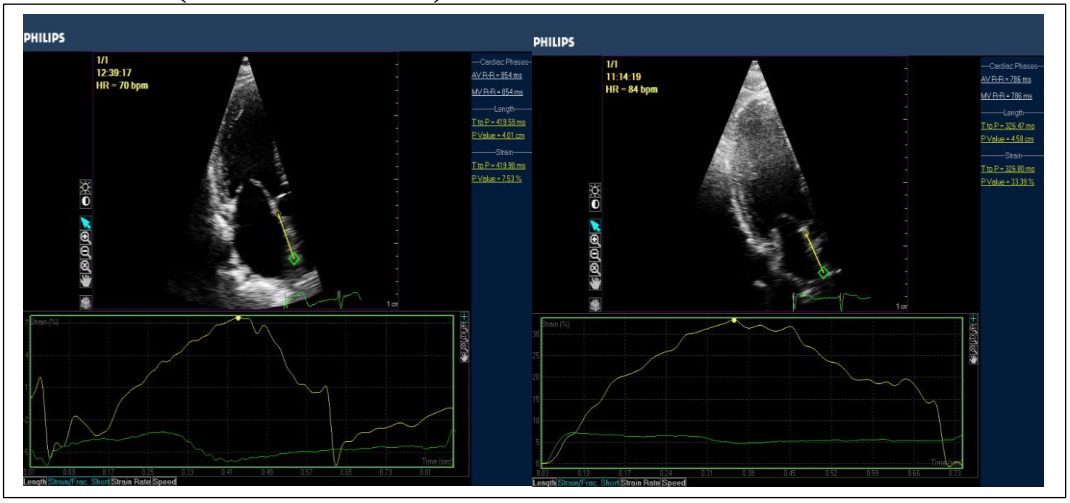


Figure 4: Two-dimensional echocardiography apical two-chamber view showing the LA anterior wall peak strain in patient with DCM (left, a 57 years old patient, NYHA class lll-lV, EF=43%, peak LA anterior wall strain= 7%. Right, a 57 years old patient, NYHA class l-ll, EF=43%, peak LA anterior wall strain= 32%)

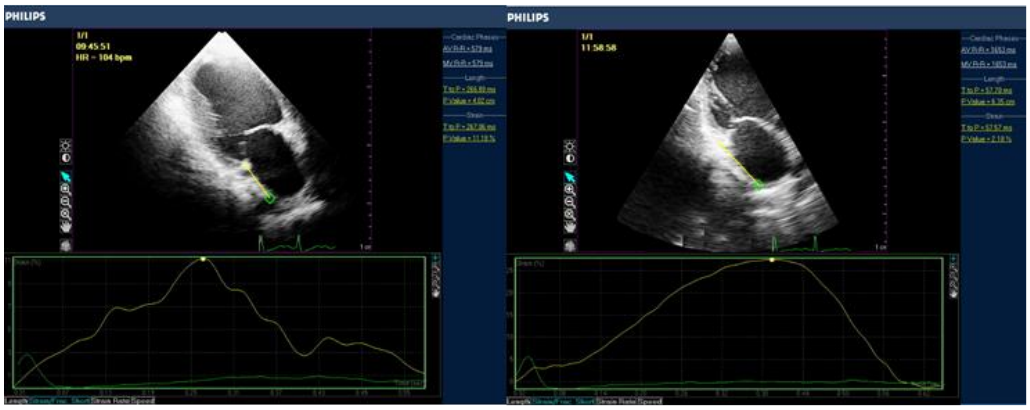


Figure 5: Two-dimensional echocardiography apical two-chamber view showing the LA inferior wall peak strain in patient with DCM (left, a 50 year old patient, NYHA class lll-lV, EF=38%, peak LA anterior wall strain= 11%. Right, a 50 year old patient, NYHA class l-ll, EF=38%, peak LA anterior wall strain= 37%)

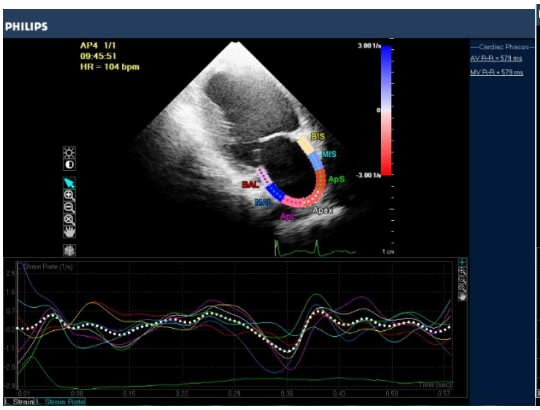


Figure 6: Two-dimensional echocardiography LA strain curves showing peak positive strain rate, early diastolic and late diastolic s train rates in a patient with DCM.

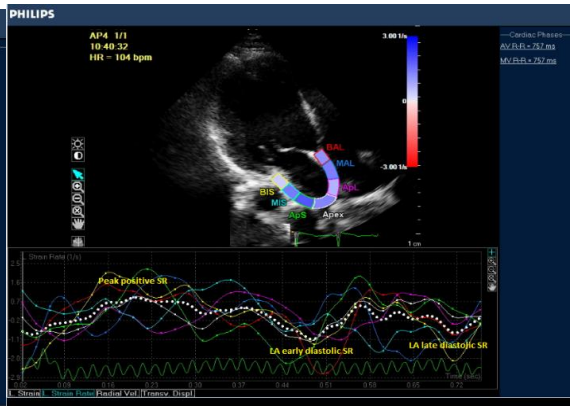


Figure 7: Two-dimensional echocardiography showing markedly reduced peak LA strain rate in a patient with DCM (strain rate 0.7 s^{-1}).

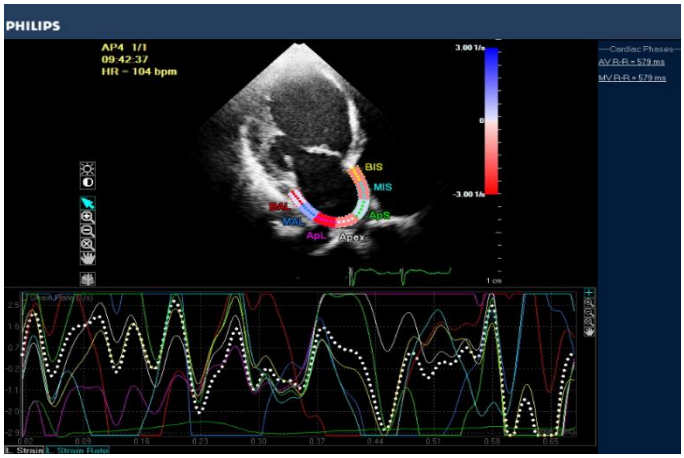


Figure 8: Two-dimensional echocardiography showing peak LA strain rate in normal control subject (strain rate 2.5 s^{-1}).

Table 1: Clinical characteristics of patient and control groups.

Variable	Patients (n=50)	Controls (n=25)	*P* value
Age (years)	51.36±7.6	39.66±8.2	0.99
Sex (men/women)	35/15	7/3	
SBP (mmgH)	118±11	124±9	0.89
DBP (mmgH)	72±9	78±6	0.95
HR (beats/min)	80±13	77±5	0.73

Data presented as mean ± SD. P > 0.05: indicates an insignificant difference; P < 0.05: indicates a significant difference; P < 0.001: indicates a highly significant difference

Table 2: Conventional echocardiographic findings in patient and control groups.

Variable	Patients (n=50)	Controls (n=25)	*P* value
LVOT diameter (cm)	2.85±0.22	2.73±25	0.65
LA diameter (cm)	3.9±0.4	3.3±0.3	0.002
LA area (cm^2)	27.5±3.4	16.4±1.5	0.004
IVS d (mm)	7.9±1.9	7.9±0.8	0.65
IVS s (mm)	10±2	10±0.8	0.64
LVID d (mm)	63.8±4.3	50.5±3.5	0.003
LVID s (mm)	50.5±3.3	32±1.4	0.002
LVPW d (mm)	7.8±1.5	7.9±0.8	0.66
LVPW s (mm)	10.1±2	9.9±0.7	0.81
EDV (ml)	186.7±22.1	110.2±26.5	<0.001
ESV (ml)	112.4±28.1	45.1±12.5	<0.001
EF %	40±7.2	62.9±5.7	<0.001
FS %	20.3±2	35.4±1.1	<0.001
SV (ml)	74.3±7	72.2±7	0.85
E wave (m/s)	0.6±0.15	0.7±0.1	0.94
A wave (m/s)	0.6±0.12	0.6±0.1	0.92
E/A ratio	1±0.4	1.1±0.1	0.98
E' wave (m/s)	0.06±0.01	0.1±0.01	2.7
E/E' ratio	10.4±4.9	6.9±0.4	0.002
MAPSE (mm)	7.2±1.1	13.5±1	<0.001

Data presented as mean ± SD. P > 0.05: indicates an insignificant difference; P < 0.05: indicates a significant difference; P < 0.001: indicates a highly significant difference

Table 8: LA function according to NYHA class

Variable	NYHA class				
	I (n=16)	II (n=21)	III (n=7)	IV (n=6)	*P* value
LAEV (ml)	16.5±1.2	17.3±1.5	19.1±1.4	21.3±2.2	0.03
LAEF (%)	35.2±1.5	33.4±1.3	31.2±0.7	30.1±1.9	0.002
LAPEV (ml)	10.3±0.6	12.1±1.1	14.2±0.9	15.5±1.2	0.01
LAPEF (%)	23.3±1.1	21.2±2.6	19.7±2.1	18.2±1.8	0.001
LAAEV (ml)	4.4±0.6	5.3±0.5	6.1±0.4	7.3±0.5	0.04
LAAEF (%)	27.5±2.1	25.3±1.6	22.5±1.9	20.2±1.4	0.001

Data presented as mean ± SD. P > 0.05: indicates an insignificant difference; P < 0.05: indicates a significant difference; P < 0.001: indicates a highly significant difference. NYHA class II, III, and IV are compared to NYHA class I.

EDV (ml)	186.7±22.1	110.2±26.5	<0.001
ESV (ml)	112.4±28.1	45.1±12.5	<0.001
EF %	40±7.2	62.9±5.7	<0.001
FS %	20.3±2	35.4±1.1	<0.001
SV (ml)	74.3±7	72.2±7	0.85
E wave (m/s)	0.6±0.15	0.7±0.1	0.94
A wave (m/s)	0.6±0.12	0.6±0.1	0.92
E/A ratio	1±0.4	1.1±0.1	0.98
E' wave (m/s)	0.06±0.01	0.1±0.01	2.7
E/E' ratio	10.4±4.9	6.9±0.4	0.002
MAPSE (mm)	7.2±1.1	13.5±1	<0.001

Data presented as mean ± SD. P > 0.05: indicates an insignificant difference; P < 0.05: indicates a significant difference; P < 0.001: indicates a highly significant difference

Table 4: LA walls strain in patient and control groups.

Variable	Patients (n=50)	Controls (n=25)	*P* value
LA septal wall peak strain %	21.7±4.4	52.3±5.2	0.001
LA lateral wall peak strain %	16.5±3.9	42.3±4.3	0.001
LA anterior wall peak strain %	18.5±4.2	46.5±5.6	<0.001
LA inferior wall peak strain %	20.1±4.3	47.6±4	<0.001

Data presented as mean ± SD. P > 0.05: indicates an insignificant difference; P < 0.05: indicates a significant difference; P < 0.001: indicates a highly significant difference

Table 7: Correlation between LA walls strain and NYHA class in patients with DCM.

Variable	NYHA Class	
	r	*P* value
LA septal peak strain	-0.72	0.001
LA lateral peak strain	-0.74	0.001
LA anterior peak strain	-0.73	0.05
LA inferior peak strain	-0.74	0.03

Data presented as mean ± SD. P > 0.05: indicates an insignificant difference; P < 0.05: indicates a significant difference; P < 0.001: indicates a highly significant difference

Table 3: LA function in patient and control groups.

Variable	Patients (n=50)	Controls (n=25)	*P* value
LA max. volume (ml)	53.1±8.6	36.3±7.5	0.001
LA min. volume (ml)	34.6±6.5	14.8±2.7	<0.001
LA pre A volume (ml)	40±7.5	21.5±5.4	0.002
LAEV (ml)	30.8±2.2	21.5±2.8	0.003
LAEF %	34.4±1.9	57.4±1.8	0.005
LAPEV (ml)	16.9±2.3	14.2±1.4	0.08
LAPEF %	20.4±2.4	38.6±1.1	0.002
LAAEV (ml)	13.2±1.3	6.3±0.8	0.06
LAAEF %	29.5±2.1	32.2±2.2	0.26

Data presented as mean ± SD. P > 0.05: indicates an insignificant difference; P < 0.05: indicates a significant difference; P < 0.001: indicates a highly significant difference

Table 5: LA strain rate and late diastolic strain rate in patient and control groups.

Variable	Patients (n=50)	Controls (n=25)	*P* value
LA SR s^{-1}	1.25±0.32	2.12±0.21	0.001
LA late diastolic SR s^{-1}	-1.29±0.81	-2.47±0.5	0.001

Data presented as mean ± SD. P > 0.05: indicates an insignificant difference; P < 0.05: indicates a significant difference; P < 0.001: indicates a highly significant difference

Table 6: Correlation between LA function measured by conventional echocardiography and NYHA class in patients with DCM.

LA function	NYHA Class	
	r	*P* value
LAEV	0.82	0.041
LAEF	0.61	0.011
LAPEV	0.72	1.583
LAPEF	0.46	0.112
LAAEV	0.60	2.319

Data presented as mean ± SD. P > 0.05: indicates an insignificant difference; P < 0.05: indicates a significant difference; P < 0.001: indicates a highly significant difference

Table 9: LA strain according to NYHA class

Variable	NYHA class				
	I (n=16)	II (n=21)	III (n=7)	IV (n=6)	*P* value
LA strain	25.5±2.1	20.2±3.2	21.4±4.1	17.2±1.5	0.001
LA SR s^{-1}	1.58±0.25	1.16±0.41	1.25±0.32	0.74±0.05	0.001
LA late diastolic SR s^{-1}	-1.42±0.51	-1.25±0.2	-1.36±0.4	-0.82±0.10	0.001

Data presented as mean ± SD. P > 0.05: indicates an insignificant difference; P < 0.05: indicates a significant difference; P < 0.001: indicates a highly significant difference. NYHA class II, III, and IV are compared to NYHA class I.

Discussion

LA function plays a central role in maintaining optimal cardiac output despite impaired LV relaxation and reduced LV compliance. Increased LA volume may be accompanied by a progressive impairment in LA function, and both may precede symptom development and adversely affect prognosis (29). In our study, LA systolic function was depressed in patients with DCM. This finding is affirmed by the concordance in several measurements of LA pump function (LAAEF, lateral mitral annulus A' velocity, and LA late diastolic strain rate). In the present study, there was significant reduction in LAAEF in DCM patients while no significant difference was observed in the LAAEV. Most likely this is because LA dilatation occurs as a compensatory response complying with increased LA volumes which aids in the preservation of cardiac output in these patients (2). It is likely that intrinsic problems with LA myocardial contractility play a role, in addition to increased LA afterload, because of the elevated LV diastolic pressures (30). A study by D' Andrea et al evaluated atrial function using myocardial strain, and showed abnormal LA systolic function, particularly in patients with idiopathic DCM (31).

Prioli A, et al recognized that abnormalities in LA pump function occur in patents with restrictive LV filling. These have been attributed to LA myopathy, and increased LA afterload attributable to the elevated late diastolic LV pressures (31). The LA plays an important role in maintaining LV filling and consequently LV stroke volume, especially when the LV is dysfunctional (32). The enlargement of the LA and the increase in LA emptying fraction are adaptive responses to impaired LV diastolic function to maintain normal LV filling pressures. Decreased LA compliance with reduced reservoir and contractile pump functions can counteract this adaptive mechanism due to disturbance of LA Frank-Starling relationship and promote symptom occurrence (33). In our study we observed that there was significant decrease in the LA reservoir function measured by LAEF in patients with DCM compared with the corresponding values in the control group.

Concerning strain parameters, there was significant decrease in the LA reservoir function when measured by strain in patients with DCM in comparison to the control group. This was evident by a decrease in the LA strain in all atrial walls (septal, lateral, anterior and inferior) of patients with DCM. Maryam E. et al reported that 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 (34). Russo et al. reported that LV longitudinal strain as a measurement of LV systolic function was the strongest predictor of the LA reservoir function because of its strong correlation with LAEV and LAEF (35).

For LA conduit function, the results of our study showed significantly lower LA conduit function in the patient with DCM evidenced by significant reduction of LA PEF and higher LA PEV compared to the control group. Ohno M. et al demonstrated that this depression of LA conduit function can be explained by the decrease in the LV filling rate early in congestive heart failure patients due to elevated LV end diastolic pressures that reduce the early diastolic left atrial - left ventricular pressure gradient and thus, decreasing conduit function (36). The same results were obtained by Bilen et al. who demonstrated impaired LA conduit function assessed by volumetric parameters in heart failure patients with preserved or reduced ejection fractions (37).

The results of our study revealed a correlation between NYHA functional class and LAEF whereas a negative correlation with LA strain (in all LA walls) was observed. Mahmoud K. et al found that LAEF were correlated with NYHA class while LA strain was negatively correlated with NYHA class (38). Similar findings were demonstrated by Bilen et al. who

found a significant negative correlation between NYHA, LAEF (LA reservoir) and LAAEF (pump function) but was not correlated significantly with conduit function (37). A study by Maryam E. et al showed a significant negative relation between LA volume and LA regional strain in 2-chamber view and total LA strain (34).

This study also demonstrated that patients in NYHA functional classes II, III, and IV had significantly lower values of LA systolic and diastolic function than patients in NYHA functional class I. Daniel A. et al found that patients with LA systolic and diastolic dysfunction presented worse NYHA functional class and more impaired LV longitudinal systolic and diastolic function compared with patients with preserved LA function. Furthermore, patients with both systolic and diastolic dysfunction of the LA had higher values of pulmonary arterial systolic pressure and pulmonary capillary wedge pressure (PCWP) compared with patients with normal LA longitudinal function (39).

Conclusion

The LA reservoir, conduit, and pump functions were significantly impaired and LA volumes were significantly increased in patients with DCM, compared with healthy controls. Atrial myocardial deformation properties, assessed by strain and strain rate imaging, are abnormal in patients with DCM. The severity of HF symptoms correlated positively with the LA reservoir function and negatively with the LA strain parameters. These findings suggest that LA systolic and diastolic dysfunction contributed to reduced functional capacity in patients with DCM and there is direct correlation between NYHA functional class and LA function.

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