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Early Detection of Left Atrial Energy Loss and Mechanics Abnormalities in Diabetic Patients with Normal Left Atrial Size: A Study Combining Vector Flow Mapping and Tissue Tracking Echocardiography

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Background: Whether left atrial (LA) functional abnormalities already exist when the LA is of normal size is unknown. The aim of this study was to explore LA energy loss and mechanics changes using vector flow mapping (VFM) and two-dimensional tissue tracking (2DTT) echocardiography in patients with diabetes and normal LA size.

Material/Methods: This study included 47 normotensive patients with diabetes and 45 controls. The following indexes were measured: LA energy loss during systole (LAELs), early diastole (LAELed), and atrial contraction (LAELac); atrial longitudinal strain during systole (SLAs), early diastole (SLAed) and late diastole (SLAac); and peak LA strain rate during systole (SRLAs), early diastole (SRLAed), and atrial contraction (SRLAac).

Results: The LAELs and LAELed decreased in diabetic patients compared with controls (P=0.002, P<0.01, respectively), whereas the LAELac increased in diabetic patients (P<0.001). The SLAs, SLAed, SRLAs, and SRLAed (all P<0.01) were all lower in diabetic patients than in controls. However, there was no difference in the SLAac and SRLAac between the two groups. Multivariate regression analysis showed that the LAELs, LAELac, and SRLAs were independently associated with HbA_{1c} in the whole study population.

Conclusions: LA energy loss and deformation mechanics are already impaired in diabetic patients with normal LA size and the long-term parameter of glycemic control was correlated with them. VFM combined with 2DTT might be a promising tool for the early detection of LA dysfunction caused by impaired glucose metabolism.

MeSH Keywords: Diabetes Mellitus • Echocardiography • Energy Transfer • Heart Atria • Mechanics

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Background

Cardiovascular complications are the major causes of mortality and disability in patients with type 2 diabetes mellitus (T2DM). Previous studies have suggested that left ventricular (LV) diastolic dysfunction is the earliest detectable functional abnormality in diabetic cardiomyopathy [1,2]. In a study of normotensive, asymptomatic T2DM patients with good glycemic control, 47% of subjects were found to have diastolic dysfunction [3]. To maintain normal cardiac output, left atrium (LA) size and function change in response to pressure or volume overload and have been studied by traditional two-dimensional echocardiography, Doppler tissue imaging (TDI), and speckle tracking echocardiography (STE, also known as two-dimensional tissue tracking in the company of Hitachi Aloka Medical Ltd., 2DTT) [4–7]. Recent years, three-dimensional (3D) echocardiography has been introduced as a more accurate tool for assessment of LA volume, but it is also lack of standardized methodology and limited normative data [8]. As a result, the biplane disk summation technique with 2D echocardiography is recommended as the standard in clinical practice for assessment of LA size [7,8]. TDI is an effective technique for assessing atrial electromechanical delays, myocardial strain and strain rate, although it is affected by myocardial tethering and acquisition angle [9,10]. On the contrary, STE allows direct and angle-independent analysis of myocardial deformation, thus providing sensitive and reproducible indexes of myocardial fiber dysfunction that overcome most of the limitations of Doppler-derived strain measures [9,11]. The feasibility and reproducibility of STE for the study of LA mechanics have been recently validated [9,11–14].

Previous studies have demonstrated that both LA size and function are markers of LV diastolic dysfunction and prognostic markers for adverse cardiovascular events [4,5,15]. However, those studies focused on volume or mechanics, and none has quantitatively assessed LA blood flow dynamics in T2DM patients and the relationship with glycemic control. In addition, most of the studies enrolled patients regardless of LA size. This raises the question of whether LA blood flow dynamics and mechanics change before the LA size increases.

In the heart, blood flow patterns can be modified by valves, chamber geometry, motions of the walls, and function of the cardiovascular system to produce hemodynamic environments that are either normal or pathological. Vector flow mapping (VFM) is a novel technique displaying velocity vectors of flow through color Doppler imaging. The accuracy of velocity vectors computed by VFM has been verified by comparing them with values computed from particle image velocimetry (PIV) [16]. Energy loss (EL) – calculated by VFM – is another flow dynamic parameter that reflects the spatial dispersion of intraventricular blood flow. It is considered a useful indicator of the efficiency of blood flow transfer and can reflect superfluous cardiac afterload caused by turbulent flow [17]. On the other hand, LA mechanics are impaired in T2DM patients [5]. With advances in the non-invasive evaluation of atrial function, STE is increasingly used to assess LA function, given its relative angle independence and ability to assess global atrial mechanics [9]. As atrial wall is thin, with less muscular mass; deformation measurements might display more variability on different ultrasound systems. So we used VFM and 2DTT (i.e. STE) in the same ultrasound machine to decrease the bias [18].

Therefore, the aim of this study was to explore LA function using VFM and 2DTT to quantify the LA EL as well as its mechanics in patients with T2DM and normal LA size.

Material and Methods

This cross-sectional study included 47 recently diagnosed normotensive (blood pressure <140/90 mmHg) patients with diabetes and 45 healthy controls of similar sex and age distributions. Diabetes was diagnosed if the fasting plasma glucose level was ≥7 mmol/L, HbA_{1c} was ≥6.5%, the OGTT plasma glucose level after 2 hours was ≥11.1 mmol/L, or a random plasma glucose was ≥11.1 mmol/L [19]. Exclusion criteria were arterial hypertension, angina pectoris, heart failure, myocardial infarction, significant valvular disease, atrial fibrillation, rheumatic diseases, congenital heart disease, obesity (body mass index (BMI) ≥30 kg/m^2), asthma, chronic obstructive pulmonary disease, neoplastic disease, cirrhosis of the liver, or kidney failure.

Body weight and height were measured, and BMI was calculated as weight (kg)/(height (m))^2. Blood pressure (BP) was measured with a calibrated sphygmomanometer after the subject had rested in the supine position for at least 10 minutes. Laboratory analyses (fasting plasma glucose or OGTT plasma glucose level after 2 hours, HbA_{1c}, total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL) and low-density lipoprotein levels (LDL)) were performed for all subjects. Fasting venous blood samples were drawn from the antecubital vein in the morning.

The study was approved by the local medical Ethics Committee, and written informed consent was obtained from all participants.

Transthoracic echocardiography

A conventional echocardiographic exam was performed using a UST-52105 probe (1–5 MHz) on a ProSound F75 ultrasound device (Hitachi Aloka Medical Ltd., Tokyo, Japan) on all subjects. Echocardiography was performed by experienced sonographers. The values of all 2D echocardiographic parameters were obtained as the average value of 3 consecutive cardiac

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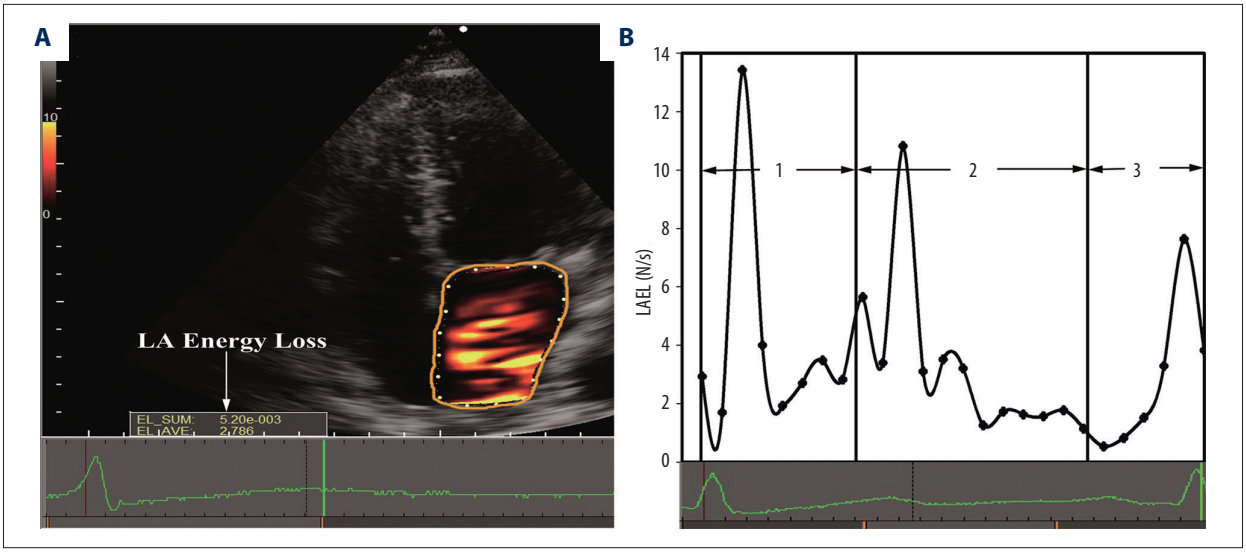

Figure 1. LA energy loss was analyzed at the apical four-chamber view. After the region of interest was determined by tracing, the distribution of EL could be displayed in two dimensions (**A**). Panel (**B**) is the LA energy loss change during one cardiac cycle, and we divided the whole cycle into three phases, where 1 represent ventricular systole (from the peak of the R wave to the onset of the T wave); 2 represents early diastole (from the onset of the T wave to the onset of the P wave); and 3 represents atrial contraction (from the onset of the P wave to the peak of the R wave).

cycles. LV and LA morphology and conventional LV systolic and diastolic parameters were analyzed.

Left ventricular end-diastolic diameters (LVEDD), posterior wall thickness (LVPW), and interventricular septal (IVS) thickness were determined according to current recommendations [20]. The left ventricular ejection fraction (EF) was calculated using the biplane Simpson's method. Transmitral Doppler flow was recorded in apical four-chamber view (A4C) by placing the sample volume at the tip of the mitral leaflets to measure early filling (E) and late filling (A) peak wave velocities and deceleration time (DT). The peak e', a' and s' wave was measured by Doppler tissue imaging on the lateral side in A4C. E/e' was calculated as a surrogate for LV filling pressure or LV diastolic stiffness [21].

The LA volume was measured using the biplane Simpson's method and normalized for body surface area (BSA). Although the use of 3D echocardiography has been introduced as a promising technique for the assessment of LA volume and LA ejection fraction [7], the 2D echocardiography remains the standard in clinical practice for assessment of LA size [8]. Maximal, precontraction, and minimal LA volumes were measured before mitral valve opening, at the beginning of the P wave, and at mitral valve closure, respectively. LA dilation was defined as a maximal 2D LA volume index >29 mL/m^2 [22]. LA total stroke volume (LASVt) was the difference between the maximal and minimal LA volumes. LA passive stroke volume (LASVp) was the difference between the maximal and precontraction LA volumes, while LA active stroke volume (LASVa) was calculated as the difference between the minimal and precontraction LA volumes. The LA passive emptying fraction (LAPEF) was calculated as the ratio of LASVp to the maximal LA volume. The LA total emptying fraction (LATEF) was calculated as the ratio of LASVt to the maximal LA volume. The LA active emptying fraction (LAAEF) was calculated as the ratio of LASVa to the precontraction LA volume.

Analysis of energy loss

The 2D color Doppler cineloop images of LA in A4C were analyzed with commercially available VFM analysis software (DAS-RS1, Hitachi Aloka Medical Ltd., Tokyo, Japan). The heart rate (HR) was calculated based on the RR interval of the cardiac cycle, which was divided into three phases: ventricular systole, early diastole, and atrial contraction. The endocardial border was manually traced at the end of atrial contraction and then automatically determined throughout the whole cardiac cycle. After the region of interest (ROI) was determined by tracing, the distribution of EL could be displayed in two dimensions (Figure 1). From the velocity vector fields of the intra-atrial blood flow, EL was calculated for each frame of the cineloop image. EL is defined as follows:

$$EL = \int \mu \left(\frac{\partial u}{\partial x} + \frac{\partial \upsilon}{\partial y} \right)^2 dx\, d\,\mathrm{y}$$

where μ indicates the blood viscosity coefficient, which was set as 0.004 Pa·s [23]. The total EL and the averaged EL were summed at each frame. The averaged EL was calculated by

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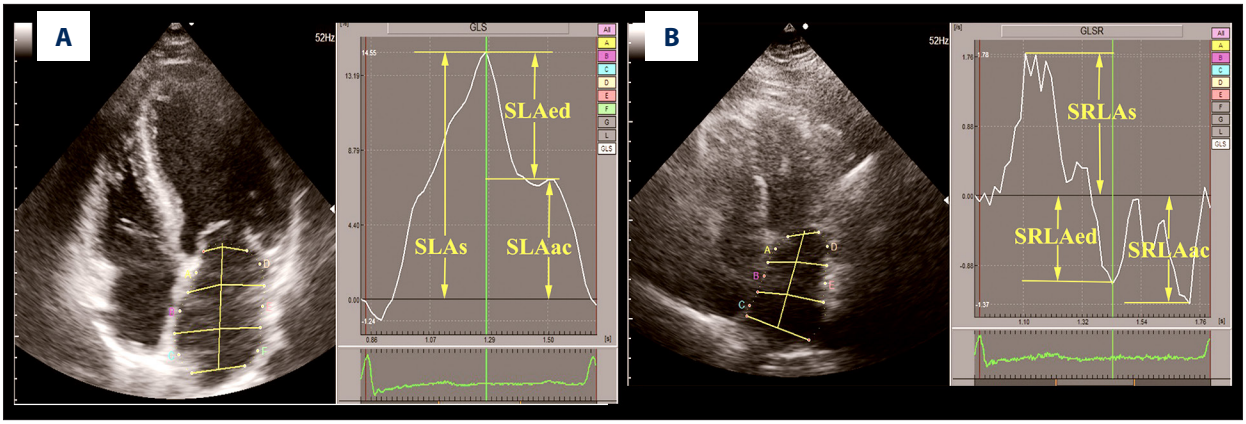

Figure 2. Longitudinal strain (**A**) and strain rate (**B**) of the LA.

dividing the total EL by the number of pixels within the ROI. The following indexes were measured: LA energy loss during systole (LAELs), early diastole (LAELed), and atrial contraction (LAELac).

Analysis of LA strain and strain rate

2DTT analyses were also performed using commercially available software (DAS-RS1, Hitachi Aloka Medical Ltd., Tokyo, Japan). Apical four-chamber and two-chamber images were recorded using conventional 2D grayscale imaging. The frame rate was set to at least 60 frames/second for all subjects. The LA endocardial border was manually delineated, and the software automatically tracked the contours on the other frames. Offline analyses were performed as previously described [4,24]. The software automatically generated curves of the LA globe longitudinal strain and strain rate. The peak systolic strain (SLAs), atrial longitudinal strain during late diastole (SLAac, defined as strain at the onset of the P wave) and early diastole (SLAed, defined as the difference between SLAs and SLAac), and peak LA strain rate during systole (SRLAs), early diastole (SRLAed), and atrial contraction (SRLAac) were obtained from curves in different phases (Figure 2). E/e'/SLAs was calculated as the surrogate for LA stiffness [25].

Reproducibility

Intra- and inter-observer variabilities for LA EL were analyzed repeatedly in 10 randomly selected subjects. The repeated analysis was performed at least 5 days after the initial analysis. To assess intra-observer variability, one observer evaluated the same studies on two separate occasions. For the inter-observer variability evaluation, two independent observers performed analyses separately.

Statistical analysis

Data were analyzed using SPSS version 19.0 (SPSS, Inc., Chicago, IL). All parameters were tested for normal distribution using the Kolmogorov-Smirnov test. Continuous variables were presented as the mean ± standard deviation (SD) and were compared using analysis of equal variance as they showed normal distributions. The differences between categorical variables were analyzed by the χ^2 test. A comparison of echocardiographic parameters between the two groups was performed using Student's *t*-test. Correlations between two parameters were analyzed by Pearson's correlation tests. Stepwise multiple regression was performed to explore the associations of glycemic control with the indexes of LA volume and function. Reproducibility was assessed by Bland-Altman analysis. *P*-values <0.05 were considered statistically significant.

Results

General characteristics

The age, gender distribution, HR, BMI, and TG of the two groups were similar. The BSA, HbA_{1c}, LDL, and TC of the diabetic patients were higher than those of the controls, whereas the HDL levels were lower in patients with diabetes. Although similar results were obtained for blood pressure, both SBP and DBP were within normal ranges (Table 1).

Between-group echocardiographic differences were found in LV diastolic function and LASVa (Table 2). There were no differences in LA volumes and other indexes of LA function.

LA energy loss and mechanics

Briefly, LA EL reached its climaxes at LV systole, early diastole, and atrial contraction (Figure 1). Compared to the controls, the LAELs and LAELed of patients with diabetes were lower (both *P*<0.01) (Table 3, Figure 3). However, the LAELac of diabetic patients was higher than that of the controls (*P*<0.001) (Table 3).

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Table 1. Demographic characteristics and clinical parameters of the study population.

Variable	Controls	DM	*P*
Sex (Male/Female)	22/23	26/21	0.342
Age (y)	49±8	52±7	0.088
BSA (m^2)	1.60±0.14	1.69±0.16	<0.01
BMI (kg/m^2)	23.46±3.02	23.86±3.09	0.534
SBP (mm Hg)	116±12	121±11	0.047
DBP (mm Hg)	71±8	74±6	0.018
HR (beats/min)	72±10	76±10	0.093
HbA_{1c} (%)	4.57±0.75	8.02±1.71	<0.01
TG (mmol/L)	1.50±0.34	1.64±0.53	0.140
HDL (mmol/L)	1.50±0.33	1.21±0.23	<0.01
LDL (mmol/L)	2.94±0.69	3.47±0.77	<0.01
TC (mmol/L)	4.57±0.97	5.88±1.41	<0.01

DM – diabetes mellitus; BSA – body surface area; BMI – body mass index; SBP – systolic blood pressure; DBP – diastolic blood pressure; HR – heart rate; HbA_{1c} – glycated hemoglobin; TG – triglycerides; HDL – high-density lipoprotein; LDL – low-density lipoprotein; TC – total cholesterol.

The SLAs, SLAed, SRLAs, and SRLAed were all lower in diabetic patients than in controls (all $P<0.01$). However, there was no difference in the SLAac ($P=0.393$) and SRLAac ($P=0.200$) between the two groups. As a surrogate of LA stiffness, the E/e'/SLAs of diabetic patients increased significantly ($P<0.001$).

Correlation and multivariate regression analysis

The HbA_{1c} level was strongly correlated with LAELac ($r=0.839$, $P<0.001$); moderately correlated with SRLAs ($r=-0.645$, $P<0.001$), E/e'/SLAs ($r=0.587$, $P<0.001$), A ($r=0.590$, $P<0.001$), e' ($r=-0.508$, $P<0.001$), E/e' ($r=0.534$, $P<0.001$), SLAs ($r=-0.464$, $P<0.001$), and SLAed ($r=-0.451$, $P<0.001$); and weakly correlated with age ($r=0.333$, $P=0.001$), SBP ($r=0.217$, $P=0.038$), DBP ($r=0.215$, $P=0.040$), E/A ($r=-0.386$, $P<0.001$), e'/a' ($r=-0.334$, $P=0.001$), DT ($r=0.318$, $P=0.002$), LAAEF ($r=0.280$, $P=0.007$), LAELs ($r=-0.224$, $P<0.001$), and SRLAed ($r=-0.364$, $P<0.001$) (Figure 4).

The multivariate regression analysis demonstrated that the LAELac (β=0.515, $P<0.001$), SRLAs (β=–0.322, $P<0.001$), LAELs (β=–0.171, $P=0.016$), and DT (β=0.157, $P=0.003$) were independently associated with HbA_{1c} in the whole study population.

Intra- and inter-observer variability

Bland-Altman analysis demonstrated that the LA EL of different phases exhibited good reproducibility (Table 4).

Discussion

This study is the first clinical comparison study of diabetic patients and controls to quantitatively evaluate LA EL using VFM. Our findings suggest that (1) LA EL changes in diabetic patients with normal LA size; (2) LA mechanics were also impaired in subjects with diabetes and normal LA size; and (3) the long-term parameter of glycemic control was correlated with LA energy loss and mechanics.

LA mechanics abnormality in diabetes

Optimal ventricular–arterial interaction is important for efficient cardiovascular performance. LV diastolic dysfunction in patients with diabetes has been well studied in previous studies, and it is considered as one of the earliest signs of diabetic cardiomyopathy [1–3]. To maintain normal cardiac output, LA size and function change in response to pressure or volume overload and have been studied by traditional two-dimensional echocardiography, TDI, and STE [4–7,14,18,26,27]. With advances in the non-invasive evaluation of atrial function, STE is increasingly used to assess LA function, given its relative angle independence and ability to assess global atrial mechanics [9]. LA enlargement and dysfunction have been considered as surrogate markers of the chronicity and severity of diastolic dysfunction. Several studies have shown that strain imaging can detect LA dysfunction before the structural changes. The decrease of LA reservoir and the increase of LA pump functions are the first manifestations of the burden of diastolic dysfunction, appearing before the LA structural changes [7,13,25,28].

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Table 2. Echocardiographic characteristics.

Variable	Controls	DM	*P*
LV (mm)	40±4	42±4	0.180
IVS (mm)	8.91±0.87	8.96±0.91	0.804
LVPW (mm)	8.80±0.81	8.85±0.83	0.767
E (cm/s)	76.76±12.47	73.89±13.42	0.292
A (cm/s)	66.37±13.27	76.70±15.45	<0.01
E/A	1.21±0.31	0.97±0.27	<0.01
e' (cm/s)	13.53±3.30	10.38±2.47	<0.01
a' (cm/s)	11.84±2.60	12.05±2.95	0.722
s' (cm/s)	11.76±1.45	11.19±1.51	0.068
e'/a'	1.12±0.38	0.98±0.22	0.027
E/e'	5.92±1.33	7.37±1.62	<0.01
EF (%)	62.60±4.60	61.46±4.77	0.247
DT (ms)	185.79±32.82	220.21±44.28	<0.01
Tei	0.48±0.06	0.47±0.10	0.628
LAVImax (mL/m^2)	26.39±6.25	26.56±5.59	0.896
LAVImin (mL/m^2)	12.73±3.44	12.53±3.30	0.362
LAVIpre (mL/m^2)	18.45±4.75	19.31±4.29	0.784
LASVt (mL)	15.66±4.06	16.02±3.92	0.670
LASVp (mL)	9.95±3.41	9.24±2.82	0.284
LASVa (mL)	5.72±2.02	6.78±2.89	0.044
LATEF (%)	55.1±7.7	56.1±8.0	0.517
LAPEF (%)	34.9±9.6	32.3±7.9	0.157
LAAEF (%)	30.8±7.4	34.8±11.9	0.059

DM – diabetes mellitus; LV – left ventricle; IVS – interventricular septum; LVPW – left ventricular posterior wall; EF – ejection fraction; DT – deceleration time; LAVImax – maximal left atrial volume index; LAVImin – minimal left atrial volume index; LAVIpre – left atrial volume index before atrial contraction; LASVt – total left atrial stroke volume; LASVp – passive left atrial stroke volume; LASVa – active left atrial stroke volume; LATEF – total left atrial emptying fraction; LAPEF – passive left atrial emptying fraction; LAAEF – active left atrial emptying fraction.

Therefore, the evaluation of LA function in diabetic patients is a key to determine early heart damage of diabetes.

In normal subjects, the LA acts as a reservoir during systole, as a conduit during early diastole, and as an active pump during late diastole [29]. Several studies have showed a reduction in LA reservoir and conduit function in diabetic patients using Doppler-derived LA strain and velocity vector imaging compared with age-matched controls [6,30]. However, most patients included in these studies had LA enlargement. In a study of diabetes patients with normal LA size, researchers found that LA deformation mechanics were also impaired in those patients detected by STE [13]. Similar changes of LA mechanics were found in our study population. The SRLAs mainly reflects LA myocardial relaxation in the longitudinal direction. In addition, the systolic descent of the mitral annulus due to LV contraction, which decreases LA pressure, contributes to LA filling [31,32]. In the present study, LA reservoir (SLAs, SRLAs, and E/e'/SLAs) function and conduit (SLAed and SRLAed) function were impaired in patients with diabetes, while an increase in LA pump function (A) was an important compensatory mechanism that facilitated LA filling.

In addition to LA mechanical change, the volume also tends to increase in patients with diabetes. When LV filling pressure rises, the LA systolic force increases under the mechanism of Frank-Starling and eventually causes LA dilation, increased contractility, and work [33]. Kadappu et al. found that LA enlargement in patients with diabetes is independent of associated hypertension and diastolic function, and it is associated

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Table 3. LA energy loss and mechanical characteristics.

Variable	Controls	DM	*P*
LAELs (N/(m·s))	5.93±1.80	4.93±1.02	<0.01
LAELed (N/(m·s))	4.95±1.68	3.75±1.77	<0.01
LAELac (N/(m·s))	4.67±2.06	8.08±3.20	<0.01
SLAs (%)	38.20±14.79	28.96±5.23	<0.01
SLAed (%)	23.45±11.70	14.54±6.57	<0.01
SLAac (%)	16.31±7.92	14.94±7.36	0.393
SRLAs (s^{-1})	1.93±0.54	1.68±0.32	<0.01
SRLAed (s^{-1})	2.40±1.00	1.76±0.38	<0.01
SRLAac (s^{-1})	1.68±0.68	1.87±0.74	0.200
E/e'/SLAs (%)	0.18±0.09	0.26±0.08	<0.01

DM – diabetes mellitus; LAELs – left atrial energy loss during ventricular systole; LAELed – left atrial energy loss during early diastole; LAELac – left atrial energy loss during atrial contraction; SLAs – left atrial strain during ventricular systole; SLAed – left atrial strain during early diastole; SLAac – left atrial strain during atrial contraction; SRLAs – left atrial strain rate during ventricular systole; SRLAed – left atrial strain rate during early diastole; SRLAac – left atrial strain rate during atrial contraction.

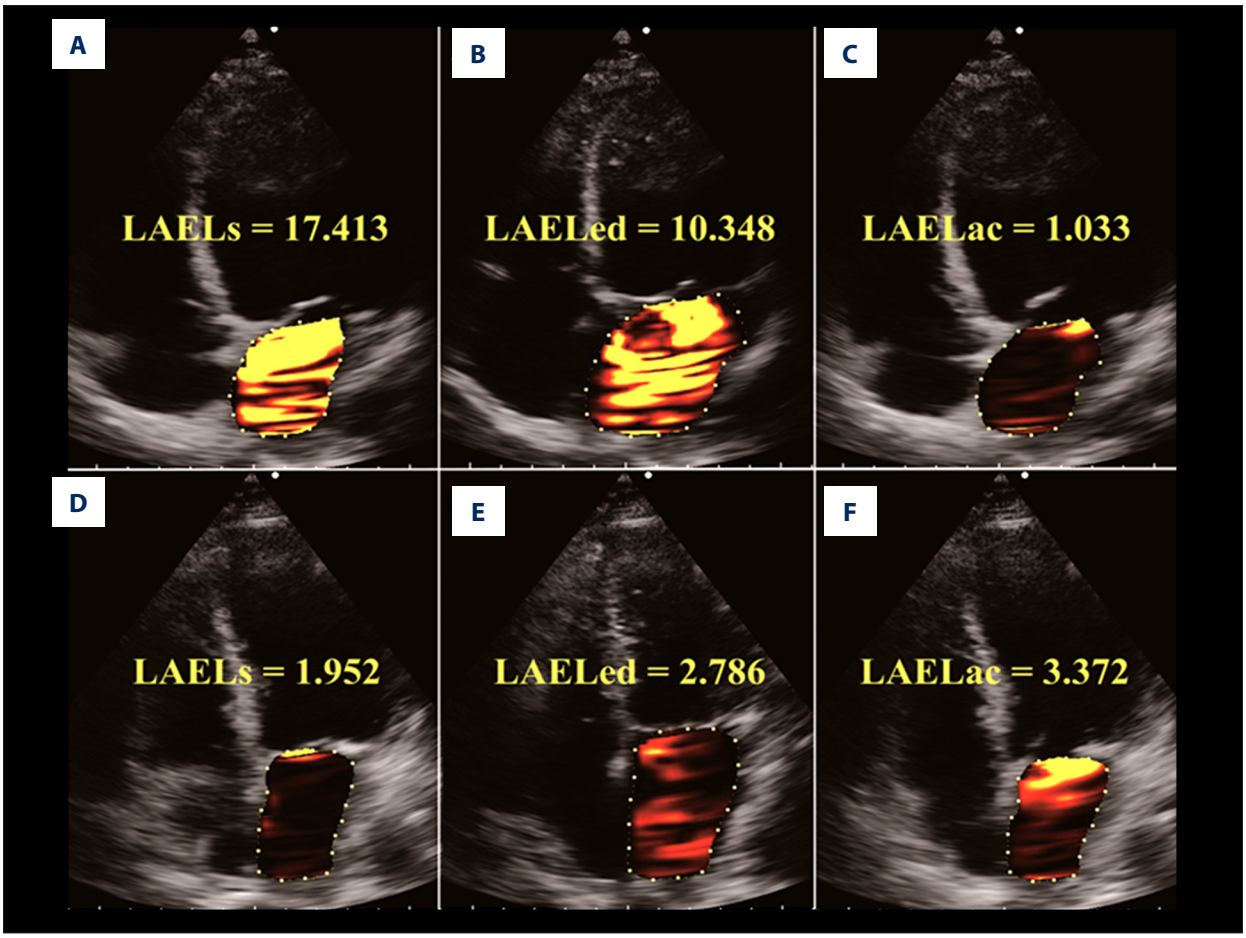

Figure 3. Difference of LA EL between patients with diabetes and controls. (**A–C**) represent controls and (**D–F**) represent diabetic patients. The LAELs and LAELed of the controls were higher than that in patients with diabetes, whereas the LAELac was lower.

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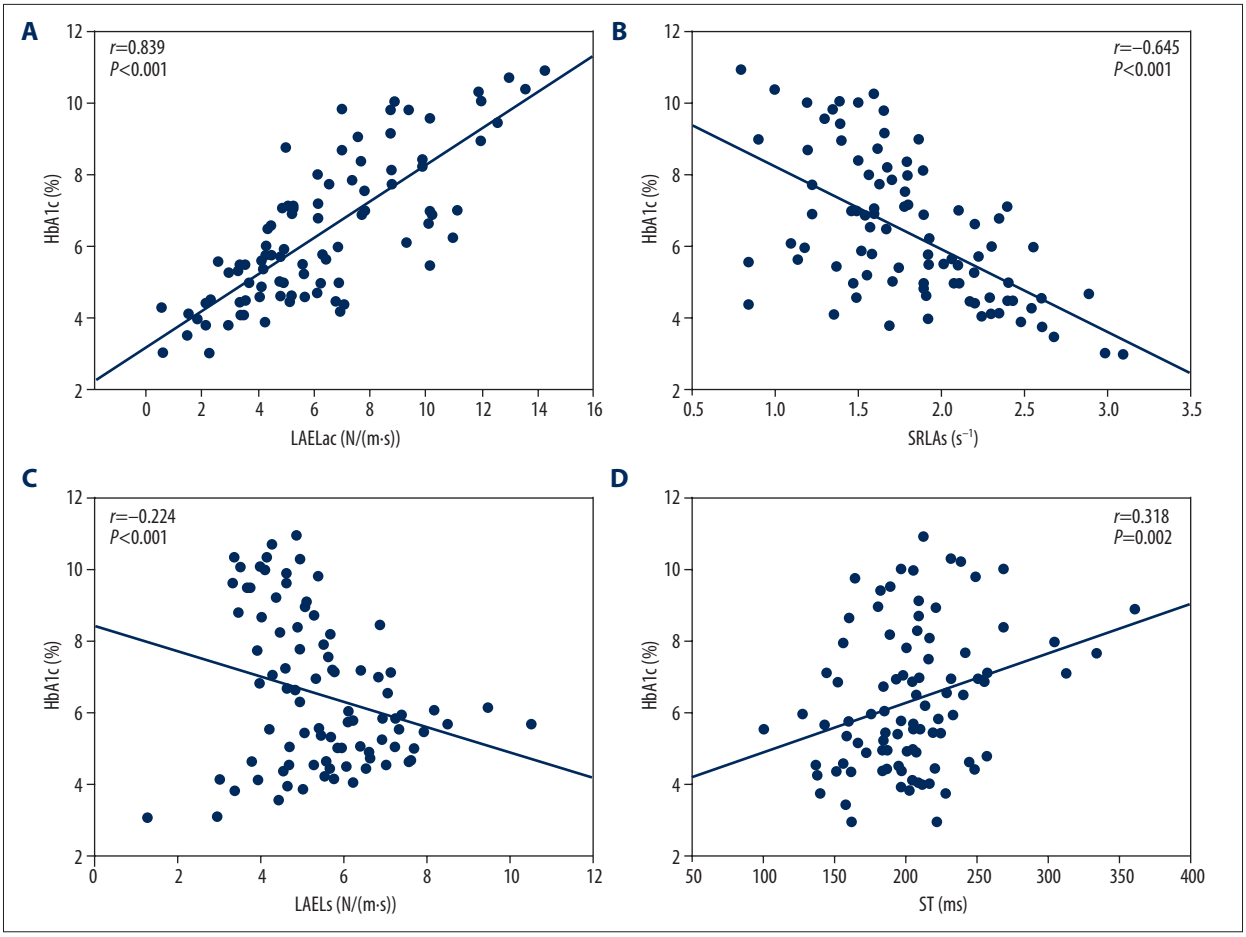

Figure 4. Correlations between HbA_{1c} and LAELac (**A**), SRLAs (**B**), LAELs (**C**), and DT (**D**).

Table 4. Variability of LA EL parameters.

Variable	Bias	ICC	95% LOA
Intra-observer			
LAELs	0.01±0.49	0.96	–0.95 to 0.96
LAELed	0.03±0.58	0.92	–1.10 to 1.17
LAELac	–0.11±0.72	0.84	–1.53 to 1.31
Inter-observer			
LAELs	0.17±0.73	0.93	–1.27 to 1.60
LAELed	–0.11±0.87	0.81	–1.81 to 1.60
LAELac	–0.12±0.65	0.79	–1.38 to 1.15

ICC – interclass correlation coefficient; LOA – limits of agreement; LAELs – left atrial energy loss during ventricular systole; LAELed – left atrial energy loss during early diastole; LAELac – left atrial energy loss during atrial contraction.

with LA dysfunction as evaluated by 2D strain [34]. However, using tissue Doppler-derived strain, Muranaka et al. determined that abnormalities in LA strain were relatively independent of LA dilation [6]. In the present study, the LA size of all subjects was within normal range, while the mechanics of the LA were already impaired. In this regard, our results suggest that LA mechanical dysfunction may precede LA enlargement.

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LA energy loss in diabetes

Another interesting finding in this study is the LA EL change at all three phases. This new parameter, EL, is a flow dynamic parameter that reflects spatial dispersion of intra-atrial blood flow. Previous study with particle image velocimetry suggests that the blood fluid dynamics in LA affords new insights into physiology and distinguishes between various states, suggesting a role in early detection of disease states and responses to therapy [9,35]. The concept of EL derives from the blood flow dynamics. To better understand why the EL differed in the two groups, we must determine what EL really means and how it works in healthy hearts. The energy of blood flow consists of two types of energy: potential energy (generated mainly by the static pressure in a circulatory system) and kinetic energy (generated by the dynamic pressure). Potential energy and kinetic energy can convert to one another [17]. For example, the driving force for early diastolic flow is the atrioventricular pressure gradient. This gradient is created partly by the elastic properties of the ventricle, which allow for the storage of potential energy in the myocardium during systole. The potential energy released during diastole is converted into kinetic energy. However, transmitral turbulent flow results in an irreversible loss of the total fluid energy [17]. Chung and colleagues studied the correlation between EL and the histopathology of an ascending aortic aneurysm and found that EL correlated with imbalances in elastin and collagen composition [36]. Normally, the aorta expands and acts as a capacitor during systole and recoils and returns the stored energy to the circulation during diastole. A greater EL represents greater inefficiency in performing this function and greater energy dissipating into the aortic wall [36]. Agati et al. quantitatively analyzed the intraventricular blood flow dynamics by particle image velocimetry in acute myocardial infarction patients, and their research revealed that the highest energy dissipation was in STEMI (ST-elevation myocardial infarction) patients with preserved global left ventricular function; such increased energy consumption with respect to controls leads to the extra effort needed to maintain adequate pump efficiency [37]. Therefore, inefficiency of blood flow transfer would lead to improper EL.

During LV contraction, LA reservoir function is determined by LA myocardial relaxation and displacement of the mitral annulus [31]. In this study, SLAs and SRLAs decreased in patients with diabetes compared with the controls. In other words, the LA passive enlargement was impaired during the atrial filling phase. LA conduit function is mainly determined by the rate of LA relaxation [38]. The reduced SLAed and SRLAed in this study indicated reduced conduit function in diabetic patients. In view of the above-mentioned facts, reservoir and conduit are more passive functions than active processes. Aside from that, some investigators have demonstrated that LA strain is related to LA structural remodeling and fibrosis of the atrial wall, as assessed by magnetic resonance imaging [39]. In patients with diabetes, the kinetic energy of blood flow converted into potential energy of the atrial wall is far from sufficient due to LA myocardial fibrosis. Thus LAELs and LAELed decreased in diabetic patients, indicating impaired reservoir and conduit function in another way. By contrast, LAELac increased significantly as a compensation for LV filling, while SLAac and SRLAac did not show much difference between the two groups. Therefore, EL is both a measurable consequence of the disease and an indicator of discomfort at the organ level and might be a more effective index to evaluate LA function.

Relationship between glycemic control and LA function

Another question is whether the impairment of LA mechanics and EL in patients with diabetes is only the consequence of structural, deformational, and blood flow dynamical changes or whether these abnormalities are a direct effect of impaired glucose metabolism. In this study, we demonstrated that nearly all changes in LA occur in parallel. In addition, we included the parameters of LA and LV structure, LV function, LA mechanics, and LA EL, and the multivariate regression analysis revealed that LAELac, SRLAs, LAELs, and DT were independently associated with HbA_{1c} in the whole study population, indicating that the long-term parameter of glycemic control has a direct impact on LA energy loss and mechanics.

Study limitations

The present investigation had several limitations. First, the relatively small number of patients represents a limitation. Therefore, our results should be considered as a preliminary suggestion and must be verified in larger and more varied cohorts. Second, dedicated software for LA strain analysis has not been released. We used the current software for LV analysis to study LA strain and strain rate. Further developments may be useful to improve tracking quality of LA mechanics, and to provide a better instrument for the study of LA functions. Third, blood flow passes through the left ventricular cavity without constraint to any single plane or predefined direction; therefore, the necessary tools used should be accurate for measuring blood flow velocity regardless of the direction in three dimensions. The VFM used in this study is based on two-dimensional color Doppler and speckle tracking data, which confines our results to one plane. Multidimensional imaging with high temporal resolution will be needed to completely elucidate the complexity of hemodynamic patterns. Fourth, we did not perform a magnetic resonance imaging evaluation as a gold standard method for measuring LA volumes and ejection fraction. The last, atrial electromechanical delays were not analyzed because the main purpose of this study was to explore the LA mechanics and energy loss. Further studies are needed.

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Conclusions

Our study showed that LA energy loss and deformation mechanics are already impaired in diabetic patients with normal LA size. The long-term parameter of glycemic control (HbA_{1c}) was correlated with LA energy loss and mechanics. Vector flow mapping combined with tissue tracking echocardiography might be a promising tool for the early detection of LA dysfunction caused by impaired glucose metabolism. Further longitudinal analyses are needed to confirm our findings and to investigate the effects of these cardiac changes on the outcomes of diabetes mellitus.

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Conflicts of interest

None.

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