Correlation of Left Ventricular Pressure Changes and Left Atrial Function on Strain Rate Imaging During Acute Left Ventricular Ischemia

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SUMMARY

The objective of the present study was to evaluate whether left ventricular (LV) pressure changes influence left atrial (LA) function during acute LV ischemia by strain rate imaging.

In 11 healthy dogs, the left anterior descending coronary artery was occluded to cause regional acute ischemia. The peak strain rate (PSR) values of the LA walls during the reservoir, conduit, and contractile phases of the LA cycle, as well as the LV pressures, were measured before and after ischemia. All PSR values increased significantly after ischemia ($P < 0.001$). Left ventricular end-diastolic pressure (LVEDP) increased after ischemia ($P < 0.0001$) and its percent change was positively correlated with the LA contractile phase and conduit phase percent changes of PSR for the anterior and lateral walls of the atrium ($r = 0.72$, 0.72, 0.83, and 0.73; $P = 0.05$, 0.05, 0.002, and 0.01, respectively).

LA function is influenced by the change of LVEDP during regional LV ischemia. There is a compensatory increase in wall motion after regional acute LV ischemia. (Int Heart J 2010; 51: 421-425)

Key words: Strain rate imaging, Left ventricular pressure, Left atrial function

The left atrium plays an important role in overall cardiac performance. It variously acts as a contractile chamber during late ventricular diastole, as a reservoir distended by the inflow from the pulmonary veins during ventricular contraction and isovolumic relaxation, and as a conduit during early ventricular diastole.[1,2] Studies of left atrial (LA) morphology by conventional echocardiography with two-dimensional measurements and assessment of LA blood flow by pulsed Doppler examination of mitral inflow or pulmonary venous flow parameters have advanced our understanding of LA function in the normal and diseased heart. However, the major limitation of these techniques is the lack of any direct assessment of atrial mechanical function. Strain rate imaging (SRI) is a new method that allows quantitative assessment of myocardial deformation,[3-5] but there have been few SRI studies of LA wall motion, especially in the diseased heart. Accordingly, this study was performed with SRI to evaluate whether pressure changes in the left ventricle affected LA wall motion after regional acute left ventricular ischemia.

METHODS

Animals: A total of 12 healthy dogs weighing 18-22 kg (mean, 18.12 ± 12.92 kg; 3 females and 9 males) were studied, but 1 died during the experiment because of ventricular fibrillation. All examinations were carried out in accordance with the regulations of the Ethical Committee of Xinjiang Medical University, China.

Surgical preparation and instrumentation: The dogs were anesthetized with alpha-chloralose (100 mg/kg intravenously (IV)), as well as fentanyl (30 mg) and pancuronium (4 mg) as needed, and were ventilated (Bird Mark 7A, USA, 15 mL/kg, 16-20/minute). Each animal was placed in the supine position, and a pericardial cradle was made after midline sternotomy and partial excision of the ribs for epicardial positioning of the ultrasound transducers. Using the standard Judkin's method, an 8F catheter was advanced into the LV cavity. Next, the left ventricular (LV) systolic pressure and left ventricular end-diastolic pressure (LVEDP) were acquired by connecting the catheter to a Medtronic Lifepark 12 monitor. After occlusion of the left anterior descending (LAD) artery for 10 minutes (1) LV apical motion became abnormal and the local myocardium developed cyanosis, (2) the apical and anterior myocardium became dyskinetic on conventional two-dimensional (2-D) images, and (3) the electrocardiogram (ECG) showed ST segment elevation and T wave inversion. Systolic blood pressure and LVEDP were measured at this time. Echocardiography was performed with a GE Vivid 7 scanner (GE Medical Systems, Horton, Norway) equipped with a 3.5 MHz phased-array transducer. Tissue velocity imaging (TVI) data were acquired at a frame rate of more than $100 s^{-1}$ and 15 complete cardiac cycles in the apical 2- and 4-chamber views were collected both at rest (before coronary occlusion) and under ischemic conditions (after 10 minutes of LAD occlusion). The pulse wave (PW) profiles of mitral flow and pulmonary venous flow

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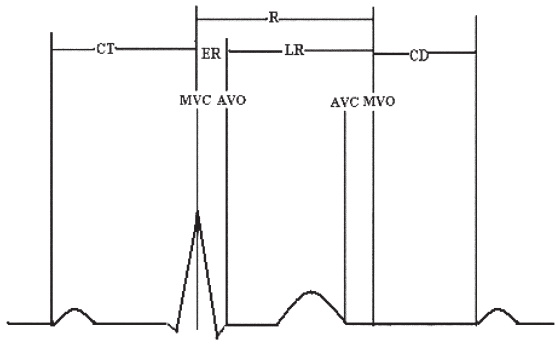

Figure 1. Diagram of the functional phases of left atria.
CT: contractile, R: reservoir, ER: early reservoir, LR: late reservoir, CD: conduit, AOV: aortic valve opening, AVC: aortic valve closure, MVO: mitral valve opening, MVC: mitral valve closure.

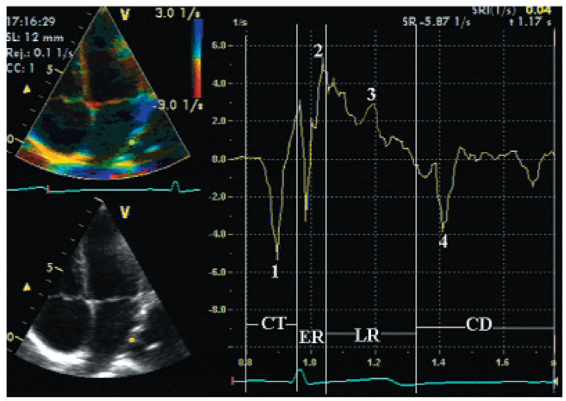

Figure 2. Strain rate curve extracted from the apical 4-chamber view. The CT, R (including ER and LR), and CD phases are shown. Peaks 1, 2, 3, and 4 represent CT-PSR, ER-PSR, LR-PSR, and CD-PSR, respectively.

were also recorded under these two sets of conditions. All data was stored on a magneto-optical disc and then transferred to an Echo PAC workstation for off-line analysis.

Measurement of strain rate (SR) parameters: Aligned with the PW profiles of transmitral flow and ECG,[6] the parts of the LA cycle were defined as follows: the LA contractile period (CT) was defined as the A-wave duration from the onset of the P wave to the R wave peak on the ECG, the LA reservoir period (R) was the interval between mitral valve closure (MVC) and mitral valve opening (MVO) corresponding to the interval from the R wave peak to the end of the T wave on the ECG, and the LA conduit period (CD) was the interval between MVO and the onset of the A wave. During the LA reservoir period, the following LV events occur: the isovolumic contraction (IVC) phase between MVC and aortic valve opening (AVO), the LV ejection (E) phase between AVO and aortic valve closure (AVC), and the isovolumic relaxation (IVR) phase between AVC and MVO. Accordingly, the R period was divided into an early reservoir period (E*R* = isovolumic contraction) and a late reservoir period (L*R* = LV ejection + IVR) (Figure 1).

Longitudinal LA wall deformation was assessed by measuring the mid-segment peak strain rate (PSR) values during the CT (CT-PSR), ER (ER-PSR), LR (LR-PSR), and CD (CD-PSR) periods (Figure 2). The apical 4-chamber view was used to assess the lateral wall and the 2-chamber view was used to assess the anterior and inferior walls. Interatrial deformation was not assessed because it is influenced by both fibrous and muscular tissue, and radial deformation of the LA walls could not be calculated because of limited spatial resolution.[3] All data were averaged over 3 consecutive cycles.

Reproducibility: Intraobserver and interobserver variability were assessed separately for each of the SR indices by using 6 data sets that were randomly selected and analyzed. For the assessment of intraobserver variability, analyses were repeated twice by the same observer within 1 week. To assess the interobserver variability, a second independent observer repeated the same analyses.

Acquisition of LA function data: Simpson's method[7-9] was used to calculate the following indices: (1) preatrial contraction LA volume (VpreA) measured at the onset of the P wave on the ECG; (2) minimum LA volume (Vmin) measured at mitral valve closure; and (3) maximum LA volume (Vmax) measured just before mitral valve opening. For assessment of LA function, 3 indicators were derived from the volume data as follows.[10-12] (1) The LA active emptying fraction (LAAEF)=(VpreA-LVmin)/VpreAV100. (2) The LA expansion index (LAEI)=(Vmax-LVmin)/VminV100. (3) The LA passive emptying fraction (LAPEF)=(VmaxL-VpreA)/VmaxV100. LV systolic function was assessed by measuring the LV ejection fraction (LVEF) according to Simpson's method.

Myocardial staining:[13-15] After the LAD was ligated and the aorta was occluded, 2 mL of Evans blue was injected into the femoral artery to define the ischemic region. Ischemic tissue was not stained, while the nonischemic region was stained blue. After 30 seconds, each dog was sacrificed by injection of 10% KCl and the heart was removed, washed free of blood with saline, and then frozen at -80°C. After 30 minutes, the heart was cut along the LV long axis from the apex to the mitral orifice. Next, the heart was cut into 1-cm slices corresponding to the cross-sectional planes of the echocardiographic images and the slices were incubated in 2,3,5-TTC solution at 37°C for 30 minutes. After TTC staining, the ischemic myocardium appeared brick-red, nonischemic myocardium appeared blue from Evans blue staining, and infarcted myocardium showed no staining (no infarcted areas were found in this experiment).

Statistical analysis: Results are presented as the mean ± standard deviation. The paired *t*-test was used to compare PSR values before and after ischemia. Pearson's correlation coefficient analysis was used to measure the strength of the association between the PSR values and pressure or LVEF. For all indices used in the correlation study, the percent change was calculated as follows: preischemic value - postischemic value/preischemic value × 100%. PSR values of the mid-segment LA wall were correlated with pressure and LVEF parameters. Estimation of intraobserver and interobserver reproducibility was performed by Bland-Altman analysis. Probability (*P*) values < 0.05 were considered to indicate statistical significance.

RESULTS

ECG and TTC staining: The ECG findings and TTC staining revealed that the anterior wall of the LV was ischemic after 10 minutes of LAD ligation in all 11 dogs, with the ischemic region being brick-red and the normal region gray-blue as shown in Figure 3.

Changes of indexes: Compared with the values before ischemia, the left ventricular end-diastolic pressure (LVEDP), left ventricular ejection fraction (LVEF), S peak and D peak values of pulmonary venous flow, Vmax, Vmin, Vpre, and LAEI of the LA were all increased after ischemia while the E/A ratio of mitral flow was decreased (Table I).

Figure 3. TTC staining of a canine heart after ischemia. Ischemic myocardium is brick-red and nonischemic myocardium is gray-blue.

Table I. Comparison of Indexes at Baseline and After Ischemia

Index	Baseline	Ischemia
Vmax (mL)	7.19 ± 1.34	9.19 ± 0.92■
Vmin (mL)	3.98 ± 1.05	5.5 ± 0.92■
Vpre (mL)	6.04 ± 1.27	8.06 ± 1.27■
LA AEF (%)	33.35 ± 13.05	30.89 ± 7.46
LA PEF (%)	15.42 ± 8.09	12.66 ± 6.46
LAEI (%)	53.05 ± 18.93	68.37 ± 17.21▲
Emax (m/s)	0.57 ± 0.11	0.55 ± 0.11
Amax (m/s)	0.46 ± 0.22	0.49 ± 0.15
E/A	1.41 ± 0.37	1.2 ± 0.35▲
DT (m/s^2)	145.12 ± 38.32	129.67 ± 19.84
Smax (m/s)	0.46 ± 0.08	0.52 ± 0.09★
Dmax (m/s)	0.38 ± 0.06	0.42 ± 0.07★
LVEF (%)	48.65 ± 9.36	25.49 ± 10.23■
LVEDP (mmHg)	7.18 ± 2.27	13.73 ± 2.41■
SBP (mmHg)	107.09 ± 46.46	115.36 ± 40.97

Vmax indicates maximum LA volume; Vmin, minimum LA volume; Vpre, preatrial contraction LA volume; LA AEF, LA active emptying fraction; LA PEF, LA passive emptying fraction; LAEI, LA expansion index; Emax, the E wave peak of mitral flow; Amax, the A wave peak of mitral flow; DT, deceleration time of the mitral E wave; Smax, S wave peak of pulmonary venous flow; Dmax, D wave peak of pulmonary venous flow; LVEF, left ventricular ejection fraction; LVEDP, left ventricular end-diastolic pressure; SBP, systolic blood pressure; and ★, ▲, and ■, $P < 0.01$, $P < 0.001$, and $P < 0.0001$ versus baseline, respectively.

Table II. Comparison of Indices for Each Wall Between Baseline and Ischemia

Index	Baseline	Ischemia
Anterior		
CT-PSR (s^{-1})	-2.26 ± 0.81	-3.27 ± 0.64■
PSR-ER (s^{-1})	2.12 ± 0.79	2.94 ± 0.64■
PSR-LR (s^{-1})	1.63 ± 0.70	2.22 ± 0.49▲
CD-PSR (s^{-1})	-1.62 ± 0.57	-2.62 ± 0.74■
Lateral		
CT-PSR (s^{-1})	-1.41 ± 0.40	-2.17 ± 0.44■
PSR-ER (s^{-1})	1.54 ± 0.49	2.46 ± 0.95■
PSR-LR (s^{-1})	1.27 ± 0.30	1.77 ± 0.50■
CD-PSR (s^{-1})	-1.03 ± 0.34	-1.84 ± 0.54■
Inferior		
CT-PSR (s^{-1})	-1.74 ± 0.31	-2.63 ± 0.63■
PSR-ER (s^{-1})	2.20 ± 0.79	2.79 ± 0.49▲
PSR-LR (s^{-1})	1.58 ± 0.55	2.37 ± 0.55■
CD-PSR (s^{-1})	-1.52 ± 0.57	-2.57 ± 0.63■

CT-PSR indicates peak strain rate of the LA contractile phase; PSR-ER, peak strain rate of the early reservoir phase; PSR-LR, peak strain rate of the late reservoir phase; CD-PSR, peak strain rate of the conduit phase; and ▲ and ■, $P < 0.001$ and $P < 0.0001$ versus baseline, respectively.

Table III. Reproducibility of SRI Indexes of Longitudinal LA Wall Deformation at Baseline

Index	Intraobserver			Interobserver		
	Mean	95%CI	(%)	Mean	95%CI	(%)
Anterior						
CT-PSR (s^{-1})	-2.49	± 0.21	8.43	-2.55	± 0.24	9.41
PSR-ER (s^{-1})	2.39	± 0.19	7.95	2.46	± 0.17	6.91
Lateral						
PSR-LR (s^{-1})	1.56	± 0.15	9.62	1.60	± 0.17	10.6
CD-PSR (s^{-1})	-1.12	± 0.11	9.8	-1.69	± 0.13	7.69
Inferior						
CT-PSR (s^{-1})	-1.77	± 0.18	10.17	-1.88	± 0.16	8.51
CD-PSR (s^{-1})	-1.60	± 0.14	8.8	-1.70	± 0.16	9.41

CT-PSR indicates peak strain rate of the LA contractile phase; PSR-ER, peak strain rate of the early reservoir phase; PSR-LR, peak strain rate of the late reservoir phase; and CD-PSR, peak strain rate of the conduit phase.

Table IV. Reproducibility of SRI Indexes of Longitudinal LA Wall Deformation After Ischemia

Index	Intraobserver			Interobserver		
	Mean	95%CI	(%)	Mean	95%CI	(%)
Anterior						
CT-PSR (s^{-1})	-3.31	± 0.32	9.7	-3.52	± 0.40	11.4
PSR-ER (s^{-1})	3.01	± 0.33	10.96	3.14	± 0.38	12.1
Lateral						
PSR-LR (s^{-1})	1.81	± 0.19	10.49	1.90	± 0.16	8.42
CD-PSR (s^{-1})	-2.02	± 0.16	7.92	-2.04	± 0.15	7.35
Inferior						
CT-PSR (s^{-1})	-2.59	± 0.21	8.11	-2.77	± 0.26	9.39
CD-PSR (s^{-1})	-2.55	± 0.16	6.27	-2.72	± 0.23	8.46

CT-PSR indicates peak strain rate of the LA contractile phase; PSR-ER, peak strain rate of the early reservoir phase; PSR-LR, peak strain rate of the late reservoir phase; and CD-PSR, peak strain rate of the conduit phase.

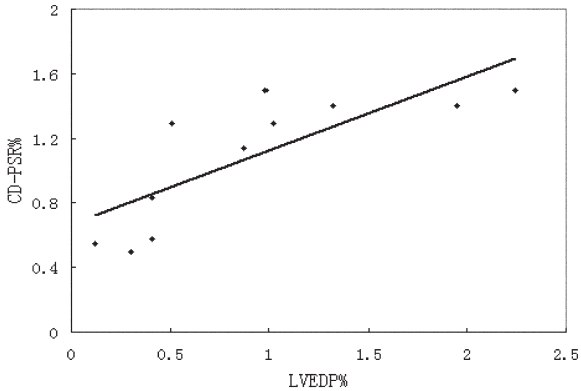

Figure 4a. Correlation between the change of the peak strain rate (PSR%) and the change of left ventricular ejection fraction (LVEF%).

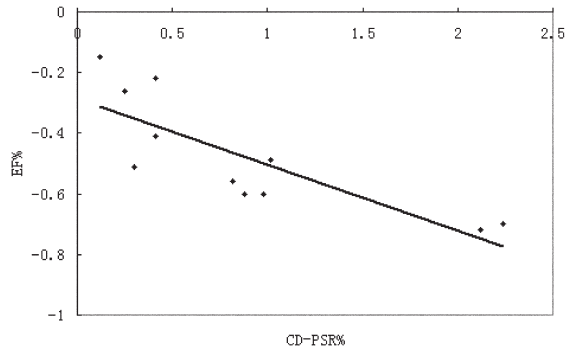

Figure 4b. Correlation between the change of the peak strain rate (PSR%) and the change of left ventricular end-diastolic pressure (LVEDP%).

Comparison of segments before and after ischemia: After ischemia, all SR values of the segments were increased compared with baseline (Table II).

Observer variability of SR parameters: Tables III and IV show the intraobserver and interobserver variability for each parameter under two different conditions. There was good intra- and interobserver agreement for assessment of LA deformation by SR parameters. The variability was generally between 6% and 10%.

Correlations: Left ventricular end diastolic pressure (LVEDP) increased after ischemia ($P < 0.0001$) and its percent change (LVEDP%) showed a positive correlation with the percent change of CT-PSR (CT-PSR%) or CD-PSR (CD-PSR%) (Figure 4a) for the anterior and lateral wall, respectively ($r = 0.72$, 0.72, 0.83, and 0.73; $P = 0.05$, 0.05, 0.002, and 0.01, respectively).

LVEF decreased ($P < 0.05$) and its percent change (LVEF%) was negatively correlated with the change of CD-PSR (CD-PSR%) (Figure 4b) for the anterior and lateral wall, respectively ($r = 0.81$ and 0.80; $P = 0.003$ and 0.003, respectively).

Discussion

SRI can be used for the quantification of regional LV wall motion by measuring the strain rate (SR) and strain values, and this method has attracted extensive attention in relation to the evaluation of LV function.[16] Sirbu[6]studied the left atrium of normal subjects using SRI and demonstrated the feasibility of calculating strain and SR values for the assessment of regional LA deformation.

Our present results also demonstrated that SRI can be used for the quantification of longitudinal myocardial LA deformation in normal and diseased hearts. The reproducibility of SRI measurements was good, with the interobserver and intraobserver variability of SR indicators of LA wall motion being comparable to that for LV indicators.[17] Thus, SRI can be used for the assessment of regional atrial wall motion.

In this study, we compared the PSR of the LA walls before and after ischemia. We found that PSR was increased during all 3 parts of the LA cycle and that the percent change of PSR (PSR%) was positively correlated with LVEDP% during the CT and CD periods. This may represent compensation by the LA when the LV is affected by ischemia because it was previously demonstrated that stretching of the atrial wall depends on the intra-atrial pressure.[18] The effect of the Frank-Starling law on the atrium manifests as a biphasic increase of the contractile force after an increase of wall stretch.[18] During the CD period, blood that enters the LA chamber from the pulmonary veins passively flows through into the dilating LV, while the atrium contracts to push blood into the left ventricle during the CT phase.[19,20] After LV ischemia leads to an increase of LVEDP (demonstrated in this study) and a decrease of LV compliance (decreased E/A ratio), the Frank-Starling mechanism will act on the atrium during the CD and CT phases, leading to increased deformation of the LA walls to maintain normal LV filling despite an increase of the trans-mitral pressure gradient and LA afterload. The increase of SR indexes during the CT phase is in accordance with a previous report that atrial contractility increases during acute ischemia.[21-23] Our correlation study showed that PSR% of the LA walls was negatively correlated with LVEF% during the CD phase, suggesting that LA wall motion was altered to compensate for a higher LVEDV during the LV filling because LVEF was decreased by ischemia, so that LV stroke volume was maintained despite the decrease of LVEF.[24]

The parameters Vmax, Vmin, Vpre and LAEI, LAAEF, and LAPEF describe the volume and functional characteristics of the left atrium during the R, CT, and CD phases of the LA cycle, respectively.[25] Sirbu[6] studied the left atrium in normal subjects by SRI and found that LAEI, LAAEF, and LAPEF were correlated with R - Tε, CT -Tε, and CD - Tε of the LA walls, respectively. In our study, we failed to find these correlations, but Vmax, Vmin, and Vpre increased after ischemia, indicating that an increase of LA wall motion compensated for the augmented LA volume during the 3 phases of the cycle. The increase of LAEI also suggested that LA function during the R phase was partially affected by regional LV ischemia.

Limitations: This study only employed a small number of animals. In addition, radial LA wall deformation could not be analyzed because of the limited spatial resolution of the current SRI technique and the very thin LA wall of the dogs. Furthermore, assessment of LA functional parameters and volumes by this noninvasive method is still limited by the need for subjec-

tive LA endocardial border tracing, which could also influence our findings.

Conclusion: Quantification of longitudinal LA wall deformation by SRI indicates that LA wall function is affected by regional LV ischemia, especially changes of LVEDP and LVEF. SRI can be a useful noninvasive technique for assessing LA mechanics that may help us to better understand the pathophysiological processes of heart disease.

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