

Comparison of Left Ventricular Contractility in Pressure and Volume Overload: A Strain Rate Study in the Clinical Model of Aortic Stenosis and Regurgitation

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Objective: The aim of this study is to compare the impact of two different loading conditions on myocardial contractility in asymptomatic patients with normal EF by using strain rate imaging (SRI). **Methods:** A total of 27 patients with severe aortic regurgitation (mean age 50 ± 11 years) and 25 patients with severe aortic stenosis (mean age 53 ± 15 years) were prospectively recruited. Fifteen healthy subjects (mean age 50 ± 6 years) were enrolled as the control group. For the evaluation myocardial contractility, longitudinal LV function was chosen and, midventricular segment shortening was analyzed for the septum, LV lateral wall from apical four-chamber view and for the anterior, inferior wall from apical two-chamber view. **Results:** Longitudinal peak systolic strain rate values of each segment derived from analysis of a total of 804 segments were significantly decreased in the patients population ($P < 0.001$). Global longitudinal peak systolic strain rate was also significantly decreased in aortic stenosis and regurgitation compared to the control group (-1 ± 0.5 , -0.9 ± 0.3 , and -1.6 ± 0.3 , $P = 0.001$). As far as the comparison between patients with aortic stenosis and aortic regurgitation, neither global strain rate nor strain rate for each wall was found to be different. **Conclusion:** We conclude that longitudinal LV function is reduced in both pressure and volume overload, and both of this overload patterns are equally harmful to the ventricle. (Echocardiography 2010;27:798-802)

Key words: aortic valvular disease, left ventricular function, strain rate

Pressure overload hypertrophy occurs in aortic stenosis (AS). Concentric hypertrophy, which consists of the addition of sarcomers in parallel and an increase in myocyte cross-sectional area, is the remodeling pattern in pressure overload. Chronic pressure overload typically results in increased wall thickness to normalize systolic wall stress with a normal chamber size.¹ In contrast, in volume overload hypertrophy such as aortic regurgitation (AR), increased diastolic wall stress leads to an increase in myocyte length with the addition of sarcomers in series, thereby engendering increased LV dilation so called eccentric hypertrophy.² In chronic AR, LV systolic function is maintained through chamber dilation and hypertrophy which also returns end diastolic wall stress to normal levels.¹

Several investigators^{3,4} have suggested that chronic volume overload is especially more harmful to the ventricle, because an increased end-diastolic and end-systolic wall stress is already present in the compensated phase of chronic regurgitation. In a different study, in the presence of normal contractility, myocardial stiffness and diastolic function were relatively more deteriorated in patients with aortic regurgitation than in patients with aortic stenosis.⁵ Different type of overload is leading to a different type of hypertrophy. Is it really possible that one type is more harmful than the other regarding myocardial contractile function? The novelty of this is to investigate this issue by a direct comparison between the two loading conditions.

Although there are only few data, we know that an early deterioration occurs in LV systolic function preceding reduced EF in asymptomatic patients with severe aortic regurgitation and aortic stenosis.^{6,7} Ejection fraction (EF) is the widely accepted and utilized method to demonstrate left ventricular (LV) dysfunction in these patient populations.⁸ However, this parameter is affected by loading conditions. Therefore, the aim of this

Conflict of interest: All authors explicitly declare that this study has no conflict of interest, any financial or other relationships.

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study is to compare the impact of two different loading conditions on myocardial contractility in asymptomatic patients with normal EF by using strain rate imaging (SRI), which describes myocardial deformation and is a less load dependent marker of myocardial contractility.⁹

Materials and Methods:

Study Population:

A total of 27 patients with severe aortic regurgitation (mean age 50 ± 11 years) and 25 patients with severe aortic stenosis (mean age 53 ± 15 years) were prospectively recruited. Fifteen healthy subjects (mean age 50 ± 6 years) were enrolled as the control group. The patients had to be in New York Heart Association functional class 1, to be in sinus rhythm, and to have normal LV function (LVEF > 50%). While severe AR was defined by echocardiographic criteria as jet area/LV outflow tract area >40%; vena contracta >0.6 cm), subjects with severe AS had an aortic valve area <0.7 cm² calculated according to continuity equation by echocardiography. Patients having additional significant valvular stenosis, regurgitations of other valves of more than mild degree, known or suspected coronary artery disease, LV wall motion abnormalities, intracardiac and/or extra cardiac shunts, all symptomatic patients having chest pain and/or dyspnea and patients with equivocal symptoms were excluded. Patients with hypertension and diabetes were also excluded. The study was approved by the local ethical committee and all patients gave written consent.

Echocardiography:

Two-dimensional and Doppler echocardiography: Using pulsed-wave Doppler, mitral and aortic flow velocities, deceleration time (DT) and isovolumetric relaxation time (IVRT) were measured. LV diameter and wall thickness were measured from the two-dimensional targeted M-mode echocardiographic tracings in the parasternal long axis, according to the criteria of the American Society of Echocardiography.¹⁰ LVEF at rest were computed from two- and four-chamber views, using a modified Simpson's biplane method. Mean ventricular wall thickness was also calculated.¹⁰ Each representative value was obtained from the average of three measurements. Myocardial velocities were recorded using a standard pulse-wave Doppler technique. The sample volume was placed at the junction of the LV wall with the mitral annulus of the lateral myocardial segments from the 4-chamber view. The basal lateral segment was used for early diastolic velocity (Em) and late diastolic ve-

locity (Am). Peak systolic velocity (Sm) was also measured.

Strain and strain rate imaging and data analysis:

Myocardial velocities were recorded by using color tissue Doppler to record low-velocity, high-intensity myocardial signals at a high frame rate 200 (per sec), giving a temporal resolution of 8 ms. The imaging angle was adjusted to ensure a parallel alignment of the beam with the myocardial segment of interest. Images were gathered with a standard ultrasound machine (Vivid 7, GE Vingmed) with a 2.5-MHz, phased-array probe. Sampling in the midmyocardial layer was performed in each segment and maintained at the same position during the cardiac cycle by manually tracking wall motion, but data were excluded if we were unable to obtain a smooth strain curve or the angle between the scan-line and wall was >20°. Images were obtained at each stage, taking care to align the ventricular walls with the ultrasound beam and to obtain the image during breath-hold if possible. At least three cardiac cycles were captured and stored digitally.

For the evaluation myocardial contractility, longitudinal LV function was chosen and, midventricular segment shortening was analyzed for the septum, LV lateral wall from apical four-chamber view and for the anterior, inferior wall from apical two-chamber view.¹¹ For each ventricular wall (septal, lateral, inferior, and anterior) curved "M-mode" lines were drawn, dividing into three myocardial segments (basal, mid, and apical). A total of $4 \times 3 = 12$ segments were analyzed. Three consecutive measurements were taken for each segment (basal, mid, and apical), and the averages were accepted as the value of the concerned segment. The average of the three segments was accepted as the strain and strain rate value of the concerned wall. Longitudinal global strain and strain rate were also calculated as the average of four LV walls (inferior, anterior, septum, and lateral).

One investigator, who was unaware of the patients' clinical status, analyzed all data from all ultrasound examination.

Feasibility and observer variability of strain and strain rate data:

We acquired images of 804 segments (12 segments \times 67 patients). Finally, strain and strain rate analysis was possible 93.3% and 91.7% of segments, respectively.

The interobserver variability was assessed by analyzing eight randomly chosen strain rate images. These images were analyzed by two independent investigators. For intraobserver variability similar dataset from eight subjects were analyzed twice by one of the investigators. The

TABLE I

Basal Characteristics in Study Groups

Variables	AS (n = 27)	AR (n = 25)	Control (n = 15)	P
Age (years)	53 ± 15	50 ± 11	50 ± 6	0.605
Sex (female/male)	12/15	11/14	6/9	0.809
Body surface area (kg/m ²)	1.77 ± 0.18	1.76 ± 0.21	1.71 ± 0.17	0.714
Total cholesterol	196.93 ± 41.70	194.38 ± 34.80	191.20 ± 32.12	0.856
Triglyceride	137.13 ± 40.76	131.45 ± 42.34	126.25 ± 48.04	0.673
Fasting plasma glucose (mg/dL)	98.14 ± 7.60	99.53 ± 6.42	97.78 ± 7.48	0.959
Systolic blood pressure (mmHg)	127.28 ± 6.49	126.06 ± 12.84	123.86 ± 10.20	0.643
Diastolic blood pressure (mmHg)	75.86 ± 7.62	61.21 ± 9.69*	73.26 ± 6.62	0.001

intraobserver and interobserver variabilities (in percentage of the mean) averaged $11 \pm 4\%$ and $15 \pm 6\%$ for strain and strain rate, respectively. The coefficient of correlation (r) for the peak systolic strain and strain rate were 0.83 ($P = 0.0001$) and 0.85 ($P < 0.0001$), respectively.

Statistical analysis: Continuous variables were presented as mean \pm standard deviation. The prevalence of categorical variables was given. Student t-test, chi-square tests, and one-way ANOVA were used for comparison of variables. SPSS for Windows version 10.0 (Chicago, IL, USA) was used for statistical analysis. The level for significance was accepted as $P < 0.05$.

Results:

Baseline characteristics of the study and control group are presented in Table I. There was no significant difference among groups regarding age, sex, biochemical parameters, body surface area (BSA), and systolic blood pressure. However,

diastolic blood pressure was significantly lower ($P = 0.01$) in patients with severe AR compared to those two other groups as expected.

Among standard echocardiographic parameters (Table II), left ventricular global systolic functions analyzed by modified Simpson were not different among groups. While left ventricular diastolic and left ventricular systolic diameters were greater in patients with AR, mean left ventricular wall thickness was increased and deceleration time, isovolumetric relaxation time was prolonged in patients with AS. There were no difference among the groups regarding tissue Doppler velocity parameters (Table II).

Longitudinal strain values in the hemodynamic overloaded patients were lower than the control group (Table III, Figure 1). Longitudinal global strain values in pressure overload, volume overload and in the control group were determined as 17 ± 7 , 12 ± 5 , and 21 ± 6 , respectively, ($P < 0.001$) (Table III).

TABLE II

Two-Dimensional and Lateral Wall Tissue Doppler Diastolic Echocardiographic Data in Groups

Variables	AS	AR	Control	P
Heart rate (per min)	72.31 ± 9.91	74.16 ± 8.18	72.85 ± 8.16	0.265
Left ventricular diastolic diameter (mm)	45.99 ± 6.45	62.35 ± 6.57	47.28 ± 3.70	≤0.001
Left ventricular systolic diameter (mm)	27.32 ± 5.54	42.00 ± 5.34	29.62 ± 2.30	≤0.001
Interventricular septum diastolic thickness (mm)	15.11 ± 2.38	9.68 ± 2.51	8.14 ± 1.35	<0.001
Posterior wall diastolic thickness (mm)	13.02 ± 2.78	10.89 ± 1.67	8.28 ± 1.27	<0.001
Mean left ventricular wall thickness (mm)	15.34 ± 3.18	11.00 ± 1.16	9.4 ± 1.03	<0.001
Left ventricular mass index (body surface area, gm/m ²)	159.77 ± 30.23	137.45 ± 22.54	81.74 ± 21.32	0.02
E velocity (cm/sn)	8.37 ± 1.47	8.72 ± 1.63	9.53 ± 1.71	0.247
A velocity (cm/sn)	9.19 ± 3.93	7.79 ± 3.29	6.21 ± 1.29	0.032
IVRT (isovolumetric relaxation time)	100.02 ± 20.48	78.57 ± 18.63	86.13 ± 14.07	0.007
Left atrium (cm)	38.50 ± 6.11	35.86 ± 9.61	35.68 ± 3.72	0.108
DT (msn) (Deceleration time)	245.74 ± 79.40	149.71 ± 35.08	170.01 ± 28.67	<0.001
Sm	7.64 ± 4.14	7.76 ± 5.13	10.64 ± 2.95	0.916
Lateral wall Em (cm/sn)	7.76 ± 5.13	7.64 ± 4.14	10.64 ± 2.94	0.897
Lateral wall Am (cm/sn)	8.06 ± 2.11	8.13 ± 2.67	7.64 ± 2.65	0.925
Ejection fraction (modified Simpson)	67.19 ± 6.89	63.84 ± 7.5	65.20 ± 3.29	0.342

TABLE III

Strain and Strain Rate in Groups

Wall	Variables	AS	AR	Control
Septum (longitudinal)	S (%)	13 ± 7	15 ± 9*	25 ± 8**
	Strain rate S (1/s)	-0.7 ± 0.4	-1 ± 0.4*	-1.4 ± 0.2**
Lateral (longitudinal)	S (%)	13 ± 7	11 ± 7*	28 ± 6**
	Strain rate S (1/s)	-0.9 ± 0.4	-0.9 ± 0.4*	-1.6 ± 0.3**
Anterior (longitudinal)	S (%)	15 ± 7	12 ± 5*	30 ± 6**
	Strain rate S (1/s)	-0.9 ± 0.3	-0.9 ± 0.4*	-1.5 ± 0.2**
Inferior (longitudinal)	S (%)	13 ± 5	13 ± 4*	29 ± 6**
	Strain rate S (1/s)	-1 ± 0.6	-0.9 ± 0.4*	-1.9 ± 0.3**
Global	S (%)	17 ± 7	12 ± 5*	21 ± 6**
	Strain rate S (1/s)	-1 ± .5	-0.9 ± 0.3*	-1.6 ± 0.3**

*P is nonsignificant between the comparison of AR and AS patients.

**P ≤ 0.001 in all study groups.

Longitudinal peak systolic strain rate values of each segment derived from analysis of a total of 804 segments were significantly decreased for both aortic stenosis and regurgitation groups (P < 0.001) (Table III, Figure 2). Global longitudinal peak systolic strain rate was also significantly decreased in aortic stenosis and regurgitation compared to the control group (-1 ± 0.5, -0.9 ± 0.3, and -1.6 ± 0.3, P = 0.001) (Figure 2).

As far as the comparison between patients with aortic stenosis and aortic regurgitation, neither global strain rate nor strain rate for each wall was found to be different (Table III).

Discussion:

Pressure overload and volume overload results in two different types of remodeling. The expectation of the study was that one kind of hypertrophy

might deteriorate the ventricular function more than the other. As a result, although ventricular function was affected in the patients group compared to control group, there was no difference in terms of longitudinal function between two types of different remodeling.

Our results were in accordance with the studies, which indicated that longitudinal LV function is impaired in patients with severe AR.^{6,12} In a different study⁷ it has been noticed that there is an early abnormality of longitudinal strain rate in aortic stenosis. Our results indicated the same longitudinal dysfunction compared to the control group. Indeed, the deterioration of contractility begins in a very early stage in pressure and volume overload, and the damage is already present at the stage of severe aortic stenosis and regurgitation regardless of the patients symptoms (P < 0.001). In other words, whether it is severe

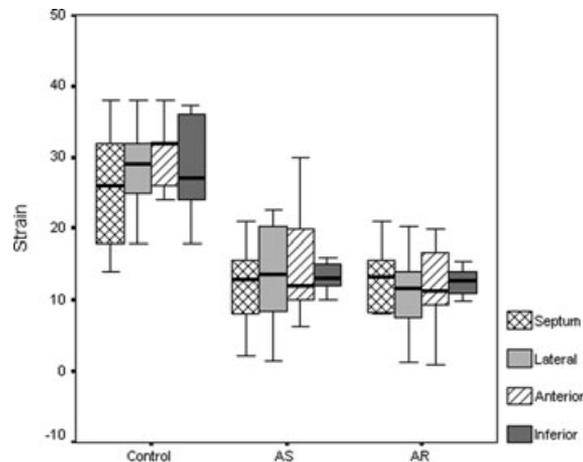


Figure 1. Longitudinal peak systolic strain for each wall in groups. AS = Aortic stenosis group, AR = Aortic regurgitation group.

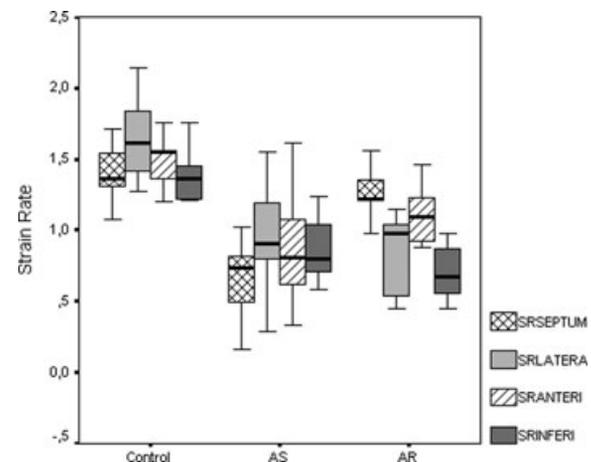


Figure 2. Longitudinal peak systolic strain rate for each wall in groups. AS = Aortic stenosis group, AR = Aortic regurgitation group.

pressure overload or severe volume overload, the longitudinal contractility of the left ventricle is affected adversely.

To our knowledge, this is the first study comparing two different loading condition to each other in terms of subtle LV dysfunction. As a result, we found no difference between pressure and volume overload regarding longitudinal LV dysfunction. In AR there is an increase in both preload and afterload, but there is pure afterload increase in AS. Although two different loading "conditions" with two different remodeling characters, in contrast to our expectation, one remodeling was not more harmful than the other regarding contractility. Since it has been known that left ventricular longitudinal functions "deteriorate" earlier than radial and circumferential functions,^{13,14} we thought assessing longitudinal function was reasonable to detect even the slightest deterioration in LV contractility.

Pressure or volume overload increases the wall stress leading to hypertrophy without adequate neoangiogenesis, which in turn leads to increased oxygen consumption and reduced coronary perfusion especially to the subendocardial layer longitudinal fibers.¹⁵ This ischemia precedes the collagen deposition.¹⁶ Indeed, it has been shown that collagen I, III and fibronectin are upregulated in aortic valve disease even with normal EF.¹⁷ Finally, whether it is an augmented preload or afterload or the combination of that, this process results in accumulation of collagen fibers, interstitial fibrosis and increase in LV mass. A common pathway, which ends as a reduction in left ventricular longitudinal function.

In brief, we conclude that longitudinal LV function is reduced in both pressure and volume overload, and both of this overload patterns are equally harmful to the ventricle.

Study Limitation:

The sample size of our study is small. This may have limited the power of the results.

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