

Evaluation of the effect of mitral stenosis severity on the left ventricular systolic function using isovolumic myocardial acceleration

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Abstract

Background: *Isovolumic acceleration (IVA) is a new tissue Doppler parameter in the assessment of systolic function of both left and right ventricles. It remains unaffected with the changes in pre- and after-load within the physiological range. The aim of our study was to assess the effect of mitral stenosis degree, which is determined by echocardiography, on the left ventricular (LV) function using IVA.*

Methods: *A total number of 62 patients with mitral stenosis (MS) and 32 healthy controls were examined. The severity of MS (mild, moderate, and severe) was determined on the basis of mitral valve area (MVA) and the mean diastolic mitral gradient findings. The peak myocardial velocities during isovolumic contraction, systole, early diastole and late diastole were measured by using tissue Doppler imaging (TDI).*

Results: *All TDI-derived global LV basal wall systolic (peak myocardial isovolumic contraction velocity, peak myocardial systolic velocity and IVA), and diastolic velocities (peak early and late diastolic velocities) were significantly decreased in the patients with MS, compared to the healthy patients ($p < 0.001$, for all). However, IVA was not different when the degree of MS was evaluated ($p = 0.114$). In addition, IVA was not correlated with the MVA ($r = 0.185$, $p = 0.150$).*

Conclusions: *Left ventricular function is impaired in patients with MS regardless of the severity of the disease. (Cardiol J 2014; 21, 4: 442–448)*

Key words: **isovolumic acceleration, mitral stenosis, left ventricular function, tissue Doppler imaging**

Introduction

Mitral stenosis (MS) still leads to significant morbidity and mortality worldwide [1]. The presence of impaired left ventricular (LV) systolic function, determined by M-mode and/or two-

-dimensional (2D) echocardiography (ECHO), is noted in 25–30% of the patients with MS [2–6]. Recently, in the studies using tissue Doppler imaging (TDI) [7–9] and strain/strain rate imaging [10, 11], which are more sensitive methods compared to the conventional ECHO, the occurrence of subclinical

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Received: 19.06.2013

Accepted: 25.06.2013

LV systolic dysfunction was confirmed even in MS patients with preserved ejection fraction (EF). The functional and/or myocardial factors, which cause impaired LV systolic function, are unclear. In the study of Lee and Lee [12], systolic dysfunction of LV was suggested to be associated with the severity of myocardial involvement in isolated mitral valve stenosis during the rheumatic attack, not with the degree of the MS demonstrated by ECHO. Furthermore, Sengupta et al. [8] showed that subclinical LV dysfunction improved following the percutaneous mitral valvuloplasty.

Isovolumic acceleration (IVA) is a new tissue Doppler parameter for the assessment of systolic function of both left and the right ventricles [13, 14]. IVA is calculated as a ratio of tissue Doppler-derived peak myocardial velocity during isovolumetric contraction (IVV) divided by the acceleration time (AT). This parameter has been validated in a variety of experimental [13, 14] and clinical [15, 16] settings. IVA remains unaffected by the changes in the preload and afterload within the physiological range [13–16]. It can detect small changes in the contractile function and is well correlated with the invasive or noninvasive measures of LV dP/dt [13, 17].

Effect of the degree of mitral valve stenosis, which is determined by echocardiographic and hemodynamic parameters, on LV function is not clearly evaluated. The aim of our study was to assess the effect of mitral valve stenosis degree, which is determined by ECHO, on the LV function using IVA.

Methods

A total number of 94 subjects, 62 isolated mitral valve stenosis patients with preserved LVEF and sinus rhythm (mean age 39 ± 8 years; 56 [90.3%] females) and 32 healthy volunteers (mean age 36 ± 8 years; 56 [81.2%] females) were included in our study. All the participants underwent both conventional echocardiography and TDI. The patients with MS were divided into three groups (mild, moderate and severe), based on their mitral valve area (MVA) determined by ECHO, and mean diastolic mitral gradients: 21 patients with mild stenosis ($MVA > 1.5 \text{ cm}^2$, mean gradient $< 5 \text{ mm Hg}$), 21 patients with moderate stenosis ($MVA = 1 - 1.5 \text{ cm}^2$, mean gradient $= 5 - 10 \text{ mm Hg}$) and 20 patients with severe stenosis ($MVA < 1 \text{ cm}^2$, mean gradient $> 10 \text{ mm Hg}$).

Patients who had coronary artery disease, moderate to severe aortic and mitral regurgitation, aortic stenosis, hyperthyroidism, chronic obstructive

pulmonary disease, atrioventricular conduction abnormality, left bundle branch block, segmental wall motion abnormalities, and severely calcified mitral valve structure were excluded in this study.

Written informed consent form was obtained from the patients following approval of the study by the institutional review board. The study was consistent with the Declaration of Helsinki.

Conventional echocardiographic examination

All the transthoracic echocardiographic (TTE) examinations were performed using GE vivid S6 Vingmed system 5 (Norway, Horten) equipped with 2.5–4 MHz transducers. All the patients were examined in the left lateral and supine positions with 2D, M-mode, pulsed, and color flow Doppler ECHO. Single lead electrocardiogram was recorded continuously. An average of at least 5 cardiac cycles was obtained for all measurements.

M-mode measurements and conventional Doppler ECHO examinations were performed based on the criteria of the American Society of Echocardiography and European Society of Echocardiography guidelines [18]. Left atrial (LA), LV end-systolic and end-diastolic dimensions were measured in the parasternal long-axis views. LVEF was estimated by Simpson's rule. Peak and mean transmitral pressures were measured via continuous wave Doppler. MVA was measured planimetrically in 2D views from the parasternal short axis and using the pressure half-time method by applying continuous wave Doppler during apical 4-chamber view of the mitral valve. The area was calculated by the mean value of 2 measurements [19]. Pulmonary artery systolic pressure (PASP) was estimated by continuous-wave Doppler imaging using the Bernoulli equation [20].

Tissue Doppler imaging

Doppler tissue ECHO was performed using transducer frequencies between 3.5 to 4.0 MHz, by adjusting the spectral pulsed Doppler signal filters until a Nyquist limit of 15 to 20 cm/s was reached, and using the minimal optimal gain. Five consecutive cycles were recorded with a frame rate greater than 150 fps. The monitor sweep speed was set at 50 to 100 mm/s to optimize the spectral display of myocardial velocities. Every effort was made to align the pulsed wave cursor so that the Doppler angle of incidence was as close to 0 as possible to the direction of these walls. In the apical 4-chamber view, the pulsed Doppler sample volume was subsequently placed at the level of LV lateral and septal basal wall at end-expiration [21].

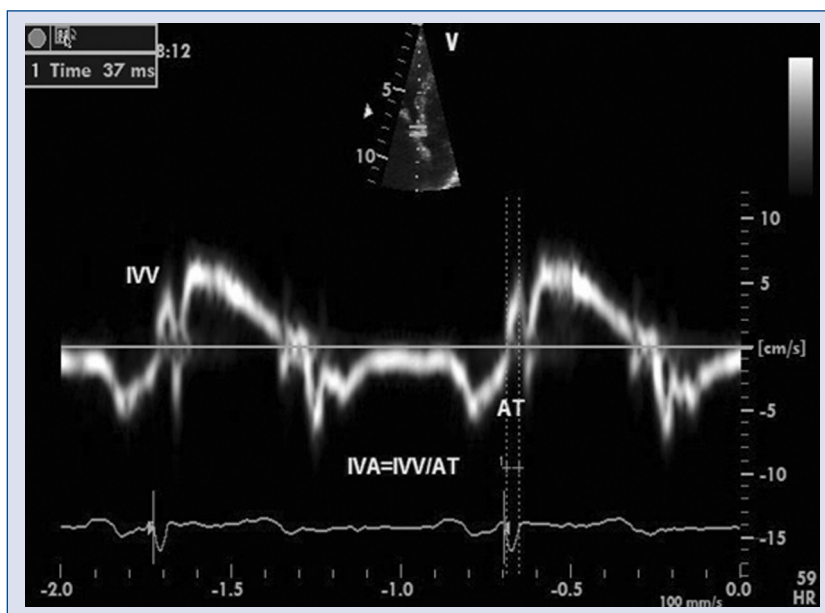


Figure 1. Tissue Doppler imaging-derived IVV and AT obtained from left ventricular septal basal wall of patients with mitral stenosis; IVV — peak myocardial velocity during isovolumic contraction; AT — isovolumic acceleration time; IVA — myocardial acceleration during isovolumic contraction.

Peak myocardial IVV, peak myocardial systolic velocity (S_m), peak early and late diastolic velocities (e' and a'), isovolumic AT, isovolumic contraction time (IVCT), isovolumic relaxation time (IVRT) and ejection time (ET) were measured. Myocardial performance index (MPI) was calculated as the sum of IVCT and IVRT divided by the ET. Myocardial acceleration during isovolumic contraction (IVA) was defined as the ratio of IVV divided by the AT (Fig. 1).

All the ECHO evaluations were performed by 2 different investigators. In order to detect the intraobserver variability, the first investigator repeated the ECHO measurements of 20 patients and the second investigator measured TDI-derived parameters of 20 patients to detect interobserver variability.

Statistics analysis

Statistical analyses were performed using the SPSS software version 17. The variables were investigated using visual and analytical methods to determine whether they were normally distributed or not. Descriptive analyses were presented as mean \pm standard deviation (SD) and categorical variables were shown as percentages. Groups were compared using the Student's t-test, Mann-Whitney U test, one-way ANOVA, and Kruskal-Wallis test (MVA, mitral valve gradient, PASP, S_m ,

e' , a' , IVCT, IVRT, AT, IVV). Fisher's exact or χ^2 tests was used to compare different groups. Mann-Whitney U test or Tukey's test was performed to determine the significance of pairwise differences using Bonferroni correction to adjust for multiple comparisons. Correlation analyses were derived by using Spearman test. An overall 5% type-I error level was used to infer statistical significance.

Results

Clinical properties

Parameters such as age, gender, body mass index, heart rate, systolic blood pressure, diastolic blood pressure, smoking, hypertension, and diabetes mellitus were similar in both MS and healthy groups (Table 1). Of the MS patients, 52 were classified in New York Heart Association functional class I or II and 10 patients were in class III.

Conventional echocardiographic parameters

LVEF, LV end-diastolic and end-systolic diameters were similar in both the patient and the control groups. As an expected result, LA diameter and PASP were significantly higher in the patients with MS. LA diameter in patients with mild and moderate MS was significantly lower than those of the patients with severe MS ($p = 0.004$); however, there was no significant difference between the

Table 1. Demographic characteristics and conventional echocardiographic parameters of the patients with mitral stenosis (MS) and healthy controls.

	Severity of MS						
	Mild (n = 21)	Moderate (n = 21)	Severe (n = 20)	P	MS total (n = 62)	Control groups (n = 32)	P
Age [years]	40 ± 9	41 ± 7	36 ± 7	0.137	39 ± 8	36 ± 8	0.163
Gender (female)	20 (95.1%)	19 (90.59%)	17 (85%)	0.541	56 (90.3%)	26 (81.2%)	0.177
Body mass index [kg/m ²]	29 ± 6	27 ± 3	27 ± 4	0.190	27 ± 5	28 ± 4	0.467
Systolic BP [mm Hg]	122 ± 12	115 ± 11	115 ± 9	0.076	117 ± 11	118 ± 10	0.677
Diastolic BP [mm Hg]	75 ± 10	71 ± 9	72 ± 8	0.360	72 ± 9	72 ± 8	0.812
Heart rate [beats/min]	80 ± 12	78 ± 10	80 ± 11	0.606	80 ± 12	78 ± 7	0.378
Current smoking	2 (9.5%)	1 (4.8%)	2 (10%)	0.790	5 (8.1%)	7 (21.9%)	0.060
Hypertension	5 (23.5%)	5 (23.8%)	2 (10%)	0.437	12 (19.4%)	4 (12.5%)	0.402
Diabetes mellitus	2 (9.5%)	1 (4.8%)	0	0.365	3 (4.8%)	0 (0%)	0.282
LVESD [mm]	30 ± 4	27 ± 4	29 ± 3	0.121	29 ± 4	28 ± 4	0.272
LVEDD [mm]	48 ± 5	47 ± 5	47 ± 5	0.738	47 ± 5	46 ± 5	0.184
LVEF [%]	63 ± 3	64 ± 2	64 ± 3	0.077	64 ± 3	65 ± 3	0.132
Left atrium diameter [mm]	39 ± 7	41 ± 4	45 ± 6*	0.003	42 ± 7	28 ± 4	< 0.001
Pulmonary artery systolic pressure [mm Hg]	33 ± 6	39 ± 10	50 ± 14	< 0.00**	40 ± 13	26 ± 4	< 0.001
Mean mitral valve area [cm ²]	1.8 ± 0.1	1.3 ± 0.1	0.8 ± 0.1	< 0.001 [#]			
Transmitral diastolic gradient [mm Hg]:							
Maximum	11 ± 4	16 ± 4	27 ± 8	< 0.001 [#]			
Mean	6 ± 2	9 ± 3	18 ± 6	< 0.001 [#]			

*p = 0.004 vs. mild and moderate; **p < 0.01 between all subgroups; [#]p < 0.001 between all subgroups; BP — blood pressure; LVEDD — left ventricular end-diastolic diameter; LVESD — left ventricular end-systolic diameter, LVEF — left ventricular ejection fraction

patients with mild and moderate MS. There was a stepwise increase in the PASP and diastolic transmitral gradients (maximum and mean) from mild to severe MS (p < 0.01 and p < 0.001, respectively). A stepwise decrease was found in the MVA from mild to severe MS (p < 0.001) (Table 1).

TDI velocities

All the TDI-derived global LV basal systolic (IVV, IVA, Sm) and diastolic velocities (e', a') were significantly decreased in the patients with MS compared to the healthy groups (p < 0.001, for all). In patients with MS, IVRT and MPI were significantly higher than the control group (p < 0.001, p = 0.007, respectively) and the ET was lower in the control group (p = 0.018). The AT and IVCT were not different among the groups (p = 0.432, p = 0.119, respectively) (Table 2).

The IVA and Sm, which indicate LV systolic function, and MPI, which shows LV both systolic and diastolic function, did not differ among the 3 MS groups (p = 0.114, p = 0.096 and p = 0.238, respectively). Excluding ET, time intervals such as

AT, IVRT and IVCT were not different among the MS groups (p = 0.005, p = 0.922, p = 0.192 and p = 0.498, respectively). The IVV, e' and a' velocities in the patients with severe MS were significantly lower than those of the patients' with mild MS (p < 0.01, for all). However, there were no significant differences between the moderate and both mild and severe MS patients (p > 0.017). Agreement of intraobserver and interobserver variabilities were obtained for the IVA (4 ± 2% and 5 ± 3%, respectively).

Correlation between TDI velocities and conventional echocardiographic parameters

MVA was positively correlated with both LV diastolic velocities (e' and a') and IVV (p < 0.01, for all). However, there were no correlations between LV systolic velocities (IVA and Sm) and the MVA (p > 0.05). Mean transmitral gradient was weakly correlated with both IVV and e' (p < 0.05). LA diameter and both systolic (IVV, IVA, Sm) and diastolic (e', a') velocities were shown to correlate (p < 0.001, for all). PASP was significantly associa-

Table 2. Tissue Doppler-derived myocardial systolic and diastolic velocities obtained from the left ventricle.

	Severity of mitral stenosis (MS)						
	Mild (n = 21)	Moderate (n = 21)	Severe (n = 20)	P	MS total (n = 62)	Control groups (n = 32)	P
IVV [cm/s]	5.6 ± 0.9	5.2 ± 0.8	4.9 ± 0.7*	0.018	5.2 ± 0.8	6.8 ± 1.2	< 0.001
Isovolumetric AT [ms]	22 ± 4	22 ± 4	22 ± 5	0.922	22 ± 4	23 ± 5	0.432
IVA [m/s ²]	2.7 ± 0.8	2.5 ± 0.6	2.3 ± 0.6	0.114	2.5 ± 0.7	3.2 ± 0.9	< 0.001
Sm [cm/s]	7.9 ± 1.2	7.3 ± 1.3	7.2 ± 1.3	0.096	7.5 ± 1.3	9.6 ± 1.3	< 0.001
e' [cm/s]	7.2 ± 3.2	5.4 ± 1.4	4.9 ± 1.0*	0.013	5.8 ± 2.3	13.1 ± 2.7	< 0.001
a' [cm/s]	8.8 ± 1.9	7.8 ± 1.7	7.1 ± 1.3*	0.008	7.9 ± 1.8	10.1 ± 2.1	< 0.001
Isovolumic contraction time [ms]	64 ± 16	68 ± 16	63 ± 15	0.498	65 ± 15	70 ± 14	0.119
Isovolumic relaxation time [ms]	81 ± 22	90 ± 21	81 ± 26	0.192	84 ± 23	68 ± 13	< 0.001
Ejection time [ms]	294 ± 27	289 ± 24 [#]	267 ± 28*	0.005	284 ± 29	298 ± 25	0.018
Myocardial performance index	0.50 ± 0.1	0.55 ± 0.1	0.55 ± 0.1	0.238	0.53 ± 0.1	0.47 ± 0.1	0.007

*p < 0.01 vs. mild; [#]p = 0.010 vs. severe; IVV — peak myocardial velocity during isovolumic contraction; AT — acceleration time; IVA — myocardial acceleration during isovolumic contraction; Sm — peak myocardial velocity during systole; e' — peak myocardial velocity during early diastole; a' — peak myocardial velocity during atrial contraction

Table 3. Correlation between tissue Doppler imaging velocities and conventional echocardiographic parameters.

	Mean MVA		Mean gradient		Left atrium diameter		PASP	
	r	p	r	p	r	p	r	p
IVV	0.387	0.002	-0.260	0.042	-0.522	< 0.001	-0.565	< 0.001
IVA	0.185	0.150	-0.147	0.255	-0.368	< 0.001	-0.384	< 0.001
Sm	0.220	0.085	-0.190	0.138	-0.541	< 0.001	-0.537	< 0.001
e'	0.348	0.006	-0.317	0.012	-0.687	< 0.001	-0.708	< 0.001
a'	0.374	0.003	-0.243	0.057	-0.387	< 0.001	-0.493	< 0.001

MVA — mitral valve area; PASP — pulmonary artery systolic pressure; IVV — peak myocardial velocity during isovolumic contraction; IVA — myocardial acceleration during isovolumic contraction; Sm — peak myocardial velocity during systole; e' — peak myocardial velocity during early diastole; a' — peak myocardial velocity during atrial contraction

ted with the parameters of LV systolic (IVV, IVA, Sm) and diastolic (e', a') function (p < 0.001, for all) (Table 3).

Discussion

In the light of these findings, it can be concluded that TDI-derived systolic and diastolic velocities are significantly reduced in the patients with MS and LV systolic dysfunction occurs independently from the severity of MS. To the best of our knowledge, this is the first study that evaluated the association between LV systolic velocities and severity of MS using TDI.

It is well known that MS affects the LV systolic function in various degrees. The probable causes can be listed as: chronically restricted

LV filling due to the structural abnormalities in the mitral valve, increased afterload, myocardial involvement during rheumatic fever, extension of the scar process from the mitral valve into the adjacent posterior basal myocardium, restriction or tethering of the posterobasal myocardium by the scarred mitral apparatus, abnormal interventricular septal motion associated with the right-ventricular overload, and the decrease in LV compliance [2, 4]. Conventional ECHO methods such as M-mode and 2D ECHO can detect one fourth of the LV dysfunction in MS [2–6]. In recent years, the studies using TDI [3–5] and strain/strain rate imaging [6, 7] demonstrated the presence of subclinical LV systolic dysfunction, which was not detected with the conventional ECHO methods in pure MS patients with preserved EF. Since the gold standard

measurement of the ventricular contractility (end-systolic elastance) requires invasive quantification [22], and most of the contractile indexes (e.g., EF, MPI, and TDI-derived velocities or strain) are highly sensitive to loading conditions, it is thought that they might not reflect the intrinsic myocardial performance [17, 23, 24].

Isovolumic acceleration is a new tissue Doppler parameter for the assessment of systolic function of both left and the right ventricles [13, 14]. It remains unaffected by the changes in the preload and afterload within the physiological range [13–16] including age, sex and body mass index [25]. It can detect even small changes in the contractile function and is well correlated with the invasive or noninvasive measures of LV dp/dt [13, 17]. Therefore, IVA can be used as a valuable and easy parameter for the quantification of global systolic function in various cardiac diseases [26, 27].

The present study shows that isolated MS may lead to significant decrease of LV systolic and diastolic function. In the studies using TDI-derived parameters, systolic velocities were demonstrated to be significantly decreased in the healthy controls, as consistent with our study [7–9]. Similar to the study by Sengupta et al. [8], Ozdemir et al. [9] demonstrated that early and late diastolic myocardial velocities were decreased in MS. On the other hand, Dogan et al. [28] did not find any differences compared to the controls. Decreased LV pre-load, impaired compliance and increased LA afterload are known changes in MS. LA size increases with the LA volume and pressure, and is associated with the initial gain in the contractile shortening. However, with progressive dilatation of the LA, which eventually leads to a threshold fiber length, atrial shortening and contractility begin to decline. Beyond the threshold, further enlargement will only result in the deterioration of atrial function. This theory was supported by decreased e' and a' velocities, and the presence of positive correlation between this decrease and MVA in our study. Previous study demonstrated that MPI and IVRT were increased and ET was shortened [29] in the patients with MS compared to the controls. In consistent with the previous studies, the present study demonstrated that ET decreased as the severity of MS increased and, MPI and IVRT increased independently from the severity of MS.

Even though IVV, IVA and Sm velocities decrease in the patients with MS compared to the control group, this decrease is independent from the degree of MS. In addition, the fact that the systolic parameters such as IVA and Sm velocities are

not correlated with MVA and the mean gradient, though weakly associated with IVV, indicates that the LV systolic dysfunction might be caused by an acute rheumatic fever leading to myocardial damage. The results of some studies [12, 30] were consistent with these findings in that the major determinant of the LV systolic dysfunction in isolated MS is impaired contractility and not the hemodynamic factors. Lee and Lee [12] evaluated the LV myocardium of 15 isolated MS patients using electron microscopy and demonstrated structural changes in LV independent from the EF and the degree of MS, determined by ECHO parameters. However, these patients with abnormal LV function always exhibit more extensive loss of myofibrils which results from either disproportion of the mitochondria-to-myofibril ratio or myofibrillar degeneration. In the study of Bilen et al. [30], which investigated the LV systolic function of mild, moderate and severe MS patients with preserved EF, using 2D speckle-tracking ECHO-derived strain; it was demonstrated that LV longitudinal function was decreased in patients with MS compared to the controls, however, this decrease was independent from the degree of MS. In our study, LV systolic function was evaluated globally with TDI-derived IVA and similar results were obtained. Furthermore, the patients were more evenly distributed into the groups in the present study.

Tayyareci et al. [26] investigated the IVA of right ventricle in prediction of the degree of MS and demonstrated that Sm, IVV and IVA of right ventricle significantly decreased in the patients with MS compared to the control group, however, they noted that only right ventricle and IVA can predict the degree of MS. Decreased IVA of LV was shown in MS patients in our study, although it was not associated with the degree of stenosis. This discrepancy might be caused by the classification differences; since Tayyareci et al. [26] grouped the MS patients into two groups (mild-moderate and severe) instead of three (mild, moderate and severe), which was helpful in the assessment of treatment strategies. Besides, the correlation of IVA with both LA diameter and PASP might be resulted from the increase in these two parameters due to hemodynamic effects of stenosis, instead of the systolic dysfunction of LV.

Limitations of the study

The current study has some limitations. First, a small number of patients included in this study. Second, systolic function parameters were not compared with the parameters obtained from

cardiac catheterization and magnetic resonance imaging. Third, the potential change in the IVA of LV was not assessed following the percutaneous balloon valvuloplasty.

Conclusions

In the light of these results, it is demonstrated that subclinical LV systolic dysfunction is present in all of the patients with MS and this condition is not affected by the degree of MS determined by ECHO.

Conflict of interest: none declared

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