

Heart Mirror **HMJ** Journal

From Affiliated Egyptian Universities and Cardiology Centers
March 2007

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Print ISSN: 1687-6652. Online ISSN: 1687-5958

Heart Mirror Journal 2007;1;36-40; originally published online March 1, 2007

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ORIGINAL ARTICLE

Ventricular Performance evaluated by TEI Index in Patients with Mitral Valve Prolapse: Doppler Tissue Imaging Study

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Background Valve prolapse is a common cardiac abnormality with a variety of clinical and echocardiographic findings. DTI can be used for assessment of both global and regional LV function with high temporal and spatial resolution.

Purpose Assessment of segmental and global LV performance in patients with MVP with pulsed wave DTI

Patients & Methods The present study enrolled 40 patients with MVP (group I), and 25 apparently healthy individuals as a control (group II). All were subjected to conventional M-mode and 2D echo Doppler and DTI examination. pulsed-wave DTI was used to assess velocity curves of basal and mid segments of the septal, lateral, anterior and inferior LV walls and the four corners of the mitral annulus together with the velocity curves of the anterolateral and postromedial papillary muscles. The following indices were measured IVRT, IVCT, CT and TEI index.

Results Group I patients had a significantly longer IVRT ($72.1 \pm 12, 72.7 \pm 17, 70.8 \pm 13, 75.8 \pm 16$ vs $62.4 \pm 17, 64.6 \pm 13, 60.4 \pm 4, 60.8 \pm 14$) $p < 0.001$ and significantly longer IVCT ($79.5 \pm 13, 77.9 \pm 13, 74.9 \pm 13, 80.4 \pm 14$ vs $60.1 \pm 11, 60.8 \pm 10, 61.4 \pm 8, 59.5 \pm 12$) $p < 0.001$ in all walls as well as both papillary muscles than in group II (control group). Subgroup IA with (MR), had a significantly higher IVCT in all segments ($81.8 \pm 14, 87.4 \pm 10, 83.7 \pm 14, 83.4 \pm 9$ vs $67.2 \pm 8, 71.7 \pm 13, 74.4 \pm 9, 72.4 \pm 11$) $p < 0.05$, also higher but not significant IVRT ($70.8 \pm 14, 78.7 \pm 18, 73.3 \pm 9, 76.8 \pm 16$ vs $70.7 \pm 11, 72.3 \pm 12, 70.5 \pm 16, 67.6 \pm 17$) $p > 0.05$ than subgroup IB (without MR). Tei index was significantly higher in group I compared to group II (0.55 ± 0.06 vs 0.43 ± 0.07) $p < 0.001$. Subgroup IA had a significantly higher Tei index than subgroup IB (0.56 ± 0.04 vs 0.49 ± 0.03) $p < 0.001$. TEI index was significantly higher in patients presented with palpitation (0.62 ± 0.08 vs 0.53 ± 0.09) $p < 0.01$ and there was no difference in those presented with or without chest pain (0.55 ± 0.10 vs 0.55 ± 0.08) $p > 0.05$.

Conclusions Patients with MVP have significantly higher TEI index than healthy control individuals denoting subtle LV dysfunction particularly those with MR.

Key Words Tissue Doppler, mitral, prolapse, left ventricle

(Heart Mirror J 2007; 1(1): 36-39)

INTRODUCTION

Mitral valve prolapse is a common cardiac abnormality affecting 2.4% of the general population (1). The structural and functional disarray of the mitral valve apparatus observed in subjects with MVP might lead, at least in theory, to dysfunction of the left ventricular muscle surrounding the mitral annulus (2, 3). Doppler tissue imaging (DTI) is a simple, reproducible, non invasive technique that can be used for assessment of regional myocardial velocities with a high temporal and spatial resolution. TEI index (which is the sum of isovolumetric contraction time IVCT and isovolumetric relaxation time IVRT divided by contraction

time) was introduced by Tei et al. as a Doppler derived index that combine both systolic and diastolic function to separate those with normal ventricular function from those with ventricular dysfunction (4). This index has been found to correlate well with invasive measures of systolic and diastolic LV function (5).

Aim of the study

Assessment of segmental and global LV performance in patients with mitral valve prolapse with pulsed wave DTI.

PATIENTS AND METHODS

This study included 40 patients with mitral valve prolapse diagnosed in our echo lab according to the criteria suggested by Freed et al. (4), namely: a) Displacement of one or both leaflets into the left atrium exceeding 2mm and b) Leaflet thickness of at least 5mm for classic prolapse and less than 5mm for non classic prolapse. Twenty five age and sex matched apparently healthy individuals were enrolled as a control group. All patients were subjected to: •Full history taking, • Physical examination. •Routine investigations. •Twelve lead ECG. •Echocardiographic examination. Doppler echocardiographic examination was done using commercially available Acuson XP10 with 2MHz transducer equipped with Doppler tissue imaging (DTI) calculation package. M-mode, two dimensional, colour Doppler and Doppler tissue examinations were done in standard parasternal long axis, short axis, apical two and four chamber views. M-mode and two dimensional echocardiography: The left ventricular internal dimensions and wall thickness were measured according to the recommendations of the American society of echocardiography (1). Ejection fraction and fractional shortening were measured in M-mode. Displacement of the mitral leaflets was measured in the parasternal long axis view. The length of the anterior leaflet and the annular diameter were measured in the same view. The thickness of the leaflets was measured at the thickest part of each leaflet from the leading to the trailing edge, excluding chordae attachment areas and focal areas of increased thickness. Colour Doppler examination: In apical four chamber view, the degree of mitral regurgitation (if present) was evaluated with respect to the ratio of the regurgitant jet area to the left atrium area. Four degrees of the mitral regurgitation were defined as: trivial (<10%), mild (10-20%), moderate (20-40%), and severe (>40%). On the bases of the presence or absence of mitral regurgitation group I patients were classified into subgroup IA (with mitral regurgitation and group IB (those without mitral regurgitation) Exclusion criteria: Patients were excluded if they had arrhythmia, coronary heart disease, congenital or rheumatic heart disease hypertensive heart disease, diabetes mellitus, and cardiomyopathy or heart failure. All medications that might affect the systolic or diastolic function of the left ventricle (e.g. beta-blockers) were discontinued for at least two days before the examination. Tissue Doppler imaging (DTI): Using pulsed wave DTI, filters and baseline were adjusted to a low velocity range(-20 to 20cm/s)with minimal gain settings (9). The sample volume was placed within the myocardium equidistant from endocardial and epicardial borders and effort was made to minimize the angle as much as possible. From apical four chamber view, using pulsed-wave DTI the myocardial velocity curves of the basal and mid segments of septal and lateral walls as well as septal and lateral aspects of mitral annulus together with mid of the anterolateral papillary muscle were recorded. From the apical two chamber view, the myocardial velocity curves of the basal and mid segments of the anterior and inferior walls as well as anterior and inferior aspects of the

mitral annulus and the mid of the postero-medial papillary muscle were recorded. The following time intervals were measured: Isovolumetric relaxation time (IVRT), ms: From the end S wave to the beginning of E wave. Isovolumetric contraction time (IVCT), ms: From the beginning of the first positive deflection after the Q wave to the onset of S wave. Contraction time (CT) ms: From the beginning to the end of S wave. TEI index was calculated as the sum of IVCT+IVRT divided by CT.

Statistics

analysis by SPSS version 11.0 statistical package. Quantitative data expressed as mean and standard deviation ($X \pm SD$) for normally distributed data and median and range for non normally distribution data. One way analysis of variance (F-test) for comparison of the means of more than two groups and student t-test for two groups of normally distribution data. Person correlation (r) used to test correlation between continuous variables. Qualitative data expressed as number and percentage and tested by Chi-square (χ^2) test. Level of significance was set as p-value <0.05.

RESULT

With mitral valve prolapse (13 males and 27 females), with a mean age $=23.9 \pm 4.3$ years and 25 apparently healthy individual (8 males and 17 females) with a mean age of 21.8 ± 4.8 years as a control group. Both groups were comparable as regards age and sex (p value >0.5).

Table 1 showed the clinical presentation of patients group: 26 (65%) patients presented by chest pain, 10 (25%) by palpitations, 24 (60%) by dyspnea and four (10%) presented by presyncope. As regards the auscultatory finding, systolic click was found in 8 (20%) patients, mid to late systolic murmur in 14 (35%) patients, both click and murmur in 10 (25%) patients and 8 (20%) patients exhibited normal auscultatory findings. Inferolateral ST, T wave changes were present in 8 (20%) patients. The prolapsing leaflet was the anterior leaflet in 26 (65%) patient and both leaflets in 14 (35%) patients. Mitral regurgitation was present in 31(67.5%) patients. As regard to conventional echocardiographic variables of both group I and group II, there was no significant difference between both groups as regard end systolic, end diastolic dimensions and ejection fraction. Group I had a significantly higher aortic root and LA dimensions, significantly increased anterior leaflet length, thickness and more posterior displacement. Mitral annular diameter was significantly higher in group I than in group II (P value <0.001) (Table 2).

Doppler tissue imaging derived time intervals (IVRT, IVCT and CT) of both anterolateral postero-medial papillary muscles were significantly longer in group I than group II. The antero-lateral and postero medial papillary muscles Parameters (IVRT, IVCT, and CT) showed a significantly higher correlation (p <0.001) with the same parameters of the underlying mid lateral and mid inferior myocardial segments

respectively denoting integrated function of the papillary muscle with the underlying segment (Tables 3 and 4).

Table 1. Clinical characteristics of group patients.

	No.	%
Clinical presentation:		
Chest pain	26	65
Palpitation	10	25
Dyspnea	24	60
Presyncope	4	10
Ausultatory findings:		
Normal	8	20
Systolic click	8	20
Mid to late systolic murmur	14	35
Systolic click & murmur	10	25
Prolapsing mitral leaflet:		
Anterior	26	65
Posterior	0	0
Both	14	35
Degree of mitral regurge:		
Non	9	22.5
Trivial	9	22.5
Mild	18	45
Moderate	4	10

Table 2. Echocardiographic variables of MVP and controls.

	MVP Mean ± SD	Controls Mean ± SD	t	P value
Aor. root. D	2.68 ± 0.28	2.38 ± 0.24	4.60	<0.001
It. atr. D	3.15 ± 0.33	2.62 ± 0.25	7.21	<0.001
Ef%	68.90 ± 3.33	69.44 ± 4.26	-0.54	>0.05
LVES	2.73 ± 0.33	2.68 ± 0.38	0.57	>0.05
LVED	4.56 ± 0.37	4.36 ± 0.51	4.71	>0.05
AMLT	4.65 ± 1.06	2.56 ± 0.32	6.06	<0.001
AMLL	2.70 ± 0.47	2.30 ± 0.13	5.05	<0.001
MAD	3.23 ± 0.44	2.67 ± 0.31	6.03	<0.001
Post. Dis.	3.80 ± 1.22	0.00		

Table 3. Shows comparison between group I and group II as regard posteromedial papillary and anterolateral papillary muscles (IVRTm, IVCTm, and CTm).

Group Papillary muscle	Group I Mean ± Sd	Group II Mean ± Sd	t	P value
Ant. lat. papillary m				
IRT	61.44 ± 13.12	71.10 ± 12.72	2.91	<0.01
CT	272.32 ± 15.57	287.55 ± 23.65	3.13	<0.001
ICT	63.04 ± 11.62	79.50 ± 17.26	4.59	<0.001
Post. med. papillary m				
IRT	61.76 ± 14.33	76.85 ± 14.53	4.11	<0.001
CT	269 ± 16.28	279.25 ± 22.85	2.02	<0.05
ICT	60.80 ± 14.05	83.50 ± 16.36	5.94	<0.001

Table 4. Correlation between time intervals of each papillary muscle and those of the corresponding myocardial segments.

Mid Lat	ALPM		IRT		ICT		CT	
	r	P value	r	P value	r	P value	r	P value
IRT	0.56	<0.001	0.62	<0.001	0.47	0.001		
ICT								
CT								
Mid inf	PMPM		IRT		ICT		CT	
	r	P value	r	P value	r	P value	r	P value
IRT	0.61	<0.001	0.82	<0.001	0.44	0.001		
ICT								
CT								

Comparison between group I and group II as regard basal and mid segments of septal, lateral, anterior and inferior walls, TDI indices. Group I indices (IVRT and IVCT) were significantly higher than group II. Contraction time was higher in group I but did not reach statistical significance (>0.05) (Table 5 and 6).

Table 5. Shows comparison between group I and group II as regard basal and mid myocardial segments of both septal and lateral walls (IVRTm, IVCTm, CTm).

Group Wall segments	Group I Mean ± Sd	Group II Mean ± Sd	t	P value
Septum Bas. segments				
IRT	72.30 ± 15.60	56.64 ± 11.29	4.68	<0.00
CT	275.90 ± 23.67	270.08 ± 17.48	1.14	>0.05
MCT	78.45 ± 19.52	55.68 ± 10.95	6.02	<0.001
Mid segments				
IRT	72.10 ± 12.80	32.40 ± 17.74	2.37	<0.05
CT	269.30 ± 24.78	266.24 ± 19.12	0.56	>0.05
ICT	79.55 ± 13.50	60.16 ± 11.10	6.29	<0.001
Lateral Wall Bas segments				
IRT	74.60 ± 14.01	55.36 ± 13.25	5.57	<0.00
CT	287.60 ± 27.03	278.40 ± 18.62	1.62	>0.05
MCT	81.90 ± 15.23	59.20 ± 12.00	6.68	<0.001
Mid segments				
IRT	72.70 ± 17.42	64.64 ± 13.05	2.12	<0.05
CT	280.70 ± 36.99	277.12 ± 17.72	0.52	>0.05
ICT	77.95 ± 13.75	60.80 ± 10.33	5.72	<0.001

Table 6. Shows comparison between group I and group II as regard basal and mid myocardial segments of anterior and inferior walls parameters (IVRTm, IVCTm, CTm).

Group Wall segments	Group I Mean ± Sd	Group II Mean ± Sd	t	P value
Anterior Wall Bas segments				
IRT	75.10 ± 14.46	66.56 ± 9.99	2.81	<0.01
CT	281.45 ± 24.96	272.32 ± 17.66	1.65	>0.05
MCT	75.25 ± 15.31	64.96 ± 10.15	3.26	<0.001
Mid segments				
IRT	70.80 ± 13.40	60.48 ± 9.82	3.57	<0.01
CT	281.40 ± 25.85	273.28 ± 13.60	0.52	>0.05
ICT	74.90 ± 13.60	61.44 ± 8.55	4.82	<0.001
Inferior Wall Bas segments				
IRT	68.90 ± 21.19	56.96 ± 10.66	5.57	<0.00
CT	275.20 ± 22.81	273.60 ± 18.33	1.62	>0.05
MCT	83.90 ± 17.40	58.56 ± 12.59	6.68	<0.001
Mid segments				
IRT	75.85 ± 16.47	60.804 ± 14.42	2.12	<0.05
CT	274.15 ± 25.42	265.12 ± 27.60	0.52	>0.05
ICT	80.40 ± 14.19	59.52 ± 12.45	5.72	<0.001

When group I was then subdivided into subgroup IA (those with MR, 22 patients) and subgroup IB (those without MR 18 patients). Subgroup IA exhibited a very highly significantly higher aortic root dimension, Anterior leaflet length, thickness, mitral annular diameter and posterior displacement than subgroup IB (p <0.001) together with a significantly higher AAML thickness P <0.5). Subgroup IA had non significantly higher LA dimension (p value =0.17). AS regard to time intervals Subgroup IA had a significantly higher IVCT, higher but non significant IVRT than subgroup IB in basal; mid segments of septal, lateral, anterior and inferior myocardial walls (Table 7). Mitral annulus derived time intervals except CT were significantly higher among subgroup IA compared to group I, II and subgroup IB.

Also they were significantly higher among group I patients than among group II patients. Contraction time was higher but did not reach statistical significance (Table 8). Mitral annulus derived global performance index (TEI index), of group I patients was significantly higher than that of group II. Still subgroup IA had a significantly higher index value than subgroup IB and group II ($p < 0.001$) (Table 8). TEI index was significantly higher in group I patients presented by palpitation than those without palpitation and was non different in those presented with and without chest pain (Table 9).

Table 7. Comparison between subgroup A and subgroup B.

Group	Subgroup IA Mean ± Sd	Subgroup IB Mean ± Sd	t	P value
Wall I segments				
Anterior Wall Bas. segments				
IR	76.73 ± 12.17	73.11 ± 17.00	0.76	>0.045
IC	82.82 ± 16.05	66.00 ± 7.37	4.38	<0.001
Mid segments				
IR	70.82 ± 14.96	70.78 ± 11.63	0.01	>0.05
IC	81.18 ± 14.53	67.22 ± 8.45	3.79	<0.001
Inferior Wall Bas. segments				
IR	74.27 ± 25.48	62.33 ± 12.04	1.95	>0.05
IC	93.91 ± 14.02	71.67 ± 12.78	5.24	<0.001
Mid segments				
IR	78.73 ± 18.97	72.33 ± 12.42	1.28	>0.05
IC	87.45 ± 10.97	71.78 ± 13.04	4.06	<0.001
Septum Bas. segments				
IR	69.82 ± 15.26	65.56 ± 13.54	1.69	>0.05
IC	84.73 ± 22.55	70.78 ± 11.54	2.53	<0.001
Mid segments				
IR	73.36 ± 9.56	70.56 ± 16.07	0.65	>0.05
IC	83.73 ± 14.84	74.44 ± 9.8	2.37	<0.001
Laterla Wall Bas. segments				
IR	75.09 ± 13.73	69.11 ± 12.62	1.69	>0.05
IC	87.27 ± 12.57	84.73 ± 15.94	2.59	<0.001
Mid segments				
IR	76.82 ± 16.64	67.67 ± 17.48	1.68	>0.05
IC	83.36 ± 9.86	72.44 ± 11.71	3.15	<0.001

Table 8. Comparison between MVP group, subgroup A and subgroup B and control group as TEI index.

	Group I	Subgroup IA	Subgroup IB	Group II	F	P value
Mitral Annulus						
IC	80.2 ± 12.16	87.45 ± 9.61	70.94 ± 8.83	59.92 ± 8.97	31.36	<0.001
CT	279.75 ± 22.1	276.7 ± 19.79	273.47 ± 24.70	274.48 ± 16.47	0.74	>0.05
IRT	72.77 ± 12.71	77.06 ± 12.09	67.52 ± 11.71	60.16 ± 8.77	9.77	<0.001
Tei Index	0.55 ± 0.06	0.56 ± 0.04	0.49 ± 0.03	0.43 ± 0.07	35.619	<0.001

Table 9. Comparison between symptomatic as regard Tei index.

Symptom	Tei Index	P value
Palpitation		
with	0.62 ± 0.08	<0.001
without	0.53 ± 0.09	
Chest Pain		
with	0.55 ± 0.10	<0.001
without	0.55 ± 0.08	

Valve prolapse is a common cardiac abnormality affecting 2.4% of the general population (1). The structural and functional disarray of the mitral valve apparatus observed in subjects with MVP might lead, at least in theory, to dysfunction of the left ventricular muscle surrounding the mitral annulus (2, 3). Doppler tissue imaging (DTI) is a simple, reproducible, non invasive technique that can be

used for assessment of regional myocardial velocities with a high temporal and spatial resolution. TEI index (which is the sum of isovolumetric contraction time IVCT and isovolumetric relaxation time IVRT divided by contraction time) was introduced by Tei et al. as a Doppler index of combined systolic and diastolic function to separate those with normal ventricular function from those with ventricular dysfunction (4). This index has been found to correlate well with invasive measures of systolic and diastolic LV function (5). The present study enrolled 40 patients with MVP (group I), and 25 apparently healthy age and sex matched individual as a control (group II). Group I were in sinus rhythm and presented by symptoms related to the MVP syndrome such as: chest pain 26 patients (65%), palpitation 10 (25%) patients, dyspnea 24 (60%) patients, presecyncope four (10%) patients. Physical examination of MVP group revealed: systolic click in 8 (20%) patients, mid to late systolic murmur in 14 (35%) patients, both click and murmur in 10 (25%) patients. Electrocardiographic ST, T wave changes in inferolateral leads were recorded in 8 (20%) patients. All these demographic characteristics are comparable to those reported by Dagdeverin et al. (8). As regards conventional echocardiographic variables of group I and group II, there was no significant differences between both groups as regards the internal dimensions and ejection fraction, however, group I had significantly higher LA diameter, aortic root dimension, anterior leaflet length, thickness, posterior displacement and mitral annular diameter than group II. These findings are in agreement with those reported by Dagdeverin et al. (8) and Weissman et al. (9). As regards TDI indices in group I had significantly higher IVRT and IVCT in basal and mid segments of septal, lateral, anterior and inferior walls. Moreover, both antrolateral and poster medial papillary muscles in group I had significantly higher IVCT, CT and IVRT than group II. These findings represent a state of subnormal or impaired regional function in group I. These findings at segmental levels has been confirmed by the statistically higher value of Tei index among group I patients compared to group II. Tei index is a globule index that was used to assess left ventricular performance. in our study its higher values among patients with MVP denoted subtle changes in both systolic and diastolic left ventricular function. Impaired diastolic function in patients with MVP was first reported in 1993 by Corrao S et al. (10) who found higher A, A/E ratio and lower E by conventional Doppler in patients with MVP and suggested that the cause may be an abnormal ventricular relaxation. Contradictory results were reported by Breithardt G et al. (11) who found increased E velocity by conventional Doppler in patients with primary MR than in control subjects. But the number of patients in this report was small (11 patients only) and they used mitral flow for assessment of diastolic function which is more load dependent than DTI derived E, A and E/A ratio. Recently, Zampoulakis J et al. (12); using TDI found that patients with MVP had some degree of diastolic dysfunction particularly after exercise. They assessed only the basal inferior segment and not all segments as in the present study. Zampoulatis J et al, reported also, that patients with MVP had less effective

contractile function when compared with healthy control group. Similar findings were reported by Agricola E et al. (13). They used TDI systolic time intervals as a potential echocardiographic indicators of subnormal LV performance. They found that the pre contraction time, contraction time and their ratio are increased in patients with asymptomatic mitral regurgitation and concluded that TDI systolic indices can identify patients with latent LV dysfunction. Despite the present study revealed that patients with MVP and MR had significantly higher IVCT and relatively higher IVRT than patients without MR this does not mean that the impaired regional function in patients with MVP is due to the presence of MR for two reasons: First, the majority of our patients had mild MR (45% had mild MR 45% without MR and only 10% had moderate MR). Second, TDI indices are relatively preload independent and this was confirmed when the MVP subgroup with no or significant MR compared with the group II. The possible explanation of this state of altered regional function in patients with MVP may be due to the presence of higher proportion of fibrin or abnormal collagen (14, 15) in the myocardium of patients with MVP leading to rigid myocardium and decreased ability for relaxation and also, reducing the contractile force of the myocardium. The higher TEI index in MVP patients presented by palpitation needs further investigations and higher number of patients. Limitations: The major limitations in the present study were angle dependency and sample volume site. However, efforts were made to minimize the angle as much as possible and to put the sample volume in the midway between endocardium and epicardium. Conclusion Patients with MVP have significantly higher TEI index than healthy control individuals denoting subtle LV dysfunction particularly those with MR.

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REFERENCES

1. Freed LA, Levy D, Levine RA, et al. Prevalence and clinical outcome of mitral-valve prolapse. *NEW ENGL J MED* New England Journal of Medicine 1999; 341(1):1-7.
2. Boudoulas H, Kolibash AJ, Jr, Baker P, et al. Mitral valve prolapse and the mitral valve prolapse syndrome: A diagnostic classification and pathogenesis of symptoms. *Am Heart J* 1989; 118(4):796-818.
3. Zuppiroli A, Rinaldi M, Kramer Fox R, et al. Natural history of mitral valve prolapse. *Am J Cardiol* 1995; 75(15):1028-32.
4. Tei C, Ling LH, Hodge DO, et al. New index of combined systolic and diastolic myocardial performance: A simple and reproducible measure of cardiac function--a study in normals and dilated cardiomyopathy. *J Cardiol* 1995; 26(6):357-66.
5. Tei C, Nishimura RA, Seward JB, et al. Noninvasive Doppler-derived myocardial performance index: Correlation with simultaneous measurements of cardiac catheterization measurements. *J Am Soc Echocardiogr* 1997; 10(2):169-78.
6. Sahn DJ, DeMaria A, Kisslo J, et al. Recommendations regarding quantitation in M-mode echocardiography: Results of a survey of echocardiographic measurements. *Circulation* 1978; 58(6):1072-83.
7. De Boeck BW, Cramer MJ, Oh JK, et al. Spectral pulsed tissue Doppler imaging in diastole: A tool to increase our insight in and assessment of diastolic relaxation of the left ventricle. *Am Heart J* 2003; 146(3):411-9.
8. Dagdeviren B, Bolca O, Eren M, et al. An unusual pulsed-wave tissue Doppler pattern in mitral valve prolapse: Spikes on systolic velocities. *Echocardiography* 2002; 19(5):367-72.
9. Weissman NJ, Pini R, Roman MJ, et al. In vivo mitral valve morphology and motion in mitral valve prolapse. *Am J Cardiol* 1994; 73(15):1080-8.
10. Corrao S, Scaglione R, Arnone S, et al. Left ventricular diastolic filling alterations in subjects with mitral valve prolapse: A Doppler echocardiographic study. *Eur Heart J* 1993; 14(3):369-72.
11. Bruch C, Stypmann J, Gradaus R, et al. Usefulness of tissue Doppler imaging for estimation of filling pressures in patients with primary or secondary pure mitral regurgitation. *Am J Cardiol* 2004; 93(3):324-8.
12. Zampoulakis JD, Karavidas AI, Matsakas E, et al. Tissue Doppler echocardiography reveals insufficient contractile reserve recruitment during effort in subjects with mitral valve prolapse and those with thick mitral valve. *Echocardiography* 2006; 23(2):114-9.
13. Agricola E, Galderisi M, Oppizzi M, et al. Pulsed tissue Doppler imaging detects early myocardial dysfunction in asymptomatic patients with severe mitral regurgitation. *Heart* 2004; 90(4):406-10.
14. Child AH. Joint hypermobility syndrome: Inherited disorder of collagen synthesis. *J Rheumatol* 1986; 13(2):239-43.
15. Yazici M, Ataoglu S, Makarc S, et al. The relationship between echocardiographic features of mitral valve and elastic properties of aortic wall and Beighton hypermobility score in patients with mitral valve prolapse. *Jpn Heart J* 2004; 45(3):447-60.