Early detection of cardiac function by tissue Doppler imaging in patients with mitral stenosis and sinus rhythm

Mitral stenozlu ve sinüs ritimli hastalarda kardiyak fonksiyonların erken dönemde doku Doppler görüntüleme ile belirlenmesi

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Objectives: We evaluated the changes in left ventricular function by means of tissue Doppler imaging (TDI) in patients with mitral stenosis (MS).

Study design: Standard echocardiographic and TDI studies were performed in 26 patients (18 females, mean age 38±7 years) with severe MS [mitral valve area (MVA) <1.2 cm^2], in 32 patients (24 females, mean age 35±9 years) with mild to moderate MS (MVA ≥1.2 cm^2), and in 25 age-matched healthy volunteers (17 females, mean age 39±6 years). All the patients were in sinus rhythm and none had hypertension or coronary artery disease. Systolic myocardial velocity, early and late diastolic velocities were measured in the basal lateral segment and basal interventricular septum from the apical four-chamber views.

Results: Left ventricular dimensions, ejection fraction, end-diastolic and end-systolic diameters, and fractional shortening of the left ventricle were similar in all the groups. Patients with MS had significantly decreased peak systolic myocardial velocities in both the lateral wall and interventricular septum of the left ventricle. In addition, early diastolic velocity and the ratio of early/late diastolic velocities were significantly lower. E-wave deceleration time and late diastolic myocardial velocities were similar in three groups. Peak systolic myocardial velocities were significantly correlated with mitral valve areas measured at the septum ($r=0.57$, $p<0.01$) and the lateral wall ($r=0.48$, $p<0.01$) of the left ventricle.

Conclusion: Our results show that, despite the presence of seemingly normal findings on standard echocardiography, TDI may provide evidence for left ventricular systolic dysfunction in patients with MS, representing early signs of myocardial abnormality.

Key words: Blood flow velocity; echocardiography, Doppler; mitral valve stenosis/ultrasonography; myocardial contraction; ventricular function, left.

Amaç: Çalışmamızda, mitral darlığı olan hastalarda doku Doppler görüntüleme ile sol ventrikül fonksiyonları incelendi.

Çalışma planı: Şiddetli mitral darlığı olan [mitral kapağı alanı (MKA) <1.2 cm^2] 26 hasta (18 kadın; ort. yaş 38±7), hafif-orta derecede mitral darlığı olan (MKA≥1.2 cm^2) 32 hasta (24 kadın; ort. yaş 35±9) ve 25 sağlıklı gönüllü (17 kadın; ort. yaş 39±6) standart ekokardiyografi ve doku Doppler görüntüleme ile incelendi. Bütün hastalar sinus ritmindeydi ve hiçbirinde hipertansiyon veya koroner arter hastalığı yoktu. Apikal dört-boşluk görüntülerde, lateral segment ve interventriküler septum bazalinden miyokardiyal sistolik hız, erken ve geç diyastolik hızlar ölçüldü.

Bulgular: Sol ventrikül boyutları, ejeksiyon fraksiyonu, diyastol ve sistol sonunda oluşan çaplar ve sol ventrikül kısalması üç grupta benzer bulundu. Mitral darlığı olan hastalarda sol ventrikül lateral duvarında ve interventriküler septumda ölçülen miyokard sistolik hızları kontrol grubuna göre anlamlı derecede düşük bulundu. Ayrıca, erken diyastolik hız ve erken/geç diyastolik hızların oranı anlamlı derecede düşüktü. E-dalgası deselerasyon zamanı ve geç diyastolik miyokard hızları üç grupta benzer bulundu. Septum ($r=0.57$, $p<0.01$) ve lateral duvarda ($r=0.48$, $p<0.01$) ölçülen miyokardiyal sistolik tepe hızlarıyla mitral kapak alanları arasında anlamlı ilişki olduğu görüldü.

Sonuç: Mitral darlığı olan hastalarda standart ekokardiyografide nispeten normal bulgular saptansa bile, doku Doppler görüntüleme sol ventrikül sistolik disfonksiyonunu gösterir bulgu sağlamaktadır. Bunlar miyokard anormalliğini yansıtan erken bulgular olarak değerlendirilebilir.

Anahtar sözcükler: Kan akım hızı; Doppler ekokardiyografi; mitral kapağı darlığı/ultrasonografi; miyokard kontraksiyonu; ventrikül fonksiyonu, sol.

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Rheumatic mitral stenosis (MS) is frequently seen in developing countries and causes significant morbidity and mortality.[1] Echocardiographic studies on left ventricular function in MS have yielded conflicting results. Despite our knowledge that myocardial function remains normal in MS, some authors have recently demonstrated abnormalities in left ventricular function.[2,3] Tissue Doppler imaging (TDI) is a new echocardiographic technique which allows quantitative measurements of myocardial contraction and relaxation velocities of a selected myocardial segment.[4] This method can provide important information on left ventricular myocardial function in patients with cardiac diseases.[5-8]

We hypothesized that patients with MS might have impaired left ventricular function and conducted a TDI study to evaluate left ventricular systolic and diastolic functions in patients with MS.

PATIENTS AND METHODS

Study population. Standard echocardiographic and TDI studies were performed in 26 patients (18 females, mean age 38±7 years) with severe MS [mitral valve area (MVA) <1.2 cm^2], in 32 patients (24 females, mean age 35±9 years) with mild to moderate MS (MVA ≥1.2 cm^2), and in 25 age-matched healthy volunteers (17 females, mean age 39±6 years).

Mitral valve area was determined by planimetric measurements and the pressure half-time method.[9] Systolic myocardial velocity, early and late diastolic velocities were measured in the basal lateral segment and basal interventricular septum from the apical four-chamber views. Exclusion criteria included the following: known coronary artery disease, diabetes mellitus, hypertension, significant aortic or mitral regurgitation, aortic stenosis, hyperthyroidism, chronic obstructive pulmonary disease, ventricular pre-excitation, atrioventricular conduction abnormalities, atrial fibrillation, or abnormal serum electrolytes.

The study protocol was approved by the Ethics Committee of the University and all subjects gave written consent to participate in the study.

Conventional two-dimensional Doppler echocardiography. A Vingmed Vivid FiVe Doppler echocardiographic unit (GE Vingmed Ultrasound, Horten, Norway) with a 2.5 MHz FPA probe was used. Examination was performed with the subject lying on the left side with the head of the bed elevated by about 30 degrees. The entire examination was recorded on a videotape, including M-mode recordings of the left ventricle during at least 10 cardiac cycles. Initially, two M-mode sequences of three cardiac cycles were retrieved from the videotape on the screen and measurements were made on frozen images by two readers with the use of electronic calipers in accordance with the recommendations of the American Society of Echocardiography.[10] Then, transthoracic echocardiographic evaluation was undertaken. Left atrial diameter, left ventricular end-systolic and end-diastolic diameters were measured by M-mode echocardiography and mitral valve areas were calculated. The mean of two values obtained by planimetric measurements and the pressure half-time method was expressed as MVA. Maximum and mean transmitral diastolic gradients were also calculated by Doppler scanning. Color-flow Doppler was used to assess valvular regurgitation. Pulmonary artery systolic pressure was estimated by continuous-wave Doppler imaging using the Bernoulli equation.[11]

Tissue Doppler imaging. Pulsed-wave TDI was performed by activating the TDI function on the same echocardiography device. Tissue Doppler imaging of the left ventricle (LV) was performed using standard apical views at a high frame rate (130±10 frames/sec) and a sector angle of less than 60 degrees. The spectral Doppler signal filters were adjusted to obtain Nyquist limits of -20 and +20 cm/sec, with the lowest wall filter settings and the minimal optimal gain, to eliminate the signals produced by transmitral flow. A 10-mm sampling gate was placed to obtain velocities from the lateral and septal corners of the mitral annulus. The peak annular velocities of systolic excursion in isovolumic contraction and ejection period (systolic myocardial velocity), and in early (early diastolic velocity) and late diastole (late diastolic myocardial velocity) were recorded and averaged over three consecutive cardiac cycles. In addition, the ratio of early/late diastolic velocities was calculated.[9] Mitral annular velocities were measured and the changes in mitral valve geometry and gradients were assessed by two observers who were blind to the data of the study. The intra- and interobserver variability in interpretation of TDI parameters was determined twice in 10 randomly selected recordings handled by the same observers and was found to be less than 4%.

Statistical analysis. The results were expressed as mean ± standard deviation (SD). Data were analyzed using one-way analysis of variance (ANOVA). Differences were considered significant when p value was less than 0.05. The intra- and interobserver agreement for echocardiographic parameters was measured

Table 1. Clinical characteristics and Doppler echocardiographic parameters of the study groups

	Mitral stenosis		
	Severe (n=26)	Mild to moderate (n=32)	Controls (n=25)
Age (years)	38±7	35±9	39±6
Gender (Female/Male)	18/8	24/8	17/8
Body mass index (kg/m^2)	23±3	22±3	23±3
Systolic blood pressure (mmHg)	112±9	110±9	111±9
Diastolic blood pressure (mmHg)	67±5	66±6	69±6
Echocardiographic parameters			
Mitral valve area (cm^2)	1.2±0.2‡	1.7±0.3‡	3.6±0.5
Maximum mitral gradient (mmHg)	19±4$^{\S,\#}$	11±2§	–
Mean mitral gradient (mmHg)	8±2$^{\S,\#}$	4±2§	–
Left atrial diameter (cm)	4.4±0.3‡	3.9±0.2†	3.5±0.2
Left ventricular end-diastolic diameter (mm)	45±4	46±5	45±5
Estimated systolic pulmonary artery pressure (mmHg)	38±5§	32±5†	28±4
Ejection fraction (%)	68±4	65±5	67±4
Fractional shortening (%)	32±4	31±4	32±3
Thickness of the interventricular septum (mm)	10.5±0.2	10.1±0.2	10.4±0.2
Thickness of the left ventricular posterior wall (mm)	9.9±0.2	9.7±0.2	9.8±0.2
Mitral regurgitation (mild/absent)	16/10	20/12	4/21

‡p<0.01, †p<0.05, and §p<0.001: compared to controls; $^{\#}$p<0.05: compared to patients with mild to moderate mitral stenosis.

with Kappa statistic analysis. All statistical data were processed using the SPSS statistical package.

RESULTS

Clinical characteristics. Age, gender, heart rate, body mass index, and blood pressure levels were similar in all the groups. The clinical characteristics of the three groups are shown in Table 1.

Echocardiographic parameters. Left ventricular dimensions, ejection fraction, end-diastolic and end-systolic diameters, and fractional shortening of the left ventricle were found similar in all the groups. Patients with severe MS had the largest left atrium, the highest diastolic transmitral gradient, and the highest estimated systolic pulmonary artery pressure (Table 1). Mitral regurgitation was detected in 16 patients with severe MS, in 20 patients with mild to moderate MS, and in four controls.

Tissue Doppler imaging findings. Mitral stenosis was associated with significantly lower peak systolic myocardial velocities in both the lateral wall and the interventricular septum of the left ventricle, indicating reduced left ventricular systolic function (Table 2). Compared to controls, early diastolic velocity and the ratio of early/late diastolic velocities were significantly lower in patients with severe or mild to moderate MS. E-wave deceleration time and late diastolic myocardial velocities were comparable to controls. Peak systolic myocardial velocities were significantly related to mitral valve areas measured at the septum (r=0.57, p<0.01) and the lateral wall (r=0.48, p<0.01) of the left ventricle.

Reader variability. The intra- and interobserver agreement for standard Doppler echocardiography and TDI studies was good, with kappa values greater than 0.70.

DISCUSSION

Systolic and diastolic dysfunction has been described in MS.[2] In patients with pure MS, varying degrees of deterioration occur in left ventricular performance. It has been demonstrated that, regardless of the level of left ventricular systolic function, varying degrees of ultrastructural pathologic alterations occur in left ventricular muscle cells.[12] Although these changes did not correlate with the severity of MS, more extensive loss of myofibrils was found in patients with abnormal left ventricular function.[12]

Tissue Doppler imaging is a recent technique in echocardiography for accurate quantification of systolic and diastolic myocardial function. There are a few reports on its utilization in evaluating systolic functions in MS.[3] A recent TDI study has shown significant improvement after percutaneous mitral comissurotomy.[13]

In our study, the most commonly used indexes of LV systolic performance, such as LV fractional shortening and LV ejection fraction, were within normal ranges, so were not helpful to identify myocardial dysfunction in both patient groups. Similarly, apart

Table 2. Tissue Doppler imaging findings obtained in the basal lateral wall and interventricular septum of the left ventricle

	Mitral stenosis		
	Severe (n=26)	Mild to moderate (n=32)	Controls (n=25)
Lateral wall			
Early diastolic velocity (cm/sec)	10±4‡	12±4†	15±3
E-wave deceleration time (msec)	63±12	64±13	62±15
Late diastolic velocity (cm/sec)	6.2±2.1	5.8±2.0	6.3±2.2
Ratio of early/late diastolic velocities	1.8±0.5†	2.1±0.6	2.2±0.7
Systolic myocardial velocity (cm/sec)	7±1‡,#	8±2†	11±2
Interventricular septum			
Early diastolic velocity (cm/sec)	11±3‡	13±4†	15±4
E-wave deceleration time (msec)	62±14	63±12	63±13
Late diastolic velocity (cm/sec)	6.5±2.1	6.0±2.2	6.2±2.0
Ratio of early/late diastolic velocities	1.9±0.6†	2.2±0.5	2.3±0.6
Systolic myocardial velocity (cm/sec)	7.1±2.1‡,#	8.2±2.1†	12.5±3.0

‡p<0.01 and †p<0.05: compared to controls; #p<0.05: compared to patients with mild to moderate mitral stenosis.

from early diastolic velocity and early to late diastolic velocity ratio, TDI parameters of left ventricular diastolic function in MS patients did not differ from those of normal controls. However, systolic myocardial velocity which is an index of left ventricular systolic function was significantly reduced in both patient groups. This TDI evidence of systolic left ventricular dysfunction, which is associated with myocardial scarring and calcification of cardiac structure, may represent early preclinical changes. These results suggest that myocardial function would inevitably be affected by myocardial scarring and calcification occurring in mitral stenosis.

Tissue Doppler imaging parameters are considered to be more sensitive than conventional mitral Doppler indexes in the assessment of left ventricular relaxation.[14-16] Our results demonstrate that, as for transmitral parameters, TDI indexes are also probably unable to identify left ventricular diastolic dysfunction in MS. In our patient groups, TDI proved superior to other echocardiographic techniques in identification of impairment in myocardial function. Peak systolic and peak early diastolic velocities, and to a lesser degree, the ratio of peak early/peak late diastolic velocities considerably enabled us to detect deterioration in LV systolic and diastolic functions in MS. With regard to left ventricular systolic function, several investigators reported that TDI-derived systolic myocardial velocity was well related to left ventricular ejection fraction.[17,18]

Our TDI finding suggesting impairment in left ventricular systolic function despite a relatively preserved left ventricular diastolic function in patients with MS seems to be inconsistent with the evidence that diastolic dysfunction usually precedes systolic dysfunction.[3,4] It may be attributed to the relatively decreased diagnostic value of TDI in evaluating left ventricular diastolic function, which may be influenced by multiple interrelated factors including heart rate, ventricular dimensions, and blood pressure. However, systolic myocardial velocity has been shown to be an appropriate parameter for global systolic function,[17] and can be used in detecting abnormal systolic function in patients with heart failure, despite the presence of normal ejection fraction.[18,19]

The abnormalities of left ventricular function in MS may be substantially related to the changes occurring in the structure of the myocardial wall. Significant decreases in systolic myocardial velocity and especially in early diastolic velocity in the basal region of the left ventricle are likely to be caused by the extension of the scarring process from the mitral valve to the adjacent myocardium.

In conclusion, our results demonstrate that patients with MS show significant TDI changes in the properties of myocardial contractility, in the face of seemingly normal myocardial contractility on standard echocardiography. These may represent early signs of myocardial abnormality despite a preserved global function, but further studies are required to clarify the clinical and prognostic value of TDI in these patients.

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