# Evaluation of the global systolic and diastolic function of the left ventricle by the total ejection isovolume index following percutaneous mitral balloon valvuloplasty: a tissue Doppler imaging study

## Perkütan mitral balon valvüloplastiden sonra global sol ventrikül sistolik ve diyastolik fonksiyonlarının total ejeksiyon isovolümetik indeks ile değerlendirilmesi: Doku Doppler ekokardiyografi çalışması

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**Objectives:** We evaluated the effect of percutaneous mitral balloon valvuloplasty (PMBV) on global systolic and diastolic functions of the left ventricle with the use of the total ejection isovolume (TEI) index.

**Study design:** The study included 76 consecutive patients (16 males, 60 females; median age 36 years; range 19 to 68 years) who underwent PMBV for isolated rheumatic mitral stenosis. Systolic and diastolic indexes were measured by pulsed Doppler tissue imaging echocardiography from the mitral lateral annulus and the TEI index was calculated before, and 48 hours and three months after PMBV.

**Results:** Concerning diastolic function parameters, there was an improvement in the maximum early diastolic velocity (p=0.001), early and late diastolic velocity ratio (p=0.02), and a decrease in the isovolumetric relaxation time (p=0.02) immediately after PMBV. Maximum systolic velocity (p=0.01) improved as a systolic function parameter. Left ventricular global function did not improve significantly 48 hours (TEI indices 0.7±0.3 *vs* 0.5±0.2, p=0.06) and three months (0.7±0.3 vs. 0.6±0.2, p=0.97) after PMBV.

**Conclusion:** Parameters of mitral annular systolic and diastolic functions seem to be improved after PMBV, accompanied by an insignificant change in the TEI index. These changes in myocardial longitudinal functions may be due to the relief of functional restriction by the mobilization of the subvalvular apparatus.

*Key words:* Balloon dilatation; blood flow velocity; echocardiography, Doppler, pulsed; heart function tests; mitral valve stenosis; myocardial contraction; ventricular function, left.

**Amaç:** Perkütan mitral balon valvüloplastinin (PMBV) global sol ventrikül sistolik ve diyastolik fonksiyonları üzerine etkisi total ejeksiyon isovolümetik (TEİ) indeks ile değerlendirildi.

**Çalışma planı:** İzole romatizmal sıkı mitral darlık nedeniyle PMBV uygulanan ardışık 76 hasta (16 erkek, 60 kadın; ortanca yaş 36; dağılım 19-68) incelendi. Mitral lateral annulustan yapılan pulse-dalga doku Doppler ekokardiyografi ile sistolik ve diyastolik fonksiyon parametreleri ve bu verilerden hesaplanan TEİ indeksi, PMBV öncesinde, işlemden 48 saat ve üç ay sonra değerlendirildi.

**Bulgular:** İşlem sonrası erken dönemde, diyastolik fonksiyon parametrelerinden maksimum erken diyastolik hız (p=0.001) ve erken-geç diyastolik hız oranında (p=0.02) artış, isovolümetrik relaksasyon zamanında düşme (p=0.02); sistolik fonksiyon göstergesi olarak da maksimum sistolik hızda (p=0.01) anlamlı artış görüldü. Global fonksiyonları yansıtan TEİ indeksinde ise, işlem öncesine göre (TEİ indeksi 0.7±0.3), işlemden 48 saat (TEİ indeksi 0.5±0.2, p=0.06) ve üç ay sonra (0.6±0.2, p=0.97) gözlenen azalma istatistiksel olarak anlamlı değildi.

**Sonuç:** Mitral annuler sistolik ve diyastolik fonksiyon göstergelerinde PMBV sonrasında iyileşme olmasına rağmen, TEİ indeksinde anlamlı değişiklik oluşmamaktadır. Mitral annuler longitudinal hareketteki değişiklikler, subvalvuler aparatusun kısmen serbestleşmesi sonucu fonksiyonel sınırlamanın ortadan kalkmasına bağlı olabilir.

*Anahtar sözcükler:* Balonla genişletme; kan akım hızı; ekokardiyografi, Doppler, pulse; kalp fonksiyon testi; mitral kapak darlığı; miyokard kontraksiyonu; ventrikül fonksiyonu, sol.

*Presented in part at the 21st National Cardiology Congress (November 26-29, 2005, Antalya, Turkey).*

*Received:* August 29, 2005 *Accepted:* November 17, 2005

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Pure mitral stenosis (MS) affects left ventricular (LV) performance as a result of myocardial and functional factors.[1-4] However, the results of the studies about the effect of percutaneous mitral balloon valvuloplasty (PMBV) on ventricular functions are controversial.[5-10]

Pulsed Doppler tissue imaging (TDI) is a relatively independent echocardiographic method from loading conditions and provides measurement of systolic and diastolic velocities of mitral and tricuspid annular motion. The Doppler total ejection isovolume (TEI) index is a combined measurement of systolic and diastolic myocardial performance. It is thought to be more reflective of overall cardiac function than systolic or diastolic function alone in both ventricles, providing a conceptually new measurement of global cardiac function. To our knowledge, there has been no report about the use of TDI-derived TEI index in assessing the effect of PMBV on LV systolic and diastolic function in rheumatic pure MS.

The aim of the present study was to evaluate the effect of successful PMBV on global systolic and diastolic LV functions by means of TDI and TDI-derived TEI index.

## PATIENTS AND METHODS

***Study population.*** The study included 76 consecutive patients (16 males, 60 females; median age 36 years; range 19 to 68 years) who underwent PMBV for isolated rheumatic MS between April 2003 and March 2005. All the patients were in sinus rhythm, with functional class II or III according to the New York Heart Association. Exclusion criteria were as follows: moderate or severe mitral regurgitation (MR), moderate or severe aortic regurgitation or stenosis, tricuspid stenosis, a previous aortic or mitral valve operation or valvuloplasty, clinical, electrocardiographic or angiographic evidence for coronary artery disease, diabetes mellitus, systemic hypertension, wall motion abnormality, bundle branch block, evidence for rheumatic activity in the preceding six months and severe mitral annular calcification. All the patients underwent PMBV by the Inoue technique after cardiac catheterization and no procedure-related complications occurred.

***Echocardiography.*** All the patients were examined in the left lateral decubitus position by M-mode, two-dimensional, Doppler and TDI echocardiography (Aloka SSD-5500, the Netherlands) using a 3.5 MHz transducer. A continuous one-lead electrocardiogram was obtained. Left atrial diameter was calculated from the parasternal long axis view by M-mode echocardiography. Left ventricular ejection fraction was calculated by the modified Simpson's rule from the apical four- and two-chamber views, mitral valve area was measured by the pressure half-time method,[11] and the peak and mean diastolic transmitral pressure gradients were assessed by continuous-wave Doppler echocardiography. Pulmonary artery pressure was derived from the tricuspid regurgitant jet velocity by the modified Bernoulli equation.[12]

***Pulsed Doppler tissue imaging.*** Pulsed-wave TDI was performed by activating the TDI function on the same echocardiographic machine. In the apical four-chamber view, the TDI cursor was placed on the lateral side of the mitral annulus. Filter settings were kept low (50 Hz), gains were adjusted to the minimal optimal level to minimize noise and eliminate signals produced by the transmitral flows, and the sample volume was 3-5 mm. A Doppler velocity range of -20 cm/s to 20 cm/s was selected. The peak systolic and diastolic velocities were measured on-line at a sweep speed of 50 mm/s. 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 motion of the mitral and tricuspid annulus. Systolic (S), early diastolic (E), and late diastolic (A) maximum velocities, isovolumetric contraction time (IVCT), ejection time (ET), isovolumetric relaxation time (IVRT), and E wave deceler-

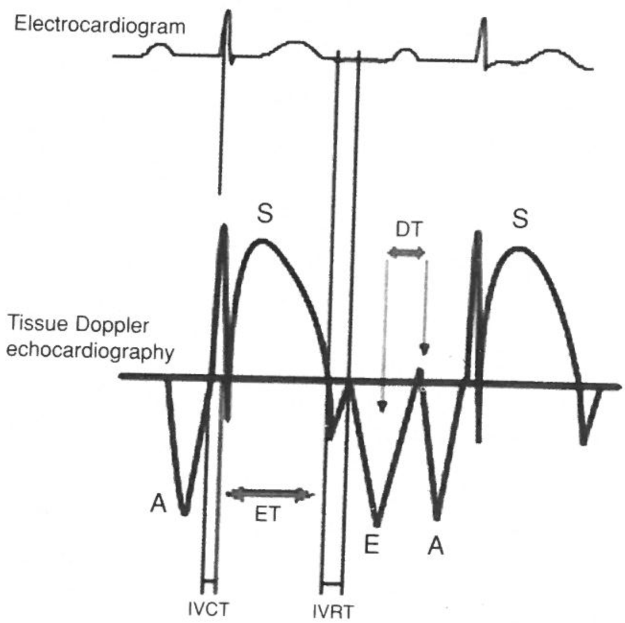


**Fig. 1.** Tissue Doppler echocardiography time intervals were measured from the Doppler velocity time intervals of the mitral lateral annular tissue. IVCT: Isovolumetric contraction time; IVRT: Isovolumetric relaxation time; S: Systolic velocity, E: Early diastolic velocity; A: Late diastolic velocity, ET: Ejection time, DT: E wave deceleration time.

ation time (DT) were measured by TDI at the sites of the mitral annulus as demonstrated in Fig. 1.

Doppler tissue echocardiography-derived systolic indexes included myocardial peak velocity of S, IVCT (from the onset of ECG QRS to the beginning of S) and ET (from the onset to the end of S wave). Diastolic indexes included peak velocities of E and A, E/A ratio, DT and IVRT (from the end of S wave to the onset of E wave). The TEI index was obtained from the mitral annulus TDI as the sum of IVCT and IVRT divided by ET. Five cardiac cycles were measured and averaged.

Echocardiographic assessments were performed at baseline, and 48 hours, and three months after PMBV. Parameters concerning myocardial systolic and diastolic functions were compared.

***Reproducibility.*** Intraobserver variability was assessed by repeating the measurements in 10 patients and on two occasions (1 to 10 days apart) under the same basal conditions. To test the interobserver variability, the measurements were performed off-line from video recordings by another observer who was unaware of the results of the first examination. Variability was calculated as the mean percentage error, derived from the difference between the two sets of measurements divided by the mean of the observations.

***Statistical methods.*** All data were expressed as a mean ± standard deviation. Observed changes after valvuloplasty were analyzed for statistical significance using the Student's paired t-test. The Pearson correlation coefficient was used for bivariate analysis. All statistical calculations were made using the SPSS for Windows ver. 10.0 statistical software package. A *p* value of less than 0.05 was considered statistically significant.

## RESULTS

Baseline evaluations revealed minimal MR in 54 patients. Immediately after PMBV, minimal MR was detected in nine patients who had no MR before valvuloplasty and, in six patients, the degree of MR increased from minimal to moderate. Significant left to right shunting was detected in two patients after valvuloplasty and they were excluded from the study. The mean left ventricle EF was 63±4% at baseline, it was 65±3% in the first month, and 64±2% in the third month (p>0.05).

A significant negative correlation was found between EF and the TEI index (r=-0.57, p=0.005). There were no correlations between the mitral annular velocities and mitral valve area or gradient. Mitral annular maximum S velocity was correlated with E velocity (r=0.61, p=0.0001), DT (r=0.47, p=0.005) and the TEI index (r=-0.35, p=0.03). A significant correlation was detected between the maximum S velocity and the maximum E velocity (r=-0.47, p=0.004), IVCT (r=-0.58, p=0.0001), and the TEI index (r=-0.46, p=0.004). There was a significant positive correlation between pulmonary artery pressures derived by echocardiography and by catheterization before PMBV (r=0.87, p=0.0001). The echocardiographic data of the patients and mitral annular pulsed TDI

**Table 1. Echocardiographic variables and mitral annular pulsed Doppler tissue imaging characteristics before and after valvuloplasty**

| | Before valvuloplasty | 48 hours after valvuloplasty | 3 months after valvuloplasty |
|---|---|---|---|
| Echocardiographic variables | | | |
| Mitral valve area ($cm^2$) | 1.1±0.2 | 1.9±0.2* | 1.8±0.2* |
| Mean mitral valve gradient (mmHg) | 10.6±2.7 | 4.0±2.9* | 6.4±4.6* |
| Left atrial diameter in the parasternal long axis (cm) | 4.6±0.6 | 4.0±0.6* | 3.9±0.5* |
| Systolic pulmonary artery pressure (mmHg) | 39.2±15.3 | 26.8±11.0* | 29.1±10.1* |
| Pulsed Doppler tissue imaging | | | |
| Peak systolic mitral annular velocity (cm/sec) | 9.0±1.7 | 9.5±2.1* | 10.6±2.1* |
| Peak early diastolic mitral annular velocity (E) (cm/sec) | 7.3±2.4 | 9.8±2.7* | 10.1±1.8* |
| Peak late diastolic mitral annular velocity (A) (cm/sec) | 8.7±2.2 | 8.7±3.5 | 8.9±4.4 |
| Isovolumetric contraction time (msec) | 85.6±13.0 | 82.5±20.7 | 81.6±18.7 |
| Ejection time (msec) | 275.8±43.1 | 283.2±33.6 | 280.0±26.7 |
| Isovolumetric relaxation time (msec) | 72.0±42.2 | 63.3±40.4* | 58.7±24.2* |
| E wave deceleration time (msec) | 96.6±62.3 | 95.5±31.1 | 109.7±30.0 |
| E/A | 0.9±0.5 | 1.3±0.7* | 1.4±0.7* |
| Total ejection isovolume index | 0.7±0.3 | 0.5±0.2 | 0.5±0.1 |

Data are expressed as mean ± standard deviation. *: p<0.05 *vs* baseline.

characteristics at baseline, 48 hours and three months after PMBV are presented in Table 1.

Forty-eight hours after PMBV, mitral valve area increased and mitral valve gradient decreased significantly ($p<0.0001$). The left atrial diameter was also lower than the baseline ($p<0.05$).

Maximum S, E velocities and E/A ratio significantly increased immediately after PMBV ($p=0.01$, $p=0.001$, $p=0.02$ respectively). The TEI index tended to decline after PMBV ($p=0.06$).

Intraobserver and interobserver variability percentages for conventional TDI-derived parameters of the mitral lateral annulus (S, E, A, IVRT, ET, IVCT, DT) ranged from 3.2% to 5.8%. Intraobserver variability for the TEI index was 3.6±2.7%; interobserver variability was 4.7±1.6%.

## DISCUSSION

Doppler tissue imaging, an echocardiographic method which is relatively independent from the volume loading conditions, enables us to assess subclinical long-axis myocardial dysfunction that cannot be detected by conventional left ventricular systolic function measurements. Pulsed TDI has been used for the evaluation of impaired systolic[13,14] or diastolic function.[15-19] Using TDI, Ozdemir et al.[1] reported significantly decreased myocardial velocities in patients with MS.

The TEI index, a combined measurement of systolic and diastolic myocardial performance, is more reflective of overall cardiac function than systolic or diastolic function alone in both ventricles, and provides a new concept about the measurement of global cardiac function.[20,21]

It has been demonstrated that the TEI index obtained by TDI correlates well with the TEI index determined by pulsed Doppler, and has the advantage of simultaneous recording of systolic and diastolic velocity patterns.[21,22]

Although it has been shown that the velocity of mitral annular motion is affected by MS, there is no report on the use of the TDI-derived TEI index to assess the effect of MS and balloon valvuloplasty on LV systolic and diastolic functions.

Several studies examined left ventricular ejection performance by angiographic and hemodynamic variables in patients with MS, with some reporting reduced performance attributable to insufficient preload, afterload mismatch, and the effects of right ventricular pressure and myocardial factors.[23]

Reduced LV end-diastolic volume[3] and increased myocardial stiffness[10] have been demonstrated in patients with MS. Abnormal passive elastic properties have also been reported in patients with severe MS arising from chamber atrophy due to unloading, myocardial fibrosis, right and left ventricular interaction, or internal restrictions due to the rigid mitral valve apparatus.[10] In addition, MS patients with normal global systolic function exhibited significantly decreased LV long-axis systolic function in the absence of segmental wall motion abnormality, suggesting a subclinic impairment in LV systolic function.[23]

There is controversy on the results of studies that used angiographic and hemodynamic variables to evaluate the effect of PMBV on systolic and diastolic functions of the left ventricle.[2,3,5-10,24]

In our study, myocardial S and E velocities, and the E/A ratio were found to increase after PMBV with no significant change in the LV ejection fraction and the TEI index. Significant improvement in TDI parameters after PMBV in these patients might indicate the presence of subclinical dysfunction underlying normal left ventricular function assessed by LV ejection fraction.

A previous study demonstrated that LV end-diastolic volume increased immediately after PMBV followed by a steady increase during a follow-up of 12 months.[3] Despite this increase in LV end-diastolic volume and a decrease in systemic vascular resistance after PMBV, LV ejection performance improved[3] as in myocardial stiffness.[10] However, in the latter study,[10] the rate of relaxation and chamber stiffness remained unchanged. These findings correlate well with our results showing no significant change in IVRT and IVCT after PMBV. The improvement in passive elastic properties after valvuloplasty can be explained by the mobilization of the subvalvular apparatus with an improvement in regional LV function.[7,10] Previous studies reported that preload increase caused a decrease in IVRT and an increase in IVCT and ET.[4,25] Although different loading conditions significantly changed the myocardial performance index, the magnitude of changes were minor (<10%).[25] Our results are compatible with these findings in patients with MS, which is a disease causing preload reduction. After PMBV, we found that increases in IVCT and ET were insignificant, and the TEI index was not influenced by the significant decrease in IVRT. In our study, although pulmonary artery pressure significantly decreased after PMBV, no significant changes were detected both in LV ejection fraction and the TEI index. As the TEI index is not greatly influenced by variations in heart rate, preload, blood pressure,[20,26,27] afterload,[28] right ventricular pressure or dilatation, and tricuspid regurgitation[29] in the clinical settings, alterations in myocardial velocities may be due to increased LV compliance, which may be the result of a relieved functional restriction caused by ventricular attachment to a thickened and immobile valve apparatus.

In conclusion, parameters of mitral annular systolic and diastolic functions seem to be improved after PMBV, accompanied by an insignificant change in the TEI index, which is thought to be more reflective of overall cardiac function than systolic or diastolic function alone in both ventricles. These changes in myocardial longitudinal functions may be due to the relief of functional restriction by the mobilization of the subvalvular apparatus.

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