

# Value of stress echocardiography in mitral stenosis

## *Mitral darlığının değerlendirilmesinde stres ekokardiyografinin değeri*

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### ABSTRACT

Mitral stenosis (MS) is a common disease that causes substantial morbidity. Timely recognition and treatment of the mitral stenotic lesion is very important. Stress echocardiography plays an important role in evaluating asymptomatic patients with significant mitral stenosis and symptomatic patients with only mild disease at rest. In patients with mitral stenosis, stress echocardiography protocols assess for the change in the mean transmitral pressure gradient and a peak pulmonary artery systolic pressure during exercise. In this review, clinical use of stress echocardiography in patients with mitral stenosis is summarized. (*Anadolu Kardiyol Derg 2013; 13: 257-60*)

**Key words:** Mitral stenosis, stress echocardiography, exercise test, dipyridamole, dobutamine, pulmonary artery systolic pressure

### ÖZET

Mitral darlığı önemli morbiditeye neden olan bir hastalıktır. Mitral darlığının zamanında tanınması ve tedavi edilmesi önemlidir. Stres ekokardiyografi ileri düzeyde mitral darlığı olan semptomsuz ve orta düzeyde mitral darlığı olup semptomlu olan hastaların değerlendirilmesinde önemli rol oynar. Stres ekokardiyografi protokolü ile ortalama mitral kapak gradyanı ve pulmoner arter sistolik basıncında egzersiz ile oluşan değişiklik saptanır. Bu derlemede, mitral darlığı olan hastalarda stres ekokardiyografinin yeri özetlenmiştir. (*Anadolu Kardiyol Derg 2013; 13: 257-60*)

**Anahtar kelimeler:** Mitral darlık, stres ekokardiyografi, egzersiz testi, dipiridamol, dobutamin, pulmoner arter sistolik basıncı

### Introduction

Several diseases have been accepted as pathological causes for mitral valve stenosis (MS), especially rheumatic valvular disease is still a prevalent in underdeveloped and developing countries (1). The main features are leaflet thickening, nodularity, and commissural fusion, all of which result in narrowing of the valve to the shape of a fish mouth. The leaflets might be calcified. Chordal fusion and shortening adds a further resistance to blood flow (2). Timely recognition and treatment of the underlying mitral stenotic lesion can prevent development of irreversible pulmonary hypertension, ventricular dysfunction and other complications (3). Patient management involves monitoring for clinical symptoms or functional deterioration assessed

by echocardiography and Doppler examination. While resting values of mitral gradients and pulmonary arterial pressures do not always reflect the severity of the disease, stress echocardiography may provide the necessary clues to determine the clinical and hemodynamic impact of MS (4).

This review evaluates whether the use of stress echocardiography to assess disease severity and to determine the optimal time for either surgical or percutaneous intervention of mitral stenosis.

### Clinical importance

Stress echocardiography plays very important role in evaluating patients with mitral stenosis. Hence, guidelines of both the American College of Cardiology/American Heart Association

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(ACC/AHA) and European Society of Cardiology (ESC) have placed emphasis on the role of exercise testing to provide objective evidence of exercise capacity, symptom status and echocardiographic parameter (1, 5). Advances in diagnosis and risk stratification, progress in percutaneous balloon valvuloplasty, surgical options including closed or open valvotomy and valve replacement have led to improved outcomes of patients with valvular heart disease in the past 5 decades (1). The most important indication for intervention in patients with significant valve disease (mitral valve area  $<1.5 \text{ cm}^2$ ) is the development of symptoms, as emphasized in recent ACC/AHA and ESC guidelines (1, 5). Although Doppler echocardiographic examination at rest is now the preferred imaging modality for the evaluation of patients with cardiac valvular disease, the current ACC/AHA guidelines have given a class I recommendation for stress echocardiography in patients with mitral stenosis and discordance between symptoms and stenosis severity (1).

### Stress echocardiography

Stress echocardiography for mitral valve disease is performed via both exercise and pharmacologic protocols. The measurement of pulmonary artery pressures and mean transmitral pressure gradient during stress echocardiography can help to distinguish those who could benefit from valvuloplasty or valve replacement from those who should be maintained on medical therapy (6-8).

### General test protocol

Stress echocardiography for mitral stenosis is performed with either exercise or pharmacologic stress. Exercise echocardiography is usually preferred over pharmacological stress because it provides information about exertional symptoms and blood pressure response (6).

**Exercise test:** Exercise echocardiography is often used to assess functional capacity and the hemodynamic response in patients with mitral stenosis (9). Exercise echocardiography can be performed using either a treadmill or a bicycle protocol. Treadmill exercise can be performed with Bruce or modified Bruce protocols, and bicycle exercise echocardiography is performed during either an upright or a recumbent posture. Workload is gradually increased until the patient achieves target heart rate or develops symptoms of fatigue or shortness of breath. Images were obtained at baseline during rest and immediately after discontinuation of exercise. The most important advantage of bicycle exercise is the chance to obtain images during the various levels of exercise. When a treadmill test is performed, scanning during exercise is not feasible, most protocols rely on immediate post exercise imaging. Therefore, the patient is moved immediately from the treadmill to an imaging bed and that imaging may be completed within 1-2 min (9). The advantage of treadmill exercise echocardiography is that it is the most commonly practiced protocol, and patients usually achieve higher workloads in exercise (10). On the other hand, the disad-

vantage is that the data acquisition is restricted to images at baseline and post-maximal exercise, and rapid position changes after exercise are required. The collection of echocardiographic data should be performed within the 1-2 minutes of the maximal exercise. The advantage of bicycle exercise echocardiography is the chance to obtain images during the various level of exercise, but elderly patients may not exercise well in this position (9).

**Dobutamine:** If pharmacologic stress is necessary, the standard dobutamine protocol using continuous intravenous infusion is used (3, 11, 12). Dobutamine echocardiography was performed using three-min stages and starting at  $5 \text{ mcg/kg/minute}$ , followed by 10, 20, 30, and  $40 \text{ } \mu\text{g/kg per min}$ . Atropine (total dose  $\leq 2 \text{ mg}$ ) was administered at the start of the  $40 \text{ } \mu\text{g/kg per min}$  stage if needed to augment heart rate (9).

Dobutamine stress echocardiography is a good alternative if the patient cannot exercise (6).

**Dipyridamole:** The standard dipyridamole protocol consists of an intravenous infusion of  $0.84 \text{ mg/kg}$  over 10 min, in two separate infusions. If no endpoint is reached, atropine is added. Aminophylline ( $240 \text{ mg iv}$ ) should be available for immediate use in case an adverse dipyridamole-related event occurs (9).

**Adenosine:** Adenosine can be used, infused at a maximum dose of  $140 \text{ } \mu\text{g/kg/min}$  over 6 min (9).

**Pacing:** Pacing is started at 100bpm and increased every 2 min by 10 bpm until the target heart rate is achieved or until other standard endpoints are reached (9).

Accordingly, we can identify two groups of patients whose symptoms do not correlate with the resting mitral valve area and gradient. The first group, who lead a sedentary life style and do not complain of symptoms, but have significant mitral stenosis. The second group, whose severe symptomatology appears to be out of proportion to their resting mitral valve area ( $>1.5 \text{ cm}^2$ ). An increase in the mitral valve area without significant changes in the transmitral gradient and pulmonary artery pressure during exercise will point less severe disease in second group from the first group (3).

The threshold values proposed by the ACC/AHA guidelines for consideration for intervention are a mean transmitral pressure gradient  $>15 \text{ mmHg}$  or a peak pulmonary artery systolic pressure  $>60 \text{ mmHg}$  during stress. In patients with pulmonary artery pressures or valve gradients above these values, percutaneous balloon valvotomy or surgical intervention is recommended, even for patients with apparently moderate mitral stenosis at rest (1, 9).

In patients who have predominantly mitral stenosis peak exercise pulmonary artery systolic pressure is inversely related to exercise capacity (13). The transmitral mean pressure gradient commonly increases during exercise, regardless of the severity of stenosis, in accordance with exercise duration and exercise induced changes in cardiac output (7, 12). Symptoms like dyspnea and fatigue that most of these patients developed during the test can be attributed to the elevated left atrial pressure caused by flow-dependent increases in gradients across

the stenotic mitral valve. Tunick et al. (4) have shown that patients with mitral stenosis who were limited by dyspnea developed a greater increase in pulmonary artery pressure during stress testing than those who were limited by fatigue. In addition, Brochet et al. (14) investigated the role of values recorded during the first stage of exercise Doppler echocardiography in asymptomatic patients. Mitral stenosis severity and rest and peak systolic pulmonary artery pressures were not different between patients who did and did not develop dyspnea. Progressions of mean gradient and relative peak systolic pulmonary artery pressure (sPAP) (ratio of sPAP/baseline sPAP) were significantly greater in patients who developed dyspnea compared with those who did not, whereas no difference was observed for absolute systolic pulmonary artery pressure progression. Onset of dyspnea was associated with a high increase of relative peak systolic pulmonary artery pressure, but not with the 60 mmHg peak systolic pulmonary artery pressure threshold. Grimaldi et al. (8) reported, predictors of adaptation to exercise were age, mean pulmonary gradient and systolic pulmonary pressure, according to multivariate analysis, best predictor was resting mean pressure gradient.

Previous studies of MS have reported an association between the echocardiographic findings and functional class and increase in plasma levels of N-terminal pro-brain natriuretic peptide (NT pro-BNP) (15). Tanboğa et al. (16) showed BNP level and sPAP better correlated with mitral valve (MV) resistance than mitral valve area (MVA) and mean MV gradient. Uçar et al. (17) found elevated plasma BNP levels in pure MS in sinus rhythm and plasma BNP levels correlated with disease severity, such as transmitral gradient, sPAP, functional capacity, left ventricular end -systolic diameter.

In a recent study by our group, we investigated whether elevated NT pro-BNP predicts pulmonary artery systolic pressure increase on exercise stress echocardiography in asymptomatic or mildly symptomatic patients with moderate to severe mitral stenosis. We demonstrated, NT pro-BNP levels correlate with functional class and echocardiographic findings in patients with mitral stenosis and indicate exercise induced augmentation of peak pulmonary artery systolic pressure >60 mmHg (18). Exercise echocardiographic methods have certain limitations the results may be affected by the person who performs the echocardiography, this point that the measurement of NT pro-BNP appears to be the method to be employed in the assessment of the severity of MS, for its features as shortness, simplicity, objectivity, and being noninvasive. Results of these studies suggest that natriuretic peptide testing may be an addition to the information obtained by echocardiography in the assessment of MS in clinical practice.

### **New stress echocardiographic techniques**

#### **3D echocardiography**

3D echocardiography enables visualization from both left ventricular and left atrial side perspectives. Evaluation of the mitral apparatus using 3D echocardiography is most useful defining the

extent and location of pathology, severity of valvular dysfunction. Three -dimensional stress echocardiography has been performed with exercise, dobutamine and dipyridamole. Multislice views from 3D echocardiography stress studies should be interpreted in a similar 2D stress studies evaluating stress-induced wall motion and thickening abnormalities (19, 20).

#### **2D Strain echocardiography**

Tissue Doppler imaging and derived strain and strain rate measurement have offered alternatives for quantification of regional contraction at rest or during stress. Strain, describes myocardial deformation, that is, the fractional change in the myocardial segment. Strain rate, is the rate of change in strain and usually expressed as 1/sec or sec<sup>-1</sup>. These techniques provide incremental information in clinical settings. For both techniques, the accuracy of measurement, however, depends on image quality and the accuracy of tracking. In expert hands, strain and strain rate parameters can improve accuracy and prognostic value of stress test echocardiogram (21).

Future clinical trials, especially in mitral stenosis patients, needs include standardization and acquisition.

### **Conclusion**

The role of stress echocardiography in assessing mitral stenosis is evolving. In mitral stenosis a patient whose symptom complex is discordant to resting hemodynamic data, stress echocardiography has been successful in clarifying the extent of valvular involvement. Together with exercise capacity and symptomatic responses to exercise, it provides the clinician with diagnostic and prognostic information that can contribute to subsequent clinical decisions. Furthermore, with a better understanding of its utility, there is an expected increase in the use of exercise echocardiography to help management decisions in patients with mitral stenosis.

All of the above-mentioned considerations clinical trials should be designed and developed on the basis of a thorough knowledge of physio-pathological, prognostic, and technical characteristics of stress echo-Doppler techniques and parameters, choosing the most performable and reproducible.

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