Factors Affecting ST Depression During Cardiopulmonary Exercise Testing in Patients With Mitral Stenosis Without Significant Coronary Lesions

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SUMMARY

Symptom-limited cardiopulmonary exercise testing was performed in 37 patients with mitral stenosis (MS) without significant coronary artery stenosis to evaluate factors affecting ST depression in exercise electrocardiograms. The degree of ST depression was not associated with gender or exercise tolerance. The incidence of significant ST depression was higher in the patients receiving than in those not receiving digitalis ($P < 0.05$). In addition, the patients with atrial fibrillation and a higher heart rate response were more likely to have a high prevalence of significant ST depression than those with sinus rhythm and a lower response ($P < 0.05$). We concluded that atrial fibrillation, a higher maximum heart rate, and oral digitalis administration were involved in ST depression during exercise testing in patients with mitral stenosis without coronary heart disease. (Jpn Heart J 2004; 45: 251-255)

Key words: Mitral stenosis, Exercise testing, ST depression, Atrial fibrillation, Digitalis

When exercise tolerance is evaluated in patients with ischemic heart diseases, the degree of ST depression is an important parameter. ST changes on exercise electrocardiograms are often encountered in patients with valvular heart disease,1) presenting problems when the activity of a patient is determined or exercise therapy is performed. In particular, in patients with mitral stenosis (MS), ST depression is often observed during exercise tests though their coronary arteries are normal.2) We performed symptom-limited exercise testing with expiratory gas analysis (cardiopulmonary exercise testing: CPX) in MS patients in whom the absence of coronary lesions was confirmed by coronary angiography, and evaluated factors affecting the ST changes.

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METHODS

Subjects: The subjects were 37 patients (11 males and 26 females; mean age, 60 years) consecutive with MS not complicated by grade 2 or greater aortic or mitral valve regurgitation who were confirmed to have normal coronary arteries by coronary angiography. The degree of coronary stenosis was evaluated using the American Heart Association classification of stenosis, and 50% stenosis or less was regarded as normal. Resting electrocardiography showed sinus rhythm in 13 patients (SR group) and atrial fibrillation in 24 (Af group). All patients were being treated with oral diuretics and 34 patients with oral digitalis. Patients with intraventricular conduction disturbance, left ventricular hypertrophy, and electrolyte disturbance were excluded.

Methods: Symptom-limited CPX using a ramp protocol with a bicycle ergometer (Lode-I Ergometer, Groningen, The Netherlands) was performed in all patients. Twelve-lead electrocardiograms were recorded by a modified Mason-Likar method. Maximum heart rate and degree of ST depression in leads II and V₅ were measured. After a 3-minute rest (sitting position) on the cycle ergometer, exercise began with a 3-minute warm up at 10 W followed by the ramp protocol (15 W/min). Heart rate (HR), ST-T changes, and arrhythmias were monitored by a 12-lead electrocardiogram using a model Case 16 exercise testing system (Marquette Electronics, Milwaukee, Wisconsin, USA). Blood pressure was also measured at 1-minute intervals by the cuff method using an automatic manometer (STBP-780B, Colin Denshi, Aichi, Japan). Ventilatory gas exchange [oxygen uptake (Vo₂), carbon dioxide output (Vco₂), and minute ventilation (VE)] was measured on a breath-by-breath basis with a gas analyzer (Aerometer AE-280s, Minato Medical Science Co, Osaka, Japan). These parameters were simultaneously displayed on a monitor using an NEC personal computer (PC-9821, NEC, Tokyo). The anaerobic threshold (AT) was determined using two methods; the V-slope method and the ventilatory equivalent method in which the ratio of the VE/Vo₂ curve inflects systematically upward. Peak Vo₂ was defined as the average of values obtained during the last 30 seconds of exercise. The degree of ST depression was measured from the J point to 80 msec. The patients were classified according to the degree of ST depression into two groups: a decrease ≥ 1.5 mm or < 1.5 mm. The former decrease was regarded as a significant change.

Analysis was performed after classifying the patients according to maximum heart rate into two groups: a good response group (heart rate at the end point was greater than a median value) and a poor response group (heart rate at the end point was less than a median value). Analysis was also performed after classifying the patients, according to functional impairment from the view point of the AT value, previously described by Weber, et al.³ into two groups with a value ≥
11.0 mL/kg/min (mild cardiac failure group) or < 11.0 mL/kg/min (severe cardiac failure group).

Statistical significance was assayed using the $\chi^2$ test, and the level of 5% was regarded as significant.

**RESULTS**

Of the 37 MS patients who underwent exercise tests, 24 (65%) showed significant ST depression while 13 (35%) did not. According to the median of the heart rate at the end point (143 beats/min), the good response group consisted of 19 patients while the other 18 patients belonged to the poor response group. By measurement of the AT, 13 patients were classified as mild cardiac failure and 24 patients as severe cardiac failure.

The degree of ST depression was not associated with gender or cardiac rhythm. The prevalence of significant ST depression was higher in the group receiving digitalis than in the group not receiving digitalis (65% vs 0%; $P < 0.05$; Figure 1). In terms of cardiac rhythm and heart rate responses, the incidence of significant ST depression was higher in the AF with the good response group than in the SR with the poor response group (85% vs 29%; $P < 0.05$; Figure 2).

However, in terms of the severity of cardiac failure evaluated by CPX, the degree of ST depression did not differ between the mild cardiac failure group (ST depression < 1.5 mm, 3 patients; ≥ 1.5 mm, 10 patients) and the severe cardiac failure group (ST depression < 1.5 mm, 10 patients; ≥ 1.5 mm, 14 patients).

![Figure 1. Degree of ST depression and its incidence according to group.](image)
DISCUSSION

Aronow and Harris\(^1\) performed symptom-limited treadmill exercise tests in 15 MS patients with normal coronary arteries and observed ST depression in 3 (20\%), suggesting the involvement of a decreased left ventricular diastolic filling rate due to MS and decreased relative coronary perfusion due to low cardiac output in ST depression. ST depression due to exercise is often associated with the imbalance between oxygen demand and supply in the subendocardium and is a useful parameter in the diagnosis of ischemic heart disease. However, the presence of ST depression does not always indicate the presence of ischemic heart disease. Its specificity was reported to be about 90\% by Bartel\(^4\). The sensitivity and specificity of the standard 12-lead exercise electrocardiography for the detection of coronary heart disease by the meta-analysis of Detrano, \textit{et al}\(^5\) were 68 ± 16\% and 77 ± 17\%, respectively. In addition to coronary heart disease, the factors associated with ST depression include intraventricular conduction disturbance, drugs (such as digitalis), electrolyte abnormalities, gender, hyperventilation, the influence of Ta waves, right ventricular load, relative myocardial ischemia, left ventricular hypertrophy, and technical factors in electrocardiography.

In this study, since patients with coronary heart disease were excluded, the cause of ST depression was not latent coronary heart disease. In the present study,
the combination of the presence of atrial fibrillation and tachycardia during exercise was associated with ST depression. We then measured exercise tolerance using CPX and investigated the relation between exercise capacity and the degree of ST depression. However, the exercise capacity of patients, which is related to cardiac output, did not affect the degree of ST depression. These results combined with those of Aronow and Harris\(^1\) suggest that disappearance of atrial contractions due to atrial fibrillation and shortening of the diastole due to tachycardia reduced coronary blood flow to the myocardium with increased oxygen demand, which then induced relative myocardial ischemia. ST depression by digitalis is well known and is often reported.\(^6\) The high incidence of ST depression in this study may be partly because many patients were being treated with oral digitalis. When MS patients receiving digitalis undergo exercise ECG and exhibit ST depression with tachycardia, this ST change may not reflect myocardial ischemia. Accordingly, these patients should be re-examined by stress myocardial scintigraphy with dipyridamole or other examinations which do not increase their heart rate.

**Conclusion:** Atrial fibrillation, a higher maximum heart rate, and oral digitalis administration may be involved in ST depression during exercise testing in patients with mitral stenosis not complicated by coronary heart disease.

**REFERENCES**