Improvement in Mitral Flow Dynamics During Exercise After Percutaneous Transvenous Mitral Commissurotomy
Noninvasive Evaluation Using Continuous Wave Doppler Technique

Jun Tamai, MD, Seiki Nagata, MD, Masashi Akiike, MD, Fuminobu Ishikura, MD, Koji Kimura, MD, Makoto Takamiya, MD, Kunio Miyatake, MD, and Yasuharu Nimura, MD, MSc

Evaluation of mitral flow dynamics during exercise is critically important in patients who receive percutaneous transvenous mitral commissurotomy (PTMC) because limited mitral flow during exercise provokes hemodynamic deterioration and involves cardiogenic symptoms in patients with mitral stenosis. To examine mitral flow dynamics during exercise, we applied continuous wave Doppler technique in 20 patients with mitral stenosis. Exercise Doppler study was performed 2 days before and 5 days after PTMC. PTMC increased mitral valve area from 1.0±0.3 (mean±SD) to 1.9±0.5 cm² and decreased mean transmitral pressure gradient from 8±2 to 4±1 mm Hg at rest. Moreover, PTMC decreased mean transmitral pressure gradient from 21±6 to 11±4 mm Hg at submaximal exercise. The extent of an increase in mitral valve area by PTMC correlated with a decrease in the mean transmitral pressure gradient at the submaximal exercise (r=−0.76, p<0.01) and that at rest (r=−0.52, p<0.05). Heart rate after PTMC during exercise was significantly lower than that before PTMC, indicating that the compensatory mechanism (tachycardia) to increase cardiac output during exercise is less necessary after PTMC. Thus, we conclude that the mitral flow dynamics during exercise is improved, as well as the resting mitral flow dynamics 5 days after PTMC, and that exercise Doppler study enabled us to make a noninvasive evaluation of the mitral flow dynamics in patients who receive PTMC. (Circulation 1990;81:46-51)

Percutaneous transvenous mitral commissurotomy (PTMC) has been shown to be a new therapy for patients with mitral stenosis. Several lines of evidence suggest that PTMC results in the separation of fused commissure comparable with surgical commissurotomy. Although improvements in mitral flow characteristics at rest were observed immediately after the procedure, this procedure is to be validated by the observation of mitral flow dynamics during exercise because mitral stenosis critically limits the mitral flow during exercise and can provoke hemodynamic deterioration. Because PTMC required less invasive technique to patients, improvements of mitral flow characteristics during exercise can be assessed immediately after the procedure. Although McKay reported considerable improvements of exercise hemodynamics 3 months after PTMC using a catheterization technique, there is no evidence of whether mitral flow dynamics during exercise are improved soon after PTMC because repeated catheterization could not be performed in this period due to technical limitations.

Doppler echocardiography is a noninvasive and reliable method to assess the mitral flow characteristics and can be applied to the exercise test. To determine whether mitral flow dynamics during exercise are improved soon after PTMC, we studied the mitral flow velocity by Doppler echocardiography 2 days before and 5 days after PTMC.
Methods

Subjects

From November 1987 to July 1988, 25 patients received PTMC in the hospital of the National Cardiovascular Center. One patient could not undergo the exercise test because of low-grade fever for 2 weeks after PTMC, and one patient declined the repeated exercise test after PTMC. Three other patients could not perform the supine bicycle exercise test before PTMC because of poor exercise capacity. Thus, the remaining 20 patients were examined in this study. Informed consent was obtained from each patient. The clinical characteristics of these patients are listed in Table 1. Patients were comprised by nine men and 11 women, and their ages were 36–62 years (mean, 49±9 years). Eleven patients had sinus rhythm, and nine patients had atrial fibrillation. None of the patients recovered from atrial fibrillation to sinus rhythm after PTMC. Medications that patients were receiving consisted of digitalis and diuretics, which were not changed until the repeated exercise test.

Left ventricular ejection fraction and mitral regurgitation were evaluated by left ventriculography before PTMC. Mitral regurgitation was again evaluated 30 minutes after PTMC. The following semiquantitative criteria were applied for the assessment of mitral regurgitation: I (mild), contrast does not outline the left atrium; II (moderate), contrast faintly outlines the left atrium, but the density is lower than that in the left ventricle; III (moderate-to-severe), contrast rapidly outlines the left atrium, and the density is equal to that in the left ventricle; IV (severe), contrast rapidly outlines the left atrium, and the density is higher than that in the left ventricle. Although mitral regurgitation was worsened in 10 patients after PTMC, the extent of the deterioration was within grade I, and none of the patients showed moderate-to-severe or severe mitral regurgitation. Aortic valve gradient was determined by pullback pressure tracing from the left ventricle to the ascending aorta. Severity of aortic regurgitation was determined by aortography and was assessed by the following criteria: I (mild), contrast does not outline the left ventricle; II (moderate), contrast faintly outlines the left ventricle, III (moderate-to-severe), contrast rapidly outlines the left ventricle, and the density is equal to that in the ascending aorta; IV (severe), contrast rapidly outlines the left ventricle, and the density is higher than that in the aorta. Tricuspid regurgitation was judged from color Doppler flow imaging.

PTMC was performed using an Inoue balloon catheter by a transseptal technique. Details of the procedure have been previously reported by Inoue et al. Briefly, a single balloon catheter was inserted into the left ventricle. The distal half of the balloon was inflated in this position, and the balloon was pulled back to the mitral valve orifice. Then, the

### Table 1. Patient Population

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<tr>
<th>Patient</th>
<th>Age/gender</th>
<th>NYHA class</th>
<th>Before PTMC</th>
<th>After PTMC</th>
<th>Symptoms</th>
<th>ECG rhythm</th>
<th>LVEF (%)</th>
<th>MR</th>
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<th>After PTMC</th>
<th>Balloon diameter (mm)</th>
<th>AS (mm Hg)</th>
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ECG, electrocardiogram; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; AS, aortic stenosis; AR, aortic regurgitation; TR, tricuspid regurgitation; SOB, shortness of breath; Af, atrial fibrillation; Sinus, sinus rhythm; PND, paroxysmal nocturnal dyspnea; Pal, palpitation. Grading of AR and MR (by angiography): 0, none; I, mild; II, moderate; III, moderate-to-severe; no patients showed severe AR or MR. Grading of TR (by color Doppler): 0, none; Mi, mild; Mo, moderate; no patients showed severe TR.
balloon was fully inflated. Thereafter, the balloon was pulled back to the left atrium and was deflated. When balloon dilatations were further required, the same procedure was repeated. The balloon diameter used in each patient is also listed in Table 1.

Exercise Test

Supine bicycle exercise testing was performed using Siemens Ergometry System 380B (Siemens AG, Erlangen, West Germany). The exercise test was performed 2 days before PTMC, and the identical protocol was repeated 5 days after PTMC. Exercise testing consisted of two stages of 3-minute intervals, starting at a work load of 0 W or 25 W (EX1) and finished at 25 W or 50 W (EX2). To determine the feasibility of Doppler study during exercise and the exercise capacity of each patient, initial bicycle exercise testing was performed 1 week before PTMC. For patients who tolerated 50 W of work load in this initial trial, bicycle exercise tests before and after PTMC were started at 25 W and increased to 50 W with a 3-minute interval. In patients who could not tolerate a 50-W work load, EX1 was started at 0 W and increased to 25 W with the same interval. In the 20 patients we examined, four patients could not perform 50-W exercise. Thus, they started the exercise test at 0 and finished at 25 W (patients 10, 16, 17, and 18 in Table 1). During the exercise test, electrocardiogram was continuously monitored. Blood pressure was measured by a sphygmomanometer every 1 minute.

The supine bicycle exercise of equivalent work load (25 W and 50 W) was also performed by six healthy subjects. Their age range was 28–33 years (mean, 30±2 years). None of them was considered a trained athlete. Informed consent was obtained from each subject. The data obtained from the healthy subjects served as a control.

Doppler Examination

Two-dimensional echocardiographic and cardiac Doppler studies were obtained with Aloka SSD-730. The continuous wave Doppler unit with mechanical scan system was operated at a frequency of 2.0 MHz. The patients were examined in the supine position at rest and during exercise. To evaluate the mitral flow velocity, the transducer was positioned at the apex to obtain a two-chamber view. The Doppler cursor was initially directed as perpendicular as possible to the mitral anulus under two-dimensional guidance, and the direction of the cursor was adjusted using audio and visual output to obtain the highest velocity of the mitral flow. Doppler signals were recorded for 15 seconds at rest and for the last 15 seconds of EX1 and EX2 on a strip-chart recorder at a paper speed of 50 mm/sec. Heart rate at each stage was calculated from the averaged number of heart beats of the simultaneously recorded electrocardiogram on the Doppler signal recording.

The mitral velocity curve was traced and analyzed on a digitizer, and the digitized flow profile was analyzed by a personal computer (NEC PC-9800, NEC Corp, Minato-Ku, Tokyo, Japan) with custom-made software. This system provides a digital printout of peak and mean transmitral pressure gradients and area under the flow velocity curve, that is, flow velocity integral (FVI). Transmitral pressure gradients were calculated using a modified Bernoulli’s equation. The time required for the pressure drop to fall to one half its initial value (pressure half-time) was measured, and mitral valve area at rest was calculated according to Hatle’s method. These measurements were done by technical assistants who had no knowledge of the patients’ profiles. An average of five cardiac cycles for sinus rhythm and 10 cycles for atrial fibrillation were used for determination of these variables.

Statistical Analysis

All variables obtained at rest and each work load (EX1 and EX2) before and after PTMC were compared by paired t test. Differences in responses of these variables to exercise before and after PTMC were compared by multiple analysis of variance (MANOVA). Linear regression was used to evaluate the relation between mitral valve area and mean transmitral pressure gradient at rest and during exercise. A p value less than 0.05 was accepted as statistically significant.

Results

Optimal Doppler signal recordings were obtained during exercise in all patients and were reproducible.
enough to assess mitral flow dynamics. No complication was noted during exercise, except for sporadic atrial premature beats during exercise and the recovery period in one patient with sinus rhythm. Figure 1 shows the representative Doppler recordings of mitral flow velocity at rest and during exercise. Mitral flow velocity markedly increased after PTMC. After the dilation of mitral valve by PTMC, the deceleration slope of the rapid filling wave became steeper at rest, and flow velocity during exercise was much lower than before PTMC.

**Changes in Mitral Flow Dynamics at Rest**

PTMC decreased pressure half-time of rapid filling wave, which indicated an increase of mitral valve area from 1.0±0.3 to 1.9±0.5 cm$^2$ (mean±SD; *p*<0.01) (Table 2). The increase in mitral valve area significantly decreased both transmitral pressure gradient and flow velocity integral at rest. The mean transmitral pressure gradient was 5 mm Hg or less in all patients after PTMC (Figure 2). Although there was no significant correlation between mitral valve area and mean transmitral pressure gradient at rest before or after PTMC (*r* = −0.25 and *r* = −0.39, respectively), a significant correlation (*r* = −0.52, *p* < 0.05) was observed between the extent of an increase in mitral valve area and a decrease in mean transmitral pressure gradient at rest after PTMC (left panel in Figure 3).

**Changes in Mitral Flow Dynamics During Exercise**

Before PTMC, transmitral pressure gradients markedly increased according to the increase in exercise work load (Table 2).

An increase in mitral valve area by PTMC effectively attenuated the extent of an increase in transmitral pressure gradient during exercise, however, the mean transmitral pressure gradient at EX2 was widely varied at 4–21 mm Hg (Figure 2). The extent of a decrease in mean pressure gradient at EX2 after PTMC highly correlated with an increase in mitral valve area at rest (*r* = −0.76, *p* < 0.01) (right panel in Figure 3).

Although resting heart rate did not change as compared with that before PTMC, heart rate during exercise showed significantly lower value than that before PTMC (*p* < 0.01, both in EX1 and EX2, by paired *t* test) (Table 2).

The mean value of pressure half-time minimally changed during exercise both before and after PTMC (Table 2), however, changes in each patient were not unidirectional (Figure 4).

Mitral flow dynamics are markedly improved after PTMC as previously shown, however, their responses to exercise were not the same as in the healthy subjects. Transmitral pressure gradient showed significant increase during exercise even after PTMC. Flow velocity integral also showed significantly higher value at rest than in healthy subjects and decreased

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**Table 2. Hemodynamic and Doppler Derived Variables During Exercise Before and After PTMC**

<table>
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<tr>
<th></th>
<th>SBP (mm Hg)</th>
<th>HR (beats/min)</th>
<th>pPG (mm Hg)</th>
<th>mPG (mm Hg)</th>
<th>FVI (cm)</th>
<th>PHT (msec)</th>
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<tr>
<td></td>
<td>Before</td>
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<td>After</td>
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<tr>
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</table>

Values are given as mean±SD for 20 patients. Before and after are values before and after PTMC.

* *p* < 0.01, compared with the equivalent work load before PTMC. Responses of pPG, mPG, and FVI to exercise after PTMC showed statistically significant differences (*p* < 0.01) from those before PTMC by MANOVA.

SBP, systolic blood pressure; HR, heart rate; pPG, peak pressure gradient; mPG, mean pressure gradient; FVI, flow velocity integral; PHT, pressure half-time; MVA, mitral valve area.
during exercise, whereas it did not change in the healthy subjects (Table 3).

**Discussion**

Although McKay reported the improvement of exercise hemodynamics 3 months after PTMC, we provided further new evidence using Doppler technique that comparable improvement of mitral flow dynamics is observed 5 days after PTMC.

**Clinical Significance of the Present Study**

In the present study, transmitral pressure gradient was markedly increased during exercise in patients before PTMC. This enhanced gradient can reflect an increase in the left atrial pressure and, hence, exacerbation of pulmonary congestion during exercise because left ventricular diastolic pressure is minimally changed due to the limited filling volume. Because the extent of an increase in transmitral pressure gradient during exercise is significantly attenuated after PTMC, pulmonary congestion during exercise can be dramatically improved.

Heart rate at the same work load was significantly attenuated after PTMC, although resting heart rate was not changed (Table 2). Tachycardia is known to be a compensatory mechanism to maintain cardiac output during exercise in patients with heart failure. Thus, attenuation of heart rate increase after PTMC indicates that improvements in mitral flow dynamics can ameliorate the hemodynamics during exercise.

**Advantages of Exercise Doppler Echocardiography**

Doppler echocardiography has been shown to be a reliable, noninvasive technique for investigating the patients with mitral stenosis and to be applicable to the exercise test. Furthermore, this technique has several advantageous points as will be described.

First, severity of mitral stenosis is usually determined by mitral valve area, mean transmitral pressure gradient at rest, or both, although the cardiogenic symptoms are usually evident only during exercise. Because the transmitral pressure gradient partly depends on the transmitral flow volume and ventricular function, patients with low cardiac output show low-pressure gradient at rest. In such patients, calculation of valve area can be erroneous, and it is difficult to determine whether mitral stenosis critically limits the transmitral flow volume during exercise and whether PTMC can improve the hemodynamic deterioration and, hence, cardiogenic symptoms. In contrast, the increase in transmitral pressure gradient during exercise indicates the limited transmitral flow volume and can certainly reflect the severity of mitral stenosis for the individual patient. The increase in pressure gradient during exercise after PTMC also clarifies whether the acquired valve area is adequate for the transmitral flow volume of the patient; mean transmitral pressure gradient at EX2 widely varied at 4–21 mm Hg, whereas that at rest was only 2–5 mm Hg after PTMC (Figure 2).

Second, when we observe the exercise mitral flow dynamics using the catheterization technique in the management of PTMC, repeated procedures increase the risk of complications and can be expensive, due to the cost of catheterization itself and hospital charges. In contrast, Doppler echocardiography is neither invasive nor risky and is suitable for repetitive assessment of the mitral flow dynamics during exercise.

Third, exercise Doppler study can be applied to the outpatients to determine the indication of PTMC and also to the patients receiving PTMC in the catheterization room, using arm exercise to evaluate the extent of a decrease in transmitral pressure gradient immediately after the procedure.

**Limitations of the Study**

Although the Doppler echocardiography provides useful information about mitral flow dynamics during
exercise, we should consider several limitations in using this technique.

First, although mitral valve area derived from pressure half-time correlated well with that from Gorlin’s formula, its application during exercise has not been established. Flow volume increase causes a decrease in pressure half-time, and can affect the relation between pressure half-time and mitral valve area during exercise. Furthermore, accurate estimation of pressure half-time is difficult because of shortened rapid-filling period, due to tachycardia especially in patients with sinus rhythm. In the present study, wide variation of changes in pressure half-time during exercise can be due, in part, to this technical limitation. Moreover, Thomas et al9 reported the inaccuracy of the pressure half-time method immediately after PTMC even at rest and cautioned the application of this method in evaluation of the immediate effect of PTMC on mitral valve area. Our data obtained 5 days after PTMC might be reliable, however, because mitral valve area obtained from pressure half-time and that from Gorlin’s formula showed high correlation 24–48 hours after PTMC.20

Second, deterioration of mitral regurgitation is a common complication with PTMC, and the presence of mitral regurgitation can blunt the precise estimation of transmitral flow dynamics. Shaikh et al21 reported that early diastolic filling is augmented by mitral regurgitation, which modifies the assessment of transmitral flow dynamics. Although we did not perform the quantitative assessment of mitral regurgitation, comparable improvement in exercise mitral flow dynamics were obtained even in the patients with mitral regurgitation because increase in mitral regurgitation was minimal and can have only a minor effect on mitral flow velocity.

Third, the exercise test in this study is not symptom limited because supine exercise is not suitable for the determination of exercise tolerance, and marked tachycardia and accelerated respiration at the peak exercise reduce the quality of the flow velocity recordings. Thus, this study could not demonstrate the improvement of exercise tolerance and, hence, changes in mitral flow dynamics at the peak exercise.

From these considerations, we conclude that PTMC by Inoue balloon catheter improves mitral flow dynamics during exercise, and that exercise Doppler study is useful for this evaluation.

Acknowledgments
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Key Word • valvular stenosis

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