Utility of Stress Doppler Echocardiography in Patients Undergoing Percutaneous Mitral Balloon Valvotomy

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A subset of patients with mitral stenosis have symptoms out of proportion to the resting hemodynamics. Exercise Doppler echocardiography is a useful diagnostic modality to determine which patients are limited by their valve obstruction and would therefore benefit from percutaneous mitral balloon valvotomy. We analyzed 11 patients who showed a peak exercise mean mitral gradient that doubled from baseline or a final gradient of >15 mm Hg. The mean mitral gradient increased from 7 ± 2 mm Hg at rest to 19 ± 6 mm Hg (*P* < .001) with exercise. All patients reported improvement in symptoms of at least 1 functional class after valvotomy. (J Am Soc Echocardiogr 2001;14: 676-81.)

Percutaneous mitral balloon valvotomy is the recommended therapeutic modality in experienced centers for selected patients with mitral stenosis. In symptomatic patients with severe mitral stenosis and favorable valve morphology, percutaneous mitral balloon valvotomy improves hemodynamics and relieves symptoms.[1] Among patients with resting hemodynamics that suggest only a mild or moderate degree of mitral stenosis, there is a subset of patients with symptoms out of proportion to the resting hemodynamics. Exercise hemodynamics may provoke findings of severe obstruction in these patients, indicating that they would benefit from intervention.[1-3]

In the past, right-sided heart catheterization with exercise was used to determine the hemodynamic response to exercise in these patients.[4,5] Doppler echocardiography permits accurate noninvasive measurement of transmitral gradients and pulmonary pressures.[2,3] This has led to the American College of Cardiology/American Heart Association (ACC/AHA) guideline recommendations that exercise Doppler echocardiography be used to assess the hemodynamic response to exercise in patients who have discordance between symptoms and resting hemodynamics.[1] However, there has not been validation of these proposed recommendations in terms of patient outcome.

The purpose of this study was to report the symptomatic outcome of patients who had symptoms out of proportion to the resting hemodynamics, underwent exercise Doppler echocardiography, and were referred for percutaneous mitral balloon valvotomy.

METHODS

Patient Selection

Patients were selected from the Mayo Clinic database, which comprised 192 adult patients with mitral stenosis who underwent percutaneous mitral balloon valvotomy from May 1984 to August 1998. In the preprocedure evaluation of these patients, exercise Doppler echocardiography had been prospectively performed in any patient who had severe symptoms of dyspnea yet had resting hemodynamics consistent with mild to moderate mitral stenosis. There were 11 patients who underwent an exercise Doppler echocardiographic test and met the following criteria: (1) a peak exercise mean transmitral gradient that doubled from baseline or (2) a final mean transmitral gradient of >15 mm Hg. In these patients the mitral stenosis was thought to be the source of the symptoms, and they underwent percutaneous mitral balloon valvotomy. No patient had severe resting pulmonary hypertension (pulmonary artery systolic pressure >50% systemic pressure) or right ventricular dysfunction. Functional status was assessed at baseline and on follow-up by using a subjective measure of the percentage of total functional capacity that was perceived by the patient.[6,7] For instance, 50% indicated that

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Table 1 Demographic and follow-up data

Patient	Age (y)	Sex	Rhythm	NYHA	% FC1	Follow-up (mo)	NYHA	% FC2
1	56	F	AF	II	30	173	I	100
2	53	F	AF	II	30	111	I	100
3	54	F	NSR	III	30	137	I	80
4	47	F	NSR	III	30	76	II	50
5	51	F	AF	III	40	59	I	70
6	62	F	NSR	III	30	52	II	50
7	61	F	NSR	II	60	46	I	90
8	44	F	AF	II	60	22	I	80
9	41	F	NSR	III	30	11	I	70
10	54	M	AF	II	60	11	I	80
11	41	F	NSR	III	30	73	I	90
Mean	51				40	70		78
SD	7				14	52		17
*P**							.0001	.0001

AF, Atrial fibrillation; *% FC,* percentage of functional capacity; *NSR,* normal sinus rhythm; *NYHA,* New York Heart Association.
*For comparison before and after percutaneous balloon valvotomy.

Table 2 Exercise Doppler echocardiographic data

Patient	% EF rest	MGr rest	MGr exe	HR rest	HR exe	SBP rest	SBP exe	PASP rest	PASP exe
1	54	6	13	80	130	105	155	35	60
2	58	7	14	60	110	115	168	43	66
3	55	6	19	63	120	138	195	30	NA
4	57	6	14	55	155	110	105	39	50
5	55	3	13	75	160	130	196	NA	NA
6	55	6	20	64	115	124	120	48	78
7	52	10	26	66	141	145	201	43	58
8	45	9	17	82	124	105	152	48	71
9	60	9	32	90	155	102	144	35	59
10	60	5	21	70	144	133	184	32	NA
11	60	10	23	68	109	90	156	44	68
Mean	56	7	19	70	133	118	161	38	64
SD	4.4	2	6	10	19	17	31	6	9
*P**			.001		.0001		.0001		.0001

EF, Ejection fraction; *exe,* exercise; *HR,* heart rate; *MGr,* mitral valve gradient (in mm Hg); *NA,* not available; *PASP,* pulmonary artery systolic pressure (in mm Hg); *SBP,* systolic blood pressure.
*For comparison between exercise and rest.

the patient was limited to 50% of the desired activity level, and 100% indicated that the patient was able to perform all daily activities without limitation. Additionally, their New York Heart Association (NYHA) functional class was recorded. All of these patients were available for follow-up. The study was approved by the Institutional Review Board, and informed consent for the procedure was obtained from all patients.

Echocardiography

All patients underwent a comprehensive 2-dimensional and Doppler echocardiogram before the percutaneous mitral balloon valvotomy. The mitral valve morphology was assessed, and all patients were thought to be suitable candidates for percutaneous mitral balloon valvotomy, based on previously published criteria, including the appearance of the mitral commissures.[8-11] A complete Doppler examination was performed, including measurements of transmitral gradient, valve area by pressure half-time method, and pulmonary pressure from the tricuspid regurgitation velocity.[12,13] In each patient, the clinical impression was that the presenting symptoms were out of proportion to the resting hemodynamics (Table 1), and exercise Doppler echocardiography was recommended for further assessment.

Symptom-limited exercise testing was performed by treadmill exercise testing in 1 patient and supine bicycle in 10 patients. The Bruce protocol was used for treadmill testing. Supine bicycle exercise testing was performed starting at 25 to 50 W and increasing by 25 W at 3-minute intervals.

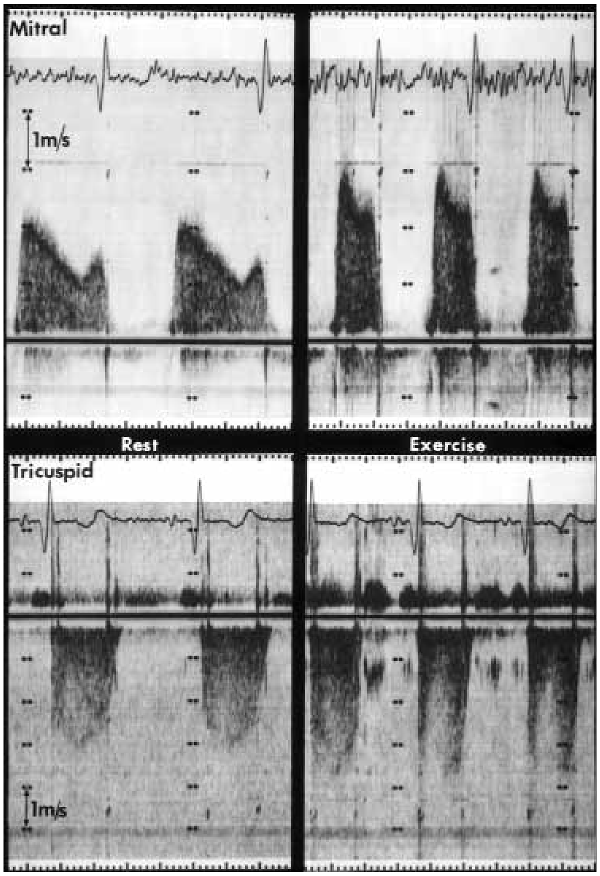

Figure 1 Doppler flow shows mean gradient across mitral valve *(top)* and tricuspid regurgitant velocity *(bottom)* at rest *(left)* and with exercise *(right)* for patient 11. Mean gradient across mitral valve increased from 10 to 23 mm Hg and tricuspid regurgitant velocity increased from 2.9 to 3.8 m/s.

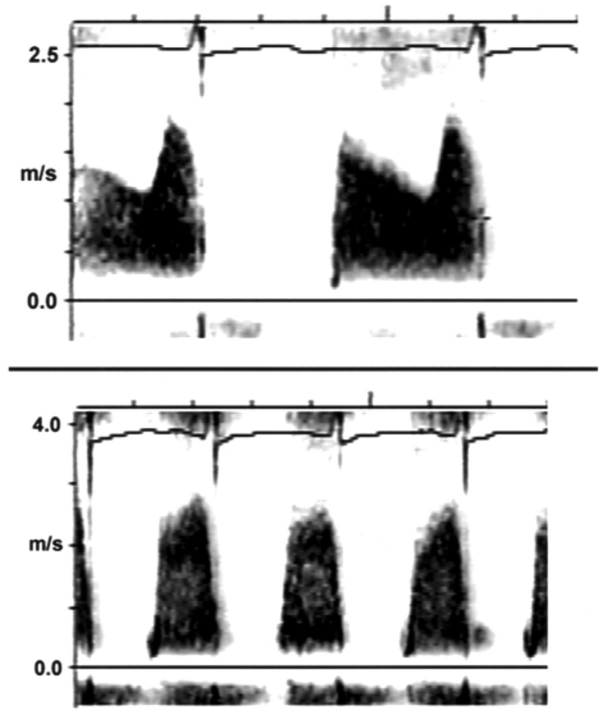

Figure 2 Doppler flow shows mean gradient across mitral valve at rest *(top)* and with exercise *(bottom)* for patient 9. Mean gradient across mitral valve increased from 9 to 32 mm Hg.

Just before the exercise tests, baseline hemodynamic measurements were repeated, consisting of transmitral gradient by continuous wave Doppler echocardiography and estimation of pulmonary artery systolic pressure by the peak velocity of continuous wave Doppler measurement of the tricuspid regurgitation signal. Measurements were an average of 3 beats for patients in sinus rhythm and 5 to 10 beats for those in atrial fibrillation. The right atrial pressure was assumed to be 10 mm Hg in all cases. Repeat Doppler echocardiography was obtained immediately in the left lateral decubitus position after cessation of upright treadmill testing. In the patients undergoing supine bicycle testing, hemodynamics were recorded during the last stage of exercise.

Percutaneous Mitral Balloon Valvotomy

The percutaneous mitral balloon valvotomy procedure was performed as previously described from our institution.[14] The double-balloon technique was used in 3 patients and the Inoue balloon was used in 8 patients. Experienced operators performed all procedures under echocardiographic guidance. The transmitral gradient was recorded by simultaneous left atrial and left ventricular pressures and cardiac output by thermodilution. A mitral valve area was calculated by the Gorlin equation.[15]

Follow-up

All patients had at least 1 follow-up visit at least 6 months after the percutaneous mitral balloon valvotomy. Telephone interviews were conducted on all patients for extended follow-up. Predefined end points for follow-up consisted of death, mitral valve replacement, repeat percutaneous mitral balloon valvotomy, and final functional status.

Statistical Analysis

Comparisons of the Doppler data at rest and during exercise were done with a paired *t* test for data with a gaussian distribution and a Newman-Keuls test for a nongaussian distribution. Similar analysis was performed to compare the perceived functional capacity at baseline and at last follow-up. All values were expressed as mean ± SD. A level of $P < .05$ was set a priori as statistically significant.

Table 3 Percutaneous mitral balloon valvotomy data

	Before			After		
Patient	MVGr	CO	MVA	MVGr	CO	MVA
1	12	4.0	1.00	5	4.5	1.80
2	9	5.5	1.50	7	6.1	2.80
3	6	3.5	1.77	4	4.7	2.58
4	7	4.9	1.48	6	5.2	1.76
5	9	5.7	1.76	5	5.2	2.20
6	6	4.7	1.48	4	4.8	2.04
7	10	6.5	1.68	4	6.7	2.86
8	8	3.1	1.27	4	3.9	1.89
9	13	5.5	1.40	5	5.4	2.30
10	6	2.5	0.90	3	3.5	2.20
11	14	4.3	1.15	7	5.6	1.88
Mean	9	4.6	1.40	5	5.1	2.21
SD	3	1.2	0.30	1	1.0	0.40
*P**				.0002	.007	.0001

CO, Cardiac output (in L/min); *MVA,* mitral valve area (in cm^2); *MVGr,* mitral valve gradient (in mm Hg).
*For comparison before and after percutaneous mitral balloon valvotomy.

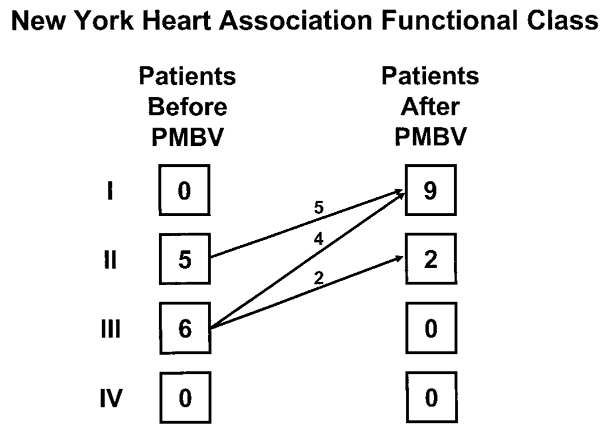

Figure 3 Boxes show numbers of patients in each New York Heart Association functional class before *(left)* and after *(right)* percutaneous mitral balloon valvotomy *(PMBV)*. Functional class improved in all patients.

RESULTS

Patient Population

The baseline clinical characteristics of the patients are summarized in Table 1. There were 10 women and 1 man, and the mean age of these 11 patients was 51 ± 7 years. All patients had rheumatic valvular heart disease. Five patients were in atrial fibrillation. Other valvular heart disease included mild mitral regurgitation in 2 patients and mild aortic stenosis in 1 patient. No patient had a history of pulmonary disease or smoking, and none had significant concomitant medical problems. No patient had clinical or echocardiographic evidence of right ventricular failure. Six patients were in NYHA class III and 5 patients were in NYHA class II.

Exercise Doppler Echocardiographic Data

The data from the exercise Doppler echocardiograms are shown in Table 2. By definition, all patients had a peak exercise transmitral mean gradient of >15 mm Hg or a doubling of the initial gradient. Overall, the mean transmitral gradient increased from 7 ± 2 mm Hg at rest to 19 ± 6 mm Hg at peak exercise ($P < .001$) (Figures 1 and 2). The pulmonary artery pressure, as estimated from the tricuspid regurgitation signal, was obtained in 8 patients, and it increased from 38 ± 6 mm Hg at rest to 64 ± 9 mm Hg at peak exercise ($P < .0001$). With exercise, baseline heart rate and systolic blood pressure of 70 ± 10 beats/min and 118 ± 17 mm Hg increased to 133 ± 19 beats/min ($P < .0001$) and 161 ± 31 mm Hg ($P < .0001$), respectively. All patients had symptoms of dyspnea at peak exercise.

Percutaneous Mitral Balloon Valvotomy

The hemodynamic results of the percutaneous mitral balloon valvotomy are shown in Table 3. The mitral valve area increased from 1.4 ± 0.3 to 2.2 ± 0.4 cm^2 ($P < .0001$), the cardiac output increased from 4.6 ± 1.2 to 5.1 ± 1.0 L/min ($P < .007$), and the catheter-derived mean gradient decreased from 9 ± 3 to 5 ± 1 mm Hg ($P < .0002$). No patient had a significant left-to-right shunt (>1.5:1.0) after the procedure as assessed by saturations. No patient had >2+ mitral regurgitation as assessed by Doppler echocardiography or left ventriculography after the procedure. There were 2 patients with trivial mitral regurgitation, 6 patients with mild mitral regurgitation, and 3 patients with moderate mitral regurgitation.

Follow-up

The patients were followed for a mean of 70 ± 52 months. One patient in atrial fibrillation had a transient ischemic attack while receiving subtherapeutic anticoagulation approximately 11 months after percutaneous mitral balloon valvotomy; he had complete neurologic recovery. All patients were alive at last follow-up, and none required repeat percutaneous mitral balloon valvotomy or mitral valve replacement. All patients reported improvement in symptoms of at least 1 functional class (Figure 3). The perceived functional capacity increased from 40% at baseline to 78% at last follow-up (Table 1).

DISCUSSION

In selected patients, percutaneous mitral balloon valvotomy can be performed by experienced centers with a high initial success rate and excellent intermediate-term outcome. It has thus been recommended as the treatment in the presence of severe limiting symptoms and severe mitral stenosis. In those patients with favorable valve morphology, percutaneous mitral balloon valvotomy has been recommended for severe mitral stenosis in mildly symptomatic patients or in asymptomatic patients if there is evidence of secondary pulmonary hypertension.[1]

There is a subset of patients who have mitral stenosis and severe limiting symptoms but resting hemodynamics that are not indicative of a severe degree of inflow obstruction. There may be other causes of the symptoms, such as left ventricular diastolic dysfunction, pulmonary disease, or deconditioning. However, some patients are truly limited by the mitral stenosis, which results in a more severe degree of obstruction during exercise caused by the tachycardia and increase in cardiac output, with elevation of left atrial pressure reflected back to the pulmonary circulation. Thus, measurement of hemodynamics with exercise should be able to identify these patients whose mitral stenosis is the limiting pathophysiologic mechanism, and these patients should have symptomatic relief after successful percutaneous mitral balloon valvotomy. Recommendations have been made in the ACC/AHA Guidelines for Valvular Heart Disease for intervening in this type of patient if there is a significant increase in transmitral gradient and pulmonary pressures with exercise, but the outcome of this intervention had not been documented.

This study examined the outcome of patients with mild to moderate mitral stenosis at rest but who had Doppler evidence of hemodynamically significant mitral stenosis during exercise. The patients were included in this study if they had symptoms disproportionate to resting hemodynamics. They prospectively underwent an exercise Doppler study. Patients with a significant elevation of transmitral gradient described as a final gradient >15 mm Hg or more than doubling of the initial resting gradient thereafter underwent percutaneous mitral balloon valvotomy. All patients had symptomatic improvement, implicating mitral stenosis as the primary cause of their symptoms. From these data, we now recommend percutaneous mitral valvotomy to patients who have these hemodynamic findings on exercise echocardiography. The indication for the percutaneous mitral balloon valvotomy in this subset of patients should be for symptomatic relief because the natural history of mild to moderate mitral stenosis is relatively benign.

There are limitations to this study. This study is a cohort observational study of a small number of patients and without a control group for comparison. We have reported only the results for the patients who had a significant increase in transmitral gradient during exercise. There were patients with similar symptoms and resting hemodynamics who did not have a significant increase in transmitral gradient; these patients did not undergo percutaneous mitral balloon valvotomy. Thus, it is unknown whether these patients would have benefited from the procedure. Benefit was defined as subjective symptomatic improvement, which can be limited by bias; objective measurement of exercise tolerance or maximum oxygen consumption was not obtained. However, the purpose of the study was to demonstrate that this particular subset of patients derives benefit in terms of symptomatic relief—the major indication for the percutaneous mitral balloon valvotomy procedure. Although the outcome of any procedure is subject to the placebo effect, the extended duration of follow-up militates against the placebo effect as having an important role in the symptomatic relief. A final limitation of this study is that there are no follow-up hemodynamic data, which is a reflection of the nature of the referral population to our institution.

Exercise Doppler echocardiography is a useful diagnostic modality for patients with mitral stenosis who have symptoms out of proportion to resting hemodynamics. If there is a significant increase in transmitral gradient during exercise, these patients have symptomatic relief from successful percutaneous mitral balloon valvotomy.

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