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Inoue Balloon Mitral Valvotomy in Patients With Severe Valvular and Subvalvular Deformity

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Objectives. **This study evaluated the immediate and long-term results of percutaneous Inoue balloon mitral valvotomy in patients with severe valvular and subvalvular deformity.**

Methods. **We reviewed the prevalvotomy transthoracic echocardiograms of patients from the North American multicenter Inoue registry with total Massachusetts General Hospital (MGH) echocardiographic scores ≥10. The echocardiograms were rescored by two investigators to assess valvular and subvalvular morphology to eliminate interinstitutional variability. Ninety patients were originally assigned scores ≥10. After rescoring, 18 patients (20%) were eliminated, leaving 72 study patients.**

Results. **Balloon mitral valvotomy was technically successful in 69 (96%) of the 72 patients. Mean (±SD) mitral valve area increased from 0.9 ± 0.3 to 1.5 ± 0.5 cm^2. An immediate optimal result, defined as ≥50% increase in mitral valve area or a final area ≥1.5 cm^2 with no major complications, was achieved in 46 patients (64%). End points for clinical follow-up (events) included mitral valve replacement, repeat valvotomy or death. At a mean follow-up of 22.9 ± 11.0 months, 22 patients (31%) required mitral valve replacement or a second valvotomy, 9 patients (13%) died, and 32 patients (45%) were in New York Heart Association functional class I or II. Univariate predictors of an immediate optimal result included sinus rhythm, male gender and a lower University of Southern California commissural calcium score. Only sinus rhythm predicted an optimal result by multivariate analysis. Actuarial 3-year event-free survival was 42%. Univariate predictors of event-free survival were a lower grade of mitral regurgitation, lower MGH total echocardiographic score, lower MGH leaflet thickness subscore and lower prevalvotomy left ventricular systolic pressure. Only grade of mitral regurgitation after valvotomy predicted event-free survival by multivariate analysis.**

Conclusions. **Inoue mitral valvotomy in patients with severe valvular and subvalvular deformity has a high technical success rate and good immediate hemodynamic result but a high cardiovascular event rate in follow-up. Mitral valve replacement should be considered in surgical candidates with an MGH total echocardiographic score ≥10 because it may be able to provide better long-term event-free survival. Balloon valvotomy remains a reasonable palliative therapeutic option for some patients with severe valvular deformity and high surgical risk.**

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Since the first description of percutaneous balloon mitral valvotomy by Inoue in 1984, it has become the procedure of choice for many patients with acquired mitral stenosis. Both immediate and long-term results have been excellent in a majority of patients, but less optimal results have been described in patients with more severe valvular and subvalvular deformity as determined by echocardiographic scoring systems. These patients obtain less optimal immediate hemodynamic results (1–8) and have a higher likelihood of restenosis (4,9,10) and a higher cardiovascular event rate (4,11,12).

Recently, the Inoue balloon has become available for clinical use in the United States. Its unique hourglass configuration results in a technically easier and quicker procedure with immediate results similar to those obtained by the single- or double-balloon method. Only a few reports describe the influence of patient selection on results of Inoue percutaneous balloon valvuloplasty in North American patients (13,14). These studies suggest that the immediate results using the Inoue balloon are less influenced by valvular and subvalvular morphology and that this procedure might be appropriate in patients with severe deformity. However, the long-term outcome of Inoue balloon valvotomy in patients with severe valvular and subvalvular deformity is not known.

This study identified a group of patients with significant valvular and subvalvular deformity and evaluated the immediate and short- and long-term results of percutaneous Inoue balloon mitral valvotomy. In addition, we identified predictors of outcome and compared two echocardiographic scoring systems currently used in selecting patients for balloon valvotomy.

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Table 1. Massachusetts General Hospital and University of Southern California Echocardiographic Scoring Systems

Massachusetts General Hospital Score	
Leaflet mobility	
Grade 1	Highly mobile valve with restriction only of leaflet tips
Grade 2	Midportion and base of leaflets have reduced mobility
Grade 3	Valve leaflets move forward in diastole mainly at base
Grade 4	No or minimal forward movement of leaflets in diastole
Leaflet thickening	
Grade 1	Leaflets near normal (4–5 mm)
Grade 2	Midleaflet thickening; marked thickening of margins
Grade 3	Thickening extends through entire leaflets (5–8 mm)
Grade 4	Marked thickening of all leaflet tissue (>8–10 mm)
Subvalvular thickening	
Grade 1	Minimal thickening of chordal structures just below valve
Grade 2	Thickening of chordae extending up to one-third of chordal length
Grade 3	Thickening extending to distal third of chordae
Grade 4	Extensive thickening and shortening of all chordae extending down to papillary muscle
Valvular calcification	
Grade 1	Single area of increased echocardiographic brightness
Grade 2	Scattered areas of brightness confined to leaflet margins
Grade 3	Brightness extending into midportion of leaflets
Grade 4	Extensive brightness through most leaflet tissue
University of Southern California Score	
Leaflet motion	
Grade 0 (mild)	H/L ratio ≥0.45
Grade 1 (moderate)	H/L ratio 0.26–0.44
Grade 2 (severe)	H/L ratio ≤0.25
Leaflet thickness	
Grade 0 (mild)	MV/PWAo thickness ratio 1.5–2.0
Grade 1 (moderate)	MV/PWAo thickness ratio 2.1–4.9
Grade 2 (severe)	MV/PWAo thickness ratio ≥5.0
Subvalvular disease	
Grade 0 (absent–mild)	Thin, faintly visible chordae tendineae
Grade 1 (moderate)	Areas of increased density equal to endocardium
Grade 2 (severe)	Areas denser than endocardium with thickened chordae tendineae
Commissural calcium	
Grade 0 (absent)	Homogeneous density of MV orifice
Grade 1 (one commissure)	Increased density of anterior/posterior commissure
Grade 2 (two commissures)	Increased density of both commissures

H/L = height/length ratio of dome of mitral valve (MV); PWAo = thickness of aortic posterior wall.

Methods

Study patients and echocardiographic scoring. The study included 72 patients from the multicenter Inoue registry with total echocardiographic scores ≥10 using the Massachusetts General Hospital (MGH) criteria (Table 1, Fig. 1). These patients were derived from the entire registry of 550 patients who underwent valvotomy at 22 centers from June 1989 to July 1992.

A total of 90 patients (from 11 of the 22 centers) had total echocardiographic scores ≥10, as scored by the individual investigators and reported to the central registry. Two investigators (J.R.P., H.C.H.) reviewed the original prevalvotomy transthoracic echocardiograms using strict criteria to eliminate interinstitutional variability in scoring. Using the MGH criteria (3), four aspects of valve morphology (leaflet mobility, thickening, calcification and subvalvular thickening) were individually graded on a scale of 1 to 4 from mild to severe. The total echocardiographic score was obtained by adding the four individual scores to yield a final score of 4 to 16. Each echocardiogram was also scored using the University of Southern California (USC) criteria (6), which assign a score of 0 to 2 to leaflet motion, leaflet thickness, subvalvular disease and commissural calcium. The total echocardiographic score consists of the sum of leaflet motion and thickness, ranging from 0 to 4. In six patients in whom only transesophageal echocardiograms were available, USC scores were not performed. After rescoring, 69 patients had total MGH scores ≥10, and 18 patients were eliminated from further analysis. Three echocardiograms could not be obtained and were included on the basis

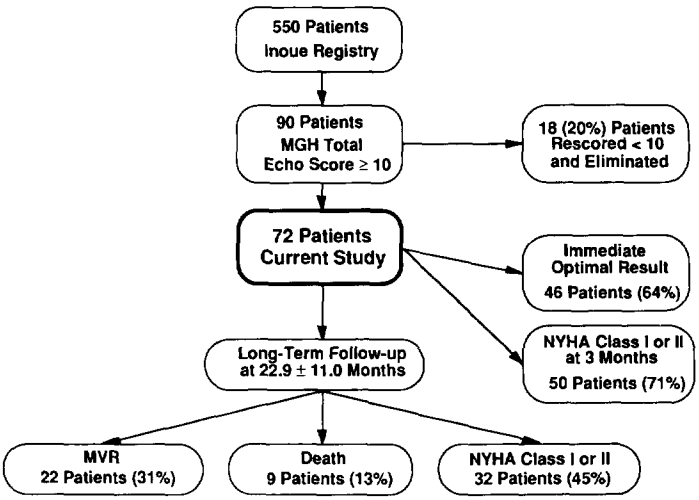

Figure 1. Flowchart of patient selection and results. The 72 study patients were selected from among 550 patients in the multicenter Inoue registry by a Massachusetts General Hospital (MGH) echocardiographic (Echo) score ≥10. Rescoring of the echocardiograms at a single center eliminated 18 patients (20%). The results of valvotomy are shown. MVR = mitral valve replacement; NYHA = New York Heart Association.

of their original scores. The final study group therefore included 72 patients.

Procedure. Inoue balloon mitral valvotomy was accomplished by the anterograde transseptal technique as previously described (13,15). Baseline hemodynamic and cardiac output measurements were obtained. The maximal balloon size was empirically chosen in relation to the patient's height. The balloon was introduced in its low profile configuration into the left atrium over a 0.025-in. (0.0635-cm) stainless steel guide wire. The balloon was maneuvered with the aid of a preformed steering stylet across the mitral valve. The initial inflation was usually performed at a diameter 4 mm less than the maximal size, and individual inflations lasted ~5 to 10 s. Subsequent inflations increased in 0.5 to 2-mm increments to the maximal balloon size until an adequate transmitral gradient reduction was achieved or until significant mitral regurgitation developed. The final hemodynamic variables and cardiac output were obtained with the catheter in the left atrium to reduce error caused by atrial septal defect blood flow. Left ventriculography was performed in most patients (86%) to compare the grade (0 to 4) of mitral regurgitation before and after valvotomy.

Assessment of results. The mitral valve area before and after valvotomy was calculated using the Gorlin formula. To evaluate immediate results, an optimal result was defined as ≥50% increase in mitral valve area or a final area ≥1.5 cm^2 with no major complications (16). Major complications were death, cardiac tamponade, systemic embolism, an increase in mitral regurgitation of three grades or a pulmonary/systemic shunt ratio ≥2.0 across the iatrogenic atrial septal defect.

End points for clinical follow-up included mitral valve replacement (or a second mitral valvotomy) and death. Otherwise, follow-up was based on New York Heart Association functional class as obtained by the individual centers.

Statistical analysis. Data were entered into an Excel spreadsheet (Microsoft Corporation) and analyzed using SPSS for Windows (SPSS Inc.) on an IBM-compatible personal computer. Twenty-six clinical, procedural, echocardiographic and hemodynamic variables were evaluated to identify predictors of an optimal hemodynamic result. An additional nine postprocedural hemodynamic variables were examined in the survival analysis. Statistical comparison of continuous variables was accomplished with the Student unpaired two-tailed *t* test. Categoric variables were compared using chi-square analysis. To identify predictors of immediate success, the Student unpaired *t* test and chi-square analysis identified univariate predictors. Logistic regression was then performed to identify which of the univariate predictors were significant by multivariate analysis. To identify predictors of event-free survival, Kaplan-Meier estimates and Cox proportional hazards regression were performed. Pearson correlation coefficients were calculated to compare echocardiographic scoring systems. All results are reported as mean value ± SD and were considered significant at $p < 0.05$.

Results

Study patients. The 72 study patients (55 women [76%], 17 men [24%]) had an average age of 63 ± 14 years (range 29 to 87) (Table 2). Before the procedure, all patients were symptomatic, and 83% were in functional class III or IV, 55% in class III and 28% in class IV. Atrial fibrillation was present in 52% of patients. Eleven patients (15%) had undergone previous surgical commissurotomy. Mean baseline mitral valve area was 0.9 ± 0.3 cm^2, and left atrial and pulmonary artery pressures were elevated (Table 2).

Mean total echocardiographic score by the MGH criteria was 11.7 ± 1.5. Individual scores for valvular thickness (3.2 ± 0.7) and valvular calcification (3.2 ± 0.6) were significantly ($p < 0.001$) higher than those for leaflet mobility (2.7 ± 0.7) and subvalvular thickness (2.7 ± 0.7). Mean total echocardiographic score by the USC criteria was 2.1 ± 0.7.

Immediate and short-term results of balloon valvotomy. Balloon mitral valvotomy was technically successful in 69 (96%) of the 72 patients. The hemodynamic variables measured and calculated before and after the procedure are listed

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Table 2. Clinical Characteristics, Echocardiographic Scores and Hemodynamic Results for 72 Study Patients

	Mean ± SD	Range
Age (yr)	63.3 ± 14.3	29–87
NYHA functional class	3.1 ± 0.7	2–4
MGH echocardiographic score	11.7 ± 1.5	10–16
Leaflet mobility	2.7 ± 0.7	2–4
Leaflet thickness	3.2 ± 0.7	2–4
Subvalvular thickness	2.7 ± 0.7	1–4
Valvular calcification	3.2 ± 0.6	2–4
USC echocardiographic score	2.1 ± 0.7	0–4
Leaflet motion	1.1 ± 0.6	0–2
Leaflet thickness	1.0 ± 0.3	0–2
Subvalvular disease	1.2 ± 0.7	0–2
Commissural calcium	1.6 ± 0.6	0–2
Cardiac output (liters/min)		
Before MV	3.7 ± 1.1	1.4–6.8
After MV	4.2 ± 1.2*	2.0–7.5
Mitral valve gradient (mm Hg)		
Before MV	13.3 ± 5.2	2.0–30.0
After MV	6.6 ± 3.2*	0–17.0
Mitral valve area (cm^2)		
Before MV	0.9 ± 0.3	0.3–2.0
After MV	1.5 ± 0.5*	0.5–3.3
Left atrial pressure (mm Hg)		
Before MV	24.0 ± 7.6	10.0–40.0
After MV	19.4 ± 6.8*	7.0–34.0
PA mean pressure (mm Hg)		
Before MV	38.5 ± 15.0	16.0–90.0
After MV	32.9 ± 14.0*	18.0–92.0
Mitral regurgitation (grade)		
Before MV	0.8 ± 0.7	0–2
After MV	1.3 ± 0.9*	0–4
No. of inflations	3.1 ± 1.6	1–8
Maximal balloon size (mm)	27.1 ± 2.0	22–30

*$p < 0.05$ before versus after mitral valvotomy (MV). MGH = Massachusetts General Hospital; NYHA = New York Heart Association; USC = University of Southern California.

in Table 2. Mean transmitral gradient decreased from 13.3 ± 5.2 to 6.6 ± 3.2 mm Hg ($p < 0.001$), and mitral valve area increased from 0.9 ± 0.3 to 1.5 ± 0.5 cm^2 ($p < 0.001$). Immediate optimal results, as previously defined, were obtained in 46 patients (64%).

Mean grade for mitral regurgitation increased from 0.8 ± 0.7 to 1.3 ± 0.9 ($p < 0.001$). Mitral regurgitation increased two or more grades in five patients (7%). Five patients (7%) experienced procedural complications. One patient had a cerebrovascular accident, and two patients required lower extremity arterial embolectomy for arterial thrombosis. One patient developed severe mitral regurgitation (grade 0 before to 4 after balloon valvotomy) that required emergency mitral valve replacement. Finally, one patient with known severe coronary artery disease experienced a myocardial infarction that was treated successfully by urgent coronary angioplasty.

Short-term results were evaluated 3 months after the procedure (Table 3). Follow-up was not available for two patients (3%). At that time, seven patients (10%) required early mitral valve replacement, mostly for mitral regurgitation. Three patients (4%) died, all of congestive heart failure. Fifty patients (71%) were in functional class I or II.

Table 3. Short- (3-month) and Long-Term Outcome for All 72 Patients

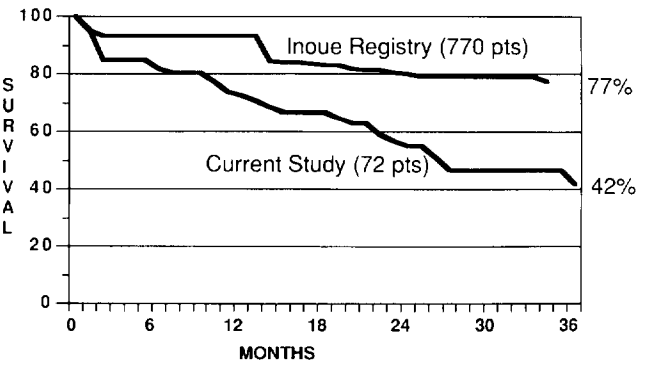
Status	Short-Term, No. of Pts (%)	Long-Term	
		No. of Pts (%)	mo (mean ± SD)
NYHA class I or II	50 (71%)	32 (45%)	22.9 ± 11.0
NYHA class III or IV	7 (10%)	4 (6%)	25.8 ± 12.8
MVR (or repeat PBV)	7 (10%)	22 (31%)	13.2 ± 10.6
Death	3 (4%)	9 (13%)	11.6 ± 13.9
Incomplete procedure	3 (4%)	3 (4%)	—
Lost to follow-up	2 (3%)	2 (3%)	—

MVR = mitral valve replacement; NYHA = New York Heart Association; PBV = percutaneous balloon valvotomy.

Long-term results of balloon valvotomy. Mean follow-up of patients who had not experienced a clinical end point (mitral valve replacement or death) was 22.9 ± 11.0 months. Follow-up was again not available for the same two patients (3%). Mitral valve replacement (or repeat valvotomy in 2 patients) was performed in 22 patients (31%) at a mean of 13.2 ± 10.6 months after valvotomy. A total of nine patients (13%) died at a mean of 11.6 ± 13.9 months. Seven patients died of progressive congestive heart failure, one of cancer and one of sepsis. Thirty-two patients (45%) were in functional class I or II at their last clinical evaluation. Figure 2 shows an event-free survival for our study patients of 42% at 3 years. Survival for unselected patients in the entire Inoue registry (17), which includes patients in the present study, is also shown in Figure 2.

Predictors of immediate and long-term results. Univariate predictors of an optimal hemodynamic result included male gender, sinus rhythm and a lower commissural calcium score (USC criteria) (Fig. 3). Eighty-eight percent of men had an optimal result compared with 60% of women ($p < 0.05$). Eighty-one percent of patients in sinus rhythm had an optimal

Figure 2. Kaplan–Meier event-free survival (freedom from death, mitral valve replacement or repeat valvotomy) for the study patients (pts) up to 3 years compared with that for the entire Inoue registry patients, including those with low echocardiographic scores (data from Feldman et al. [17]).



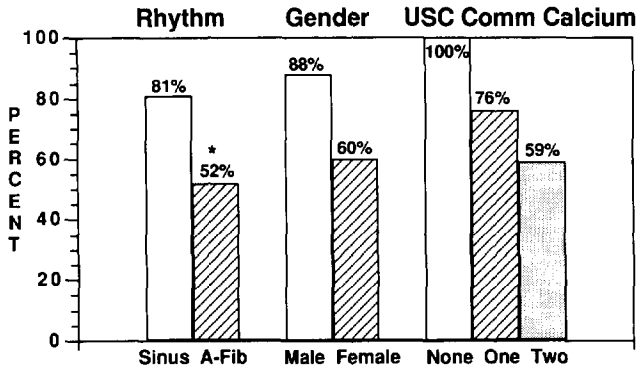


Figure 3. Univariate predictors ($p < 0.05$) of an optimal immediate result, defined as ≥50% increase in mitral valve area or a final area ≥1.5 cm^2 with no major complications. The percent of patients achieving an optimal result for each variable is plotted on the **ordinate**. Only sinus rhythm was predictive of an optimal result in multivariate analysis (*$p < 0.05$). A-Fib = atrial fibrillation; comm = commissural; USC = University of Southern California echocardiographic score.

result versus 52% of those in atrial fibrillation ($p < 0.05$). The USC commissural calcium score ($p < 0.01$) also predicted success, with an optimal result inversely proportional to the number of commissures calcified. Valves with both commissures calcified had a 59% success rate, and those with one calcified had a 76% success rate; only two patients in this series had no commissural calcium, and an optimal result was obtained in both. Neither total echocardiographic score predicted early outcome ($p = 0.36$ and $p = 0.42$ for MGH and USC scores, respectively). Multivariate analysis by logistic regression using the previous three variables identified only sinus rhythm as predicting success ($p < 0.05$).

Event-free survival was defined as freedom from mitral valve replacement (or repeat valvotomy) and death. Univariate predictors of improved event-free survival were a lower MGH total echocardiographic score ($p < 0.05$), lower MGH leaflet thickness subscore ($p < 0.05$), lower prevalvotomy left ventricular systolic pressure ($p < 0.05$) and smaller degree of mitral regurgitation as measured by contrast ventriculography after valvotomy ($p < 0.01$). Multivariate analysis using these four variables identified only degree of mitral regurgitation after valvotomy ($p < 0.05$) as predictive of event-free survival. Figures 4 and 5 demonstrate event-free survival by MGH total echocardiographic score and grade of mitral regurgitation after valvotomy.

Influence of echocardiographic score. Reevaluation of the original echocardiograms resulted in the elimination of 18 of the 90 echocardiograms (20%) from the study population due to rescoring below 10. Twenty-eight percent of the echocardiograms had the same total MGH echocardiographic score as was originally reported by the individual centers. Only 8% were rescored with the identical four subcomponent scores.

Comparison of the MGH and USC echocardiographic scores demonstrated a significant positive correlation both between total scores and between several of the individual components of each scoring system. Total echocardiographic

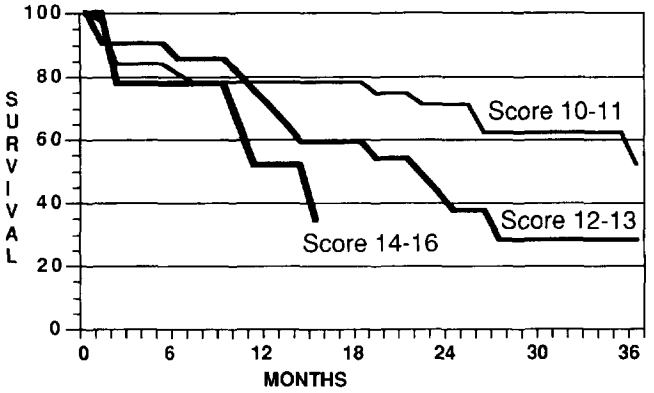


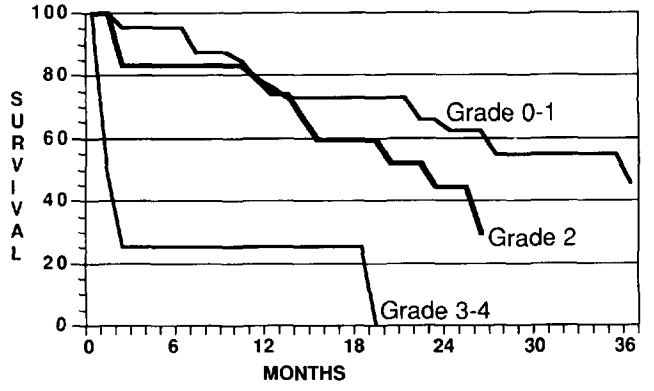
Figure 4. Kaplan–Meier 3-year event-free survival is shown for patients with Massachusetts General Hospital total echocardiographic scores of 10 to 11, 12 to 13 and 14 to 16. This variable was a significant univariate predictor of outcome ($p < 0.05$).

scores were correlated with a correlation coefficient of 0.46 ($p < 0.001$). Subscores for leaflet motion ($r = 0.59$, $p < 0.001$) and subvalvular disease ($r = 0.71$, $p < 0.001$) were highly correlated, but the scores for valvular thickness ($r = 0.01$, $p = 0.91$) and calcification ($r = 0.14$, $p = 0.29$) did not correlate.

Discussion

We identified 72 patients from the North American multicenter Inoue registry with severe valvular and subvalvular disease as defined by a total MGH echocardiographic score ≥10. Such patients are usually considered poor or suboptimal candidates for both balloon valvotomy and surgical commissurotomy (18), but few studies have specifically examined outcomes after Inoue balloon valvotomy. In the present study, we attempted to carefully define this group of patients by reviewing all the echocardiograms at a central site, which resulted in elimination of 20% of patients with echocardiograms previously scored as ≥10 at contributing registry insti-

Figure 5. Actuarial 3-year event-free survival for patients with severe valvular and subvalvular deformity grouped by the grade of mitral regurgitation after valvotomy. Mitral regurgitation was graded (none to 4+) by left ventriculography and was the only significant predictor of poor long-term outcome identified by multivariate Cox regression analysis.



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tutions. In addition, to our knowledge we obtained the first long-term follow-up of such patients after Inoue balloon valvotomy in North America.

Early valvotomy results. A number of investigators have reported the results of Inoue balloon valvotomy, both here and abroad (13–15,19–22). The results of the North American multicenter registry are typical (13,14). In general, mitral valve area increases from 1.0 to 1.8 cm^2 with an immediate success rate of ~75% and a low rate of major complications (14). Complications may include severe mitral regurgitation, systemic embolism, cardiac tamponade and significant interatrial shunts.

Several studies have also examined the early results of Inoue valvotomy in patients with a suboptimal morphology (13,15,19). Feldman et al. (13) described the results of valvotomy in 44 patients with an MGH echocardiographic score >8. Their postvalvotomy mitral valve area was 1.7 ± 0.5 cm^2, which was similar to the result obtained in 105 patients with echocardiographic scores ≤8. They concluded that valve deformity did not have a significant effect on early results with the Inoue balloon. In contrast, Hung et al. (19) reported the results of Inoue valvotomy in 74 Chinese patients with severe valvular and subvalvular calcification. Although the mitral valve area increased to 1.8 ± 0.5 cm^2, valvular morphology was a significant predictor of a suboptimal hemodynamic result. Likewise, Nobuyoshi et al. (15) described the results of Inoue valvotomy in 106 Japanese patients; the early hemodynamic and symptomatic improvement was significantly worse in 10 patients with rigid valves. The final mitral valve area in these patients increased to 1.6 ± 0.7 cm^2, and only 60% of patients improved symptomatically compared with 95% of the remaining patients.

Our patients with severe valvular and subvalvular disease are similar to those in previous studies of less selected patients with more pliable valves with regard to gender, incidence of previous commissurotomy and severity of mitral stenosis but were older by ~10 years. In the present study, valvotomy was technically successful in 96% of patients, a rate similar to those reported in large series of patients with lower mean echocardiographic scores (13–15,19,21). However, the immediate hemodynamic result (1.5 ± 0.5 cm^2) was lower than the result in the entire Inoue balloon registry (1.8 ± 0.6 cm^2) (14,17). Similarly, by a previous definition of optimal hemodynamic success, 64% of our patients with severe valvular and subvalvular disease achieved an optimal result compared with 74% in the entire registry (14).

Compared with previous studies, we confirmed that balloon valvotomy can be safely performed in patients with a suboptimal morphology with an acceptable but smaller improvement in mitral valve area. Previous reports from the Inoue multicenter registry failed to demonstrate short-term differences in such patients, probably because of greater interinstitutional variability in echocardiographic scoring, the inclusion of patients with scores between 8 and 10 and the much smaller number of patients with an echocardiographic score ≥10.

Short-term follow-up. Short-term results were evaluated at 3 months, by which time 10% of patients required mitral valve replacement, usually for mitral regurgitation. Seven percent of patients had a significant increase in grade of mitral regurgitation immediately after the procedure, which appeared to be similar to that reported in other series and in the registry as a whole (13–15,19,21,22). However, mean grade of mitral regurgitation increased more in these patients from a higher baseline, and more patients required early mitral valve replacement for mitral regurgitation than in previous series. Neither left ventriculography nor echocardiographic Doppler examination was performed in seven patients. It is unlikely that the incidence of severe mitral regurgitation would have been higher if these patients were included, because six were free of events at last follow-up, and one died of a cerebral vascular accident.

The mechanism of severe mitral regurgitation with the Inoue balloon was previously examined by Herrmann et al. (23), who demonstrated that the most frequent causes of regurgitation were rupture of the chordae tendineae and tearing of a leaflet, usually the posterior one. One would expect that leaflet tears would be more frequent in more calcified valves and that chordal rupture would be more frequent in patients with severe subvalvular deformity. Echocardiograms after valvotomy were not examined in the present study, but none of the echocardiographic variables within this selected patient group predicted the occurrence of mitral regurgitation. Previous studies with a larger range of echocardiographic scores have also failed to identify specific predictors of this complication (14,16,23).

Long-term follow-up. Several previous investigators have examined the intermediate and long-term results of balloon valvotomy. Palacios (24) described results in 320 patients after single- and double-balloon valvotomy and reported by actuarial estimates an event-free survival of 77%, with 19% requiring mitral valve replacement at 2 years. Three-year event-free survival was 70%. In contrast, patients with MGH echocardiographic scores >8 had poorer results, with a 3-year event-free survival of 46% (24). Cohen et al. (11) provided 5-year (mean 3) actuarial data for 145 patients after predominantly single-balloon procedures. They reported a similar 2-year event-free survival of 74% and a 5-year event-free survival of 51%. In that study, patients with MGH echocardiographic scores >8 had an event-free survival of 58% at 2 years and 28% at 5 years (11). Finally, a preliminary study from the Inoue multicenter registry (17) reported by actuarial methods an event-free survival of 77% at 3 years.

In the present study, we demonstrated a poorer outcome in patients with severe valvular and subvalvular disease. With a 2-year mean follow-up, mitral valve replacement was required in 31% of patients, and only 45% were in functional class I or II. Actuarial event-free survival was only 42% by 3 years, comparable to that achieved with the single- and double-balloon techniques in similar patients (11,24). These results are less than half that achieved in less selected patient series (11,17,24). We therefore demonstrated that both the short- and long-term results of Inoue valvotomy in patients with

severe valvular and subvalvular disease are very similar to those obtained with the single- or double-balloon techniques. The unique geometry of the Inoue balloon appears to offer no advantage in this highly selected group of patients.

Predictors of outcome. Factors that have previously been demonstrated to adversely affect the early hemodynamic results of balloon valvotomy include atrial fibrillation (2,4,7,19), echocardiographic morphology (2–7,9,19), balloon size (2,5–7,25), advanced age (4,19) and cardiac output (6,25). In the present study, we confirmed that atrial fibrillation and commissural calcium (USC score) were associated with less hemodynamic improvement. In addition, we demonstrated in this highly selected study group with severe valvular deformity that female gender had an adverse effect on early outcome.

It is likely that atrial fibrillation is a marker of more severe or long-standing mitral stenosis, or both, which may be less amenable to balloon dilation. Similarly, because the mechanism of successful percutaneous balloon valvuloplasty requires separation of fused commissures (1,3), it is not surprising that better results are obtained in valves with less commissural calcium. It is less clear how gender influences outcome, but this variable was not independently significant in multivariate analysis. More male than female patients were in sinus rhythm (56% vs. 46%), but this difference was not statistically significant.

Several investigators have demonstrated that echocardiographic variables can predict long-term outcome with single- and double-balloon techniques (4,9–11). Chen et al. (20) demonstrated in young Chinese patients that severe valvular and subvalvular disease increased the rate of restenosis after Inoue valvotomy, although Herrmann et al. (14) did not find a higher rate of early restenosis in a previous study of North American patients.

However, with a more homogeneous group of patients with severe valvular and subvalvular disease and longer follow-up, the present investigation demonstrated a high rate of mitral valve surgery, need for repeat valvotomy and death. Univariate predictors of event-free survival included MGH total echocardiographic score and leaflet thickness subscore, postvalvotomy grade of mitral regurgitation and prevalvotomy left ventricular systolic pressure. Event-free survival was particularly poor in patients with an Massachusetts General Hospital score $\geq$12 (Fig. 4). Only postvalvotomy mitral regurgitation grade was predictive of long-term outcome in multivariate analysis. Although the incidence of severe mitral regurgitation produced by valvotomy in this study was not different from that in previous investigations, mean grade of mitral regurgitation both before and after valvotomy was higher. This suggests that small increases in mitral regurgitation grade may be less well tolerated in this older patient group and that patients with severe valvular deformity and more than mild preexisting mitral regurgitation are at greatest risk for poor long-term outcomes.

Finally, we compared the MGH criteria and USC echocardiographic score criteria. The subscores for leaflet motion and subvalvular disease were highly correlated, as were the total echocardiographic scores. However, the subscores for leaflet thickness did not correlate, possibly because of difficulty in eliminating the subvalvular apparatus from measurements of the USC subscore. Although the USC commissural score was predictive of immediate results, only the MGH score predicted event-free survival.

Study limitations. This was a retrospective study and has the usual limitations attributed to this form of analysis. In addition, an inherent selection bias was incurred because investigators chose patients for valvotomy and because the study patients were selected on the basis of one (MGH) scoring system. In particular, comparisons of the relative predictive value of the two scoring systems used in this study as well as comparisons of one to the other must be interpreted cautiously. Finally, the older age of our study patients may have influenced the decision for operation and limits comparison of event-free survival with that for the entire Inoue registry.

Clinical implications. Percutaneous balloon mitral valvotomy is a safe and efficacious treatment modality for the majority of patients with acquired mitral stenosis. However, proper patient selection is essential to achieve optimal results. In the present investigation, we demonstrated that both immediate and long-term results of Inoue balloon valvotomy are adversely influenced by severe valvular and subvalvular deformity. Procedural technical success remains high in such patients, but smaller mitral valve areas are achieved, and the long-term event-free survival is <50% of that achieved in unselected patients. The most important predictor of event-free survival was the severity of mitral regurgitation after valvotomy. Mitral valve replacement may result in better long-term relief of mitral valve obstruction in symptomatic surgical candidates with total MGH echocardiographic scores $\geq$10, although comparative studies of event-free survival will need to include prosthetic valve complications as well. Balloon valvotomy remains a reasonable palliative therapeutic option for some patients with severe valvular deformity and high surgical risk.

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