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Mechanisms and Outcome of Severe Mitral Regurgitation After Inoue Balloon Valvuloplasty

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Objectives. The purpose of this study was to assess the incidence, mechanism and outcome of severe mitral regurgitation after treatment of mitral stenosis with percutaneous mitral valvuloplasty using the Inoue balloon.

Background. Severe mitral regurgitation occurs in up to 15% of percutaneous balloon valvuloplasty procedures for acquired mitral stenosis. The incidence and mechanism of production of mitral regurgitation with the recently introduced single-balloon Inoue technique have not been characterized.

Methods. We examined the incidence, mechanism, predictors and outcome of severe mitral regurgitation after Inoue balloon valvuloplasty in 280 patients in the North American multicenter registry. Twenty-one patients who developed either clinically significant or angiographically severe regurgitation were identified, and their echocardiograms were reviewed to determine the mechanism of regurgitation. These patients were then compared with the remaining patients without severe regurgitation to identify predictors of this outcome.

Results. The incidence of severe regurgitation in this study was 7.5%, and the mean grade of angiographic regurgitation in these patients increased from 0.9 ± 1.0 to 2.8 ± 0.7 ($p < 0.05$). The most common cause of regurgitation (43%) was rupture of chordae tendineae to the anterior or posterior mitral leaflet. Tearing of a leaflet (usually the posterior one) occurred in 30% of patients; and no recognizable structural abnormality, with wide splitting of the commissures and a central regurgitant jet, was present in five patients (26%). All patients with definite posterior leaflet tears had heavily calcified leaflets. Patients who developed severe regurgitation had fewer balloon inflations and a higher grade of preexisting mitral regurgitation but were otherwise similar to the remaining patients without severe regurgitation. During 6-month follow-up, 71% of the patients with severe regurgitation were treated surgically; the grade of regurgitation decreased in four patients (19%), and five patients (24%) have not required mitral valve replacement during 18 ± 5 months of follow-up.

Conclusions. Severe mitral regurgitation is a relatively infrequent complication of Inoue balloon valvuloplasty and results from disruption of the valve integrity, including chordal rupture and leaflet tearing. Careful balloon positioning may help avoid chordal rupture, and heavily calcified posterior leaflets may be at greater risk of tearing. Most patients who develop severe regurgitation will require nonemergency mitral valve replacement.

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Mitral regurgitation occurs in up to 50% of patients after percutaneous balloon valvuloplasty for acquired mitral stenosis (1–3). In most cases, the regurgitation is mild and only minimally detracts from the clinical improvement provided by the relief of mitral valve obstruction. However, severe mitral regurgitation may occur in up to 15% of procedures and often requires intensive medical therapy or surgery (1,2,4,5).

The mechanism for production of valvular regurgitation has been described in a small number of patients and involves disruption of the integrity of one or more parts of the valvular apparatus (4,6,7). In these reports, valvuloplasty was performed with a double-balloon technique. The single-balloon Inoue technique, recently introduced in the United States, has gained increasing favor as studies have demonstrated its safety, efficacy and ease of use (8–11). In the present investigation, we examined the incidence, mechanism, predictors and outcome of severe mitral regurgitation after Inoue single-balloon valvuloplasty in a large group of patients in a multicenter registry.

Methods

Study group. The study group was derived from 15 centers participating in the North American multicenter registry of patients undergoing percutaneous balloon valvuloplasty with the Inoue technique (11). Data from 280 procedures performed between June 1989 and March 1992 were collected on standardized forms and reported to a

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central registry. The specific study group for this investigation comprised 21 patients (7.5%) who developed severe mitral regurgitation after valvuloplasty. Nineteen patients had severe (grade 3 or 4) regurgitation on ventriculography (n = 16) or by echocardiography (n = 3). Two additional patients with moderate (grade 2) regurgitation after valvuloplasty were also included in the study because they required early mitral valve replacement for symptoms in the absence of significant residual mitral stenosis.

Valvuloplasty procedure. Percutaneous balloon valvuloplasty was performed with an Inoue balloon using an anterograde transseptal approach, as previously described (8,9,11). An initial balloon size was chosen on the basis of patient height, and subsequent dilations were performed in an incremental stepwise fashion until adequate reduction in transmitral gradient was achieved or mitral regurgitation developed (11,12). Techniques used to assess the development of regurgitation during the procedure included changes in the size of left atrial *v* waves, angiographic grade by repeated left ventriculography (13) and color flow and Doppler echocardiography. The mean maximal balloon diameter was 27 ± 2 mm (range 22 to 31).

Echocardiographic analysis. Echocardiograms recorded before valvuloplasty from patients who developed severe mitral regurgitation were reviewed by two investigators (H.C.H. and J.A.C.L.). An echocardiogram recorded within 24 h after valvuloplasty was available in 20 of the 21 patients, and these studies were compared with those obtained before the procedure. Transesophageal studies were available in five patients.

The mechanism of regurgitation was determined by consensus and classified as follows. 1) *Chordal rupture* was considered to be the mechanism producing regurgitation when a free chord was visible in association with a flail or prolapsed leaflet causing moderate or severe mitral regurgitation. 2) *Leaflet tears* were either visible or inferred from the appearance of one or multiple Doppler jets seen across the valve leaflets. Jets directed toward the interatrial septum were considered to be due to posterior leaflet disruption, whereas laterally directed jets were considered related to the anterior leaflet. 3) *No recognizable structural abnormality* was the classification utilized for patients with centrally directed regurgitant jets that were seen not to traverse the valve leaflets. This regurgitant flow probably results from failure of leaflet coaptation during systole and may have occurred because of "excessive" widening of the commissures beyond the point at which the leaflets could adequately coapt because of either leaflet abnormalities or coexistent subvalvular disease.

The mechanism of mitral regurgitation was further classified as either *definite* (when by consensus there was enough echocardiographic evidence for a particular mechanism) or *probable* (when such a mechanism could be inferred but not directly ascertained despite review and comparison of all echocardiographic studies recorded before and after the procedure). Finally, valvular morphology was assessed using the Massachusetts General Hospital scoring system (14,15).

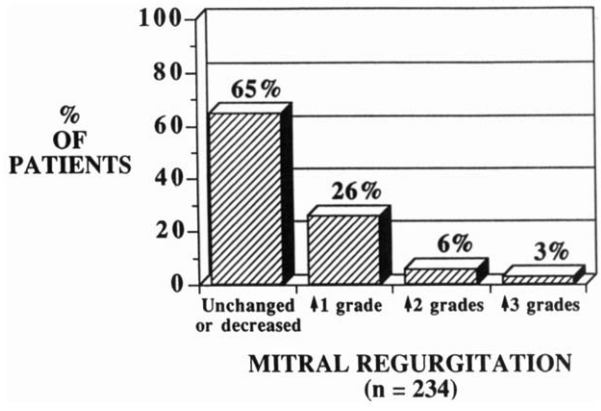

Figure 1. Frequency distribution of the change in mitral regurgitation grade as assessed by left ventriculography in 234 patients.

Statistics. Data from all 280 procedures were entered into a spreadsheet (Microsoft Excel) on a Macintosh IIcx computer (Apple Computer) and are shown as mean value ± SD (Statview Statistical Software). Comparisons before and after valvuloplasty were made by analysis of variance with the Scheffé F test for multiple comparisons. Comparisons between patients with and without mitral regurgitation were assessed by linear regression analysis. Differences were considered significant at $p < 0.05$.

Results

Incidence of mitral regurgitation. The mean age (± SD) of the 280 patients in the entire registry was 53 ± 15 years. At baseline, these patients had a mean echocardiographic score of 7.5 ± 2.5 and were in New York Heart Association functional class 2.8 ± 0.7. Balloon valvuloplasty resulted in an increase in calculated mitral valve area from 1.0 ± 0.3 to 1.8 ± 0.6 cm^2 ($p < 0.05$).

Two hundred thirty-four patients (84%) had left ventriculography before and after valvuloplasty. The mean grade of mitral regurgitation increased from 0.5 ± 0.6 to 1.0 ± 0.9 ($p < 0.05$). The frequency distribution of the change in regurgitation grade is shown in Figure 1; 91% had an increase of ≤1 grade, and 9% had an increase of ≥2 grades. In the 21 patients (7.5%) with severe regurgitation after valvuloplasty constituting the study population, the mean grade of mitral regurgitation increased from 0.9 ± 1.0 to 2.8 ± 0.7 ($p < 0.05$).

Mechanism. The mechanism producing mitral regurgitation was established with certainty in 16 (80%) of the 20 patients who had both severe regurgitation and available echocardiograms; a probable mechanism was identified in 3 additional patients (Table 1). The most common cause of regurgitation was rupture of chordae tendineae to the anterior (n = 6) or posterior (n = 3) leaflet, which accounted for nearly 50% of cases (Table 1, Fig. 2 and 3). Tearing

Table 1. Mechanism of Production of Severe Mitral Regurgitation in 20 Patients After Inoue Balloon Valvuloplasty*

	Chordal Rupture		Tears		
	Ant	Post	Ant	Post	Commis
Definite	6	3	1	3	2
Probable	—	—	—	2	3
Total	6	3	1	5	5
	9		6		5

*Mechanism could not be determined in one patient, and one patient had both posterior and commissural tears. Ant = anterior; Commis = commissural; Post = posterior.

of a leaflet (usually the posterior one) was present in 30% of patients (Table 1, Fig. 4), and "overdilation" with wide splitting of the commissures and a central regurgitation jet was present in five patients (26%). The anterior leaflet was very pliable and demonstrated excessive mobility in two of the six patients who developed chordal rupture. All three of the patients with definite posterior leaflet tears had a heavily calcified posterior leaflet.

Predictors. To identify predictors of severe mitral regurgitation, the 21 patients in the study group were compared with the remaining 259 patients in the multicenter registry (Table 2). Patients with severe mitral regurgitation had fewer balloon inflations (2.2 ± 1.2 vs. 3.0 ± 1.6, $p < 0.05$) and a higher grade of preexisting mitral regurgitation (0.9 ± 1.0 vs. 0.5 ± 0.6, $p < 0.05$). The two groups did not differ with respect to age, functional class before valvuloplasty, hemodynamic variables before and after valvuloplasty and maximal balloon size used or maximal balloon size normalized for body surface area. Furthermore, there were no differences in echocardiographic variables, including leaflet mobility, thickening, valvular calcification, subvalvular disease, total score and left atrial enlargement.

Outcome. During 6-month follow-up, 15 patients (71%) underwent mitral valve replacement (Fig. 5); surgery was performed as an emergency procedure in 1 patient, within 30 days in 9 additional patients and before 60 days in 5 patients. In the six remaining patients with minimal symptoms, the grade of regurgitation lessened in four and remained the same or worsened in two. The two patients with persistent severe regurgitation have had no surgical treatment and have minimal symptoms 14 and 21 months, respectively, after their procedure. One of the four patients with lessened regurgitation required valve replacement for mixed regurgitation and recurrent stenosis 19 months after valvuloplasty. Thus, 18 (86%) of 21 patients either were surgically treated or had persistent severe mitral regurgitation at a mean follow-up interval of 18 ± 5 months. The mechanism of mitral regurgitation did not differ between patients who did or did not require valve replacement. Specifically, the causes of regurgitation in the four patients whose condition improved by 6 months were ruptured chord to the anterior leaflet, no recognizable structural abnormality, posterior leaflet tear and unknown.

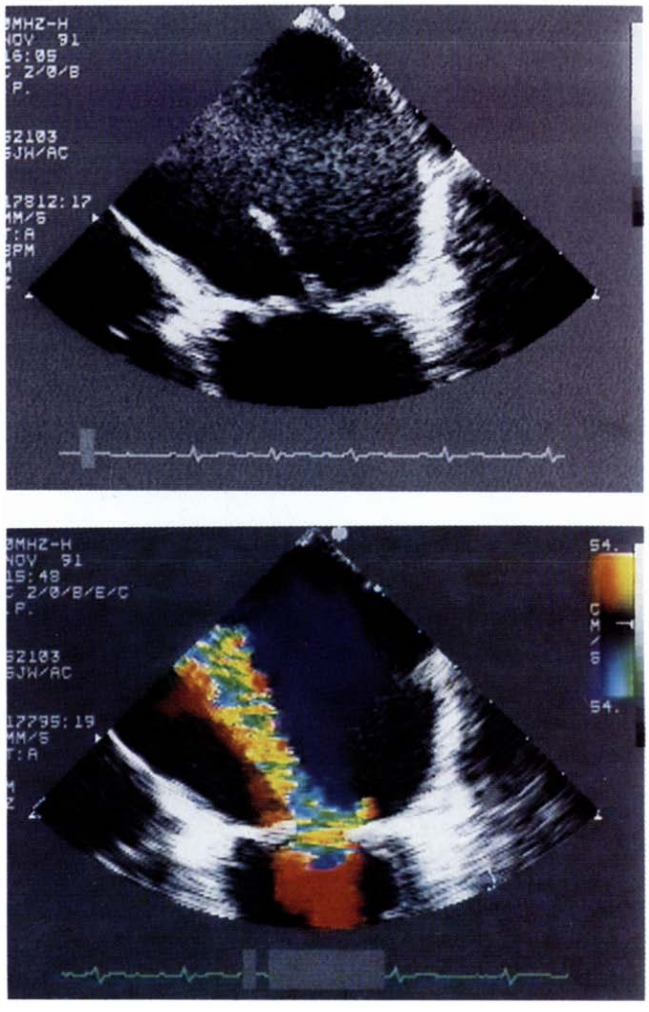

Figure 2. Sequence of frames from a transesophageal echocardiogram obtained immediately before mitral valve replacement in a patient with severe mitral regurgitation after Inoue balloon valvuloplasty. **Upper panel** demonstrates prolapse of the posterior leaflet with an attached chord into the left atrium during systole. **Lower panel** shows a central and septally directed Doppler color flow jet of severe mitral regurgitation.

Discussion

Percutaneous balloon valvuloplasty with the Inoue device has demonstrated high efficacy and improved procedural ease compared with other techniques (8–11). In this investigation, we demonstrated a low rate (7.5%) of severe mitral regurgitation as a complication of Inoue balloon valvuloplasty due to disruption of the valvular apparatus.

Previous studies. Several previous studies have examined the incidence of mitral regurgitation after balloon valvuloplasty (Table 3). In general, the grade of mitral regurgitation was unchanged in up to 50% of patients, was slightly increased in 33% and was severe (increase ≥2 grades) in

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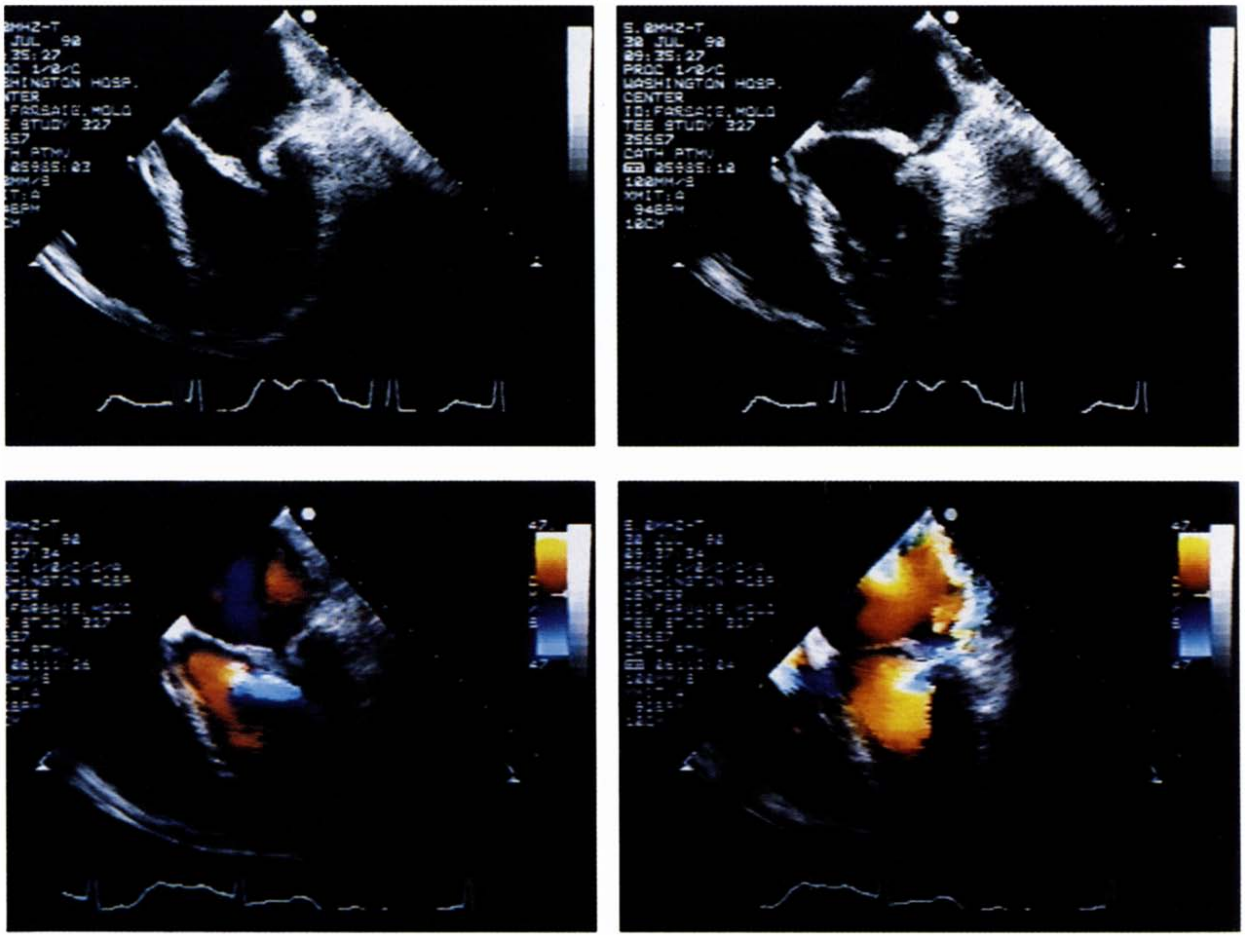


Figure 3 (above). Frames from a transesophageal echocardiogram obtained during a valvuloplasty procedure just after balloon inflation. **Upper panels,** An excessively mobile anterior leaflet during diastole **(left panel)** is seen prolapsing into the left atrium with an attached flail chord **(right panel). Lower panels,** Doppler color flow imaging demonstrates an associated laterally directed jet due to severe regurgitation.

Figure 4 (below). Transthoracic parasternal view echocardiographic frames from a patient who developed severe mitral regurgitation after Inoue balloon valvuloplasty. **Left panel,** The mitral valve is seen during early diastole. **Right panel,** Doppler color flow imaging demonstrates a wide-based, posterior and laterally directed jet across the anterior mitral valve leaflet, illustrating an anterior leaflet tear.

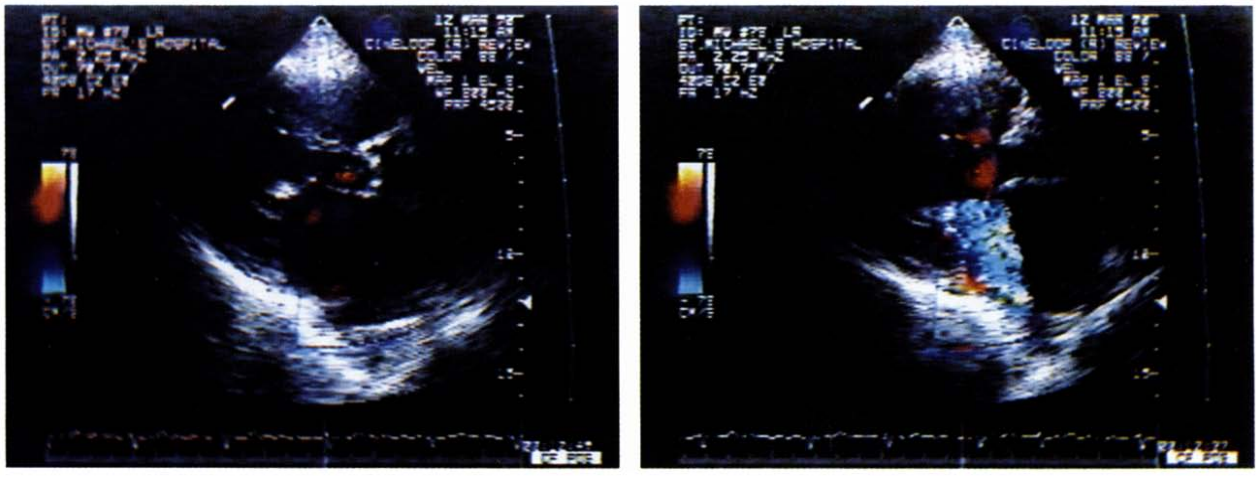


Table 2. Comparison of Selected Variables in Patients Developing Severe Mitral Regurgitation After Inoue Balloon Valvuloplasty and Those Without Severe Mitral Regurgitation

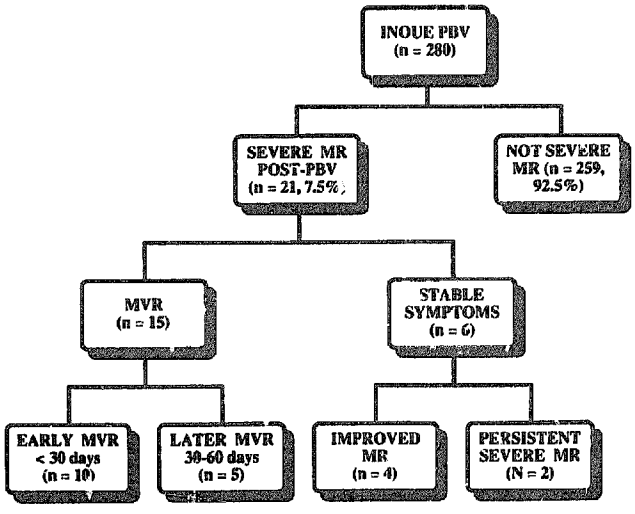
	Severe MR (n = 21)	Not Severe MR (n = 259)
MR grade		
Pre	0.9 ± 1.0	0.5 ± 0.6*
Post	2.8 ± 0.7	0.8 ± 0.7*
Inflation (no.)	2.2 ± 1.2	3.0 ± 1.6*
Echo score	7.6 ± 2.0	7.5 ± 2.6
MVA (cm^2)		
Pre	0.9 ± 0.2	1.0 ± 0.3
Post	1.5 ± 0.5†	1.8 ± 0.6
Max balloon size (mm)	27 ± 2	27 ± 2
Max balloon size/BSA (mm/m^2)	16.4 ± 1.5	16.2 ± 2.2

*$p < 0.05$. †This is a minimal valve area calculated in the presence of severe regurgitation using a forward Fick or thermodilution cardiac output. Values presented are mean value ± SD. BSA = body surface area; Echo = echocardiographic; Max = maximal; MR = mitral regurgitation; MVA = mitral valve area; post and pre = after and before, respectively, Inoue balloon valvuloplasty.

approximately 8% of procedures (1–5,7,10,14,15). The incidence of mild regurgitation was higher in studies using Doppler echocardiography (4,15) and was similar with various non-Inoue balloon techniques. In the present study using the Inoue technique, we demonstrated a similar incidence of mild and severe regurgitation of 26% and 9%, respectively, in the patients who had left ventriculograms obtained before and after valvuloplasty; the incidence of severe regurgitation was 7.5% for the total registry population.

Several studies have attempted to compare in a nonrandom fashion the incidence of mitral regurgitation after double-balloon valvuloplasty with that after the Inoue technique. The incidence of severe regurgitation was higher with the double-balloon technique (8% vs. 3%, p = NS) in one study (10) and higher with the Inoue balloon (19% vs. 4%, $p < 0.05$) in the other study (3). It is likely that patient selection and learning curve effects, particularly the careful use of a stepwise inflation technique with the Inoue balloon (12), may bias the results in these nonrandomized comparisons of devices.

Figure 5. Clinical outcome of patients with mitral regurgitation (MR) after Inoue balloon valvuloplasty. The specific study group comprised 21 patients who developed severe regurgitation as a result of the procedure. MVR = mitral valve regurgitation; PBV = percutaneous balloon valvuloplasty.



Mechanism of mitral regurgitation. Essop et al. (4) examined the mechanism of production of regurgitation in 40 patients undergoing double-balloon valvuloplasty. Seven patients (17%) had severe regurgitation due to posterior (n = 5) and anterior (n = 1) leaflet tears, and one patient had avulsion of a portion of papillary muscle. The mechanism of mild regurgitation was more commonly widening at the site of commissural splitting (4), which may reflect the inability of leaflets to coapt adequately once the commissures are fully opened because the leaflets are immobile or subvalvular disease has impaired their range of motion. O'Shea et al. (6) described six patients (4% of procedures) with unusual valvular disruptions after double-balloon valvuloplasty. Mechanisms of regurgitation included posterior leaflet rupture and tears in the anterior leaflet. In addition, they described one patient with only mild regurgitation due to rupture of an anterior leaflet chord (6).

The present study includes the largest series of patients with severe regurgitation to undergo careful echocardiographic analysis. Chordal rupture, particularly to the anterior leaflet, was the single most common cause of mitral regurgitation. This complication may be more common with the Inoue balloon because it is steered across the mitral valve with an internal stylet from a posterior location in the left atrium after crossing the interatrial septum. Despite partial inflation of the balloon as it is advanced across the valve, the tip may become entangled in the anterior leaflet chords, which can then be disrupted during inflation. Careful attention to the balloon position and its free movement toward the left ventricular apex before inflation may help to minimize this complication. Anterior leaflet chordal rupture was also noted in two patients with a highly mobile anterior leaflet, a situation that may increase the potential for the balloon to become entrapped in the chordae tendineae (Fig. 3).

Posterior leaflet tears were another common cause of severe regurgitation, as noted in previous studies utilizing the double-balloon technique (4,5). In most instances the patient had a heavily calcified posterior leaflet, a predisposing factor that has been noted by other investigators (7).

Predictors of severe regurgitation. Previous studies have attempted to identify factors associated with the development of mitral regurgitation after balloon valvuloplasty. In the M-HEART multicenter registry (1), the effective balloon dilating area was greater in patients who developed regurgitation, although the range of balloon sizes was wide. A similar result was found by Roth et al. (2), but other studies (4,16) were unable to demonstrate a correlation

Table 3. Frequency of Change in Mitral Regurgitation Grade After Balloon Valvuloplasty in Published Studies

Reference (first author)	No. of Pts	Grade of MR			Method	
		Unchanged (%)	+1 Grade (%)	+≥2 Grades (%)	MR Assessment	PBV
Herrmann (1)	48	69	19	13	LVg	S + D
Roth (2)	157	55	31	13	LVg	D
Ruiz (3)	222	50	46	4	LVg	D
Essop (4)	40	41	28	17	LVg	D
	40	18	67	15	Pulsed Doppler	D
Sancho (5)	197	69	22	9	LVg	R
Vahanian (7)	189	74	26	7	LVg	T
Abdullah (10)	60	78	20	2	LVg	D
Herrmann (14)	52	44	48	8	LVg	S + D
Abascal (15)	24	54	33	13	Pulsed Doppler	D

D = double balloon; LVg = left ventriculography; MR = mitral regurgitation; PBV = percutaneous balloon valvuloplasty; Pts = patients; R = retrograde transarterial; S = single balloon; T = trefoil balloon.

between balloon size and the development of mitral regurgitation.

A high echocardiographic score indicating a nonpliable valve was associated with regurgitation in one study (9) but not in others (15,16). In both the present study and a previous one from the North American registry of Inoue balloon investigators (11), echocardiographic variables of valvular morphology were not correlated with the development of mitral regurgitation. In fact, none of the variables studied, except the number of balloon inflations and the preexisting grade of regurgitation, influenced the development of regurgitation after valvuloplasty. The smaller number of inflations in the patients who developed severe regurgitation probably reflects the early discontinuance of the procedure.

Follow-up. Most (70% to 80%) of the patients in this series of severe mitral regurgitation required mitral valve replacement during short-term follow-up. Although several patients in this and other (2) studies experienced an improvement in the grade of mitral regurgitation assessed immediately after valvuloplasty, most patients with severe (grade 3 to 4) regurgitation will need surgery (4,7,9). The similar distribution of mechanisms producing regurgitation in patients with improvement makes it unlikely that the cause of regurgitation alone will allow prediction of the subsequent need for mitral valve replacement.

Study limitations. This is a multicenter study, and our results could be influenced by individual center variability in the grading of valve morphology and regurgitation or its clinical significance and by incomplete reporting or data collection. These problems were minimized in the study group of patients with regurgitation by having the echocardiographic videotapes reviewed by two investigators at a central site and by the definition of severe regurgitation that was chosen. Pathologic correlation of the echocardiographic findings was not performed; however, several previous reports have documented echocardiographic correlation with observations at operation in this setting (7,9). Similarly, Essop et al. (4) demonstrated good correlation between angiographic and Doppler echocardiographic assessments of regurgitation after valvuloplasty.

Summary and clinical implications. This study demonstrates that severe mitral regurgitation is a relatively infrequent complication of Inoue balloon valvuloplasty, occurring in approximately 7.5% of procedures. Regurgitation is produced by disruption of the valve integrity and is usually due to chordal rupture or leaflet tearing. It is possible that careful balloon positioning may help in avoiding chordal rupture. Leaflet tears are not easily predictable, but heavily calcified posterior leaflets may be at greater risk for tearing. Patients who develop mild and moderate grades of regurgitation can be followed-up medically, but most patients with severe regurgitation will require nonemergency mitral valve replacement.

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