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Progression to Moderate or Severe Mitral Regurgitation After Percutaneous Transvenous Mitral Commissurotomy Using Stepwise Inflation Technique

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Abstract

Progression to moderate or severe mitral regurgitation (MR) was studied after Inoue balloon percutaneous transvenous mitral commissurotomy (PTMC) using the stepwise inflation technique, performed at increments of 1 mm of balloon diameter, in 49 consecutive patients with rheumatic mitral stenosis (aged from 32-73 years; 8 males, 41 females).

The patients were classified on the basis of the degree of MR after PTMC, compared with that before PTMC, into either Group A, development of moderate or more severe ($\geq$ grade 2) MR ($n=8$) or Group B, no increase in MR or development of mild (grade 1) MR ($n=41$). Progression to moderate or severe MR was significantly associated only with advanced age (60 ± 8 vs 52 ± 10 years, $p<0.05$) and narrower mitral valve area (0.87 ± 0.35 vs 1.11 ± 0.29 cm^2, $p<0.05$), but other characteristics before PTMC were similar in both groups. There was no difference between the two groups in the total number and degree of balloon inflation. Immediately before the final inflation, the left atrial mean pressure and *v* wave pressure were decreased in smaller degrees in Group A compared with Group B (-2 ± 2 vs -5 ± 4 mmHg, $p<0.05$; -2 ± 2 vs -6 ± 6 mmHg, $p<0.05$, respectively). Thus, the stepwise inflations require careful monitoring of changes in the left atrial pressure and waveform to recognize the aggravation of MR, especially in older patients with severe stenosis.

Patients who do not have a significant drop in left atrial mean pressure and *v* wave pressure during stepwise inflations of the balloon might be at risk of development of moderate or severe MR after further dilations.

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Key Words

Mitral valve stenosis, Valvuloplasty, Mitral regurgitation

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INTRODUCTION

Percutaneous transvenous mitral commissurotomy (PTMC) has proved to be an effective procedure for the treatment of symptomatic mitral stenosis, and the efficacy and safety of this treatment have been established[1-3]. Both immediate and long-term results are excellent in the majority of patients, but the development of mitral regurgitatiton (MR) is still a major problem associated with this procedure. The grade of MR after PTMC, even if severe MR is infrequent, is the most important predictor of event-free survival[4]. The purpose of this study was to examine clinical characteristics in patients who developed moderate or severe MR after Inoue balloon PTMC using the stepwise inflation technique.

METHODS

We studied 49 consecutive patients with mitral stenosis who underwent PTMC from April, 1991 through May, 1997 ; eight were men and 41 were women ; 16 showed sinus rhythm and 33 atrial fibrillation. All patients underwent two-dimensional and Doppler echocardiography, coronary arteriography, and left ventriculography prior to the PTMC procedure. The mitral valve echocardiographic score[5] was used to evaluate morphologic features, including leaflet mobility, valvular thickening, valve calcification, and subvalvular thickening. Each feature was graded on a score of 0+ to 4+, and the total score was obtained by summing the four scores. The severity of MR before PTMC was graded angiographically from 0 (no regurgitation) to 4+ according to the method of Sellers *et al*[6]. Exclusion criteria included MR $\geq 3+$ on left ventriculography, associated significant aortic valve regurgitation or stenosis, active endocarditis, or contraindications to transseptal puncture such as large left atrial thrombus. Patients with markedly severe valve deformity or calcification observed by echocardiography and X-ray fluoroscopy were also excluded. Informed consent was obtained from each patient before PTMC. The patients were divided into two groups after PTMC, as follows : patients with development of moderate or more severe ($\geq 2+$) MR after PTMC (Group A ; $n=8$) ; and patients without increase in MR or with development of mild (1+) MR (Group B ; $n=41$).

Selected abbreviations and acronyms

PTMC = percutaneous transvenous mitral commissurotomy

PTMC was performed with an Inoue balloon using an anterograde transseptal approach as previously described[7,8]. Baseline hemodynamic determinations were recorded, and cardiac output was determined by the thermodilution technique. The mitral valve area was calculated using Gorlin's formula[9]. The maximal nominal inflated balloon diameter was selected in relation to the patient's height. A 24 mm balloon was selected for patients $\leq$ 147 cm in height, a 26 mm balloon for those 148–160 cm, a 28 mm balloon for those 161–180 cm, and a 30 mm balloon for those > 180 cm. The balloon size was calibrated using test inflations prior to insertion into the patient. Increasing volumes of contrast medium were used to inflate the balloon in steps of 1 mm per each inflation. The initial inflation was performed at a diameter 4 mm less than the maximal nominal size. Subsequent inflations were performed at increments of 1 mm diameter with the predetermined volume of the contrast medium to achieve the desired balloon diameter. After each inflation, the balloon catheter was withdrawn into the left atrium, and the transmitral gradient, the left atrial pressure, and the pressure waveform were reassessed immediately. Auscultation and color Doppler examination or left ventriculography were performed as needed to evaluate whether there was any progression of MR. If no increase in MR, no reduction by half in the transmitral gradient, and no increase by 2 mmHg or more in the left atrial mean and v wave pressures were noted, the subsequent inflations was performed at an increment of 1 mm balloon diameter. Five consecutive cardiac cycles were analyzed for each hemodynamic determination. This stepwise process was repeated until the transvalvular gradient was reduced as much as possible without a significant increase in MR or until the balloon was inflated to 1 mm diameter greater than the nominal size (overinflation). After valvuloplasty, hemodynamics and cardiac output were reassessed. Left ventriculography

Table 1 Baseline characteristics

	Group A (n=8)	Group B (n=41)	p value
Age (yr)	60±8	52±10	<0.05
Female gender (%)	88	83	NS
NYHA functional class	2.3±0.4	2.5±0.5	NS
Echocardiographic score (total)	9.1±1.5	9.0±1.8	NS
Leaflet mobility	2.0±0.2	2.0±0.5	NS
Valvular thickening	2.4±0.5	2.4±0.5	NS
Valve calcification	2.4±0.5	2.3±0.5	NS
Subvalvular thickening	2.4±0.7	2.3±0.6	NS
Cardiac output (l/min)	3.4±0.9	4.0±0.9	NS
Mitral valve area (cm^2)	0.87±0.35	1.11±0.29	<0.05
LA mean pressure (mmHg)	18±5	17±7	NS
LA v wave pressure (mmHg)	24±9	22±9	NS
Transmitral gradient (mmHg)	12±4	11±6	NS
Mitral regurgitation (grade)	0.9±0.6	0.6±0.7	NS
Grade 0 or 1+	7 (88%)	37 (90%)	NS
Grade 2+	1 (13%)	4 (10%)	NS

Group A: patients with development of moderate or more severe (≥ grade 2) mitral regurgitation (MR),
Group B: patients without increase in MR or with development of mild (grade 1) MR.
NYHA = New York Heart Association; LA = left atrial.

was performed to evaluate any change in MR in comparison with that before PTMC.

Statistical comparisons between the two groups of patients were conducted using an unpaired t-test. Categoric variables were compared using χ^2 analysis. All results are presented as mean±SD, and a p value<0.05 was considered significant.

RESULTS

The baseline clinical, hemodynamic and echocardiographic data for the two groups are listed in **Table 1**. Progression to moderate or severe MR was significantly associated only with advanced age and more severe stenosis. However, other characteristics before PTMC were similar in both groups.

Fig. 1 shows the changes observed in the degree of MR immediately after PTMC. Of eight patients in Group A, five showed moderate (2+) MR and three severe (3+) MR, but there was no patient with 4+ MR. In Group B, MR increased from grade 0 to 1+ in five patients, which was not considered a significant progression. In one patient with 2+MR before PTMC, MR decreased to 1+ after the procedure. There was no difference between Groups A and B in the total number of inflations or the final balloon inflation size (**Table 2**). Overinflation of the balloon was not associated with the development of moderate or severe MR. However, a sudden increase in MR occurred with an associated increase in left atrial mean pressure and/or v wave pressure with only an increment of 1 mm diameter balloon size in Group A.

Fig. 2 shows the changes in the mean transmitral gradient, left atrial mean pressure, and left atrial v wave pressure before inflation, immediately before final inflation, and after final inflation. After final inflation, transmitral gradient, left atrial mean pressure, and v wave pressure were significantly higher in Group A compared with Group B. Immediately before the final inflation, left atrial mean and v wave pressures were significantly higher in Group A compared with Group B (16±5 vs 12±4 mmHg for left atrial mean pressure, $p<0.05$; 24±8 vs 16±6 mmHg for left atrial v wave pressure, $p<0.01$). At this time before the final inflation, the

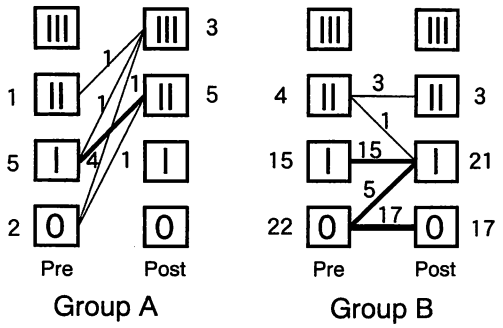

Fig. 1 Angiographic changes observed in the degree of mitral regurgitation before (Pre) and after (Post) PTMC in the two groups
Explanation of the groups as in Table 1.

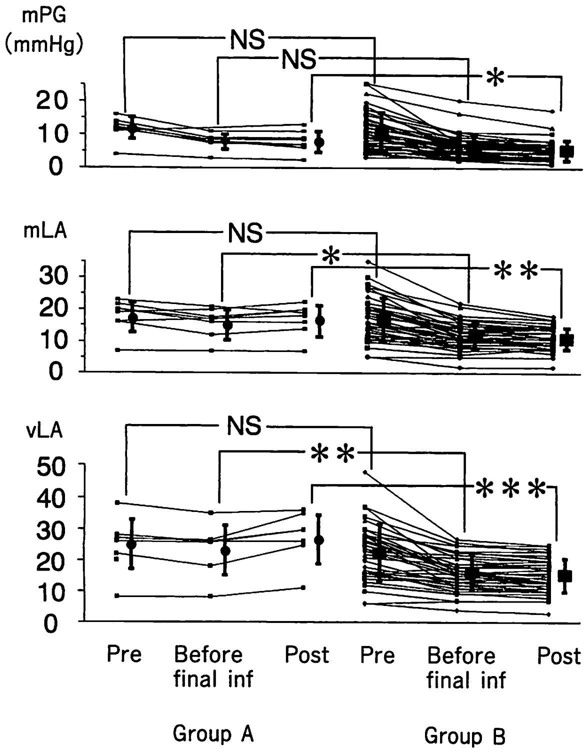

Fig. 2 Mean mitral pressure gradient (mPG), left atrial mean pressure (mLA), and left atrial *v* wave pressure (*v*LA) before PTMC (Pre), immediately before the final inflation (Inf), and after the final inflation (Post)
*$p<0.05$, **$p<0.01$, ***$p<0.001$.
Circles: Group A, squares: Group B.
Explanation of the groups as in Table 1.

decreases in left atrial mean and *v* wave pressures were significantly smaller in Group A compared with Group B (-2 ± 2 vs -5 ± 4 mmHg for the change of left atrial mean pressure, $p<0.05$; -2 ± 2 vs -6 ± 6 mmHg for the change of left atrial *v* wave pressure, $p<0.05$), but the decreases in the mean mitral pressure gradient did not differ between Groups A and B (-4 ± 1 vs -4 ± 4 mmHg).

Table 2 Balloon inflations

	Group A (n=8)	Group B (n=41)
Number of balloon inflations	4.5±2.0	4.9±1.3
Final balloon inflation size		
Underinflation	3 (38%)	15 (37%)
Nominal size	2 (25%)	10 (24%)
Overinflation	3 (38%)	16 (39%)

Explanation of the groups as in Table 1.

The change in the mitral valve area after PTMC is shown in **Fig. 3**. The area increased in both groups after PTMC. However, the area after PTMC in Group A was significantly smaller than that in Group B (1.27 ± 0.35 vs $1.77+0.40\ cm^2$, $p<0.01$), although the area before PTMC in Group A was also smaller than that in Group B. In Group A, in spite of the progression of significant MR, the mitral valve area measured by Gorlin's method was smaller compared with that in Group B.

DISCUSSION

The development of MR or the aggravation of pre-PTMC mild MR is frequently observed during PTMC, but the development of clinically relevant regurgitation is a rare complication[1,4,10,11]. Although patients with mild MR can safely undergo PTMC, severe (3+ and 4+) MR is generally considered to be a contraindication to this procedure. For patients with moderate (2+) MR before the procedure, PTMC may be indicated when the degree of mitral stenosis is severe and the clinical symptoms are mainly due to stenosis[2]. In this study, we performed PTMC in five patients who had 2+ MR before PTMC. However, it progressed to 3+ MR after PTMC in only one patient. In the other four patients with 2+ MR before PTMC, the procedure did not aggravate the grade of regurgitation.

Some investigators have identified anatomic and procedural factors as predictors of progression of MR after PTMC[1,12,13], but others could

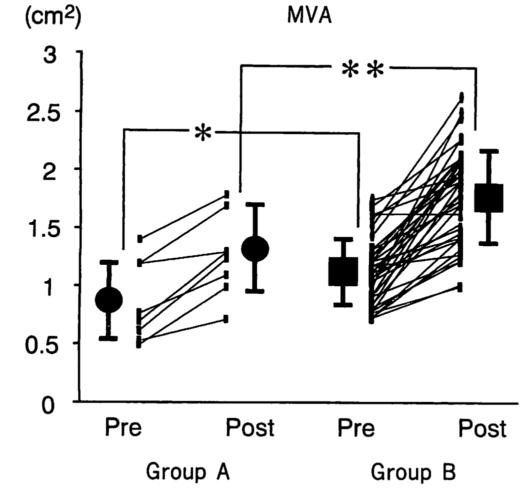

Fig. 3 Mitral valve area (MVA) before (Pre) and after (Post) PTMC in Group A (*circles*) and Group B (*squares*)
*$p<0.05$, **$p<0.01$.
Explanation of the groups as in Table 1.

not find any correlation between the production or aggravation of MR and mitral anatomy assessed by echocardiography[14–17]. In the present study, we attempted to carefully evaluate patients by echocardiography before PTMC, but the echocardiographic scores, considered either in total or separately for each component, were similar in both groups with and without progression to moderate or more severe (≥ 2+) MR. As mentioned in the methods, we did not perform PTMC for patients with severe valvular calcification visible on X-ray fluoroscopy as well as markedly severe valvular and subvalvular lesions as assessed by echocardiography. That may be the reason why the baseline echocardiographic scores were the same in both groups. Iung *et al.*[18] recently reported that a rough grading of mitral anatomy assessed by fluoroscopy as well as echocardiography was useful, and that the grade was one of the significant predictors of immediate results. However, they also mentioned the limitation of the evaluation of mitral anatomy only by echocardiography. Some properties of the mitral valve, which cannot be estimated by echocardiographic mitral valve morphology, may have significant effects on the progression of regurgitation.

Inoue balloon PTMC is performed by most operators using the stepwise inflation technique to avoid occurrence of massive MR. Two-dimensional echocardiography plus color flow imaging monitoring of the procedure are also recommended[2,3,10,16]. Therefore, stepwise inflation with the Inoue balloon was expected to reduce the aggravation of MR and, when possible, permit the inflation to be stopped before the MR becomes even worse. However, recent studies[3,17,18] reported that the Inoue balloon and double-balloon techniques yield similar results with respect to the progression of regurgitation as well as other clinical results. Feldman *et al.*[19] pointed out the limitation of this echocardiographic monitoring, in which the detection of a small increase of MR in color Doppler imaging may make the operator more hesitant to proceed with further inflation. They reported that a significant increase in MR (≥ 2+) was associated with fewer balloon inflations, underinflated balloon size and lower echocardiographic scores[16,19]. In our study, the progression of MR (≥ 2+) was not dependent on the number of inflations or balloon inflation size, whether of nominal size or undersize or oversize inflation. However, the progression of MR was observed more frequently in older patients and in patients with more severe stenosis. It is still controversial whether the immediate results may be influenced by age or the extent of valve deformity[16,18,20,21]. Sancho *et al.*[20] reported that none of the parameters reflecting valve anatomy could be predictors of progression of MR, but that age was one of the independent predictors. Iung *et al.*[18] also showed that the risk of inadequate immediate results increased, in particular in patients with lower initial mitral valve area and greater age. Our findings support these observations.

We have previously reported that, in patients without progression of MR after PTMC, the decreases in the left atrial mean and *v* wave pressures during undersize inflations were larger than those in patients with progression of MR[22]. With regard to the change of left atrial pressure, there seems to be a close relationship to the state of enlargement of the mitral valve. In patients who have suboptimal decline in the left atrial mean pressure and *v* wave pressure during stepwise inflations, there is a possibility that the increase in MR may occur to some extent after the first stepwise inflations of the balloon, although the evidence for such a speculation is lacking. Despite these considerations, it remains our opinion that, to detect the progression of MR, stepwise inflation using the Inoue balloon requires careful monitoring of the changes in the left atrial mean and v wave pressures, not in the mitral valve gradient, especially in the older patients with severe stenosis. Although the number of patients developing moderate or severe MR was small, patients who have suboptimal decrease in left atrial mean and v wave pressures after the first stepwise inflations of the balloon might be at risk of development of moderate or severe regurgitation after further dilations.

要　約

段階的拡張法による経皮的経静脈的僧帽弁交連裂開術における中等度以上の僧帽弁逆流の発生・悪化に関する検討

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経皮的経静脈的僧帽弁交連裂開術(PTMC)における合併症としての僧帽弁逆流(MR)は，その後の長期予後を規定する最も重要な因子である．本研究では段階的拡張法による PTMC に際し，中等度以上の逆流の発生・増悪に関して検討した．

段階的拡張法により PTMC を施行した連続 49 例(32–73 歳；男性 8 例，女性 41 例)を対象とした．段階的拡張は身長から選択したバルーンの最大規定径より 4 mm 減の径から 1 mm ごとに拡張した．僧帽弁圧較差が半減せず，かつ平均左房圧(mLA)あるいは左房 v 波(vLA)が 2 mmHg 以上明らかに増加しない場合は更に拡張を行い，最大規定径より 1 mm 大きい径を最終とした．心エコー図検査は術前後および術中僧帽弁逆流の増悪が疑われた際に施行した．PTMC 前後に左室造影を行い，逆流が発生・悪化し II 度以上になった A 群(8 例)とそのようにならなかった B 群(41 例)に分け，比較検討した．

A 群では B 群に比し高齢であり(60±8 vs 52±10 歳，$p<0.05$)，裂開前の弁口面積は小さかったが(0.87±0.35 vs 1.11±0.29 cm^2，$p<0.05$)，その他の血行動態の指標や心エコースコアでは術前に差はみられなかった．最終拡張直前の圧較差は A，B 両群で差はなかったが，mLA，vLA は A 群では B 群に比して有意に高かった．また，この最終拡張直前における mLA，vLA の減少程度は A 群では B 群に比して有意に小さかった(mLA：−2±2 vs −5±4 mmHg，$p<0.05$；vLA：−2±2 vs −6±6 mmHg，$p<0.05$)．最終拡張後の弁口面積は，A 群では B 群より小さく(1.27±0.35 vs 1.77±0.40 cm^2，$p<0.01$)，圧較差，mLA，vLA は A 群では B 群に比して有意に大きかった．拡張回数，最終拡張径と II 度以上の逆流の発生・悪化とは関連はなかった．

段階的拡張中に mLA，vLA に明らかな低下がみられない例では，拡張を続けた際に中等度以上の僧帽弁逆流の発生・悪化が起こりうるため，特に高齢者，術前の弁口面積が小さい重症例では左房圧の変化に注意を要すると考えられた．

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