CLINICAL STUDY

Long-Term Prognosis of Patients Who Underwent Percutaneous Transvenous Mitral Commissurotomy for Mitral Stenosis

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Summary

The long-term prognosis for up to 20 years of patients who have undergone percutaneous transvenous mitral commissurotomy (PTMC) for mitral stenosis (MS) is unknown.

We examined 77 of 93 patients (83%) with MS and who underwent PTMC from 1989 to 2002 at our institute, as well as the occurrence of either one of the following clinical endpoints until September 1, 2018: all-cause death or repeat intervention for the mitral valve.

The mean follow-up duration was 20.5 ± 7.3 years. The mean age was 51 ± 11 years. Overall, the 20-year survival rate was 71% ± 5%; without any intervention, the 20-year survival rate was 40% ± 6%. In patients who achieved good immediate results (i.e., mitral valve area (MVA) of ≥ 1.5 cm^2 without mitral regurgitation (MR) of > 2/4 after PTMC), the 20-year survival rate was 80% ± 6%; without any intervention, the 20-year survival rate was 54% ± 7%.

In our 20-year observational study, patients who have undergone PTMC for MS had favorable prognosis, especially in those who achieved good immediate results. In those who had poor immediate results, careful follow-up is needed because they might have more clinical event and any intervention for the mitral valve.

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Key words: Inoue balloon, Mitral valve area, Survival rate

Percutaneous transvenous mitral commissurotomy (PTMC) for mitral stenosis (MS) was first reported by Inoue[1)] in 1984 and has been demonstrated worldwide since then. In Japan, PTMC is now an established treatment for MS because of its good midterm prognosis.[2)] However, unlike the reports on surgical mitral commissurotomy (i.e., closed mitral commissurotomy and open mitral commissurotomy),[3-5)]even in Japan, those for PTMC have mostly been on midterm prognosis for around 10 years,[6,7)] and only few have reported on the long-term prognosis after PTMC. In this study, we examined the long-term prognosis of PTMC for up to 20 years.

Methods

Study population: We retrospectively examined 93 patients with MS who underwent PTMC at Niigata University Medical Hospital from 1989 to 2002. MS was diagnosed by echocardiography or cardiac catheterization. Mitral regurgitation (MR) was diagnosed by echocardiography or left ventriculography. Left atrial diameter and ejection fraction were measured by echocardiography before PTMC. The mitral valve area (MVA) was calculated using Gorlin's formula.[8)] PTMC was performed on patients with severe MS (MVA ≤ 1.5 cm^2) and favorable valve morphology in the absence of left atrial thrombus or moderate to severe MR. Mitral valve morphology was assessed by Wilkins score,[9)] which included valve calcification, leaflet mobility, leaflet thickening, and disease of the subvalvular apparatus. Each parameter had a scale of 1-4. Wilkins score was obtained by adding all parameter scores, of which score of less than 8 was eligible for PTMC.

The local ethics committee of Niigata University School of Medical and Dental Sciences approved this study.

PTMC technique: PTMC was performed with an Inoue balloon using an antegrade transseptal approach, as previously described.[10,11)] The maximal nominal inflated balloon diameter was selected according to the patient's height. Inflation was initially performed at a diameter of 4 mm less than the maximal nominal size and was increased stepwise by 1 mm each inflation. This stepwise process was repeated until the transvalvular pressure gradient was reduced as much as possible without a significant increase in MR by left ventriculography or until the balloon was inflated to a diameter of 1 mm greater than the nominal size (overinflation).

Follow-up and endpoints: The occurrence of any of the

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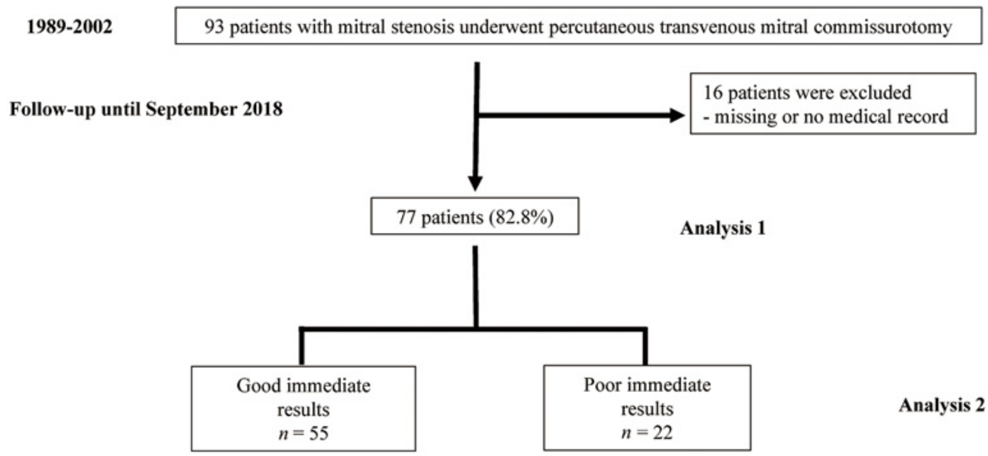

Figure 1. Study population. *Good immediate results are defined as mitral valve area of ≥ 1.5 cm^2 without mitral regurgitation of > /4 immediately after percutaneous transvenous mitral commissurotomy; results other than this are defined as poor immediate results.

Table I. Baseline Characteristics of the Entire Population

	All patients *n* = 77
Age, years	51 ± 11
Female sex, *n* (%)	61 (79)
Height (cm)	155 ± 8
Weight (kg)	52 ± 9
NYHA functional class, *n* (%)	
I	4 (5)
II	57 (74)
III	16 (21)
IV	0 (0)
Previous commissurotomy, *n* (%)	12 (16)
Atrial fibrillation, *n* (%)	57 (74)
Ejection fraction, %	59 ± 10
Left atrial diameter, mm	51 ± 10
Preoperative mitral valve area, cm^2	1.1 ± 0.3
Preoperative mean mitral gradient, mmHg	11 ± 5
Final mitral valve area, cm^2	1.8 ± 0.4
Final mean mitral gradient, mmHg	5 ± 2
Balloon size, *n* (%)	
22 mm	5 (6)
24 mm	24 (31)
26 mm	39 (51)
28 mm	9 (12)

Values are Mean ± SD. NYHA indicates New York Heart Association.

Table II. Outcomes of the Entire Population

	All patients (*n* = 77)
Death, *n* (%)	26 (34)
Cardiovascular	12 (16)
Intervention, *n* (%)	32 (42)
Repeat PTMC	2 (3)
MVR	30 (39)

PTMC indicates percutaneous transvenous mitral commissurotomy; and MVR, mitral valve replacement.

clinical endpoints until September 1, 2018, was examined by medical record review or interview (analysis 1). The clinical endpoints were defined as either all-cause death or repeat intervention with mitral valve replacement (MVR) or PTMC. Furthermore, we compared patients with good immediate results and those with poor immediate results (analysis 2). Good immediate results were defined as MVA of ≥ 1.5 cm^2 without MR of > 2/4[12,13] after PTMC; findings other than this were defined as poor immediate results.

Statistical analysis: Values were expressed as mean ± standard deviation. Continuous variables were compared using paired *t*-test. Categorical variables were compared using Chi-square test. The cumulative event-free survival curves were determined by an actuarial method using Kaplan-Meier estimates. The probability of event-free survival was compared among subgroups using the log-rank test. A P value of < 0.05 was considered significant. Analysis was performed using SPSS version 25 (SPSS, Inc., Chicago, IL, USA).

Results

Follow-up was completed for 77 patients (83%). We excluded 16 patients due to loss of contact or because there was no preserved medical record. The mean follow-up duration was 20.5 ± 7.3 years. Of the 77 patients, 55 had good immediate results and 22 had poor immediate results (Figure 1).

Entire population (analysis 1): The baseline characteristics of the entire population are detailed in Table I. The mean age at the time of intervention was 51 ± 11 years, and 79% were women; 12 patients underwent a previous mitral commissurotomy. The MVA increased from 1.1 ± 0.3 to 1.8 ± 0.4 cm^2 after PTMC. None of the patients had severe adverse events, including severe MR requiring emergency surgery in the acute phase. During the follow-up, 26 patients (34%) died, 12 of which were cardiovascular-related. Thirty-two patients (42%) under-

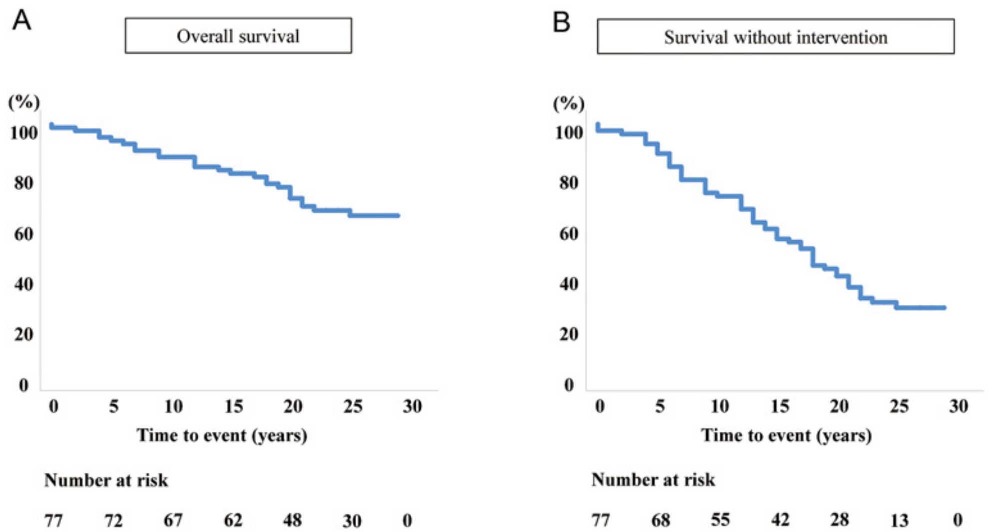

Figure 2. Kaplan-Meier curve of the overall population (analysis 1). **A:** The 10- and 20-year survival rates without all-cause death are 87% ± 4% and 71% ± 5%, respectively. **B:** The 20-year survival rate without intervention is 40% ± 6%.

Table III. Baseline Characteristics of Both Groups

	Good immediate results *n* = 55	Poor immediate results *n* = 22	Good versus poor
Age, years	50 ± 11	55 ± 9	$P = 0.049$
Female sex, *n* (%)	41 (75)	20 (91)	$P = 0.13$
Height, cm	156 ± 8	152 ± 7	$P = 0.053$
Weight, kg	53 ± 9	49 ± 8	$P = 0.069$
NYHA functional class, *n* (%)			$P < 0.001$
I	4 (7)	0 (0)	
II	46 (84)	11 (50)	
III	5 (9)	11 (50)	
IV	0 (0)	0 (0)	
Previous commissurotomy, *n* (%)	8 (15)	4 (18)	$P = 0.73$
Atrial fibrillation, *n* (%)	38 (69)	19 (86)	$P = 0.16$
Ejection fraction, %	60 ± 8	56 ± 12	$P = 0.18$
Left atrial diameter, mm	50 ± 10	53 ± 10	$P = 0.28$
Preoperative mitral valve area, cm^2	1.2 ± 0.3	0.9 ± 0.3	$P < 0.01$
Preoperative mean mitral gradient, mmHg	11 ± 5	10 ± 4	$P = 0.48$
Final mitral valve area, cm^2	2.0 ± 0.3	1.3 ± 0.2	$P < 0.01$
Final mean mitral gradient, mmHg	5 ± 2	6 ± 2	$P = 0.06$
Final mitral regurgitation, *n* (%)			$P < 0.01$
0	27 (49)	3 (14)	
1	19 (35)	12 (55)	
2	9 (16)	5 (23)	
3	0 (0)	2 (9)	
4	0 (0)	0 (0)	
Balloon size, *n* (%)			$P = 0.11$
22 mm	2 (4)	3 (14)	
24 mm	17 (31)	7 (32)	
26 mm	27 (49)	12 (55)	
28 mm	9 (16)	0 (0)	

Values are mean ± SD. NYHA indicates New York Heart Association.

went repeat intervention for the mitral valve; MVR was performed on 30 patients (39%) and repeat PTMC on 2 (3%) (Table II). The Kaplan-Meier curve of the entire population is shown in Figure 2. The 10-year survival rate was 87% ± 4%, and the 20-year survival rate was 71% ± 5%. Without any mitral intervention, the 20-year survival rate was 40% ± 6%.

Good immediate results versus poor immediate results

Table IV. Outcomes of Both Groups

	Good immediate results *n* = 55	Poor immediate results *n* = 22
Death, *n* (%)	14 (26)	12 (55)
Cardiovascular	7 (13)	5 (23)
Intervention, *n* (%)	20 (36)	12 (55)
Repeat PTMC	2 (4)	0 (0)
MVR	18 (33)	12 (55)

PTMC indicates percutaneous transvenous mitral commissurotomy; and MVR, mitral valve replacement.

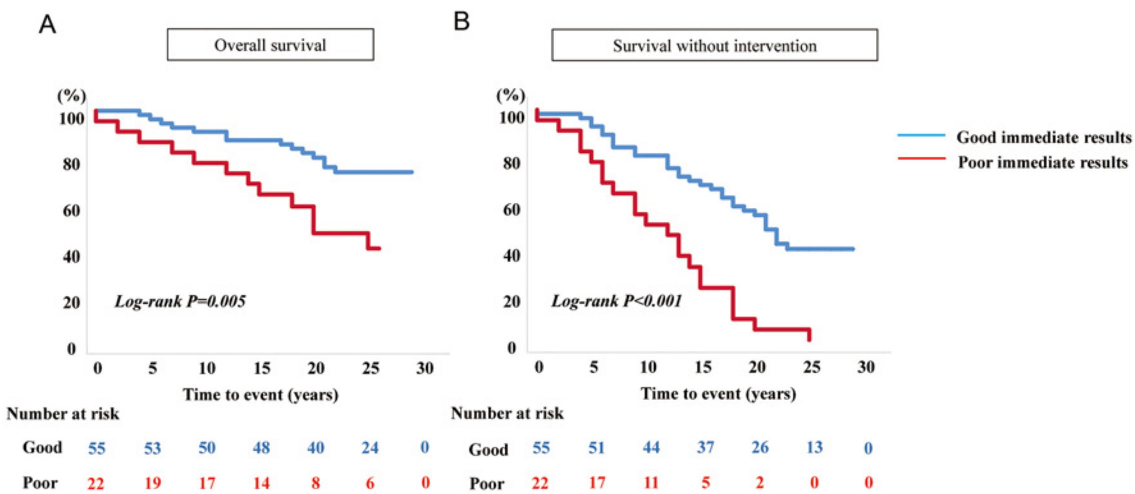

Figure 3. Kaplan-Meier curves of both groups (analysis 2). **A:** In the group with good immediate results, the 10- and 20-year survival rates without all-cause death are 91% ± 4% and 80% ± 6%, respectively. **B:** The 20-year survival rate without intervention is 54% ± 7% in the group with good immediate results and only 5% ± 4% in the group with poor immediate results.

(analysis 2): The baseline characteristics of patients according to the immediate results are described in Table III. Compared with patients with good immediate results, those with poor immediate results were significantly older, had higher New York Heart Association (NYHA) functional class, had smaller MVA both before and after PTMC, and had more severe MR after PTMC.

During the follow-up, 14 patients (26%) with good immediate results and 12 (55%) with poor immediate results died. Repeat mitral intervention was performed on 20 patients (36%) who had good immediate results and on 12 patients (55%) who had poor immediate results (Table IV). The Kaplan-Meier curves of both groups are shown in Figure 3. Overall survival was significantly better in patients who had good immediate results than in those who had poor immediate results (log-rank P = 0.005). Likewise, survival without any mitral intervention was significantly better in those with good immediate results than in those with poor immediate results (P < 0.001). In patients who had good immediate results, the 10-year survival rate was 91% ± 4% and the 20-year survival rate was 80% ± 6%; without any mitral intervention, the 20-year survival rate was 54% ± 7%. On the other hand, in those with poor immediate results, the 10-year survival rate was 77% ± 9% and the 20-year survival rate was 58% ± 11%; without any intervention, the 20-year survival rate was only 5% ± 4% (Table V).

Discussion

This study revealed that the prognosis of patients with MS who underwent PTMC at Niigata University Medical Hospital was favorable. At 20 years after PTMC, 71% ± 5% of all patients and 40% ± 6% of those who did not receive any intervention for the mitral valve survived. In particular, in those with good immediate results, 80% ± 6% of all patients and 54% ± 7% of those who did not receive any intervention for the mitral valve survived after 20 years of the PTMC. We believe that this is the first study to report about the long-term prognosis (up to 20 years) of PTMC in Japanese population.

Reports on the long-term (>10 years) prognosis after PTMC are few, even in Japan. Bouleti *et al*.[12)] reported that of the 1,024 patients (mean age, 49 years) followed up for a median of 10.7 years after PTMC, the 20-year survival rates were 73% ± 2% overall and 34% ± 2% for those who did not receive intervention. Among patients who obtained good immediate results (n = 912), the 20-year survival rates were 75% ± 2% overall and 38% ± 2% without intervention. On the other hand, for surgical commissurotomy,[3-5)] the 20-year survival rate was reported to be 60%-70%, and the 20-year rate for freedom from reoperation was 50%-80%. Considering these previously reported results of PTMC and surgical commissurotomy, the long-term prognosis of our patients was relatively satisfac-

Table V. Prognosis of All Patients, Those with Good Immediate Results and Those with Poor Immediate Results

	All patients $n = 77$	Good immediate results $n = 55$	Poor immediate results $n = 22$
20-year survival rates, %	71 ± 5	80 ± 6	58 ± 11
20-year survival rates without intervention, %	40 ± 6	54 ± 7	5 ± 4

tory.

The reported predictors of poor long-term outcome after PTMC were Wilkins score of >8, increasing age, prior surgical commissurotomy, higher NYHA functional class, higher final mean gradient, MR of > 2, and smaller final MVA.[12-15] These data suggested that the achievement of good immediate results may be difficult in patients with poor mitral valve characteristics secondary to old age or prior surgical commissurotomy.

In this study, the long-term prognosis depended on the achievement of good immediate results in the acute phase of PTMC. Mitral restenosis is a major cause of repeat intervention. It has been reported that the MVA decrease by 0.2 cm^2 and that restenosis occur every 5 years.[13,15,16] Therefore, if patients could not obtain an MVA of ≥ 1.5 cm^2 in the acute phase, restenosis can occur earlier, requiring early repeat intervention. Similar to previous reports, our study suggested that the achievement of good immediate results may be difficult in patients who are relatively old and have high NYHA functional class and small MVA before and after PTMC and severe MR after PTMC. In this study, half of the patients who had good immediate results survived for 20 years without any mitral intervention.

Study limitations: This study was a single-center study on a small number of patients. Most of the patients were followed up outside our hospital; therefore, we could not ascertain the occurrence of heart failure or embolism after PTMC, as well as examine valve function.

Conclusions

In our 20-year observational study, patients who have undergone PTMC for MS had favorable prognosis, especially in those with good immediate results. In those with poor immediate results, careful follow-up is need because they might have more clinical event and any intervention for the mitral valve.

Acknowledgments

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Disclosure

Conflicts of interest: All authors have no conflicts of interest to declare.

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