JACC Vol. 32, No. 4
October 1998:1009–16



# Retrograde Nontransseptal Balloon Mitral Valvuloplasty: Immediate Results and Intermediate Long-Term Outcome in 441 Cases—A Multicenter Experience

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***Objectives.*** **Our aim was to present the immediate and intermediate long-term results of the application of retrograde nontransseptal balloon mitral valvuloplasty (RNBMV) in four cooperating centers from Greece and India.**

***Background.*** **RNBMV is a purely transarterial method of balloon valvuloplasty, developed with the aim to avoid complications associated with transseptal catheterization. Only single-center experience with RNBMV has been previously reported.**

***Methods.*** **The procedure was attempted in 441 patients with symptomatic mitral stenosis (320 women, 121 men, mean age [± SD] 44 ± 11 years, mean echocardiographic score [± SD] 7.7 ± 2.0) from 1988 to 1996. Three hundred eighty-five patients with successful immediate outcome were followed clinically for a mean [± SD] of 3.5 ± 1.9 (range, 0.5–9.1) years.**

***Results.*** **A technically successful procedure was achieved in 388 (88%) cases. The echocardiographic score ($p < 0.001$), male gender ($p = 0.005$), preprocedural mitral regurgitation ($p = 0.007$) and previous surgical commissurotomy ($p = 0.029$) were unfavorable predictors of immediate outcome. Complications included death (0.2%), severe mitral regurgitation (3.4%) and injury of the femoral artery (1.1%). Event-free (freedom from cardiac death, mitral valve surgery, repeat valvuloplasty and NYHA class > II symptoms) survival rates (± SEM) were 100%, 96.9 ± 0.9%, 89.8 ± 1.9% and 75.5 ± 5.5% at 1, 2, 4 and 9 years, respectively. The echocardiographic score ($p < 0.001$), NYHA class ($p = 0.008$) and postprocedural mitral valve area ($p = 0.009$) were significant independent predictors of intermediate long-term outcome.**

***Conclusions.*** **Multicenter experience indicates that RNBMV is a safe and effective technique for the treatment of symptomatic mitral stenosis. As with the transseptal approach, patients with favorable mitral valve anatomy derive the greatest immediate and intermediate long-term benefit from this procedure.**

**(J Am Coll Cardiol 1998;32:1009–16)**



More than a decade after its introduction by Inoue et al. (1), percutaneous balloon mitral valvuloplasty has been established as an effective alternative to surgery for the treatment of mitral stenosis. In its most widely employed variations, the technique of valvuloplasty involves puncture of the interatrial septum (1–5) and is associated with a small risk of serious complications including cardiac perforation, cardiac tamponade or the creation of a significant left-to-right interatrial shunt (6,7). In an effort to obviate the need for transseptal catheterization, an alternative purely transarterial technique [retrograde nontransseptal balloon mitral valvuloplasty (RNBMV)] was developed at the University of Athens, Athens, Greece. This approach is based on the use of a specially designed, externally steerable left atrial (LA) guiding catheter (Cordis, Europa N.V.-Cat # 5RE-692) by means of which entry into the LA is achieved retrogradely via the left ventricle (LV) (8,9).

Published data have so far reported only single-center experience with RNBMV (10–13). In the present study, the results of its application in four cooperating centers from two countries are presented for the first time with emphasis placed on the assessment of immediate results, development of complications and intermediate long-term outcome of this technique.

## Methods

**Study population.** From April 1988 until September 1996, RNBMV was attempted by independent operators in 441 consecutive cases at the Athens University (n = 293), Onassis Cardiac Surgery Center (n = 31) and Tzannio Hospital (n = 16) in Greece and at the All India Institute of Medical Sciences

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Manuscript received December 8, 1997; revised manuscript received April 13, 1998, accepted June 1, 1998.

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0735-1097/98/$19.00
PII S0735-1097(98)00357-X

**Abbreviations and Acronyms**

FA = femoral artery
FU = follow-up
LA = left atrial, left atrium
LV = left ventricle, left ventricular
MR = mitral regurgitation
MVA = mitral valve area
MVR = mitral valve replacement
NYHA = New York Heart Association
RNBMV = retrograde nontransseptal balloon mitral valvuloplasty

(n = 101) in New Delhi, India. Baseline characteristics of the total patient population, as well as of the subgroups of Greek and Indian patients, are summarized in Table 1. All patients were symptomatic. Patients in atrial fibrillation were anticoagulated for at least 2 months prior to valvuloplasty. Patients with more than moderate mitral regurgitation (MR) or echocardiographic evidence of LA thrombus were not considered eligible for RNBMV. Echocardiographic score $> 8$ (14) was present in 131 patients (29.7%); subvalvular thickening grade $\geq 3$ was present in 83 (18.8%) patients. Fluoroscopic valve calcification was present in 114 patients (25.9%).

**Preprocedural evaluation.** Within 48 h prior to valvuloplasty, all patients underwent a diagnostic workup including evaluation of clinical status and echocardiographic examination.

Assessment of functional capacity was based on the criteria of the New York Heart Association (NYHA). Echocardiographic examination included M-mode, two-dimensional and Doppler echocardiography. Transesophageal echocardiograms were also performed in all but the first 41 treated patients. In addition to the assessment of mitral anatomy, echocardiography focused on the detection of LA thrombi and on the quantification of concomitant MR and aortic or tricuspid valve disease.

**Cardiac catheterization and valvuloplasty.** The study protocol was approved by the committees on human research of the participating institutions. Written informed consent was obtained by all patients after detailed description of the procedure.

Diagnostic cardiac catheterization and RNBMV were performed as previously described (9–13) (Fig. 1). In India, a sheathless technique was employed in the majority of cases; for the insertion of the balloon catheter in these procedures, the groin incision was dilated with a 10 F dilator. At the Greek centers, insertion of the balloon catheter was performed through either an adjustable introducer (Medina-Schneider, Europe, used during our early experience) or a 12 F sheath (William Cook Europe, Bjaeverskov, Denmark, employed in the last 250 Greek patients in this series).

In a total of 438 completed procedures, the single-balloon technique was used in 240 cases [conventional single balloon in 220; Inoue balloon catheter modified by elongation of the catheter shaft in 20 cases (12)], the twin-balloon (bifoil) technique in 194 cases and the double-balloon bifemoral

**Table 1.** Baseline Characteristics of the Study Population

| Characteristic | Total (n = 441) | Greek pts (n = 340) | Indian pts (n = 101) | p Value |
|---|---|---|---|---|
| Age, years | 44 ± 11 | 49 ± 11 | 28 ± 8 | < 0.001 |
| Males/females | 121/320 | 63/277 | 58/43 | < 0.001 |
| Body surface area, $m^2$ | 1.62 ± 0.18 | 1.68 ± 0.16 | 1.48 ± 0.7 | < 0.001 |
| NYHA class | | | | 0.014 |
| II | 72 (16.3%) | 65 (19.1%) | 7 (6.9%) | 0.004 |
| III | 324 (73.5%) | 241 (70.9%) | 83 (82.2%) | 0.024 |
| IV | 45 (10.2%) | 34 (10%) | 11 (10.9%) | NS |
| Atrial fibrillation | 202 (45.8%) | 186 (54.7%) | 16 (15.8%) | < 0.001 |
| Previous commissurotomy | 20 (4.5%) | 18 (5.3%) | 2 (1.9%) | NS |
| Associated cardiac disease | | | | 0.020 |
| Mild or moderate aortic valve disease | 98 (22.2%) | 86 (25.3%) | 12 (11.9%) | 0.004 |
| Substantial aortic stenosis | 1 (0.2%) | — | 1 (1%) | NS |
| Conduction defect | 4 (0.9%) | 4 (1.2%) | — | NS |
| Substantial CAD | 3 (0.7%) | 3 (0.9%) | — | NS |
| LV ejection fraction (%) | 61 ± 13 | 60 ± 13 | 64 ± 10 | 0.006 |
| Echocardiographic score | | | | |
| Leaflet mobility | 2.1 ± 0.6 | 2.2 ± 0.6 | 1.9 ± 0.5 | < 0.001 |
| Leaflet thickening | 2.3 ± 0.6 | 2.3 ± 0.6 | 2.3 ± 0.5 | NS |
| Leaflet calcification | 1.3 ± 0.9 | 1.4 ± 0.9 | 1.0 ± 0.2 | < 0.001 |
| Subvalvular thickening | 2.0 ± 0.8 | 2.0 ± 0.7 | 2.1 ± 0.6 | NS |
| Total score | 7.7 ± 2.0 | 7.8 ± 2.0 | 7.4 ± 1.6 | NS |
| Mitral regurgitation | | | | 0.001 |
| Mild | 74 (16.8%) | 69 (20.3%) | 5 (4.9%) | 0.001 |
| Moderate | 2 (0.5%) | 2 (0.6%) | — | NS |

Plus-minus values are mean ± SD. CAD = coronary artery disease. Pts, patients.

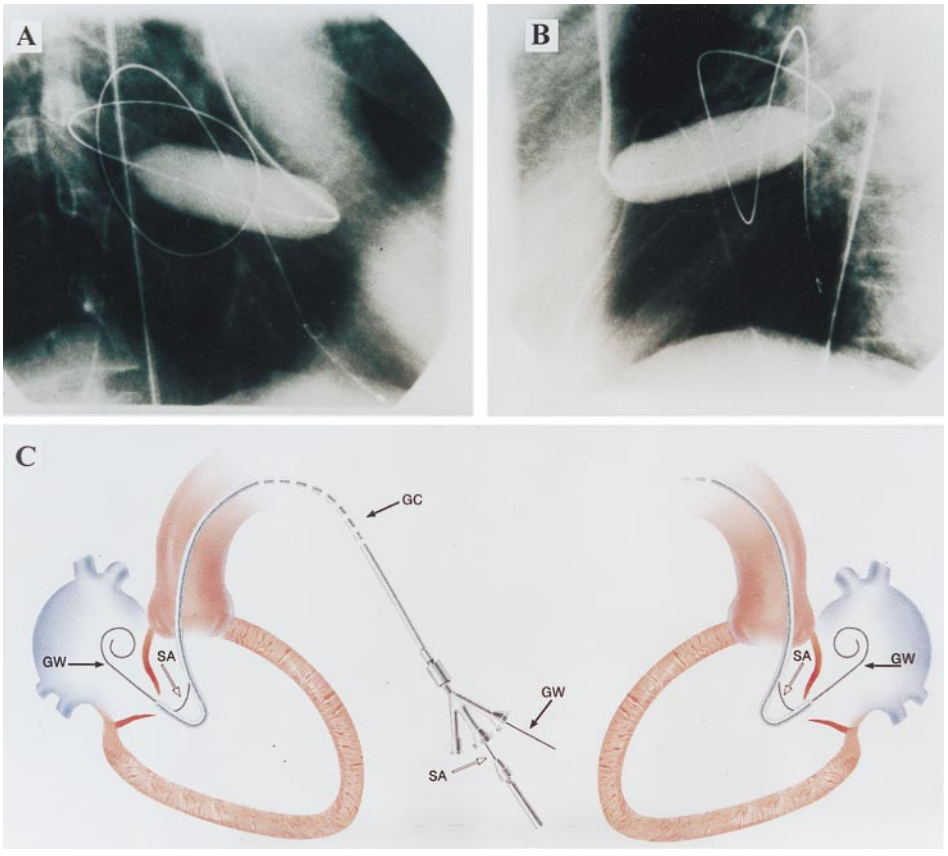



**Figure 1.** Ventriculographic frames of a single valvuloplasty balloon dilated across the stenotic mitral valve in the right anterior oblique (**A**) and left anterior oblique (**B**) projections. (**C**): schematic representation of the steerable left atrial guiding catheter (GC) in the right anterior oblique **(left)** and left lateral projection **(right)**. By external manipulations of the steering arm (SA), the catheter's distal tip is curved so as to point directly at the mitral orifice. The guidewire (GW) is stabilized within the left atrium by the formation of spirals.

technique in four cases. The right brachial artery approach was employed once.

During all procedures, preventive measures taken against subvalvular damage included the following 1) Curving of the LA catheter's distal tip was always performed in the apical region of the LV, and only then was the catheter rotated counterclockwise and retracted to reach a point immediately below the mitral valve. 2) Correct positioning of the catheter was subsequently confirmed either by the recording of LA pressures through the catheter or by the unobstructed forward advancement of a J wire through its lumen into the LA cavity. 3) An additional safety check was performed after the introduction of the stiff guidewire into the LA, by the insertion of a flow-directed catheter into the LV over it. The balloon was inflated in the LV outflow tract with a dilute dye solution or carbon dioxide and was advanced toward the mitral valve; its unobstructed movement was considered as proof of the fact that the guidewire had passed correctly through the LV inflow tract and had not become involved with the chordae tendineae (10–12).

When involvement of the LA catheter with the subvalvular apparatus was suspected, the catheter was either advanced toward the LV apex and positioning manipulations were repeated, or it was retracted into the ascending aorta after complete release of its curved tip and was reintroduced into the LV with the help of a guidewire (10–12). Performance of these actions was necessitated very rarely and was successful at all times.

**Clinical follow-up.** Clinical follow-up (FU) data were obtained at 3, 6, and 12 months after RNBMV and at 1-year intervals thereafter by direct interview with the patients. Endpoints of FU were cardiac death, mitral valve replacement (MVR), repeat balloon mitral valvuloplasty and the development of NYHA class III or IV symptoms. Causes of death were ascertained from patients' medical records and their attending physicians.

**Statistical analysis.** All continuous variables are presented as mean ± SD. Baseline and their corresponding postprocedural data were compared with use of the paired *t* test. For comparisons of means of continuous data from two independent groups, the two-sample *t* test for independent samples with equal or unequal variances was used where appropriate. To compare data from different institutions, one-way analysis of variance (ANOVA) was employed. In addition, where appropriate, continuous variables were categorized by use of clinically reasonable cutoff points to define subgroups for the purposes of analysis. Discrete data were compared by chi-square analysis. To identify predictive factors for a technically successful procedure as well as for the development of significant MR, multiple stepwise logistic regression analysis was employed on significant explanatory variables from the univariate analysis of demographic, hemodynamic, echocardiographic and procedural variables. To identify independent predictors of event-free survival, multiple stepwise Cox regression analysis was performed on significant explanatory variables from the univariate Cox proportional hazards regression

**Table 2.** Immediate Hemodynamic Results in 438 Completed Procedures

| Variable | Before RNBMV | After RNBMV | p Value |
|---|---|---|---|
| Heart rate, bpm | 82 ± 12 | 81 ± 12 | NS |
| Mean left atrial pressure, mm Hg | 26 ± 8 | 13 ± 6 | < 0.001 |
| Mean transmitral gradient, mm Hg | 18 ± 7 | 6 ± 3 | < 0.001 |
| Mitral valve area, $cm^2$ | 1.0 ± 0.3 | 2.1 ± 0.5* | < 0.001 |
| Cardiac output, liter/minute | 4.0 ± 0.8 | 4.5 ± 0.8 | < 0.001 |
| Mean pulmonary artery pressure, mm Hg | 37 ± 10 | 27 ± 7 | < 0.001 |
| Pulmonary resistance, $dynes \cdot s \cdot cm^{-5}$ | 241 ± 132 | 250 ± 126 | NS |

*Estimated in 423 procedures without severe mitral regurgitation. RNBMV = retrograde nontransseptal balloon mitral valvuloplasty; bpm = beats per minute.

on demographic, hemodynamic, echocardiographic and procedural variables. Analysis was performed in two steps, the first including only baseline variables and the second including procedural and postprocedural variables as well. All final models were tested for two- and three-way interactions. Kaplan-Meier estimates were used to determine event-free survival rates for the entire FU population as well as for patient subgroups defined on the basis of the independent predictors of long-term event-free survival. Event-free survival rates were expressed as estimated rate ± SEM. All analyses were performed by use of the SPSS version 7.5 statistical package. A value of $p < 0.05$ was accepted as statistically significant.

## Results

**Immediate results of RNBMV.** Baseline hemodynamic measurements and immediate results of RNBMV are shown in Table 2. The procedure was completed in 438 cases. One case of procedure abortion occurred early in the experience of the center of origin in a patient with enlarged aorta and LV due to aortic regurgitation in whom, although the guidewire was in place, the length of the catheter proved insufficient for the balloon to be positioned across the mitral valve. In the remaining two cases of abortion, the procedure was completed by the transseptal Inoue technique—with which operators were more familiar at the time—in an effort to conserve time as the patients developed pulmonary edema while LA entry was being attempted.

Successful introduction of the guidewire into the LA was achieved within 1–10 min in 440 procedures. The mean duration of the procedure from the introduction of the LA catheter into the LV until the removal of the balloon-guidewire assembly was 24.6 ± 8 min (12–60 min); mean fluoroscopy time was 14.8 ± 6 min (6–25 min).

A technically successful procedure, defined as an increase in MVA ≥ 50% with postprocedural MVA ≥ 1.5 $cm^2$ and final MR ≤ grade 2+, was achieved in 388 cases (88%). Among the 53 technical failures, 15 (3.4%) developed significant (> grade 2+) MR, 35 (7.9%) had a suboptimal result (increase in MVA < 50% and/or final MVA < 1.5 $cm^2$) while in three cases retrograde balloon mitral dilatation was not attempted, as mentioned above.

**Table 3.** Independent Predictors of Immediate Procedural Outcome

| Variable | b ± SE | Relative Risk | p Value |
|---|---|---|---|
| Echocardiographic score | 0.98 ± 0.15 | 2.65 | < 0.001 |
| Male gender | 1.42 ± 0.50 | 4.13 | 0.005 |
| Baseline mitral regurgitation | 1.19 ± 0.44 | 3.29 | 0.007 |
| Previous commissurotomy | 1.98 ± 0.91 | 7.29 | 0.029 |
| Balloon type | 1.15 ± 0.43 | 3.17 | 0.008 |
| Constant | −10.93 ± 1.42 | | < 0.001 |

b ± SE = regression coefficient ± standard error.

Stepwise multiple logistic regression analysis identified the echocardiographic score, male gender, preprocedural MR and previous commissuroromy as significant unfavorable predictors of immediate outcome (Table 3). Compared with patients with higher echocardiographic scores, those with scores ≤ 8 had a greater postprocedural MVA (2.23 ± 0.49 vs. 1.8 ± 0.42 $cm^2$, $p < 0.001$), a lower rate of significant postprocedural MR (1.3% vs. 8.5%, $p < 0.001$) and a higher rate of procedure success (97% vs. 66.4%, $p < 0.001$).

The use of the Inoue balloon catheter was associated with a higher success rate than the use of the other balloon types; conversely, use of the single-balloon was associated with the lowest success rate.

**Complications.** Cardiac perforation, cardiac tamponade or embolic events were not encountered. There was one procedure-related death (0.2%) in a patient who developed severe MR after valve dilatation and died after urgent MVR.

*Mitral regurgitation.* The degree of MR increased by one grade in 78 patients (18%), by two grades in 15 patients (3.4%), by three grades in 5 patients (1.1%) and by four grades in 2 patients (0.5%). Overall, 15 patients (3.4%) had MR > grade 2+ at the end of the procedure. Emergency MVR was necessitated in 2 of these patients (0.5%), 1 of whom died soon after its completion, as mentioned above. Ten of the remaining 13 patients were eventually treated surgically within a period of 6.6 ± 8 months (range, 1–27 months). Finally, 3 patients were maintained stable under medical therapy for at least 6 months after valvuloplasty, but data regarding their course thereafter are not available.

Transesophageal echocardiography and examination of the mitral valve after surgery revealed severe MR to be caused by noncommissural anterior mitral leaflet tears in all cases. Preprocedural MR ($p = 0.003$), the echocardiographic score ($p = 0.008$) and NYHA functional class ($p = 0.038$) were significant independent predictors of the development of severe MR after RNBMV.

*Bleeding and vascular complications.* Bleeding requiring transfusion occurred in 4 (0.9%) patients (one of whom had had sheathless RNBMV) while significant groin hematoma

was noted in 5 patients (3 who had undergone sheathless procedures and 2 Greek patients who were also part of the group with severe bleeding).

Significant weakening of the femoral pulse was noted in 5 (1.1%) patients (2 of them after sheathless valvuloplasty). All were treated effectively: one patient underwent femoral artery (FA) balloon angioplasty, 3 were treated by thrombolysis and one presented no functional problems and required no special treatment.

*Arrhythmias and intraventricular conduction disturbances.* Ventricular extrasystoles or salvos of nonsustained ventricular tachycardia were recorded in most patients during the procedure. Transient disturbances of atrioventricular conduction were noted in 6 patients (1.4%), lasting 30 min in one case and 3 h in another, without need for special treatment. Disturbances of intraventricular conduction persisting for more than 24 h were observed in 10 patients (2.3%). Conduction was restored on the second day in 7 patients and during the first week in 2 patients while the defect persisted for 3 months in one case.

**Hospital stay.** Mean hospital stay in the present series was 1.58 ± 0.57 days (range, 1–4 days). Discharge was originally permitted 48 h post-RNBMV, but in the last 100 Greek patients and all Indian patients, hospital stay was reduced to 24 hs. Cases in which hospitalization was prolonged included all 5 patients with weakening of the femoral pulse, 4 patients with severe postprocedural MR and 4 patients with bleeding complications.

**Follow-up.** Of the 388 patients who had a successful RNBMV, 3 patients did not return for reevaluation; the remaining 385 patients were followed for 3.5 ± 1.9 years (range, 0.5–9.1 years). FU duration was 3.8 ± 1.9 years and 2.6 ± 1.2 years for Greek and Indian patients, respectively. Seventeen patients were lost during FU and were censored at the time of their last evaluation, while 1 patient died of pancreatic cancer 34 months after the procedure and was censored at the time of her death.

There was one cardiac death which occurred 26 months after the procedure. Recurrence of NYHA class > II symptoms occurred in 35 patients, at a mean of 3.0 ± 1.6 years after RNBMV (range, 1.0–7.0 years); 19 patients were treated by MVR, 2 patients underwent successful repeat RNBMV, while 14 patients were maintained under medical treatment.

The estimated event-free survival rates (freedom from cardiac death, MVR, repeat valvuloplasty and NYHA class > II) at 1, 2, 4 and 9 years were 100%, 96.9 ± 0.9%, 89.8 ± 1.9% and 75.5 ± 5.5%, respectively (Fig. 2). Rates during 4 years post-RNBMV were similar for Greek and Indian patients (1 year: 100% vs. 100%; 2 year: 96.9 ± 1.1% vs. 96.8 ± 2.2%; 4 year: 89.4 ± 2.1% vs. 91.9 ± 3.9%, respectively, $p = 0.673$). Multiple stepwise Cox regression analysis on baseline variables identified the echocardiographic score ($p < 0.001$), NYHA functional class ($p < 0.001$), and preprocedural transmitral pressure gradient ($p = 0.008$) as significant independent predictors of long-term event-free survival after RNBMV. When procedural and postprocedural variables were included in the analysis, postprocedural MVA emerged as a significant predictor of long-term event-free survival ($p = 0.009$), while preprocedural pressure gradient was displaced from the model (Table 4). Testing of the final Cox model for two- and three-way interactions revealed postprocedural MVA ($p = 0.009$) and the interaction between NYHA functional class and echocardiographic score ($p < 0.001$) as the only independent predictors of long-term event-free survival. Further analysis in this respect was of limited value in our population because of the small size of several resulting subpopulations, in which the occurrence or absence of events had disproportionate effects on survival rates.

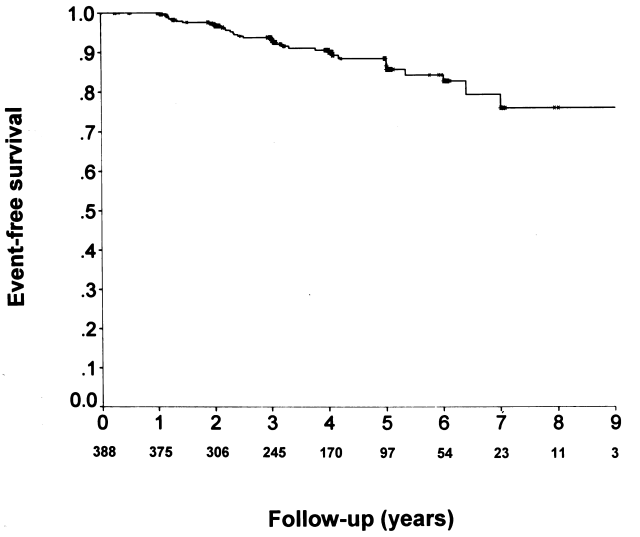



**Figure 2.** Kaplan-Meier event-free survival curve for the entire follow-up population. The number of patients available for observation at the end of each year of follow-up is depicted under the horizontal axis.

The FU patient group was divided into subgroups on the basis of the three independent significant predictors of long-term outcome identified by the expanded model of Cox analysis, and 9-year event-free survival rates for each subgroup were estimated and compared. Rates were significantly higher in patients with echocardiographic scores ≤ 8 versus > 8 (88.1 ± 4.8 vs 35.9 ± 15.8%, $p < 0.001$, Fig. 3), in patients with a postprocedural MVA ≥ 2 $cm^2$ versus < 2 $cm^2$ (88.1 ± 3.6 vs. 57.5 ± 10.7, $p < 0.001$, Fig. 4) and in patients in lower versus higher NYHA functional class (NYHA class II: 97.8 ± 2.2%, NYHA class III: 76.1 ± 5.7% and NYHA class IV: 31.9 ± 23.1%, $p < 0.001$, Fig. 5).

**Table 4.** Independent Predictors of Long-Term Event-Free Survival

| Variable | b ± SE | Relative Risk | p Value |
|---|---|---|---|
| Echocardiographic score | 0.43 ± 0.08 | 1.54 | < 0.001 |
| NYHA functional class | 0.92 ± 0.34 | 2.49 | 0.008 |
| Postprocedural mitral valve area | 1.84 ± 0.71 | 6.31 | 0.009 |

b ± SE = regression coefficient ± standard error.

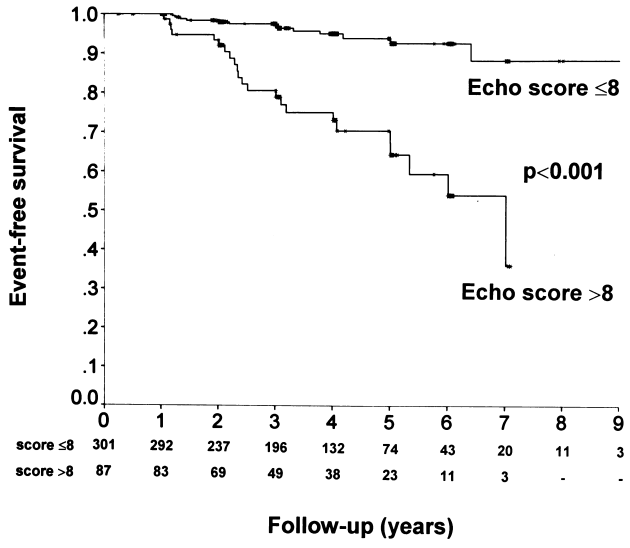



**Figure 3.** Kaplan-Meier event-free survival curves for patients with echocardiographic score ≤ 8 versus > 8. Format as in Figure 2.

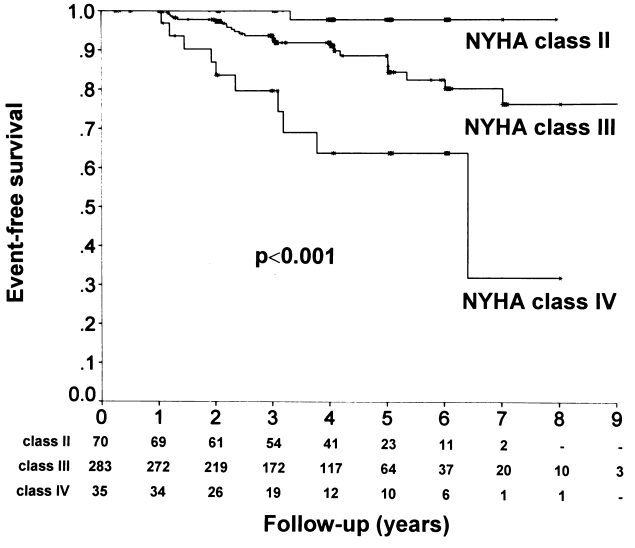
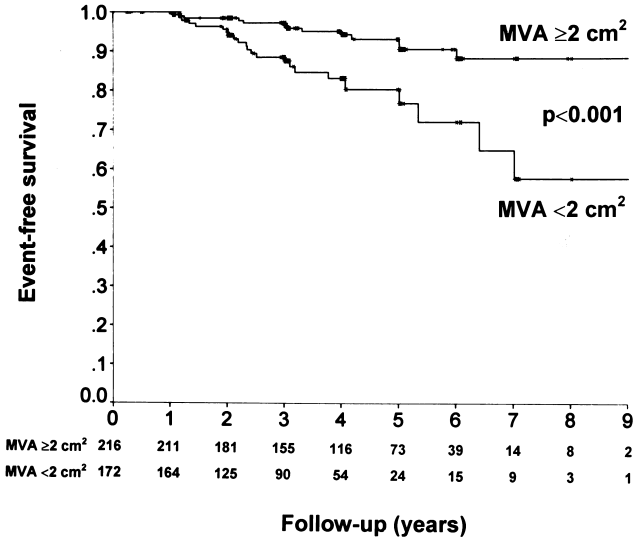



**Figure 5.** Kaplan-Meier event-free survival curves according to baseline symptom severity. Format as in Figure 2. NYHA = New York Heart Association.

**Effect of operator experience on immediate results, complications and intermediate long-term outcome.** The mean postprocedural MVA, rate of successful immediate result, rate of suboptimal result, incidence of significant final MR, mean procedure duration, mean fluoroscopy time and 4-year event-free survival rates were compared between the cooperating centers and (with the exception of the last variable) between the first 100 and the subsequent 192 procedures performed at the center of origin. Procedure duration and fluoroscopy time were significantly shorter in high case-volume compared with low case-volume centers, as well as in the last 192 compared with the first 100 procedures performed at the center of origin ($p < 0.001$ for all comparisons). No other significant differences were revealed.

**Figure 4.** Kaplan-Meier event-free survival curves for patients with postprocedural mitral valve area (MVA) ≥ 2cm$^2$ versus < 2cm$^2$. Format as in Figure 2.




## Discussion

The present study demonstrated that RNBMV, performed in centers with varying degrees of experience, produced a good immediate outcome with an acceptable complication rate in selected patients with symptomatic mitral stenosis. The benefit from this procedure was maintained during intermediate long-term FU in the majority of cases.

**Retrograde LA catheterization.** Multicenter application of RNBMV confirmed previous experience regarding the feasibility and safety of retrograde LA catheterization (8–13). LA access by means of the special guiding catheter was achieved invariably in this series, requiring a maximum of 10 min and contributing to the favorable profile of RNBMV with regard to total duration and duration of fluoroscopy. Steering of the LA catheter within the LV was uneventful, even in patients with marked mitral subvalvular deformity.

Avoidance of the technically demanding transseptal catheterization probably also accounts for the steep learning curve indicated by the comparison between early and late experience at the center of origin and between results at the different centers in the present study. A considerable impact of the learning effect on the success and safety of balloon mitral valvuloplasty has been demonstrated in reports with the transseptal technique (6,15–17).

Use of the route for LA access proposed by RNBMV may prove particularly beneficial for patients in whom transseptal catheterization is difficult to perform as are those with thickened interatrial septum (usually resulting from previous cardiac surgery), chest wall malformations or anomalies of the inferior vena cava. Furthermore, it offers an alternative for

"bailing-out" in case of a failed transseptal procedure. Conversely, it is not an option in patients with a prosthetic aortic valve.

**Immediate and intermediate long-term outcome of RNBMV—comparison with transseptal mitral valvuloplasty.** Conclusions regarding comparison of RNBMV with transseptal balloon mitral valvuloplasty based on the present report should be drawn with caution, taking into account potential differences between our patient population and those of reports employing the transseptal approach, particularly in North American centers, which have often included large numbers of nonideal candidates for balloon mitral valvuloplasty.

Keeping these considerations in mind, it could be stated that multicenter application of RNBMV produced comparable results to those yielded by the transseptal approach in single large-volume center and multicenter studies, with respect both to procedure success rates and magnitude of immediate hemodynamic alterations (6,15,17–23), as well as to the clinical course of patients during long-term FU (24–26).

The inverse relation between the extent of mitral valve deformity and the benefit derived by transseptal balloon mitral valvuloplasty has been well-established (14,18,23,27–29). Our data indicate that this is equally true in the case of RNBMV. The echocardiographic score was the most important independent predictor of immediate results in the present study, and patients with a score $\leq 8$ had significantly higher rates of procedure success, greater final MVA and a lower incidence of significant postprocedural MR, compared with patients with higher echocardiographic scores.

The intermediate long-term event-free survival after RNBMV was also predicted independently by mitral anatomy, with estimated 9-year rates being 88% for patients with echocardiographic scores $\leq 8$ versus 36% for those with scores $> 8$. Additional significant predictors of event-free survival included the NYHA functional class and postprocedural MVA, revealing intermediate long-term prognosis after RNBMV as a function of disease severity at the time of the intervention and immediate procedural results; such a concept has also been outlined by the results of operators performing the transseptal approach (24,26).

**Complications of RNBMV.** The safety profile of RNBMV was favorable in the present series. Cardiac perforation and cardiac tamponade were not encountered in any case, in contrast to rates ranging between 0.2% and 6.7% with the transseptal technique (6–7,15,17,19–21). While nontransseptal LA entry diminishes the risk of LA wall injury, the possibility of LV perforation might be expected to persist with RNBMV; we attribute the lack of its occurrence to two procedural elements: 1) the stabilization of the guidewire within the LA throughout the procedure, which decreases significantly the likelihood of displacement of the balloon from the mitral orifice during inflation, and 2) the position of the guidewire within the LV, which constrains the balloon catheter's tip during its insertion into this chamber and prevents it from approaching closely the LV apex.

Development of severe MR was the most significant complication in the present series, occurring in 3.4% of cases compared with rates between 1% and 17% reported during transseptal valvuloplasty (6,7,19–22,30–32). The etiologic diversity of severe MR development following the latter technique (30–32) was not encountered with RNBMV; absence of its induction by papillary muscle or chordal rupture attests to the safety of retrograde LA catheterization.

Concerns regarding retrograde mitral valvuloplasty have focused predominantly on the possibility of FA injury as a result of its cannulation by large introductory sheaths. The rate of this complication in our study (1.1%) was not insignificant, although it was lower than that previously encountered with balloon aortic valvuloplasty (27,33), probably as a result of the young age of our patients. FA damage occurred exclusively in either sheathless procedures or during the early experience in Greece, when comparably more traumatic sheaths were employed. In contrast, use of 12 F sheaths in the last 250 Greek patients did not lead to FA damage. Further reduction of the incidence of this complication may be anticipated by future use of sheaths of smaller caliber in appropriate cases (e.g., use of 10 F sheaths when use of a single 25-mm balloon is planned for mitral valve dilatation).

**Conclusions.** The first multicenter application of RNBMV yielded immediate and intermediate long-term results similar to those achieved with the transseptal technique. Transarterial LA access avoided serious complications associated with transseptal catheterization, whereas it occasionally led to FA injury. Overall consideration of RNBMV suggests that it represents a reliable alternative to the transseptal approach, and may thus help broaden the application of percutaneous balloon mitral valvuloplasty.

## References

1. Inoue K, Owaki T, Nakamura T, et al. Clinical application of transvenous mitral commissuroromy by a new balloon catheter. J Thorac Cardiovasc Surg 1984;87:394–402.
2. Lock JE, Khalilullah M, Shrivastava S, et al. Percutaneous catheter commissurotomy in rheumatic mitral stenosis. N Engl J Med 1985;313:1515–8.
3. Palacios IF, Block PC, Brandi S, et al. Percutaneous balloon valvotomy for patients with severe mitral stenosis. Circulation 1987;75:778–84.
4. Al Zaibag M, Kasab SA, Ribeiro PA, Fagih MR. Percutaneous double balloon mitral valvotomy for rheumatic mitral valve stenosis. Lancet 1986; 1:757–61.
5. Babic UU, Grujicic S, Popovic Z, et al. Percutaneous transarterial balloon dilatation of the mitral valve: five year experience. Br Heart J 1992;67:185–9.
6. The National Heart, Lung and Blood Institute Balloon Valvuloplasty Registry. Complications and mortality of percutaneous balloon mitral commissurotomy. Circulation 1992;85:2014–24.
7. Harrison JK, Wilson JS, Hearne SE, Bashore TM. Complications related to transvenous mitral commissurotomy. Cathet Cardiovasc Diagn 1994 (Suppl. 2):52–60.
8. Stefanadis C, Kourouklis C, Stratos C, et al. Retrograde left atrial catheterization with a new steerable cardiac catheter. Am Heart J 1990;119:375–80.
9. Stefanadis C, Kourouklis C, Stratos C, et al. Percutaneous balloon mitral valvuloplasty by retrograde left atrial catheterization. Am J Cardiol 1990;65: 650–4.
10. Stefanadis C, Stratos C, Pitsavos C, et al. Retrograde nontransseptal balloon mitral valvuloplasty: immediate results and long-term follow-up. Circulation 1992;85:1760–7.

11. Stefanadis C, Toutouzas P. Retrograde nontransseptal mitral valvuloplasty. In: Topol EJ, ed. Textbook of Interventional Cardiology. Philadelphia: WB Saunders Company, 1994:1253–67.
12. Stefanadis C, Stratos C, Kallikazaros I, et al. Retrograde nontransseptal balloon mitral valvuloplasty using a modified Inoue balloon catheter. Cathet Cardiovasc Diagn 1994;33:224–33.
13. Bahl VK, Juneja R, Thatai D, et al. Retrograde nontransseptal balloon mitral valvuloplasty for rheumatic mitral stenosis. Cathet Cardiovasc Diagn 1994;33:331–4.
14. Wilkins GT, Weyman AE, Abascal VM, et al. Percutaneous balloon dilatation of the mitral valve: an analysis of echocardiographic variables related to outcome and the mechanism of dilatation. Br Heart J 1988;60: 299–308.
15. Nobuyoshi M, Hamasaki N, Kimura T, et al. Indications, complications and short-term clinical outcome of percutaneous transvenous mitral commissurotomy. Circulation 1989;80:782–92.
16. Tuzcu EM, Block PC, Palacios IF. Comparison of early versus late experience with percutaneous mitral balloon valvuloplasty. J Am Coll Cardiol 1991;17:1121–4.
17. Vahanian A, Acar J. Mitral valvuloplasty: The French experience. In: Topol EJ, ed. Textbook of Interventional Cardiology. Philadelphia: WB Saunders Company, 1994:1206–25.
18. Palacios IF, Block PC, Wilkins GT, Weyman AE. Follow-up of patients undergoing percutaneous mitral balloon valvotomy. Analysis of factors determining restenosis. Circulation 1989;79:573–9.
19. Herrmann HC, Kleaveland JP, Hill JA, et al., for the M-Heart group. The M-Heart percutaneous balloon mitral valvuloplasty registry: initial results and early follow-up. J Am Coll Cardiol 1990;15:1221–6.
20. Herrmann HC, Ramaswamy K, Isner JM, et al. Factors influencing immediate results, complications and short-term follow-up status after Inoue balloon mitral valvotomy: a North American multicenter study. Am Heart J 1992;124:160–6.
21. Arora R, Kalra GS, Murty GSR, et al. Percutaneous transatrial mitral commissurotomy: Immediate and intermediate results. J Am Coll Cardiol 1994;23:1327–32.
22. Chen CR, Cheng TO. Percutaneous mitral valvuloplasty by the Inoue technique: a multicenter study of 4832 patients in China. Am Heart J 1995;129:1197–203.
23. Iung B, Cormier B, Ducimetiere P, et al. Immediate results of percutaneous mitral commissuroromy. A predictive model on a series of 1514 patients. Circulation 1996;94:2124–30.
24. Cohen DJ, Kuntz RE, Gordon SPF, et al. Predictors of long-term outcome after percutaneous balloon mitral valvuloplasty. N Engl J Med 1992;327: 1329–35.
25. Palacios IF, Tuzcu ME, Weyman AE, et al. Clinical follow-up of patients undergoing percutaneous mitral balloon valvotomy. Circulation 1995;91: 671–6.
26. Dean LS, Mickel M, Bonan R, et al. Four-year follow-up of patients undergoing percutaneous balloon mitral commissurotomy. A report from the National Heart, Lung and Blood Institute Balloon Valvuloplasty Registry. J Am Coll Cardiol 1996;28:1452–7.
27. Block PC, Palacios IF. Aortic and mitral balloon valvuloplasty: The United States experience. In: Topol EJ, ed. Textbook of Interventional Cardiology. Philadelphia: WB Saunders Company, 1994:1189–1205.
28. Reid CL, Chandraratna AN, Kawanishi DT, et al. Influence of mitral valve morphology on double-balloon catheter balloon valvuloplasty in patients with mitral stenosis. Analysis of factors predicting immediate and 3-month results. Circulation 1989;80:515–24.
29. Post JR, Feldman T, Isner J, Herrmann HC. Inoue balloon mitral valvotomy in patients with severe valvular and subvalvular deformity. J Am Coll Cardiol 1995;25:1129–36.
30. Essop MR, Wisenbaugh T, Skoularigis J, et al. Mitral regurgitation following mitral balloon valvotomy. Differing mechanisms for severe versus mild-to-moderate lesions. Circulation 1991;84:1669–79.
31. Herrmann HC, Lima JAC, Feldman T, et al., for the North American Inoue Balloon Investigators. Mechanisms and outcome of severe mitral regurgitation after Inoue balloon valvuloplasty. J Am Coll Cardiol 1993;22:783–9.
32. Padial LR, Freitas N, Sagie A, et al. Echocardiography can predict which patients will develop severe mitral regurgitation after percutaneous mitral valvulotomy. J Am Coll Cardiol 1996;27:1225–31.
33. McKay RG. Balloon valvuloplasty for treating pulmonic, mitral and aortic valve stenosis. Am J Cardiol 1988;61:102G–108G.