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Late clinical and echocardiographic follow up after percutaneous balloon dilatation of the mitral valve

Carlos E Ruiz, He Ping Zhang, Habib Gamra, John W Allen, Francis Y K Lau

Abstract

***Objective*—To assess the outcome after attempted percutaneous balloon dilatation of the mitral valve in patients with severe mitral stenosis between February 1986 and June 1992.**

***Design*—Clinical state, mitral valve area, and restenosis at follow up were analysed. Mitral valve area as determined by the Gorlin formula, planimetry, and Doppler methods was compared before and after dilatation and at follow up.**

***Setting*—University hospital.**

***Patients*—176 patients had serial clinical and Doppler echocardiographic follow up and 44 of them also underwent recatheterisation.**

***Result*—At follow up 93% of patients were in New York Heart Association functional class I or class II. Mitral valve area (planimetry) increased from 0·97(0·24) cm² before to 1·86(0·39) cm² after dilatation ($p = 0·0001$) and then decreased to 1·72(0·39) cm² at follow up ($p < 0·001$); mitral valve area (Doppler) increased from 1·01 (0·24) to 1·89 (0·42) cm² ($p = 0·0001$) and then decreased to 1·78(0·40) cm² ($p < 0·05$). The overall restenosis rate was 15% and over 90% of the patients were free from cardiovascular events. Age, valvar calcification, echocardiographic score, and mitral valve area after dilatation were found to be determinant predictors of restenosis. In patients who underwent recatheterisation, mitral valve area by the Gorlin method at follow up was comparable with that by planimetry and Doppler methods whereas a significant discrepancy between the three methods was noted immediately after dilatation.**

***Conclusion*—Balloon dilatation of the mitral valve provided sustained anatomical and functional improvement in over 80% of patients at late follow up. Older age, heavy calcification, high echocardiographic score, and suboptimal immediate results are significant predictors of restenosis. Doppler echocardiographic examination is the procedure of choice for follow up evaluation.**

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Department of Cardiology, Loma Linda University Medical Center, Loma Linda University, Loma Linda, California, USA
Carlos E Ruiz
He Ping Zhang
Habib Gamra
John W Allen
Francis Y K Lau

Correspondence to: Dr Carlos E Ruiz, Department of Cardiology, RMMC 2426, Loma Linda University Medical Center, Loma Linda University, 11234 Anderson Street, Post Office Box 2000, Loma Linda, California 92354-0200, USA.

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Since percutaneous balloon dilatation of the mitral valve was introduced by Inoue *et al* in 1984,[1] the procedure has been successfully used as an alternative to surgical commissurotomy.[2-4] Although the immediate efficacy of balloon dilatation of the mitral valve has been extensively studied, reports of its long-term outcome are few.[5-7] Restenosis was reported to be influenced by age and heavy valvar calcification after surgical commissurotomy[8 9] but few reports discussed this issue after balloon dilatation of the mitral valve.

The aim of our study was to (*a*) evaluate the follow up results of balloon dilatation of the mitral valve up to five years in a patient population with a high proportion of heavily calcified valves; (*b*) determine which factors influence restenosis; and (*c*) compare the value of invasive and non-invasive techniques for measuring mitral valve area after balloon dilatation of the mitral valve.

Methods

This study was carried out on 176 patients who underwent percutaneous balloon dilatation of the mitral valve and serial clinical follow up evaluation with Doppler echocardiographic studies between February 1986 and June 1992. The mean (SD, range) follow up period was 16 (13, 1 to 66) months. According to the protocol and clinical indications, 44 of those patients underwent repeat catheterisation at a mean follow up of 19 (11, 2 to 51) months, including three patients who had a second balloon dilatation of the mitral valve. There were 143 (81%) women and 33 (19%) men with a mean age of 49 (14, 23 to 83). Before dilatation, 110 patients (63%) were in New York Heart Association (NYHA) functional class III or IV; 68 (39%) were in atrial fibrillation; 41 (23%) had an echocardiographic score >8; 91 (52%) had 0 or 1 + and 85 (48%) had 2 to 4 + valvar calcification; and 10 (6%) had 2 + mitral regurgitation. Demographic characteristics and clinical profile of the 44 patients who underwent repeat catheterisation were similar to those of the whole group.

The procedure was performed as previously described.[3] Follow up clinical evaluation and Doppler echocardiographic assessment were performed every three months during the first year, every six months during the second year, and at yearly intervals thereafter. An informed consent was obtained from each patient.

Mitral valve area was determined by cross sectional echo planimetry from the short axis view at the level of the tips of the mitral leaflets. Continuous wave Doppler echocardiographic recording was obtained from the apical four chamber view while the

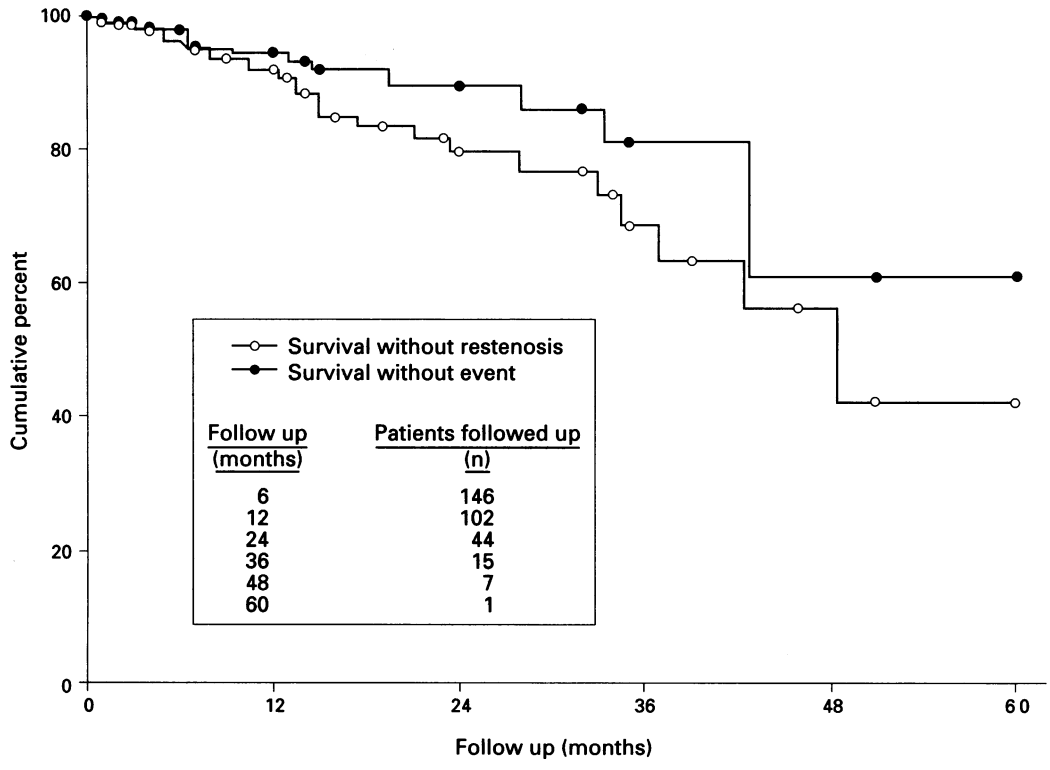

Figure 1 Plot of cumulative survival rates without restenosis and without cardiovascular events in 176 patients after percutaneous balloon dilatation of the mitral valve.

transducer was angled. Visual and auditory monitoring was used to locate the maximal velocity across the mitral valve. Mitral valve area was then determined from pressure half time. Mitral valve area after dilatation was assessed by Doppler echocardiography 24 hours after the procedure.

In the group of patients who underwent repeat catheterisation, mitral valve area was determined by the Gorlin formula. A transseptal procedure was performed to estimate accurately the mitral valve gradient. Cardiac output was measured by thermodilution unless severe tricuspid regurgitation was present, in which case the Fick method was used.

The severity of mitral regurgitation before and after dilatation was determined by ventriculography and was graded on a 0 + (no regurgitation) to 4 + (severe) scale according to the degree of opacification of the left atrium and pulmonary veins.[10]

The degree of valvar calcification was graded fluoroscopically from 0 + (no calcium) to 4 + (dense valvar and subvalvar calcium). On the basis of calcification, patients were separated into two groups: group 1, 0 or 1 + ; group 2, 2, 3, or 4 +.

Table 1 Significant independent predictors of restenosis at follow up by univariate Cox proportional hazard regression analysis in 176 patients who underwent percutaneous balloon dilatation of the mitral valve

	Estimate of variable (SEM)	*Risk ratio*	*p Value*
Age	0·0456 (0·0157)	1·05	0·004
Valvar calcification	0·6316 (0·1776)	1·88	0·0004
Echo score	0·1750 (0·0756)	1·19	0·02
Mitral valve area after dilatation	−2·0536 (0·5210)	0·13	0·0001

The severity of leaflet immobility, valve thickness, calcification, and submitral involvement was assessed by echocardiography and each feature was graded on a score of 0 to 4 +; higher scores represented more abnormal structure. The total echo score was the sum of the four scores.[11 12]

Restenosis was defined as a decrease in mitral valve area >50% from the original gain together with mitral valve area <1·5 cm^2 at follow up by either the cross sectional echo planimetry or the Doppler method. Survival without cardiovascular event was taken as no stroke, no mitral valve replacement, no surgical mitral commissurotomy, no repeat balloon dilatation of the mitral valve, and no cardiac death.

STATISTICAL ANALYSIS

Haemodynamic values and mitral valve area before dilatation, immediately after dilatation, and at follow up by invasive and non-invasive methods were compared by paired and unpaired *t* tests, Wilcoxon sign rank test, and rank sum test. Multivariate and univariate Cox proportional hazard regression analyses were used to identify which factors may affect restenosis. Cumulative % of survival without restenosis and without cardiovascular events was determined by the Kaplan-Meier method as well as stratified analysis and log rank test for two group comparisons. Results are presented as means (SD) and $p < 0·05$ was considered significant. All statistical analyses were performed with SAS version 6·04 software (Cary, North Carolina, USA).

Results

CLINICAL FOLLOW UP

At follow up, 119 (67·6%) patients were in NYHA functional class I and 45 (25·6%) in

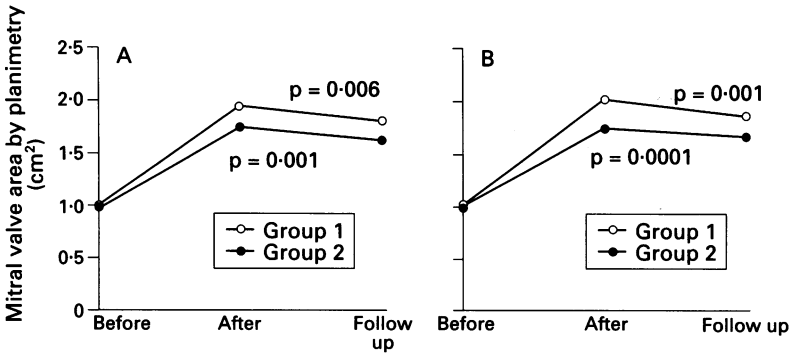

Figure 2 Comparison of mitral valve area before and after dilatation of the valve and at follow up according to the degree of valvar calcification in 176 patients (group 1 comprises patients with 0 to 1 + calcification and group 2 patients with 2 to 4 + calcification). (A) Mitral valve area as measured by cross sectional echo planimetry. (B) Mitral valve area as determined by Doppler pressure half time.

Table 2 Comparison of mitral valve area before and after percutaneous balloon dilatation of the mitral valve and at follow up (group 1, valvar calcification 0 or 1 + ; group 2 valvar calcification 2, 3, or 4 + ; values are means (SD))

Mitral valve area (cm²)	*Group 1 (n = 91)*	*Group 2 (n = 85)*	*p Value*
Planimetry:			
Before	0·99 (0·22)	0·96 (0·26)	0·3
After	1·95 (0·41)	1·76 (0·34)	0·001
Follow up	1·80 (0·39)	1·63 (0·39)	0·006
Decrease	0·16 (0·35)	0·14 (0·28)	0·8
Doppler:			
Before	1·02 (0·24)	1·00 (0·23)	0·7
After	2·02 (0·44)	1·76 (0·36)	0·0001
Follow up	1·87 (0·40)	1·68 (0·38)	0·001
Decrease	0·15 (0·44)	0·09 (0·34)	0·3

class II. Only 12 (6·8%) patients were in class III or IV. Three patients (1·7%) underwent a second balloon dilatation of the mitral valve, nine (5%) had mitral valve replacement, and three (1·7%) died.

DOPPLER ECHOCARDIOGRAPHIC AND HAEMODYNAMIC FOLLOW UP

In 176 patients who had Doppler echocardiographic studies at follow up, mitral valve area by planimetry increased from 0·97 (0·24) cm² before to 1·86 (0·39) cm² after dilatation ($p = 0·0001$) and then decreased to 1·72 (0·39) cm² at follow up ($p \leqslant 0·001$); the mean decrease in mitral valve area was 0·15 (0·32) cm² ($p = 0·0001$). Mitral valve area by Doppler increased from 1·01 (0·24) to 1·89 (0·42) cm² ($p = 0·0001$) and then decreased to 1·78 (0·40) cm² at follow up ($p < 0·05$); the mean decrease in mitral valve area was 0·12 (0·39) cm² ($p = 0·0001$). Although the difference between mitral valve area after dilatation and that at follow up was significant, the area at follow up was still significantly larger than that before dilatation as determined by both planimetry and Doppler; and 134 (76%) patients still had a mitral valve area >1·5 cm² at follow up. Restenosis had developed in 26 (15%) patients.

Seven variables—age, sex, heart rhythm, NYHA functional class before dilatation, echocardiographic score, valvar calcification, and mitral valve area after dilatation—were used in the Cox proportional hazard regression model to determine which factors may affect restenosis. Mitral valve area after dilatation ($p = 0·0001$) and echo score ($p \leqslant 0·01$) were shown to be significant predictors for restenosis by multivariate analysis. Univariate analysis identified age, valvar calcification, echo score, and mitral valve area after dilatation as significant determinants of restenosis (table 1). Figure 1 shows the cumulative % of survival without restenosis and cardiac events during a five year follow up by Kaplan-Meier analysis.

When patients were separated according to the degree of valvar calcification, 91 were in

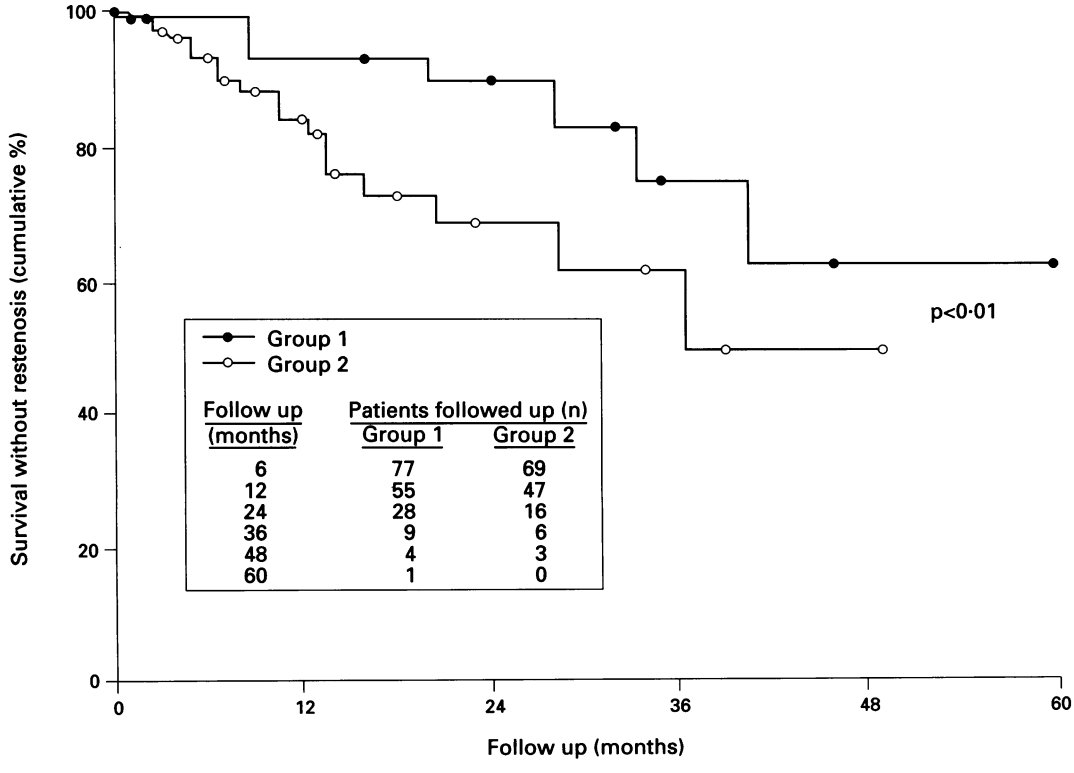

Figure 3 Plot of cumulative survival rate without restenosis in group I (calcification 0–1 +) and group II (calcification 2–4 +) after percutaneous balloon dilatation of the mitral valve. The survival rate without restenosis was significantly higher in group 1 than in group 2 by log rank test.

Table 3 Comparison of mitral valve area as determined by Gorlin formula, cross sectional echo planimetry, and Doppler methods before and after percutaneous balloon dilatation of the mitral valve and at follow up in 44 patients who underwent repeat catheterisation (values are means (SD))

Mitral valve area (cm²)	*Gorlin*	*Planimetry*	*Doppler*
Before	0·87 (0·19)	0·96 (0·24)*	0·95 (0·21)†
After	2·43 (0·62)	1·87 (0·41)‡	1·90 (0·47)§
Follow up	1·94 (0·67)	1·77 (0·41)	1·80 (0·45)

*p ⩽ 0·05, Gorlin *v* planimetry; †p ⩽ 0·05, Gorlin *v* Doppler; ‡p ⩽ 0·0001, Gorlin *v* planimetry; §p ⩽ 0·0001, Gorlin *v* Doppler. No significant differences were found between mitral valve areas as determined by planimetry and Doppler methods.

group I and 85 were in group II. The mean (SD) follow up period was 17 (14) months in group 1 and 15 (12) months in group 2 ($p = 0·2$). Seventy one patients (78%) in group I were in NYHA functional class I *v* 48 patients (56%) in group 2 ($p < 0·01$) at follow up. One death occurred in group 1 and two in group 2; two patients had mitral valve replacement in group 1 and seven in group 2. Table 2 shows the comparative results between the two groups, of mitral valve area before and after dilatation and at follow up. Figure 2 shows that mitral valve area was significantly larger in group 1 than in group 2 immediately after dilatation and at follow up. The trend towards a decrease in mitral valve area at follow up occurred in parallel in both groups. The cumulative % of survival without restenosis was significantly higher in group 1 than in group 2 ($p < 0·01$, fig 3).

In the 44 patients who underwent repeat catheterisation at follow up, we compared mitral valve area before and after dilatation and at follow up as determined by Gorlin, planimetry, and Doppler methods (table 3). From the table, the mean mitral valve area immediately after dilatation was about 0·5 cm² larger by the Gorlin formula than by either planimetry or Doppler ($p = 0·0001$). This significant discrepancy between invasive and non-invasive methods disappeared at follow up.

The incidence of significant mitral regurgitation (⩾2 +) had decreased from 18% immediately after dilatation to 14% at follow up.

Discussion

This report clearly shows that the enthusiasm for the initial reports of balloon dilatation of the mitral valve has more than one reason to persist because the long-term success is as encouraging as the short-term.

Indeed, in this series with a high proportion of patients with heavy valvar calcification, the five year cumulative survival rate without cardiovascular events is still over 60%, which is comparable with the results reported by Cohen *et al.*[13] Ninety three per cent of the patients remained in NYHA functional class I or class II during the five year follow up. More objectively over 75% of the patients still had a mitral valve area >1·5 cm².

Restenosis seems to be highly related to the patient's baseline characteristics—namely, old age, heavy valvar calcification, high mitral valve echo score, and suboptimal initial results. Furthermore, restenosis seems to be a continuous process and is likely to increase gradually with time. The time to restenosis is difficult to predict and therefore a serial clinical and Doppler echocardiographic follow up is necessary to detect early restenosis.

Anatomical restenosis as determined by Doppler echocardiography was not always associated with recurrent symptoms. In our study 27% of the patients with restenosis were still in NYHA functional class I. This indicates that the rate of restenosis in our series would be much lower than 15% if we only considered the symptomatic patients and those in whom a second balloon dilatation of the mitral valve or surgery were required. These were the criteria for restenosis in previous reports after closed and open surgical commissurotomy. John *et al*[8] reported a restenosis of 4·2% at five years and 15·6% at 20 years in a population much younger (mean age 27) than ours and with only 15% of calcified valves. Lyons *et al*,[14] however, documented restenosis in 25% of the patients at five years; and Heger *et al* reported a 28% rate of restenosis 12 years after closed commissurotomy.[15] Houseman *et al* reported a 16% rate of restenosis 10 years after open surgical commissurotomy.[16] On the basis of the same criteria, the rate of restenosis would be only 5% in our patients, which is highly encouraging compared with these other studies. In a recent randomly conducted study, comparing balloon dilatation of the mitral valve with closed mitral commissurotomy, Turi *et al* found no significant differences in mitral valve area between the two techniques for a follow up period of eight months.[17]

The issue of how to manage the restenosis and symptomatic patients is of great importance. Based on a previous report,[18] which showed that short-term results of balloon dilatation of the mitral valve in patients who had had surgical commissurotomy are similar to those found in unoperated patients,[18] we could extrapolate that repeat balloon dilatation of the mitral valve after restenosis could be beneficial particularly in patients who have benefited from a first procedure for two years or more. Patients who restenose within two years of a first dilatation, may not benefit much from a second procedure and surgery is probably a better alternative. This early restenosis is highly associated with unfavourable mitral valve structure that may cause difficulty and insufficiency of commissural splitting. Further follow up studies are needed to support this recommendation.

Another important issue is what kind of surgical procedure should be done in those patients with restenosis. Ellis *et al* showed that patients over 40 with a calcified valve are at higher risk of restenosis after closed commissurotomy.[9] Houseman *et al* found similar results in patients with "poor leaflet condition" after open commissurotomy.[16] These

reports support our findings and indicate that patients who did not benefit much from balloon dilatation of the mitral valve are unlikely to benefit from a surgical commissurotomy and therefore a mitral valve replacement is probably the treatment of choice for those patients.

It is important to note that atrial septal defects and significant mitral regurgitation as seen in some patients after balloon dilatation of the mitral valve seem to recede at follow up. Atrial septal defect was detected by colour Doppler in only 6% of the patients at follow up and has not required surgical repair by itself in our experience. Also, mitral regurgitation seems to decrease or remain unchanged at follow up in most of our patients. The few patients in whom mitral valve replacement for severe mitral regurgitation was necessary during the follow up period already had significant mitral insufficiency immediately after the procedure.

The question of whether or not a repeat catheterisation needs to be undertaken after balloon dilatation of the mitral valve is becoming much less controversial. In fact, Block *et al* reported that the discrepancies of mitral valve area immediately after dilatation between the Gorlin method and Doppler echocardiography was not found at follow up.[7] Our results corroborate those findings that suggest that repeat catheterisation is not necessary to evaluate these patients at follow up. Doppler echocardiography is an accurate and reliable tool for follow up of these patients in addition to the clinical evaluation. Furthermore, the difference in cost between catheterisation and Doppler echocardiography is obvious. For all these reasons, we think that a repeat catheterisation is indicated only in selected patients to solve possible discrepancies between clinical and Doppler echocardiographic findings.

Mitral valve areas as determined by echo planimetry and Doppler pressure half time are often consistent, but discrepancies are sometimes encountered. We recommend for that reason to rely on the same method to determine restenosis.

LIMITATIONS OF THE STUDY

The major limitation of this study is that we were only able to have follow up Doppler echocardiographic studies in 176 patients, which is 35% of our total patient population undergoing balloon dilatation of the mitral valve. These patients who had follow up may still be considered as a representative sample because their age, sex, severity of clinical symptoms, valvar calcification, echo score, cardiac rhythm, mitral valve area, and degree of mitral regurgitation before and after balloon dilatation of the mitral valve were similar to those of the rest of our patient population.

Another important limitation which should be noted is that although the study period was over five years, the mean follow up period was less than two years. This may cause underestimation of survival rates without restenosis and cardiovascular events because of the small sample size after that period.

In conclusion from our study we are able to show that balloon dilatation of the mitral valve provides encouraging late success that compares well to that found in patients undergoing surgical mitral commissurotomy. Old age, heavy calcification, high echo score, and suboptimal initial results are important risk factors for restenosis. Larger numbers of patients and longer follow up periods are required to determine the long-term efficacy of balloon dilatation of the mitral valve.

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