Age, a predictive factor for the reduction in the mean transmitral pressure gradient after percutaneous balloon mitral valvotomy

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Aging; Follow-up studies; Mitral valve; Stenosis; Valvular surgery.

Background. **The aim of this study was to evaluate the changes in mitral valve area and mean transmitral pressure gradient before and after percutaneous balloon mitral valvotomy and at 2 years of follow-up. We hypothesized that the patient's age would be an important determinant for the success of balloon valvotomy.**

Methods. **We studied 24 patients with mitral stenosis (6 men and 18 women with an average age of 58 years, range 39 to 80 years), who underwent percutaneous balloon mitral valvotomy. Two-dimensional and Doppler echocardiographic examinations were taken before, immediately after and at a mean follow-up of 24 months (range 12 to 73 months). The correlation between the changes in the mitral valve area or mean transmitral pressure gradient and age was assessed with rank correlation and with stepwise multiple linear regression analysis correcting for sex, days of follow-up, heart rate score, pulmonary hypertension, mitral regurgitation and Wilkins score at follow-up.**

Results. **Changes in the mitral valve area did not correlate with age. The reduction in mean transmitral pressure gradient at follow-up was associated with age with a 20.6% less reduction in mean transmitral pressure gradient (95% confidence interval 3.5-40.4%, $p < 0.021$) for every other year of the patients' age. When comparing changes in mean transmitral pressure gradient before and after percutaneous balloon mitral valvotomy, the strength and consistency of the association with age appeared similar (mean transmitral pressure gradient -0.9 ± 3.0 vs -2.8 ± 3.4 mmHg).**

Conclusions. **Age is a predictive factor for the reduction in mean transmitral pressure gradient after percutaneous balloon mitral valvotomy. This suggests that a better outcome is to be expected in younger patients, independently of the list of factors taken into consideration in our study.**

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The research has been conducted in full accordance with ethical principles as stated by the Declaration of Helsinki and free and informed consent of the subjects involved was obtained.

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Introduction

Several studies have demonstrated that percutaneous balloon mitral valvotomy is a safe and effective procedure for the treatment of patients with symptomatic mitral stenosis with immediate results that may be comparable to surgical commissurotomy[1-9].

This procedure has not only been successfully performed in younger patients with optimal anatomy but also in elderly patients unfit for surgery or in selected elderly patients with a good echocardiographic score[10-16].

The aim of this study was to evaluate the changes in mitral valve area and mean transmitral pressure gradient before and after percutaneous balloon mitral valvotomy and at 2 years of follow-up, hypothesizing that patients' age would be an important determinant for the success of balloon valvotomy, and to study the extent to which these changes are related to the patients' age.

Methods

Patient population. The study included 24 patients (6 men, 18 women, average age 58 years, range 39-80 years) with mitral stenosis undergoing percutaneous balloon mitral valvotomy between May 1992 and October 2000. All patients had been submitted to two-dimensional and Doppler echocardiographic examinations immediately before and immediately after (mean 3 ± 3 days following the pre-procedural echocardiogram) the procedure and at a mean follow-up of 2 years (range 12 to 73 months).

Before valvuloplasty, 8 patients had sinus rhythm, 14 had atrial fibrillation, and 2 were pacemaker-dependent. Six patients were in NYHA functional class IV, 15 were in NYHA class III, and 3 patients were in NYHA class II.

Thirteen patients had at least one coronary risk factor. Four had hypertension, 1 was diabetic, 2 had a history of coronary disease, 3 had a history of cerebrovascular disease, and 3 had hypercholesterolemia.

No patient had previous percutaneous balloon mitral valvotomy.

Four patients had previous surgical commissurotomy (21 to 32 years before), one had previous aortic valve replacement, one had previous repair of coarctation of the aorta, and one had concomitant moderate aortic stenosis.

Echocardiographic analysis. Two-dimensional and Doppler echocardiography were performed in all patients before percutaneous balloon mitral valvotomy, after 3 ± 3 days) following the pre-procedural echocardiogram and at a mean follow-up of 24 ± 19 months.

All echocardiographic measurements were recorded on videotape and reviewed for subsequent analysis by two independent observers who were unaware of the patients' catheterization data. A Toshiba 160 SSH ultrasound imager (Toshiba Medical Systems, West Sussex, UK) was used in the study. The mitral valve area was calculated using the pressure half-time method[17] from the continuous wave Doppler mitral velocity profile, averaging 3 to 5 beats in patients in sinus rhythm and 5 to 10 beats in those with atrial fibrillation. The mean transmitral pressure gradient was calculated from the same tracings using the simplified Bernoulli equation. The Wilkins echocardiographic score (from 0 to 4) was assigned for leaflet mobility, valvular thickening, valvular calcification and subvalvular thickening. The scores of the four individual features were added in each patient to obtain a total echocardiographic score (range 0 to 16)[18].

Mitral regurgitation was graded as none, trivial, mild, mild-moderate or moderate.

Pulmonary hypertension was classified as follows: normal for a systolic gradient across the tricuspid valve < 25 mmHg; mild for a gradient ranging from 25 to 40 mmHg; moderate for a gradient ranging from 40 to 60 mmHg; severe for a gradient > 60 mmHg.

We generated a heart rate score on the basis of the following categories: sinus rhythm, atrial fibrillation, and pacing rhythm.

Statistical analysis. Results are expressed as means ± SD unless otherwise stated. The distribution of the variation of the mitral valve area and of the mean transmitral pressure gradient was gaussian. The correlation between the variation of the mitral valve area and of the mean transmitral pressure gradient and age was first assessed using Pearson rank correlation analysis. Simple and stepwise multiple linear regression analysis was used to assess the importance, together with age, of sex, days of follow-up, heart rate score, pulmonary hypertension, severity of mitral regurgitation at follow-up, and Wilkins score at follow-up[19,20], considered as categorical where appropriate. Interactions between selected variables were allowed to enter if they had additional predictive power. Results of linear regression are expressed as the percentage variation of the relative risk (RR), with 95% confidence intervals (CI). The power of the study was calculated with type I error (α) 0.05 and type II error (β) 0.2[21]. Analyses were performed using Stata 5 software (Stata Corp., College Station, TX, USA).

Results

Baseline characteristics and initial results are summarized in table I. The mean mitral valve area was 1.16 ± 0.37 cm^2 before percutaneous balloon mitral valvotomy, increasing to 1.70 ± 0.40 cm^2 after an average of 3 days following the procedure and increasing further to 1.74 ± 0.64 cm^2 at a mean follow-up of 2 years.

The mean transmitral pressure gradient was 7.1 ± 3.8 mmHg before percutaneous balloon mitral valvotomy, decreasing to 5.0 ± 1.7 mmHg after an average of 3 days following the procedure, and reaching 5.2 ± 2.3 mmHg at a mean follow-up of 2 years.

The changes occurring in the mean mitral valve area and mean transmitral pressure gradient comparing the two measures before and after the procedure and at follow-up are shown in table II.

A rank correlation scatter diagram of the age and mean transmitral pressure gradient changes at follow-up together with a regression line are shown in figure 1. The correlation rank test (r^2 = -0.09, $p > 0.05$) suggests that in our patients the mitral valve area changes were not correlated with age. Furthermore, univariate and multivariate linear regression analyses showed that, within our population, age seemed to be unrelated to the changes in the mitral valve area.

The change in the mean transmitral pressure gradient at follow-up was correlated to the patients' age (r^2 = 0.178, $p < 0.039$). Univariate analysis demonstrated that this association was statistically significant with a 13% reduction in the mean transmitral pressure gradient at follow-up (95% CI 0.7-27.1%, $p < 0.04$) for every year increase in the patients' age. Multivariate analysis yielded similar results, with a 20.6% reduction in the mean transmitral pressure gradient (95% CI 3.5-40.4%, $p < 0.021$) for every year increase in the patients' age when correcting for sex, days of follow-up, pulmonary hypertension, mitral regurgitation, heart rate score, and Wilkins score.

A rank correlation scatter diagram of the age and mean transmitral pressure gradient changes immediately after the procedure together with the regression line are shown in figure 2. The mean transmitral pressure gradient change after the procedure correlated with the patients' age (r^2 = 0.129, $p < 0.01$). Stepwise linear regression univariate analysis was not significant, with an 11.3% reduction in the mean transmitral pressure gradient (95% CI -2.3 to 26.8%, $p < 0.11$) for every year increase in the patients' age. Multivariate analysis

Table I. Characteristics of the 24 patients in whom balloon mitral valvuloplasty was performed.

No. patients	24	Mitral area (cm^2)	
Sex (M/F)	6/18	Pre-intervention	1.16 ± 0.37
NYHA class		Post-intervention	1.70 ± 0.40
II	3	Follow-up	1.74 ± 0.64
III	15	MPG (mmHg)	
IV	6	Pre-intervention	7.1 ± 3.8
Sinus rhythm	8	Post-intervention	5.0 ± 1.7
Atrial fibrillation	14	Follow-up	5.2 ± 2.3
Paced rhythm	2	Mitral regurgitation	
Previous commissurotomy	4	Pre-intervention	
Concomitant aortic stenosis	1	None	2
Previous aortic valve replacement	1	Trivial	11
Mitral valve morphologic score		Mild	10
Pre-intervention		Mild-moderate	1
Mobility	2.0 ± 0.4	Moderate	0
Thickening	2.0 ± 0.2	Follow-up	
Calcification	1.5 ± 0.7	None	1
Subvalvular thickening	1.7 ± 0.5	Trivial	11
Total echocardiographic	7.3 ± 1.2	Mild	5
Post-intervention		Mild-moderate	1
Mobility	1.6 ± 0.5	Moderate	6
Thickening	2.0 ± 0.0		
Calcification	1.4 ± 0.6		
Subvalvular thickening	1.5 ± 0.6		
Total echocardiographic	6.6 ± 1.2		
Follow-up			
Mobility	1.8 ± 0.6		
Thickening	2.0 ± 0.0		
Calcification	1.4 ± 0.7		
Subvalvular thickening	1.6 ± 0.6		
Total echocardiographic	6.8 ± 1.5		

MPG = mean transmitral pressure gradient.

Table II. Mean mitral valve area and mean pressure gradient changes: comparison between follow-up and pre-intervention; post-intervention and pre-intervention; post-intervention and follow-up.

Follow-up vs pre-intervention	
Months	24 ± 19
Mitral valve area (cm^2)	0.58 ± 0.63
MPG (mmHg)	-1.90 ± 3.01
Post-intervention vs pre-intervention	
Days	3 ± 4
Mitral valve area (cm^2)	0.54 ± 0.28
MPG (mmHg)	-2.13 ± 3.22
Post-intervention vs follow-up	
Months	24 ± 19
Mitral valve area (cm^2)	-0.04 ± 0.56
MPG (mmHg)	0.24 ± 2.09

MPG = mean transmitral pressure gradient.

demonstrated that this association became significant when adding the follow-up mitral regurgitation data to the model, with a 17.0% reduction in the mean transmitral pressure gradient (95% CI 3.3-32.5%, $p < 0.016$) for every year increase in the patients' age. A similar result was obtained when we corrected for sex, days of follow-up, pulmonary hypertension, mitral regurgitation, heart rate score, and Wilkins score with a 22.2% reduction in the mean transmitral pressure gradient (95% CI 2.0-46.5%, $p < 0.033$).

Patients improved clinically after 2 years of follow-up. Seventeen (71%) of the 24 patients improved by at least one functional class: 65% of the patients aged between 30 and 59 years, and 75% of the patients aged between 60 and 80 years. Five patients remained in the same functional class and in only 2 cases was a worsening by one functional class observed (Fig. 3).

Discussion

Our results indicate that the reduction in the mean transmitral pressure gradient after an average of 2 years of follow-up correlates with the patients' age, with a 20.6% decrease in the mean transmitral pressure gradient for every year increase in the patients' age. When comparing the changes in the mean transmitral pressure gradient before and immediately after percutaneous balloon mitral valvotomy, the strength and consistency of the association with age appeared similar.

Nevertheless, the mitral valve area did not show any statistically significant relationship to the patients' age, in contrast with the findings of a recent study by Krasuski et al.[22] having a larger sample of patients, though

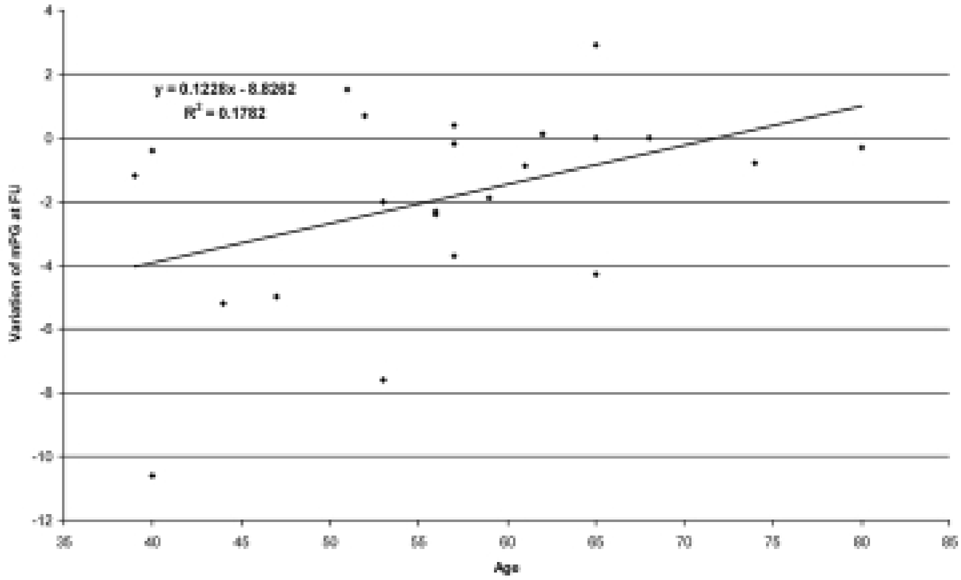

Figure 1. *Scatter diagram showing the changes in the mean transmitral pressure gradient (mPG) prior to the procedure through follow-up (FU) and age at the time of intervention.*

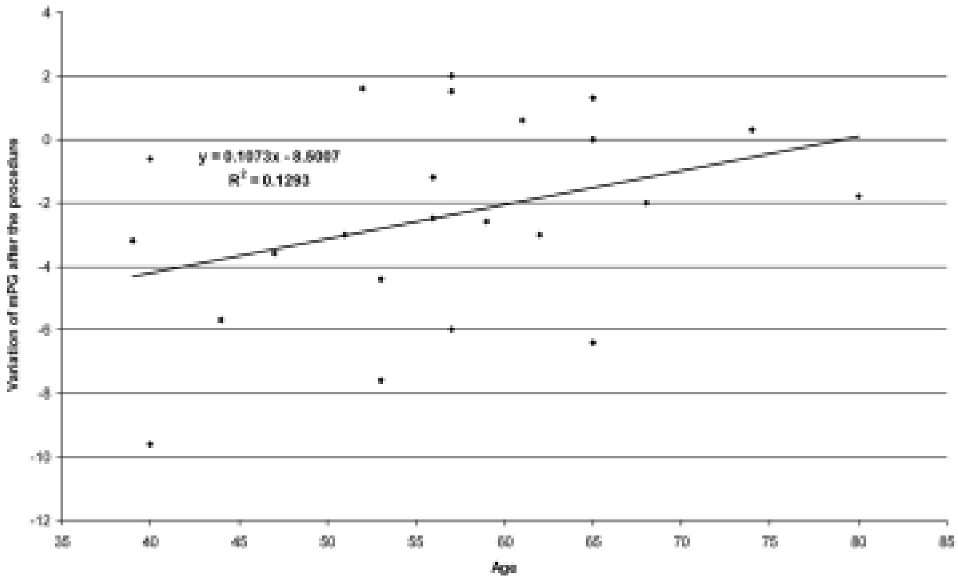

Figure 2. *Scatter diagram showing the changes in the mean transmitral pressure gradient (mPG) prior to the procedure through post-intervention and age at the time of the procedure.*

not considering variations in the mean transmitral pressure gradient. However, the determination of the mitral valve area on the basis of pulmonary hypertension is dependent upon the left ventricular compliance and volume loading conditions. These can explain the lack of correlation.

The calculation of the mitral valve area by the Doppler pressure half-time method is a reliable non-invasive tool for the determination of the orifice area in patients undergoing percutaneous balloon mitral valvotomy and is sufficiently accurate to assess the results of this procedure 24 to 48 hours after valvuloplasty[23-26]. The calculation of the mitral valve area by planimetry is often a good alternative but it is not always possible to obtain adequate cross-sectional images of the mitral orifice and therefore has a restricted application in such patients.

The interobserver variability was always < 5% and was controlled for by an independent physician.

The limited number of patients included in the present study did not allow to assess whether this association is truly linear and the variation from the mean follow-up appears to be a limitation.

Age seems to be inversely related to the reduction in the mean transmitral pressure gradient after percutaneous balloon mitral valvotomy. A larger sample of pa-

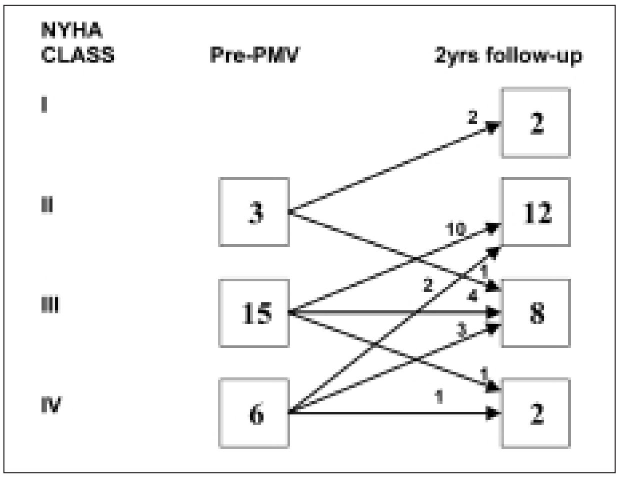

Figure 3. *Changes in the patients' NYHA class before percutaneous balloon mitral valvotomy (PMV) through 2 years of follow-up.*

tients may help to reduce uncertainty and the width of the CI, inevitably large with such a small number of patients. We conclude that, similar to what observed in other studies[22], our results suggest a better outcome of percutaneous balloon mitral valvotomy in younger patients, at least in terms of the mean transmitral pressure gradient, independently of sex, days of follow-up, pulmonary hypertension, mitral regurgitation, heart rate score, and Wilkins score and that elderly patients should be aware of this limitation.

References

1. Inoue K, Owaki T, Nakamura T, Kitamura F, Miyamoto N. Clinical application of transvenous mitral commissurotomy 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 I, Block PC, Brandi S, et al. Percutaneous balloon valvotomy for patients with severe mitral stenosis. Circulation 1987; 75: 778-84.
4. McKay RG, Lock JE, Safian RD, et al. Balloon dilation of mitral stenosis in adult patients: postmortem and percutaneous mitral valvuloplasty studies. J Am Coll Cardiol 1987; 9: 723-31.
5. Vahanian A, Michel PL, Cormier B, et al. Results of percutaneous mitral commissurotomy in 200 patients. Am J Cardiol 1989; 63: 847-52.
6. Abascal VM, Wilkins GT, O'Shea JP, et al. Prediction of successful outcome in 130 patients undergoing percutaneous balloon mitral valvotomy. Circulation 1990; 82: 448-56.
7. The National Heart, Lung and Blood Institute Valvuloplasty Registry Participants. Multicenter experience with balloon mitral commissurotomy NHLBI Balloon Valvuloplasty Registry Report on immediate and 30-day follow-up results. Circulation 1992; 85: 448-61.
8. Kawanishi DT, Rahimtoola SH. Catheter balloon commissurotomy for mitral stenosis: complications and results. J Am Coll Cardiol 1992; 19: 192-5.
9. Carroll JD, Feldman T. Percutaneous mitral balloon valvotomy and the new demographics of mitral stenosis. JAMA 1993; 270: 1731-6.
10. Zaki A, Salama M, El Masry M, Elhendy A. Five-year follow-up after percutaneous balloon mitral valvuloplasty in children and adolescents. Am J Cardiol 1999; 83: 735-9.
11. Kothari SS, Kamath P, Juneja R, Bahl VK, Airan B. Percutaneous transvenous mitral commissurotomy using Inoue balloon in children less than 12 years. Cathet Cardiovasc Diagn 1998; 43: 408-11.
12. Shaw TR, Elder AT, Flapan AD, Essop AR. Mitral balloon valvuloplasty for patients aged over 70 years: an alternative to surgical treatment. Age Ageing 1991; 20: 299-303.
13. Sutaria N, Elder AT, Shaw TR. Long-term outcome of percutaneous mitral balloon valvotomy in patients aged 70 and over. Heart 2000; 83: 433-8.
14. Sutaria N, Elder AT, Shaw TR. Mitral balloon valvotomy for the treatment of mitral stenosis in octogenarians. J Am Geriatr Soc 2000; 48: 971-4.
15. Herrmann HC, Wilkins GT, Abascal VM, et al. Percutaneous balloon mitral valvotomy for patients with mitral stenosis. Analysis of factors influencing early results. J Thorac Cardiovasc Surg 1988; 96: 33-8.
16. Rediker DE, Block PC, Abascal VM, et al. Mitral balloon valvuloplasty for mitral restenosis after surgical commissurotomy. J Am Coll Cardiol 1988; 11: 252-6.
17. Hatle L, Angelsen B, Tromsdal A. Noninvasive assessment of atrioventricular pressure half-time by Doppler ultrasound. Circulation 1979; 60: 1096-104.
18. Wilkins GT, Weyman AE, Abascal VM, Block PC, Palacios IF. Percutaneous balloon dilatation of the mitral valve: an analysis of echocardiographic variables related to outcome and mechanism of dilatation. Br Heart J 1988; 60: 299-308.
19. Clayton D, Hills M. Statistical models in epidemiology. Oxford: Oxford University Press, 1996: 367.
20. Gardner M, Altman DG. Statistics with confidence. London: BMJ, 1989.
21. Pocock SJ. Clinical trials. London: John Wiley & Sons, 1995: 127-41.
22. Krasuski RA, Warner JJ, Peterson G, et al. Comparison of results of percutaneous balloon mitral commissurotomy in patients aged ≥ 65 years with those in patients aged < 65 years. Am J Cardiol 2001; 88: 994-1000.
23. Chen C, Wang Y, Guo B, Lin Y. Reliability of the Doppler pressure half-time method for assessing effects of percutaneous balloon valvuloplasty. J Am Coll Cardiol 1989; 13: 1309-13.
24. Abascal VM, Wilkins GT, Choong CY, et al. Echocardiographic evaluation of mitral valve structure and function in patients followed for at least 6 months after percutaneous balloon mitral valvuloplasty. J Am Coll Cardiol 1988; 12: 606-15.
25. Reid CL, McKay CR, Chandraratna PA, et al. Mechanisms of increase in mitral valve area and influence of anatomic features in double-balloon, catheter balloon valvuloplasty in adults with rheumatic mitral stenosis: a Doppler and two-dimensional echocardiographic study. Circulation 1987; 76: 628-36.
26. Otto CM, Davis KB, Holmes DR Jr, et al. Methodologic issues in clinical evaluation of stenosis severity in adults undergoing aortic or mitral balloon valvuloplasty. The NHLBI Balloon Valvuloplasty Registry. Am J Cardiol 1992; 69: 1607-16.