Original Article

Mitral valve calcium assessment: An independent predictor of balloon valvuloplasty results

Ricardo A. Sarmiento a, b, *, Raúl Solernó b, Rodrigo Blanco a, Federico Giachello b, Agustin Hauqui b, Martín Oscos b, Federico Blanco a, Gerardo Gigena a, Jorge Lax a, Pablo Pedroni b

* Department of Interventional Cardiology, Hospital General de Agudos Dr. Cosme Argerich, Ciudad Autónoma de Buenos Aires, Argentina
b Department of Interventional Cardiology, Hospital de Alta Complejidad en Red – El Cruce, Florencio Varela, Argentina

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Objective: Percutaneous mitral valvuloplasty (PMV) is an effective treatment for patients with mitral valve stenosis. Echocardiographic score (ES) is a useful predictor of outcomes. However, mitral valve calcium (MVC) has been shown to predict immediate results even in patients with otherwise low ES. We sought to evaluate the usefulness of MVC assessment as a predictor of immediate and long-term outcomes after PMV.

Methods: PMV was performed in 168 consecutive patients. Clinical and echocardiographic variables were analyzed. Patients were classified into 2 groups: group 1: minimal MVC and group 2: moderate to severe MVC. Primary success was defined as post-PMV mitral valve area (MVA) > 1.5 cm² in the absence of major complications. Restenosis (RE) was defined as a decrease in MVA >50% of initial gain or a final MVA <1.5 cm².

Results: Mean age was 46.5 ± 11 years, and 86.9% (146) were women. Forty-two patients (25%) had mild MVC (group 1), and 75% of the patients had moderate to severe MVC (group 2). Procedural success was achieved in 95.2% and 76.2% for groups 1 and 2, respectively, p = 0.01. MVA after PMV was 1.82 cm² (IQR 25–75 = 1.60–2.00) in group 1 and 1.67 cm² (IQR 25–75 = 1.44–1.97) in group 2, p = 0.02. After 48 months, 28.2% of patients presented RE. Multivariate analysis identified the presence of MVC as an independent predictor of poor immediate results (HR = 0.12, 95% IC 0.03–0.91) and RE (HR = 1.94, 95% CI = 1.02–5.21).

Conclusion: Our study shows that the presence of MVC may predict immediate and long-term outcomes after PMV.

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1. Introduction

Percutaneous mitral valvuloplasty (PMV) has been well established as an effective treatment for patients with symptomatic severe mitral valve stenosis.1–6 Immediate postprocedural and long-term results depend on clinical and echocardiographic findings.7–10 Mitral valve morphology is currently assessed by the Wilkins transthoracic echo score (ES) in which leaflet thickening, calcification, mobility, and subvalvular fusion are determined.9,10 A low echocardiographic score (≤8) is indicative of a pliable, non-calciﬁed valve with little subvalvular fusion and has been shown to have a good correlation with procedural success and lower rates of restenosis (RE). Higher scores are indicative of more calcified, immobile and thickened valve leaflets with subvalvular fusion and are associated with lower procedural success rates and a higher incidence of RE.11 However, the individual weight of each of the echocardiographic components is not well established. Sutaria et al12 and Cannan et al13 have shown that commissural calcification is a useful predictor of outcomes in patients with otherwise low echo scores (<8) and that the presence of calcification in one or more commissure predicts poor immediate and long-term results.

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The purpose of our study was to determine the usefulness of valve calcification assessment as a predictor of immediate and long-term outcomes after PMV.

2. Methods

2.1. Patients

PMV was performed in 168 consecutive patients in 2 public hospitals in Argentina, from January 1993 to December 2015. The study protocol was approved by the Ethics Committee of both hospitals.

2.2. Echocardiographic assessment

All patients underwent full transthoracic cross-sectional echocardiography within one month before PMV. Mitral valve apparatus morphology was evaluated with the Abascal and Wilkins score. This involves semiquantitative assessment of leaflet mobility and thickening, subvalvular changes, and valve calcification; each abnormality has a possible score of 0–4, corresponding to zero/mild to severe abnormality and giving a possible total echo score between 0 and 16. All patients were screened for the presence of left appendage thrombus using a transesophageal echocardiography within 24 h before the PMV. Echocardiographic variables were assessed before and immediately after the procedure, at one month, six months, and annually during the follow-up.

Patients were classified into the following 2 groups, in a retrospective analysis, according to the degree of mitral valve calcification: group 1: minimal valve calcification (0–1 point in the ES) and group 2: moderate to severe valve calcification (2–4 points in ES). For each group, the following variables were analyzed: age, ES, heart rhythm, mitral valve area (MVA), systolic pulmonary artery pressure (sPAP), mean diastolic mitral gradient, balloon size, left atrium diameter, and New York Heart Association (NYHA) functional class.

2.3. Procedural technique

Standard hemodynamic data, including left ventricular, left atrial, right ventricular, and systolic pulmonary artery pressures, were recorded before and immediately after the procedure. Cardiac output was determined by the Fick method, and MVA was calculated with the Gorlin formula. Percutaneous mitral valvuloplasty was performed with the Inoue single-balloon technique as previously described. The procedure was performed through an anterograde approach across the mitral valve by performing a transeptal puncture. The Inoue single-balloon technique included sequential increases in balloon size, assessing echocardiographic parameters regarding the valve gradient and the degree of mitral regurgitation after each inflation. Maximum balloon size was determined by the following formula: (patient height [cm]/10) + 10. Echocardiographic guidance was used in every case.

Left ventriculography was performed to assess the presence and severity of mitral valve regurgitation (MR) based semiquantitatively and graded on a scale from 1 to 4, according to the Sellers’ classification.

2.4. Outcomes

Primary success was defined as post-PMV mitral valve area ≥1.5 cm² in the absence of major periprocedural complications: significative mitral regurgitation (≥2 Sellers’ classification), in-hospital death, cardiac tamponade, and systemic embolism. RE was defined as a decrease in mitral valve area >50% of initial gain or a final MVA <1.5 cm².

2.5. Statistical analysis

Categorical variables are expressed as frequencies and percentages and were analyzed by the χ² test. Continuous variables are expressed as mean ± standard deviation or median and interquartile range (IQR 25–75%), and comparison of parametric and nonparametric values between the two groups was performed by means of two-tailed Student t-test or Kruskal–Wallis test, as appropriate. The association between demographic, clinical, and hemodynamic variables with PMV success and with the mitral calcium score was evaluated. To identify predictors of successful outcomes, all variables were tested independently in a univariate logistic regression model. For those variables with a p value < 0.05 in the univariate analysis, a stepwise logistic regression model was used to identify independent predictors of immediate success and a Cox regression model was used to determine independent predictors of RE during follow-up. All the analysis was performed using the Statistix 7.0 software package, and a p value < 0.05 was considered statistically significant.

3. Results

A total of 168 patients with symptomatic rheumatic mitral stenosis were treated with PMV. Mean age was 46.5 ± 11 years and 86.9% (146) were women. One hundred five patients (62.5%) were in NYHA functional class II and 57 patients (33.9%) in NYHA functional class IV. Atrial fibrillation was present in 51 patients (30.5%). Mitral regurgitation was observed in 109 patients (mild MR in 105 and 4 patients, who were deemed to be inoperable, had moderate MR). Median MVA before PMV was 0.90 cm² (IQR 25–75 = 0.87–1.00 cm²), median sPAP was 44 mmHg (IQR 25–75 = 35–52 mmHg), and median wedge pressure was 23 mmHg. Median ES was 7 (IQR 25–75 = 6–9) and 30.9% of the patients had an ES > 8. Forty-two patients (25%) had mild valve calcification (group 1), and 75% of the patients had moderate to severe valve calcification (group 2).

Table 1 shows echocardiographic and hemodynamic findings before and after PMV.

Procedural success was achieved in 95.2% of patients in group 1 and 76.2% in group 2 (p = 0.01). The median valve area after PMV was 1.75 cm² (IQR = 1.6–2.0 cm²). MVA observed in group 1 was 1.82 cm² (IQR 25–75 = 1.60–2.00) and it was 1.67 cm² (IQR 25–75 = 1.44–1.97) in group 2 (p = 0.02). Mitral valve regurgitation was observed in 151 patients after PMV (80.9% of patients in group 1 and 92.8% in group 2, p = 0.04). Among these patients, 80.7% had mild MR and 19.3% moderate MR (Table 2). No patient required mitral valve replacement surgery due to severe mitral valve regurgitation. Three in-hospital deaths occurred (2.2%). One patient died due to infective endocarditis, another patient died because of sepsis and one of the patients suffered disseminated intravascular coagulation. Univariate analysis showed that the presence of atrial fibrillation, a higher echocardiographic score, and the presence of moderate to severe mitral valve calcification were found to be predictors of poorer immediate results (Table 3). Multivariate analysis identified the presence of moderate to severe mitral valve calcification as the only independent predictor of a lower immediate success achievement rate (HR = 0.12, 95% CI = 0.03–0.91, p = 0.03).

After a median follow-up of 48 months (IQR 25–75 = 24–48 months), 86% of patients remained asymptomatic. Four deaths were observed (1 in group 1 and 3 in group 2). A gradual reduction in MVA was seen in both groups. RE rates of 16.4%, 20.7%, 27.4%, and
**Table 1**

Echocardiographic and hemodynamic parameters before and after percutaneous mitral valvuloplasty.

| Echocardiographic findings | Pre-PMV n = 168 | Post-PMV n = 168 |
|---------------------------|----------------|-----------------|
| LVDD mm – median (IQR 25–75%) | 49 (45–52) | 49 (45–52) |
| LVSD mm – median (IQR 25–75%) | 30 (26–32) | 30 (26–32) |
| SF % – median (IQR 25–75%) | 39 (33–44) | 39.5 (35–44.2) |
| LA mm – median (IQR 25–75%) | 53 (49–58) | 50 (47–54) |
| MVA cm – median (IQR 25–75%) | 0.90 (0.87–1.00) | 1.75 (1.6–2.0) |
| MVG mmHg – median (IQR 25–75%) | 11 (9–16) | 5 (3–6.25) |
| sPAP mmHg – median (IQR 25–75%) | 45 (35–52) | 30 (27–40) |
| MR – no. (%) | 109 (64.9) | 151 (89.8) |
| MILD MR – no. (%) | 105 (96.3) | 122 (80.7) |
| Moderate MR – no. (%) | 4 (3.6) | 29 (19.3) |
| Mild ASD – no. (%) | 35 (20.8) | 35 (20.8) |
| **Hemodynamic parameters** | | |
| MVA cm – median (IQR 25–75%) | 0.88 (0.75–1.00) | 1.70 (1.50–2.00) |
| MVG mmHg – median (IQR 25–75%) | 15 (11–19.2) | 6.5 (4.2–8.57) |
| sPAP mmHg – median (IQR 25–75%) | 44 (31.2–58.7) | 24.5 (18–30) |
| Wedge mmHg – median (IQR 25–75%) | 23 (17–30) | 15.5 (11.2–17) |
| CO I/min – median (IQR 25–75%) | 4.2 (3.6–5.0) | 4.5 (3.62–5.5) |

**PMV** = percutaneous mitral valvuloplasty; **LVDD** = left ventricle diastolic diameter; **IQR** = interquartile range; **LVSD** = left ventricle systolic diameter; **SF** = shortening fraction; **LA** = left atrium; **MVA** = mitral valve area; **MVG** = mean valve gradient; **sPAP** = systolic pulmonary artery pressure; **MR** = mitral regurgitation; **ASD** = atrial septal defect; **CO** = cardiac output.

**Table 2**

Baseline clinical and echocardiographic characteristics and immediate results in both groups.

| Variable | Group 1 (n = 42) | Group 2 (n = 126) | p value |
|----------|----------------|----------------|---------|
| Age – yr – mean ± SD | 39.5 ± 10.5 | 46.6 ± 13 | 0.005 |
| Atrial fibrillation – no. (%) | 6 (14.3) | 55 (32.7) | 1.00 |
| Female gender – no. (%) | 36 (85.7) | 110 (87.6) | 0.89 |
| NYHA FC II – no. (%) | 28 (66.6) | 77 (61.1) | 0.89 |
| NYHA FC III – no. (%) | 13 (30.9) | 44 (34.9) | 0.89 |
| NYHA FC IV – no. (%) | 1 (2.3) | 5 (3.9) | 0.89 |
| Pre-PMV MVA – cm² (IQR 25–75%) | 0.90 (0.83–1.00) | 0.90 (0.81–1.00) | NS |
| ES – value (IQR 25–75%) | 6 (5–7) | 8 (6–9) | 0.002 |
| ES > 8 – no. (%) | 7 (16.6) | 55 (32.7) | 0.003 |
| sPAP pre-PMV – mmHg (IQR 25–75%) | 47 (34–59) | 42 (35–50) | 0.07 |
| MVG – mmHg (IQR 25–75%) | 11.0 (9–16) | 11 (9–14) | NS |
| Immediate success – no. (%) | 40 (95.2) | 96 (76.2) | 0.01 |
| Post-PMV MVA – cm² (IQR 25–75%) | 1.82 (1.16–2.0) | 1.67 (1.44–1.97) | 0.02 |
| MR post-PMV – no. (%) | 34 (80.9) | 117 (92.8) | 0.04 |

Group 1 = minimal valve calcification; Group 2 = moderate to severe valve calcification.

**NYHA FC** = New York Heart Association functional class; **PMV** = percutaneous mitral valvuloplasty; **MVA** = mitral valve area; **IQR** = interquartile range; **ES** = echocardiographic score; **sPAP** = systolic pulmonary artery pressure; **MVG** = mean valve gradient; **MR** = mitral regurgitation.

28.2% were seen at 12, 24, 36, and 48 months, respectively. The presence of an ES > 8 (p = 0.03), moderate to severe mitral valve calcification (p = 0.01), and a MVA post-PMV <1.8 cm² (p < 0.01) were identified as predictors of RE after univariate analysis (Table 4). On multivariate analysis, the presence of moderate to severe mitral valve calcification (HR = 1.94, 95% CI = 1.02–5.21, p = 0.03) and an MVA post-PMV <1.8 cm² (HR = 2.6, 95% CI = 1.08–6.25, p = 0.01) was significantly correlated with RE at follow-up.

**4. Discussion**

Since 1984, PMV has become the treatment of choice in patients with rheumatic mitral valve stenosis in the absence of significant mitral regurgitation and favorable anatomic features. Several studies have shown good immediate results as well as in the long-term follow-up. Procedural success is seen in 80% of cases with a range between 73% and 99% according to published data. While Palacios et al. have reported a procedural success rate of 71.1% in...

**Table 3**

Predictors of immediate success: univariate analysis.

| Variable | Successful PMV (n = 136) | Nonsuccessful PMV (n = 32) | p value |
|----------|----------------|----------------|---------|
| Age – yr – mean ± SD | 43.5 ± 12.8 | 46.2 ± 14 | 0.77 |
| Female gender – no. (%) | 119 (87.5) | 27 (84.3) | 0.80 |
| NYHA FC III–IV – no. (%) | 46 (33.8) | 17 (53.1) | 0.06 |
| Atrial fibrillation – no. (%) | 35 (25.7) | 16 (50) | 0.01 |
| Pre-PMV MVA – cm² (IQR 25–75%) | 0.88 (0.75–1.02) | 0.90 (0.75–0.97) | 0.71 |
| ES – value (IQR 25–75%) | 7.0 (5.2–8.7) | 8.5 (7.7–10.0) | 0.002 |
| ES > 8 – no. (%) | 37 (27.2) | 15 (46.5) | 0.03 |
| MVC >1 – no. (%) | 96 (70.5) | 30 (93.75) | 0.01 |
| sPAP pre-PMV – mmHg (IQR 25–75%) | 42.5 (34–52) | 38 (34–64) | 0.83 |
| Balloon diameter – mm (IQR 25–75%) | 28 (26–30) | 28 (24–30) | 0.94 |

PMV = percutaneous mitral valvuloplasty; NYHA FC = New York Heart Association Functional Class; MVA = mitral valve area; IQR = interquartile range; ES = echocardiographic score; MVC = mitral valve calcification; sPAP = systolic pulmonary arterial pressure.
the Massachusetts General Hospital experience, lung et al\textsuperscript{8} reported a procedural success rate of 85% with a very low incidence of severe mitral regurgitation (3.4%).

Percutaneous mitral valvuloplasty results are strongly related to patient’s selection, and echocardiographic valve morphology assessment plays a special role in decision making. Well-trained cardiologists evaluated all our patients and the Abascal-Wilkins score was always considered to decide whether a PMV was suitable. This score evaluates leaflets’ thickness and mobility, commissural and valve calcification, and subvalvular changes. Patients are classified with a maximum score of 16. Those patients with an ES < 8 are considered adequate candidates for PMV and they certainly have the best immediate and long-term results.

The mechanism by which PMV achieves successful results is by commissural splitting, and severe valve calcification is likely to prevent this mechanism. Therefore, we decided to use a simple score obtained with the evaluation of the degree of valve calcification.

Immediate success was achieved in 80.1% (136) of our patients, and median MVA increased from 0.90 to 1.75 cm\(^2\). This was observed more frequently in patients with mild valve calcification (group 1) than those patients with moderate to severe valve calcification (group 2) and this finding was statistically significant. Median MVA observed in group 1 was significantly larger than that observed in group 2. Certain clinical and echocardiography features correlated with poor immediate results: ES > 8, presence of atrial fibrillation, and the presence of moderate to severe valve calcification. Multivariate analysis showed that moderate to severe valve calcification was the only predictor of lower procedural success rates (HR = 0.12, 95% CI = 0.03-0.91, p = 0.03).

Fatkin et al\textsuperscript{10} have shown the negative influence of commissural calcification in their study comprising 30 patients. Cannan et al\textsuperscript{11} retrospectively evaluated the morphology of the mitral valve apparatus on baseline echocardiogram in 149 patients, concluding that the presence of commissural calcification is a strong predictor of poor PMV results. In 2014, Dreyfus et al\textsuperscript{12} evaluated the immediate results of PMV on 464 patients divided into 3 groups according to the degree of mitral valve calcification. They found the best immediate results achieving the largest MVA in those with the lowest degrees of valve calcification.

Nevertheless, most of the published studies correlate their results with the Abascal-Wilkins score, without mentioning the severity of the valve calcification degree. These studies, including our findings, have shown the influence of the degree of mitral valve calcification on PMV results. Mitral valve calcification is easily assessed on echocardiography and results in a better post-PMV predictor than a low ES (<8).

During a follow-up period of 48 months, 86% of our patients remained asymptomatic. The rate of RE gradually increased along the study period, reaching 28.2% at the fourth year of follow-up. Univariate analysis found an ES > 8, the presence of MVC and a post-PMV MVA <1.8 cm\(^2\) as predictors of RE. After multivariate analysis, the presence of moderate to severe valve calcification and a post-PMV MVA were found as independent predictors of RE (HR = 1.94, 95% CI = 1.02–5.21 and HR = 2.6, 95% CI = 1.08–6.25, respectively).

Studies evaluating long-term follow-up regarding the presence of valve calcification are scarce. Tuzcu et al\textsuperscript{13} evaluated the presence and degree of mitral valve calcification on fluoroscopy and long-term results of PMV. We must consider the strong limitations of fluoroscopy for this purpose. Results on patients with a high ES (>10) were reported by Pos et al\textsuperscript{14} Commissural calcification was evaluated according to a score proposed by the University of South California. Immediate results were related with the calcium score, although it did not predict events in follow-up. Similar findings were obtained by Salarifar et al\textsuperscript{15} on 87 patients during a six-week follow-up. Hernandez et al\textsuperscript{16} reported 7 patients who developed severe mitral regurgitation after PMV. Six of them required early mitral valve replacement. Five of these patients had evidence of commissural calcification on anatomic pathological examination. Although Dreyfus et al\textsuperscript{12} study did not find a relation between MR development and the degree of mitral calcification, in our study, the incidence of MR after PMV in patients with moderate to severe mitral valve calcification was significantly higher.

Our study had some limitations. We have to consider that although patients were evaluated prospectively according to Abascal-Wilkins score, the analysis of the degree of mitral valve calcification was performed retrospectively. Finally, although a long recruitment period might have influenced the learning curve, all the procedures were made by the same operator, and the materials and techniques have not suffered major changes over time.

5. Conclusions

Our study shows that a simple method to assess the degree of mitral valve calcification may predict immediate and long-term results post-PMV and should always be considered while selecting patients. Although the presence of mitral valve calcification should not prevent PMV, poorer results could be expected when higher degrees of calcification are found, while those patients with lower levels of mitral valve calcification might still benefit with PMV, even with higher ES.

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Conflict of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject discussed in the manuscript.

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| Table 4 | Predictors of restenosis (univariate analysis). |
|---------|-----------------------------------------------|
| Variable | Hazard ratio (95% CI) | p value |
| Age | 1.04 (0.76–1.18) | 0.91 |
| Female gender | 0.84 (0.62–1.06) | 0.84 |
| NYHA FC III-IV | 1.20 (0.81–2.34) | 0.36 |
| Atrial fibrillation | 1.37 (0.94–3.28) | 0.09 |
| Post-PMV MVA <1.8 cm | 3.59 (1.2–7.4) | –0.01 |
| ES >8 | 2.32 (1.05–7.2) | 0.03 |
| MVC >1 | 2.57 (1.09–8.0) | 0.01 |
| sPAP >50 mmHg | 1.21 (0.76–2.9) | 0.28 |

NYHA FC = New York Heart Association Functional Class; PMV = percutaneous mitral valvuloplasty; MVC = mitral valve area; ES = echocardiographic score; MVC = mitral valve calcification; sPAP = systolic pulmonary arterial pressure.
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