Pulmonary artery pressures and outcomes after MitraClip

Yonatan Rashi¹, Dan Haberman²*, Ivaylo Tonchev¹, Alona Peretz¹, Anna Turyan Medvedovsky¹, Israel Gotsman³, Saar Minha³, Lion Poles², Sara Shimon³, Sorel Goland², Gidon Y. Perlman¹, Haim D. Danenberg¹, Ronen Beer³ and Mony Shuvy¹

¹Heart Institute, Hadassah-Hebrew University Medical Center, Jerusalem, Israel; ²Heart Center, Kaplan Medical Center, Hebrew University, Jerusalem, Israel; ³Cardiology Department, Shamir Medical Center (Assaf-Harofeh Campus), Zerifin, Israel

Abstract

Aims We evaluated the impact of MitraClip on systolic pulmonary artery pressure (sPAP) and the effects of baseline sPAP on outcomes.

Methods and results In a cohort of patients who underwent MitraClip implantation, three groups were defined according to pre-procedure sPAP levels. Clinical and echocardiographic data were compared. The study included 177 patients: 59 had severe pulmonary hypertension (PHT), 96 had mild to moderate PHT, and 22 had no PHT. In patients with pre-existing severe PHT, sPAP was reduced from 70.8 ± 9.2 to 56.8 ± 13.7 mmHg (P < 0.001), sPAP remained unchanged in patients with mild to moderate PHT but was significantly increased from 30.8 ± 4.3 to 38.6 ± 8.3 mmHg in the no-PHT group (P < 0.001). Improvement of sPAP was observed in 77% of severe PHT group, while worsening of sPAP was more common among patients with no-PHT (57% compared with 33% among the mild to moderate PHT and 7% in the severe PHT group, respectively, (P < 0.001)). One year survival was similar among the study groups.

Conclusions MitraClip decreases PHT among patients with severe PHT. A concerning finding is that most patients with no-PHT increase their sPAP.

Keywords Mitral regurgitation; Transcatheter mitral valve repair; MitraClip; Pulmonary hypertension; Heart failure

Introduction

Mitral regurgitation (MR) is the most common valve disease and the second-most common indication for valve surgery in the United States and Europe.¹,² Pulmonary hypertension (PHT) is a common finding among patients with MR and has been associated with increased mortality after mitral valve (MV) surgical intervention.³,⁴ The percutaneous edge-to-edge MV repair with MitraClip (Abbott, Menlo Park, CA, USA) is a well-established treatment for high surgical risk MR patients with more than 100 000 procedures performed. However, the impact of MitraClip on systolic pulmonary artery pressure (sPAP) and the effects of baseline sPAP on MitraClip outcomes are unclear.

The haemodynamic effects of MitraClip are complex. Repair of MR may decrease the post capillary pulmonary pressure but might create relative mitral stenosis.⁵ Trans-mitral increased gradient and the haemodynamic effects of the iatrogenic atrial septal defect (iASD) may affect post-procedural sPAP, in relation with pre-procedure values.

The German Transcatheter Mitral Valve Intervention (TRAMI) registry showed that MitraClip decreased the sPAP among patients with severe PHT, while among patients with no PHT, there was no change in sPAP.⁶ This lack of improvement in sPAP after MV intervention was also shown in patients who underwent MV surgery.⁷ Although MitraClip might be beneficial in reducing sPAP among patients with severe PHT, their long-term survival remained low⁶,⁸ and in
fact, in the recent Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation (COAPT) trial, patients with sPAP $> 70$ mmHg were excluded. Furthermore, there is even disagreement regarding the definition of the severity of PHT, several studies defined severe sPAP as greater than $50$ mmHg, while others defined it as greater than $60$ mmHg. Only few studies have examined the interrelations between PHT and MitraClip performance. The purpose of our study is to evaluate the impact of MitraClip in patients with pre-existing severe, mild to moderate, and no PHT.

**Methods**

**Study design**

An observational, retrospective cohort study was performed.

**Study population**

We studied a cohort of consecutive patients who underwent MitraClip implantation between September 2014 and September 2019, in two Israeli medical centres: Hadassah University Medical Center in Jerusalem and Kaplan Medical Center in Rehovot. Patients were followed for at least 6 months until 30 March 2020. We excluded from the analysis four patients who underwent combined MV and tricuspid valve (TV) clipping, seven patients who died within a week of the MitraClip implantation, 10 patient with unmeasurable TV pressure gradient or missing data. Six patients who underwent redo MitraClip procedure were considered as separate cases. A multidisciplinary heart team of non-interventional cardiologists, interventional cardiologists, cardiothoracic surgeons, and anaesthesiologists has assessed the patients, and all were deemed as high risk for surgery. The study protocol was approved by the institutional ethical committee, and all patients received thorough verbal and written explanations about MitraClip implantation procedure and signed informed consent.

**Echocardiographic assessment**

Transthoracic echocardiography and transesophageal echocardiography were performed to evaluate severity of MR and to assess suitability for MitraClip implantation. MR severity was initially assessed by integrated multi-parametric visual evaluation tool in accordance with standard clinical practice (incorporating 2D, spectral and colour Doppler images), using an ordinal scale (grading 0—no MR, 1 + mild MR, 2 + moderate MR, 3 + moderate to severe MR, and 4 + severe MR). Systolic pulmonary artery pressure was estimated by calculating the amount of maximal tricuspid pressure gradient using continuous-wave Doppler and the estimated right atrial pressure based on inferior vena cava size and changes during inspiration. Three groups were defined according to pre-procedure sPAP levels: no PHT (sPAP $\leq 35$ mmHg), mild to moderate PHT ($35 < \text{sPAP} < 60$ mmHg), and severe PHT (sPAP of $\geq 60$ mmHg). In addition, we collected echocardiographic data of left ventricle (LV) end diastolic and systolic diameter, LV ejection fraction, mean MV gradient, tricuspid regurgitation (TR) severity grade, and LV and right ventricle (RV) dysfunction grades. All echocardiographic data were collected at three stages: before the procedure, before discharge from the hospital, and at the first follow-up visit at 6 month.

We evaluated baseline characteristics, clinical and procedural data including complications and New York Heart Association (NYHA) class at 6 months, and 1 year after the procedure. Procedural success was defined as a residual MR grade of 2+ or less after clip implantation in accordance with MVARC definition. After up to 6 months, and then every 6 months to a year, patients were invited for follow-up at the clinic that including general questioner, physical examination, and transthoracic echocardiography.

**Invasive measurements**

Pressure reading from the left atrium was measured before the procedure using the trans-septal Sheath, during the procedure using the MitraClip guide after clip delivery system removal.

**Statistical analysis**

Most of the analysis was performed by comparing the comparing three groups of baseline PHT severity. Age, sPAP, MV gradient, and other continuous parameters were expressed as mean $\pm$ standard deviation and compared with one-way ANOVA test in case of three groups and paired $t$-test in case of comparing two groups.

Sex, clinical background disease, NYHA class, PHT severity grade, and other ordinal or nominal parameters were expressed as percentage and compared with $\chi^2$ square test for nominal parameters and McNemar test for ordinal parameters. Kaplan–Meier method was used for survival analysis and the log-rank test to compare the groups. The SPSS software (Version 25) was used for analysis, and $P$ value $< 0.05$ was considered to be significant.
Results

The study included 177 patients that underwent MitraClip procedure between September 2014 and September 2019 (Table 1).

Ninety-four per cent were an elective procedure, and 6% were an urgent MitraClip procedure. Mean age was 74.8 ± 10 years old, 58% of patients were men, and most patients had functional MR and were in NYHA class of III or IV. The median Euroscore was 6.4% with interquartile range of 4% to 11.8%. Fifty-seven patients were implanted with single clip, 108 with 2 clips and 22 with three clips. One hundred and seventy patients were implanted with either NT or NTR, and 17 were implanted with XTR.

Improvement in MR severity to grade +2 or less was achieved in 88.5% of patients. Five patients had peri-procedural complications resulted including tamponade, hemotorax, right atrial dissection, leaflet tear, and hemodynamic collapse. Stroke or clip embolization was not observed. Improvement in NYHA class was shown in 84% of patients, and 40% of them improved their NYHA class by at least 2 degrees 6 month follow-up.

The cohort was divided into three groups according to baseline sPAP values, 59 patients (33.3%) were classified as severe PHT group, 96 patients (54.2%) as mild or moderate PHT group, and 22 patients (12.5%) as no-PHT group. Most baseline characteristics were similar between the three groups apart of atrial fibrillation, which was more common among patients with severe PHT (Table 1). Baseline left atrial V-wave was not significantly different among PHT groups. The baseline echocardiographic findings and invasive measurements are presented in Table 2.

The average post procedure sPAP of the entire cohort was decreased from 54.1 to 49.9 mmHg (P < 0.001), an 8% decrease from baseline. The percentage of patients who were classified as severe PHT was reduced from 34% to 20% post-procedure (P < 0.001) (Figure 1).

Changes of post-procedural sPAP were correlated with baseline pulmonary pressures. In patients with pre-existing severe PHT, sPAP was reduced from 70.9 ± 9.3 mmHg to

Table 1 Baseline characteristics (n = 177)

| Variable               | No PHT (n = 22) | Mild or moderate (n = 96) | Severe PHT (n = 59) | P value |
|------------------------|-----------------|--------------------------|---------------------|---------|
| Age                    | 73.8 ± 10.7     | 73.5 ± 10.4              | 76.2 ± 9.4          | 0.270   |
| Gender (Male)          | 46%             | 57%                      | 64%                 | 0.291   |
| BMI                    | 26.1 ± 4.9      | 28.1 ± 5.6               | 26.5 ± 5            | 0.101   |
| Euroscore (%)          | 8.4 ± 6.8       | 11.3 ± 11.3              | 8.4 ± 8.3           | 0.156   |
| Functional MR          | 67%             | 78%                      | 60%                 | 0.069   |
| NYHA class III/IV      | 91%             | 99%                      | 100%                | 0.014   |
| CVA                    | 46%             | 70%                      | 61%                 | 0.086   |
| Post MI                | 39%             | 62%                      | 43%                 | 0.062   |
| Post PCI               | 33%             | 57%                      | 46%                 | 0.162   |
| Pacemaker              | 50%             | 34%                      | 36%                 | 0.381   |
| S/P CABG               | 27%             | 31%                      | 19%                 | 0.248   |
| AF/flutter             | 27%             | 43%                      | 58%                 | 0.034   |
| Diabetes               | 23%             | 46%                      | 36%                 | 0.091   |
| Post CVA/TIA           | 14%             | 18%                      | 18%                 | 0.868   |
| Oncological disease    | 23%             | 20%                      | 19%                 | 0.917   |
| HTN                    | 82%             | 91%                      | 83%                 | 0.293   |
| Hyperlipidaemia        | 86%             | 81%                      | 72%                 | 0.283   |
| Smoking                | 44%             | 42%                      | 42%                 | 0.991   |
| CKD IV                 | 65%             | 53%                      | 63%                 | 0.479   |
| COPD                   | 9%              | 18%                      | 10%                 | 0.313   |
| OSA                    | 6%              | 12%                      | 12%                 | 0.582   |
| Asthma                 | 6%              | 3%                       | 2%                  | 0.795   |
| Haemoglobin (g/dL)     | 11.3 ± 1.3      | 11.9 ± 1.9               | 11.7 ± 1.6          | 0.316   |
| Creatinine (mmol/L)    | 155 ± 119       | 142 ± 113                | 140 ± 81            | 0.849   |
| GFR                    | 53 ± 32         | 57 ± 28                  | 54 ± 38             | 0.788   |
| Albumin (g/L)          | 38.6 ± 7.1      | 37.1 ± 4.6               | 36.8 ± 4.8          | 0.521   |
| Antiplatelets          | 53%             | 50%                      | 48%                 | 0.930   |
| ACEi or ARBs           | 50%             | 79%                      | 71%                 | 0.022   |
| Anticoagulants         | 28%             | 49%                      | 65%                 | 0.025   |
| Beta blockers          | 82%             | 89%                      | 88%                 | 0.681   |
| Digoxin                | 9%              | 11%                      | 12%                 | 0.919   |

ACEi, angiotensin converting enzyme inhibitor; AF, Atrial fibrillation; ARB, angiotensin receptor blocker; BMI, body mass index; CABG, coronary artery bypass graft; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; GFR, glomerular filtration rate; HTN, hypertension; LV, left ventricle; LVEF, left ventricle ejection fraction; MI, myocardial infarction; OSA, obstructive sleep apnoea; PCI, percutaneous coronary intervention; PHT, pulmonary hyper tension; RV, right ventricle; TIA, transient ischemic attack; TR, tricuspid regurgitation; Significant P Value (P < 0.05) in bold.

Table 2 Baseline echocardiographic findings and invasive measurements (n = 177)

| Variable               | No PHT (n = 59) | Mild to moderate (n = 96) | Severe PHT (n = 22) | P value |
|------------------------|-----------------|--------------------------|---------------------|---------|
| LVEF (%)               | 49 ± 17         | 39 ± 15                  | 44 ± 18             | 0.119   |
| MR severity grade      | Moderate 4.5%   | 7.1%                     | 3.8%                | 0.886   |
|                       | (+2)            |                          |                     |         |
|                       | Mod-severe 18.2%| 21.2%                    | 17.3%               |         |
|                       | (+3)            |                          |                     |         |
|                       | Severe 77.3%    | 71.8%                    | 78.8%               |         |
|                       | (+4)            |                          |                     |         |
| TR severity grade      | Non-mild 36.4%  | 23.2%                    | 10.5%               | 0.101   |
|                       | Moderate 40.9%  | 46.2%                    | 42.1%               |         |
|                       | Severe 22.7%    | 30.8%                    | 47.4%               |         |
| RV dysfunction         | Non 63.2%       | 69.8%                    | 53.7%               |         |
|                       | Mild 10.5%      | 11.6%                    | 25.9%               |         |
|                       | Moderate 15.8%  | 11.6%                    | 18.5%               |         |
|                       | Severe 10.5%    | 7%                       | 1.9%                |         |
| LV dysfunction         | Non 33.3%       | 23.3%                    | 48.1%               | 0.045   |
|                       | Mild 19%        | 12.2%                    | 11.1%               |         |
|                       | Moderate 4.8%   | 20%                      | 9.3%                |         |
|                       | Severe 42.9%    | 44.4%                    | 31.5%               |         |
| V-wave (mmHg)          | 30.1 ± 11.4     | 33.8 ± 14.1              | 33.5 ± 12.40.719    |         |

LVEF, left ventricle ejection fraction; PHT, pulmonary hyper tension; RV, right ventricle; sPAP, systolic pulmonary artery pressure; TIA, transient ischemic attack; TR, tricuspid regurgitation.
56.9 ± 13.7 mmHg (P < 0.001), while in patients with mild or moderate PHT, the average sPAP (48.9 ± 6.2 mmHg) remained unchanged. In patients without pre-procedure PHT, there was a significant increase in sPAP from 30.8 ± 4.4 mmHg to 38.6 ± 8.3 mmHg (P < 0.001). In all groups, the initial trends in pulmonary blood pressure were remained unchanged during the follow-up period (Figure 2).

There was a significant V-wave reduction before and after the procedure (33.8 to 18.1 mmHg, P = 0.001) in the entire cohort. Higher V-wave at baseline was correlated with more prominent decrease in V-wave, $R^2 = 0.701$.

The change in V-wave was least prominent in the No PHT group, compared with the moderate and severe PHT groups.

This change, however, was not statistically significant (8.8, 15.8, and 16.9 mmHg, respectively, $P = 0.215$).

Significant changes in sPAP (defined as an increase/decrease of at least 5 mmHg compared with baseline pressures) occurred in most of patients and were related to baseline sPAP. Improvement of sPAP was observed in 77% of the severe PHT group, compared with 37% and 5% among the mild to moderate PHT and no PHT groups, respectively ($P < 0.001$). Worsening of sPAP was more common among patients with no PHT (57% compared with 33% among the mild to moderate PHT and 7% in the severe PHT group, respectively ($P < 0.001$) (Figure 3). The number of patients in each PHT severity group, pre-procedure, and post-procedure severity

---

**Figure 1** Alternations in PHT severity of the study population at different time periods: baseline, few days after MitraClip and 1–6 months follow-up. PHT, pulmonary hypertension.

**Figure 2** Systolic pulmonary artery pressure according to pre-procedure PHT severity groups. (A) Box plot of sPAP—median, interquartile range (IQR) and 95% confidence interval. (B) Column chart of sPAP—mean ± SD. PHT, pulmonary hypertension; sPAP, systolic pulmonary artery pressure.
group is presented in Figure 4. Improvement in NYHA class was also associated with severity of baseline PHT, occurring in 92.5% of patients with severe PHT compared with only 80% in patients with non-severe PHT ($P = 0.049$).

To further explore the potential factors that might be associated with the increase in sPAP among the no PHT group, we evaluated the post-procedure mitral valve gradients (MVGs). The average MVG of the entire cohort was 4.1 ± 2.1 mmHg, and 31 patients (19%) had a MVG ≥ 6 mmHg. MVG ≥ 6 mmHg was significantly more common among no PHT group, 38% compared with 16% of the rest of the cohort, ($P = 0.032$) and was associated with less improvement in NYHA class. Only 72% of patients with MVG ≥ 6 mmHg had improvement in their NYHA class compared with 87% among the rest of the cohort ($P = 0.048$).

LV, and RV functions, and the severity of TR were similar between the study groups and were not significantly changed after MitraClip (Table 3).

To further evaluate the impact of post-procedural residual MR and baseline severe TR on pulmonary pressures, we repeated the analysis after excluding 22 patients with residual MR ($>2$) at the end of the procedure, and similar results were observed. The low rate of improvement in sPAP in the low PHT group was consistent. After excluding patient with severe TR (62 patients, 33%), there was no significant change in the results, and the impact of baseline PHT on outcomes remained unchanged.

**Figure 3** Significant alternations in systolic pulmonary artery pressure, defined as at least change of 5 mmHg, according to baseline PHT severity groups. PHT, pulmonary hypertension.

**Figure 4** Alternations between the severity of PHT groups, pre-procedure (left) and immediately after (right). A black line indicates a static state, a green line indicates improvement, and a red line indicates deterioration. For example, among 90 patients with mild to moderate PHT at baseline, 17 patients improved, 14 patients worsened, and 59 patients remained with mild to moderate PHT. PHT, pulmonary hypertension.
Fifty per cent of patients had same degree of ASD at 6 month follow-up. The presence of ASD was similar in the three baseline PHT groups. sPAP was not statistically different between patient with or without ASD at 6 month follow-up.

One year survival was similar among the study groups (88%, 86%, and 83% in the no PHT, mild to moderate PHT, and severe groups, respectively, \( P = 0.33 \)) in Kaplan–Meier analysis (Figure 5A).

We also analysed outcomes according alteration in sPAP after the MitraClip. Patients who worsened their sPAP were less likely to improve their NYHA class (66% compared with 90% in the rest on the cohort, \( P = 0.003 \)). There was no correlation between survival and post-procedural sPAP trends—decreased, not changed or increased (1 year survival 83%, 82%, and 88%, respectively; \( P = 0.71 \)) (Figure 5B).

When comparing no PHT with both PHT groups, NYHA class improvement was less significant in the no PHT group, \( P = 0.045 \) (Table 3).

### Discussion

The study analysed the effect of MitraClip procedure on sPAP and outcomes in relation to pre-existing sPAP. We showed an improvement of sPAP among the entire cohort and a decrease in the number of patients with severe PHT (sPAP ≥ 60 mmHg) from more than one-third of the cohort at baseline to only one-fifth following MitraClip. Changes of post-procedural sPAP were directly related to baseline sPAP. Greater improvement in PHT was observed in patients who had severe pre-procedure PHT. In patients with mild to moderate PHT, sPAP remained unchanged. Although patients with no PHT at baseline worsened their sPAP following the procedure, this was not associated with effects upon survival. These results remained unchanged after excluding patients with significant post-procedural residual MR and patients with severe TR.

Pulmonary hypertension is common among patients with MV disease due to backwards transmission of elevated left atrial pressure. At early stages, pulmonary vascular resistance is normal (isolated post-capillary PHT), chronic left atrial pressure elevation might promote pulmonary vascular remodeling, which will develop to pulmonary vascular component of PHT. Our findings suggest that although the clinical baseline characteristics of study groups were similar, the reduction in PHT was observed only in patients with severe PHT. The explanation for these findings is not clear given the various determinants of PHT in patients with chronic MR who underwent MitraClip procedure. It is reasonable to assume

### Table 3 Echocardiographic and NYHA class changes by pre-procedure PHT severity (n = 177)

| Variable                | No PHT | Mild to moderate PHT | Severe PHT | \( P \) value total |
|-------------------------|--------|----------------------|------------|---------------------|
| LV EF (%)               | 49 ± 13| 52 ± 16              | 38 ± 3     | 0.35 <0.01          |
| MR severity grade       |        |                      |            |                     |
| Non-moderate            | 5%     | 7%                   | 2%         | 88%                 |
| Mod-severe              | 18%    | 21%                  | 18%        | 5%                  |
| Severe                  | 77%    | 72%                  | 80%        | 7%                  |
| TR severity grade       | 0.189  | 0.962                | 0.307      | 0.885               |
| Non-mild                | 29%    | 14%                  | 10%        | 10%                 |
| Moderate                | 47%    | 48%                  | 38%        | 48%                 |
| Severe                  | 24%    | 38%                  | 52%        | 42%                 |
| RV dysfunction          | 0.392  | 0.484                | 0.149      | 0.380               |
| Non                     | 50%    | 66%                  | 50%        | 70%                 |
| Mild                    | 14%    | 7%                   | 28%        | 11%                 |
| Moderate                | 22%    | 16%                  | 19%        | 11%                 |
| Severe                  | 14%    | 11%                  | 3%         | 8%                  |
| LV dysfunction          | 0.172  | 0.65                 | 0.615      | 0.448               |
| Non                     | 37%    | 24%                  | 56%        | 56%                 |
| Mild                    | 19%    | 10%                  | 15%        | 9%                  |
| Moderate                | 0%     | 20%                  | 12%        | 15%                 |
| Severe                  | 44%    | 46%                  | 17%        | 20%                 |
| NYHA                    |        |                      |            |                     |
| Pre FU                  | <0.01  | Pre Pre <0.01        | Pre FU <0.01 | 0.045*             |
| I                       | 0%     | 0%                   | 0%         | 8%                  |
| II                      | 9%     | 1%                   | 0%         | 75%                 |
| III                     | 55%    | 56%                  | 47%        | 17%                 |
| IV                      | 36%    | 43%                  | 53%        | 0%                  |

LVEF, left ventricle ejection fraction; NYHA, New York Heart Association class; PHT, pulmonary hypertension; RV, right ventricle; TIA, transient ischemic attack; TR, tricuspid regurgitation. \( P \) value calculated by McNemar test.

*Non-PHT compared with both PHT groups.
that MR reduction improve the post-capillary component; therefore, patients with severe PHT at baseline (which have high post capillary pressure) decrease their sPAP and consequently improve NYHA class. Similar trend was shown in the TRAMI registry, a significant reduction of 10 mmHg in sPAP values in patients with severe PHT at baseline.

On the other hand, procedural factors like iASD and elevated MVG following clip implantation can promote an increase in pulmonary pressure. Post-MitraClip iASD often promotes immediate volume and pressure relief of the left atrium and marked decrease in pulmonary capillary wedge pressure. However, right to left shunt is also associated with RV dilatation and PHT as well as worse clinical outcomes and increased long-term mortality among patients after MitraClip. Elevated MV pressure gradient after MitraClip implantation might also impact outcomes and indeed Neuss et al. showed that the increased residual MVG > 5 mmHg was a significant outcome predictor. We showed that patients with no PHT at baseline had a significant increase of 8 mmHg in sPAP after MitraClip. It is possible that this concerning finding was caused by the haemodynamic effects of residual shunt, and increased trans-mitral gradient were translated to an increase in PHT. Indeed, our findings suggest that patients with no PHT are more likely to have ≥6 mmHg post-procedural MVG. The increase in MVG was associated with decrease improvement in NYHA class.

There was no significant difference in TV gradient or RV function between the three baseline PHT groups, which could have explained this increase in sPAP.

This kind of trend, baseline sPAP pressures below 36 mmHg population resulted in higher sPAP post-procedure, was also demonstrated in TRAMI registry but was not further elaborated. The increase in PHT as well as the relative modest improvement in NYHA class should be considered in the selection of patients for MitraClip. In addition, the quality of the implantation should be analysed carefully, and repositioning of the clip may be considered in the case of an elevated pressure gradient over the MV particularly in this population.

While other studies have shown lower survival in patients with pre-procedural severe PHT, their survival was similar in our study. To further evaluate this issue, we performed a log-rank analysis for patients who had improved their pulmonary pressure compared with patients whose sPAP had worsened or remained unchanged and showed that survival was similar. This suggests that there was no association between alternations in pulmonary pressures and mortality. The similar survival might be related by the older age and the

![Figure 5](image-url)
comorbidities of the cohort; however, we cannot exclude that our study was underpowered to show a survival difference between the study groups.

Limitations

There are several limitations to this study. First, the present study is a retrospective analysis of collected data from two medical centres in Israel, representing relatively small studied cohorts of patients. Validation in a large multicentre prospective study is required. Second, invasive right heart catheterization—the gold standard of PHT diagnosis—was not performed.

Third, as mentioned before the cut-off for definition on severe PHT is undetermined, we chose to use 60 mmHg as the cut-off. Utilizing additional cut-offs (55 and 50 mmHg) in repeated analysis demonstrated similar results, assist to transcend this limitation.

Finally, similar mortality rate in our study might be related to the relatively small number of patients. The impact of PHT on mortality among patient who were treated with MitraClip should be evaluated in larger studies.

Conclusions

Percutaneous MV repair improves sPAP. The reduction in sPAP was attributed mainly to patients with severe PHT at baseline. Increase in sPAP among patients with normal PHT at baseline and higher rates of elevated MV gradients are concerning findings. Additional studies are required to shed light on this phenomenon.

Impact on daily practice

MitraClip procedure reduces sPAP, especially in patients with pre-procedural severe PHT. In patients with no PHT, sPAP may increase significantly and result in clinical benefit attenuation.

Conflict of interest

None declared.

References

1. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Fleisher LA, Jneid H, Mack MJ, McLeod CJ, O’Gara PT, Rigolin VH, Sundt TM 3rd, Thompson A. 2017 AHA/ACC Focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2017; 70: 252–289.

2. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Jung B, Lancellotti P, Lansac E, Rodriguez Munoz D, Rosenhek R, Sjogren J, Tornos Mas P, Vahanian A, Walther T, Wendler O, Windecker S, Zamorano JL. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J 2017; 38: 2739–2791.

3. Lam CS, Boogaard BA, Kane GC, Enders FT, Rodeheffer RJ, Redfield MM. Age-associated increases in pulmonary artery systolic pressure in the general population. Circulation 2009; 119: 2663–2670.

4. Szwejkowski BR, Elder DH, Shearar F, Jack D, Choy AM, Pringle SD, Struthers AD, George J, Lang CC. Pulmonary hypertension predicts all-cause mortality in patients with heart failure: a retrospective cohort study. Eur J Heart Fail 2012; 14: 162–167.

5. Feldman T, Guerrero M. Assessing the balance between less mitral regurgitation and more residual transmitial pressure gradient after MitraClip. JACC Cardiovasc Interv 2017; 10: 940–941.

6. Tigges E, Blankenberg S, von Bardeleben RS, Zurn C, Bekeredjian R, Ouarrak T, Sievert H, Nickenig G, Boekstegers P, Senges J, Schillinger W, Lubos E. Implication of pulmonary hypertension in patients undergoing MitraClip therapy: results from the German transcatheter mitral valve interventions (TRAMI) registry. Eur J Heart Fail 2018; 20: 585–594.

7. Ghoreishi M, Evans CF, DeFilippi CR, Hobbs G, Young CA, Griffith BP, Gammie JS. Pulmonary hypertension adversely affects short- and long-term survival after mitral valve operation for mitral regurgitation: implications for timing of surgery. J Thorac Cardiovasc Surg 2011; 142: 1439–1452.

8. Matsumoto T, Nakamura M, Yew W, Hussaini A, Ram V, Makar M, Gurudevan SV, Trento A, Siegel RJ, Kar S. Impact of pulmonary hypertension on outcomes in patients with functional mitral regurgitation undergoing percutaneous edge-to-edge repair. Am J Cardiol 2014; 114: 1735–1739.

9. Mack MJ, Abraham WT, Lindenfeld J, Bolling SF, Feldman TE, Grayburn PA, Kapadia SR, McCarthy PM, Lim DS, Udelson JE, Zile MR, Gammie JS, Gillinov AM, Glower DD, Heimansohn DA, Suri RM, Ellis JT, Shu Y, Kar S, Weissman NJ, Stone GW. Cardiovascular outcomes assessment of the MitraClip in patients with heart failure and secondary mitral regurgitation: design and rationale of the COAPT trial. Am Heart J 2018; 205: 1–11.

10. Zoghbi WA, Enriquez-Sarano M, Foster E, Grayburn PA, Kraft CD, Levine RA, Nihoyannopoulos P, Otto CM, Quinones MA, Rakowski H, Stewart WJ, Waggoner A, Weissman NJ. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. J Am Soc Echocardiogr 2003; 16: 777–802.

11. Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Baron-Esquivias G, Baumgartner H, Borger MA, Carrel TP, De Bonis M, Evangelista A, Falk V, Lung B, Lancellotti P, Pierard L, Price S, Schafers HJ, Schuler G, Stepinska J, Swedberg K, Takkenberg J, Von Oppell UO, Windecker S, Zamorano JL, Zembala M. Guidelines on the management of valvular heart disease (version 2012): the Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Eur
12. Stone GW, Adams DH, Abraham WT, Kappetein AP, Genereux P, Vranckx P, Mehran R, Kuck KH, Leon MB, Piazza N, Head SJ, Filippatos G, Vahanian AS. Clinical trial design principles and endpoint definitions for transcatheter mitral valve repair and replacement: part 2: endpoint definitions: a consensus document from the mitral valve academic research consortium. J Am Coll Cardiol 2015; 66: 308–321.

13. Schueler R, Ozturk C, Wedekind JA, Werner N, Stockigt F, Mellert F, Nickenig G, Hammerstingl C. Persistence of iatrogenic atrial septal defect after interventional mitral valve repair with the MitraClip system: a note of caution. JACC Cardiovasc Interv 2015; 8: 450–459.

14. Biaggi P, Felix C, Gruner C, Herzog BA, Hohlfeld S, Gaemperli O, Stahli BE, Paul M, Held L, Tanner FC, Grunenfelder J, Corti R, Bettes D. Assessment of mitral valve area during percutaneous mitral valve repair using the MitraClip system: comparison of different echocardiographic methods. Circ Cardiovasc Imaging 2013; 6: 1032–1040.

15. Toyama K, Rader F, Kar S, Kubo S, Shiota T, Nishioka T, Siegel RJ. Iatrogenic atrial septal defect after percutaneous mitral valve repair with the MitraClip system. Am J Cardiol 2018; 121: 475–479.

16. Del Trigo M, Bergeron S, Bernier M, Amat-Santos IJ, Puri R, Campelo-Parada F, Altisent OA, Regueiro A, Eigler N, Rozenfeld E, Pibarot P, Abraham WT, Rodes-Cabau J. Unidirectional left-to-right interatrial shunting for treatment of patients with heart failure with reduced ejection fraction: a safety and proof-of-principle cohort study. Lancet (London, England) 2016; 387: 1290–1297.

17. Block PC. The transseptal conundrum. JACC Cardiovasc Interv 2015; 8: 460–461.

18. Neuss M, Schau T, Isotani A, Pilz M, Schopp M, Butter C. Elevated mitral valve pressure gradient after MitraClip implantation deteriorates long-term outcome in patients with severe mitral regurgitation and severe heart failure. JACC Cardiovasc Interv 2017; 10: 931–939.

19. Al-Bawardy R, Vemulapalli S, Thourani VH, Mack M, Dai D, Stebbins A, Palacios I, Inglessis I, Sakhuja R, Ben-Assa E, Passeri JJ, Dal-Bianco JP, Yucel E, Melnitchouk S, Vlahakes GJ, Jassar AS, Elmariah S. Association of pulmonary hypertension with clinical outcomes of transcatheter mitral valve repair. JAMA Cardiology 2020; 5: 47–56.