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Use of MitraClip for mitral valve repair in patients with acute mitral regurgitation following acute myocardial infarction: Effect of cardiogenic shock on outcomes (IREMMI Registry)

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ORIGINAL STUDIES

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Use of MitraClip for mitral valve repair in patients with acute mitral regurgitation following acute myocardial infarction: Effect of cardiogenic shock on outcomes (IREMMI Registry)

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Abbreviations: AMI, acute myocardial infarction; CS, cardiogenic shock; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; MVARC, Mitral Valve Academic Research Consortium; NYHA, New York Heart Association; PMVR, percutaneous mitral valve repair; SPAP, systolic pulmonary arterial pressure.

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Abstract

Objectives: To assess outcomes in patients with acute mitral regurgitation (MR) following acute myocardial infarction (AMI) who received percutaneous mitral valve repair (PMVR) with the MitraClip device and to compare outcomes of patients who developed cardiogenic shock (CS) to those who did not (non-CS).

Background: Acute MR after AMI may lead to CS and is associated with high mortality.

Methods: This registry analyzed patients with MR after AMI who were treated with MitraClip at 18 centers within eight countries between January 2016 and February 2020. Patients were stratified into CS and non-CS groups. Primary outcomes were mortality and rehospitalization due to heart failure. Secondary outcomes were acute procedural success, functional improvement, and MR reduction. Multivariable Cox regression analysis evaluated association of CS with clinical outcomes.

Results: Among 93 patients analyzed (age 70.3 ± 10.2 years), 50 patients (53.8%) experienced CS before PMVR. Mortality at 30 days (10% CS vs. 2.3% non-CS; p = .212) did not differ between groups. After median follow-up of 7 months (IQR 2.5–17 months), the combined event mortality/re-hospitalization was similar (28% CS vs. 25.6% non-CS; p = .793). Likewise, immediate procedural success (90% CS vs. 93% non-CS; p = .793) and need for reintervention (CS 6% vs. non-CS 2.3%, p = .621) or re-admission due to HF (CS 13% vs. NCS 23%, p = .253) at 3 months did not differ. CS was not independently associated with the combined end-point (hazard ratio 1.1; 95% CI, 0.3–4.6; p = .889).

Conclusions: Patients found to have significant MR during their index hospitalization for AMI had similar clinical outcomes with PMVR whether they presented in or out of cardiogenic shock, provided initial hemodynamic stabilization was first achieved before PMVR.

KEYWORDS
acute myocardial infarction, cardiogenic shock, MitraClip, mitral regurgitation, percutaneous mitral valve repair

1 | INTRODUCTION

Acute mitral regurgitation (MR) may develop in the setting of an acute myocardial infarction (AMI) as a result of papillary muscle dysfunction or rupture. Acute MR is a severe complication that may occur in up to 3% of AMI patients, is more prevalent in patients presenting with hemodynamic instability, and has been linked to a worse prognosis even in the modern era of transcatheter reperfusion.[1-4] Acute MR without papillary muscular rupture may induce severe MR due to leaflet tethering produced by the sudden onset of regional or global left ventricular dysfunction and can lead to pulmonary edema or cardiogenic shock (CS) during the acute or subacute phase of the MI.[5] Thus, more commonly patients who present with AMI may also be found to have severe functional mitral regurgitation. Although percutaneous revascularization may improve the degree of MR,[4] in some cases, MR remains unaltered or worsens, potentially leading to clinical deterioration that may prompt intervention.

Until recently, the only intervention for correcting MR was surgery; however, surgery is associated with high rates of morbidity and increased mortality nearing 20–25%.[6] Additionally, patients treated solely with medical therapy have the highest mortality rates.[7] Therefore, the development of less invasive interventions for repairing MR would be beneficial. The method of percutaneous mitral valve repair (PMVR) with the MitraClip device (Abbot Vascular, Santa Clara, California) has been shown to be a safe and effective technique for reducing MR in patients who are at high risk for open-heart surgery,[8] and this method can improve symptoms, quality of life, and prognosis in patients with functional MR.[9-12] Whereas most MR cases are in patients who are in a stable clinical situation with advanced functional

class and chronic MR, patients with acute MR are underrepresented in registries and randomized trials.

Although experiences with MitraClip for correcting MR following AMI have been reported,[13-17] data on the effect of this treatment in patients who develop CS during the event are lacking, and the issue remains understudied. The aim of this registry-based study was to assess procedural, clinical, and echocardiographic outcomes of patients with acute MR after AMI who were treated by PMVR with the MitraClip device and to assess whether patients who developed CS had different outcomes from those who did not (non-CS).

2 | METHODS

We performed a registry-based record review study by assessing all consecutive patients who were found to have severe MR when presenting with AMI and who underwent PMVR with the MitraClip device in 18 centers worldwide between January 2016 and January 2020. A list of participating centers is shown in Table S1.

3 | PATIENT POPULATION

3.1 | Inclusion criteria

Patients were included in the study who had an AMI in the prior 4 weeks and experienced symptomatic severe MR that was diagnosed by transthoracic echocardiogram or transesophageal echocardiogram following current guidelines and recommendations.[18,19] Symptoms of MR were different from heart failure to CS. All patients were considered by a heart team to be at high risk for conventional surgery.

3.2 | Exclusion criteria

Patients were excluded if their anatomy was not suitable for MitraClip implantation.

All patients were cared for following current practice guidelines for both AMI and acute heart failure.[6,20] Administration of intravenous diuretics and inotropes/vasopressors and indication for mechanical ventilation or circulatory support before PMVR were conducted based on attending team criteria. Patients with CS included those patients who fulfilled the CS definition of the Society for Cardiovascular Angiography and Intervention Stage C-E.[21] The timing of shock evaluation to classify patients was the time of MitraClip strategy decision.

3.3 | Procedure

All procedures were performed in a cardiac catheterization laboratory or in a hybrid room, and patients were under general anesthesia using transesophageal echocardiogram and fluoroscopic guidance. Preprocedural transthoracic and transesophageal echocardiography were performed in all patients for semiquantitative MR analysis and to assess morphologic suitability for MitraClip implantation.

3.4 | Study end points

Baseline and echocardiographic features and immediate procedural outcomes were collected. Procedural and clinical adverse events during follow-up were defined according to the Mitral Valve Academic Research Consortium.[22] Technical success was defined as correct implantation of at least one clip and the absence of procedural mortality or emergent cardiovascular intervention related to the device or the access site. Immediate procedural success was defined as technical success associated with a reduction of MR to ≤2+. Procedural success at 30-days follow-up was defined as device success in the absence of life-threatening bleeding, major vascular or structural complications, MI, severe acute kidney injury, or hemodynamic instability. Total mortality and admission due to heart failure were the main clinical end-points. Secondary outcomes were acute procedural success, periprocedural complications, functional improvement, and MR reduction.

Echocardiographic and clinical follow-up were carried out per New York Heart Association functional classification. Patients were contacted by phone if necessary. Data collection was approved by the local ethics committee of every institution and written informed consent was obtained.

3.5 | Statistical analysis

Continuous variables were summarized as mean ± *SD* or as median and interquartile range (IQR). Comparisons were made using unpaired Student's *t*-test or the nonparametric Wilcoxon rank sum test if data did not follow a normal distribution. Distribution normality was assessed with the Shapiro–Wilk test. Categorical variables were described as percentages and were compared using Chi-square test for frequencies greater than 5 and Fisher exact test for frequencies less than 5. Survival curves for time-to-event were constructed using all available follow-up data with Kaplan–Meier estimates. Comparisons between CS and non-CS patients were performed using the log-rank test. A Cox-regression analysis adjusted by age, EuroScore II, and acute procedural success was performed to evaluate the independent effect of CS on clinical events. A p-value <.05 was considered statistically significant. Statistical analyses were performed using SPSS version 25.0. (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.).

4 | RESULTS

A total of 93 records in the IREMMI registry of patients who had mitral valve repair with the MitraClip device between January 2016

TABLE 1 Baseline characteristics

	Total *n* = 93	CS *n* = 50	Non-CS *n* = 43	*p*-value
Variables				
Age, years	70 ± 10	68 ± 10	72 ± 9	.061
Male, *n* (%)	45 (48)	25 (50)	20 (46)	.836
Diabetes, *n* (%)	40 (43)	23 (46)	17 (40)	.672
Hypertension, *n* (%)	65 (70)	33 (66)	32 (74)	.486
BMI (kg/m$^{2)}$	26 ± 5	26 ± 4	26 ± 5	.574
Dyslipidaemia, *n* (%)	58 (62)	28 (56)	30 (69)	.192
COPD, *n* (%)	16 (17)	7 (14)	9 (21)	.417
Previous MI, *n* (%)	53 (57)	28 (56)	25 (58)	1.000
Previous stroke, *n* (%)	13 (14)	9(18)	4 (9)	.368
Previous CABG, *n* (%)	25 (27)	14 (28)	11 (25)	.817
Previous CKD, *n* (%)	45 (48)	20 (40)	25 (58)	.081
Euroscore 2, mean ± *SD*	16 ± 15	21 ± 18	11 ± 8	.001
Infarct location				.013
Anterior	32 (35)	23 (46)	9 (21)	
Inferior	44 (47)	16 (32)	28 (65)	
Lateral	15 (16)	10 (20)	5 (12)	
Undetermined	2 (2)	1 (2)	1 (2)	
STEMI, *n* (%)	68 (73.1)	39 (78)	29 (67.4)	.502
Multivessel disease, *n* (%)	73 (78)	38 (76)	36 (83)	.404
Primary PCI, *n* (%)	66 (71)	38 (76)	28 (65)	.159
MCS				
IABP/Impella	36 (38)	33 (66)	3 (7)	<.001
VA ECMO	6 (6)	6 (12)	0 (0)	.028
Vasoactive drugs	43 (46)	41 (82)	2 (4)	<.001
LVEF (%)	36 ± 12	34 ± 12	38 ± 11	.079
MR grade 4+, *n* (%)	77 (83)	43 (86)	34 (79)	.377
Systolic PAP (mmHg)	54 ± 19	53 ± 21	55 ± 18	.793

Abbreviations: BMI, body mass index; CABG, coronary artery by-pass graft; CKD, chronic kidney disease; COPD, Chronic obstructive pulmonary disease; CS, cardiogenic shock; IABP, intraaortic balloon pump; LVEF, left ventricle ejection fraction; MCS, mechanical cardiac support; MI, myocardial infarction; MR, mitral regurgitation; NCS, non-cardiogenic shock; PCI, percutaneous coronary intervention; PAP, pulmonary artery pressure; STEMI, ST-segment elevation myocardial infarction; VA ECMO, veno-arterial extracorporeal membrane oxygenation.

and February 2020 were included in the study. The mean ± *SD* patient age was 70.3 ± 10.2 years and included 48 (51.6%) women and 45 (48.4%) men. Characteristics of the population are in Table 1. Patients were divided into CS and non-CS groups. Of the 93 patients, 50 (53.8%) were in CS prior to MitraClip procedure. SCAI categories of cardiogenic shock were A 24.7%, B 21.5%, C 36.6%, D 15.1%, and D 2.1%. Compared with non-CS patients, patients with CS were younger (68 ± 10 vs. 72 ± 9 years; p = .061), had a lower prevalence of chronic kidney disease (40 vs. 58%; p = .081), had higher surgical risk (21 ± 18% vs. 11 ± 8% Euroscore II; p = .001), and had shorter time elapsed between MI and MitraClip placement (24 ± 22 vs. 33 ± 23 days; p = .069) (Table 1). The prevalence of multi-vessel disease was high (CS, 76% vs. non-CS, 83%; p = .404) and similar between groups and anterior wall MI was more frequent in the CS group (CS, 46% vs. non-CS, 21%; p = .013). The percentage of primary percutaneous coronary intervention was equivalent. Complete revascularization was achieved in 86% of patients with multivessel disease, with no difference between CS and non-CS patients (p = .562). CS patients were prescribed vasoactive drugs more frequently (82 vs. 4%, p < .001) and were more likely to have IABP/Impella pumps (66 vs. 7%, p < .001) or venoarterial extra-corporeal membrane oxygenation (12 vs. 0%, p = .028). Of the patients with IABP, 3 non-CS patients received prophylactic IABP implantation after diagnosis with severe MR. Preprocedural MR was 4+ in 86% of CS patients and 79% in non-CS patients (p = .377). Left ventricular ejection fraction was lower in CS patients, but no differences were observed regarding systolic pulmonary arterial pressure (SPAP). Six patients were reported to have partial or complete papillary muscle rupture.

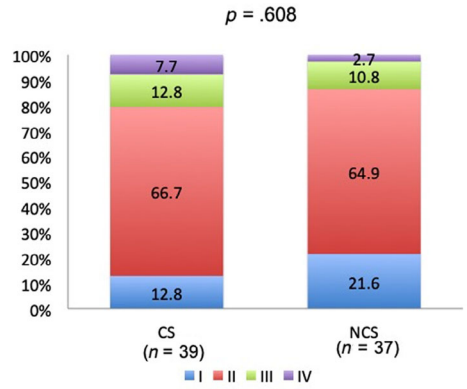

FIGURE 1 New York Heart Association functional class at 3 months [Color figure can be viewed at wileyonlinelibrary.com]

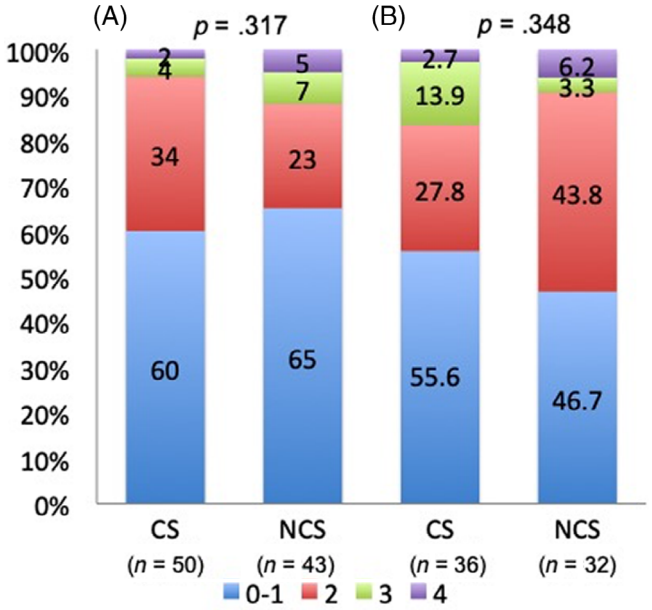

FIGURE 2 MR reduction postprocedural (panel a) and at 3 months (panel b) [Color figure can be viewed at wileyonlinelibrary.com]

4.1 | Procedural characteristics

Technical success was achieved in 100% of patients. MitraClip NT and NTR devices were used in 80 patients, XTR devices were used in 10 patients, and a combination of clips was used in 3 patients. More than 1 clip was used in 58.1% of patients. Immediate procedural success was high, with no difference between groups (CS, 90% vs. non-CS, 93%, p = .793). However, mean procedure length was longer in patients with CS than in non-CS patients (143 ± 113 vs. 82 ± 44 min; p = .003).

The percentage of in-hospital major complications (including partial clip detachment, air embolism, MI, stroke, vascular injury, pericardial effusion, and bleeding events) was low after procedure and did not differ between groups (CS, 4% vs. non-CS, 7%, p = .659). Overall, mean SPAP was significantly decreased after the procedure (before, 54 ± 19 mmHg vs. after, 44 ± 20 mmHg; p < .001), with no difference between groups. The mean mitral valve gradient increased significantly after procedure (before, 1.7 ± 0.9 mmHg vs. after, 3.3 ± 1.6 mmHg; p < .001). After PMVR, the gradient did not differ between CS and non-CS patients (CS, 3.7 ± 1.9 mmHg vs. non-CS, 3.6 ± 1.7 mmHg; p = .741).

4.2 | Clinical follow-up

At 30-day follow-up, mortality was higher in the CS group (10 vs. 2.3%), but the difference was not significant (p = .207). Procedural success at 30 days was lower in patients with CS, but the difference was not significant (CS, 59% vs. non-CS, 74%; p = .136).

At 3-month follow-up, there were no differences in the percentage of re-admissions due to heart failure (CS, 13% vs. non-CS, 23%, p = .253) or repeated MitraClip intervention or surgery (CS, 6% vs. non-CS, 2.3%; p = .621). New York Heart Association functional classifications improved significantly compared with baseline, but no differences were observed between groups (Figure 1). Likewise, echocardiographic evaluation during this period showed a marked reduction in MR with no difference between groups (Figure 2). Reduction in SPAP persisted, and no differences were observed between groups (CS, 40 ± 13 mmHg vs. non-CS, 44 ± 19 mmHg; p = .441).

After a median follow-up of 7 months (range 0–81 months, IQR 2.7–17), overall mortality did not differ between groups (CS, 16% vs. NCS, 9.3%; p = .377), and the combined event mortality/rehospitalization due to heart failure was similar (CS, 28% vs. NCS, 26%; p = .793). Survival curves for both end-points are shown in Figure 3.

In a Cox-regression analysis adjusted by age, Euroscore II, and procedural success, CS was not independently associated with the combined end-point (hazard ratio [HR], 1.1; 95% CI, 0.3–4.6; p = .889). The only variable independently associated with the combined end-point was the immediate procedural success (HR, 0.1; 95% CI, 0.01–0.6; p = .012). Univariate and multivariate analyses are shown in Table 2.

5 | DISCUSSION

To our knowledge, this is the largest registry-based study evaluating the outcomes of patients who developed acute MR after AMI and who received PMVR with the MitraClip device. Our data suggest that this procedure may be a safe and effective strategy for reducing MR and improving prognosis in such high-risk populations. Also, we observed no differences in outcomes after PMVR in patients with CS, suggesting that CS may not be an important factor for precluding implementation of the therapy, providing that clinical stabilization could be achieved to receive PMVR.

MR after AMI is a serious complication that occurs in roughly 3% of cases. Complete papillary muscle rupture is uncommon (0.25% of MIs in the percutaneous coronary intervention era) and is often fatal.[23] However, acute MR due to leaflet tethering, partial papillary muscle

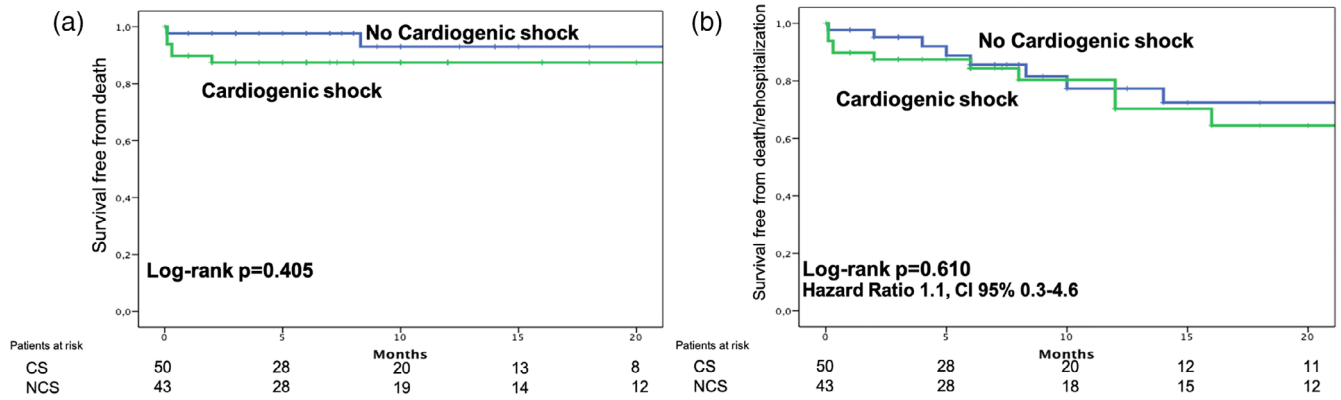

FIGURE 3 Kaplan–Meier survival curves comparing CS and non-CS groups. Panel a: Survival free from death. Panel b: Survival free from death and rehospitalization due to heart failure [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 2 Univariate and multivariate predictors of combined death/rehospitalization due to heart failure during follow-up

	Univariate			Multivariate		
	HR	95% CI	*p*	HR	95% CI	*p*
Age	0.99	0.95–1.03	.651	1.05	0.97–1.13	.227
CKD	1.11	0.48–2.60	.810			
DM	1.90	0.81–4.46	.140			
EuroScore II	1.02	0.99–1.05	.087	1.02	0.99–1.06	.154
Pre IHD	0.98	0.38–2.56	.979			
LVEF	0.99	0.95–1.03	.592			
Cardiogenic shock	0.97	0.42–2.24	.936	1.1	0.3–4.6	.889
Procedural success	0.18	0.06–0.57	.004	0.10	0.02–0.60	.012
MCS	0.60	0.23–1.54	.288			

Abbreviations: CI, confidence interval; CKD, chronic kidney disease; DM, Diabetes Mellitus; HR, hazard ratio; IHD, ischemic heart disease; LVEF, left ventricular ejection fraction; MCS, mechanical cardiac support.

rupture, or new onset of left ventricular dysfunction may be more frequent, with a possible prevalence of 35%, according to a study of a series of MI treated by primary percutaneous coronary intervention.[4] In a cohort of surgical patients, complete papillary muscle rupture after MI-related MR was responsible for 45% of cases,[24] which means that severe functional MR after MI is common and may cause deterioration in a patient's condition enough to justify intervention.

Regarding treatment of MR (excluding complete papillary muscle rupture), it has been reported that revascularization by means of primary percutaneous coronary intervention can significantly improve the degree of MR and therefore should be a first line treatment.[4] In our study, primary percutaneous coronary intervention was carried out in almost 72% of cases. However, even after successful percutaneous revascularization, the degree of MR may worsen, and further treatment may be required. When CS develops within the context of MR, mortality rises significantly, and stabilization through pharmacological afterload reduction and/or mechanical circulatory support may be lifesaving. However, the use of this advanced support should not be a destination therapy, but rather a bridge to a subsequent interventional therapy focused in correcting MR.[1,6,25]

Until recently, cardiac surgery was the only option available for the treatment of MR, and a systematic review revealed a pooled 30-day mortality rate of 19%, with some studies showing mortality rates as high as 39%.[7] Notwithstanding, in recent years PMVR has been extensively developed, and MitraClip is the device that has been used for PMVR most extensively so far.

MitraClip has been shown to be safer than conventional surgery, although less effective.[26] In real-world registries of patients with both degenerative and functional MR and who are at high-risk for surgery, MitraClip use is associated with clinical improvements and a significant reduction of MR.[10,11,27] However, most MitraClip interventions performed to date have been in patients who were in a stable clinical situation with advanced functional class and chronic (not acute) MR. Our data suggest that MitraClip could be a safe and effective alternative to surgical intervention in clinically unstable patients who have a high risk of 30-day mortality, and this therapy may even be safe for the 10% of patients who develop CS, which is encouraging.

In our study, we saw that clinical results of PMVR did not differ significantly between CS and non-CS patients, despite the poorer

clinical situation and lower left ventricular ejection fraction in patients with CS. This underscores the fact that in a CS scenario, the main component responsible for clinical deterioration is the MR and its deleterious hemodynamic effects rather than the role of pump failure. This could explain the difference in mortality observed in our series compared with classic series of CS following MI[28] or in those series of PMVR in cardiogenic shock patients where patients were in a clinical unstable condition but after mainly a long-standing ischemic or non-ischemic cardiomyopathy in an end-stage situation.[29-31] On the other hand, the time from MI to MR treatment was several weeks in our patient sample, and this could be related to the intention to stabilize the clinical condition with the belief medical therapy was the only option for the MR, since patients were not surgical candidates and the MitraClip approach was rather new in this setting. However, treating the MR quickly produces such positive clinical benefits that the intervention should not be delayed. Thus, we advocate for early MR correction irrespective of lower left ventricular ejection fraction and development of CS.

There are several potential advantages of using PMVR with MitraClip. First, this treatment can lead to a rapid decrease in left ventricular, left atrium, and pulmonary artery pressures and an increase of cardiac output after a successful correction of the MR,[32] which may lead to a fast recovery. Second, the technique reduces risk of left ventricle damage induced by the systemic inflammatory response, free radical injury, and myocardial oxidative stress associated with cardiopulmonary bypass.[33] Moreover, MitraClip may also avoid the restraint of the mitral annular motion caused by mitral rings or prosthesis and the development of abnormal septal motion that may negatively impact left ventricle performance. In addition, acute MR often develops in a previously normal mitral valve, which usually translates into optimal leaflet tissue and coaptation for device therapy. Furthermore, the use of MitraClip does not preclude a delayed cardiac surgery in case the device fails. Finally, a relevant number of unstable patients are on double or triple antithrombotic therapy after MI, and MitraClip may help prevent significant bleeding complications that are common after open-heart surgery and that may negatively impact the prognosis of unstable patients. However, challenges when implementing this therapy exist. Treating acute MR is one of the most technically challenging MitraClip procedures. Lesion complexity, a small atrium that makes performing a high puncture difficult, the clinical situation of the patient, and the risk of impingement in papillary muscle make these cases very demanding. The fact that the only independent factor associated with clinical outcomes was immediate technical success underscores the relevance of the high level of experience required for the implanting team.

Interestingly, a recent review of shock management after MI[25] only considers mitral valve surgery for acute MR after MI. Our data suggest that, given the favorable safety/efficacy profile, PMVR should at least be considered in patients with this condition if the attending team has enough experience. This strategy may be of special interest in patients with CS, which represent complex cases where effective and fast recovery with a low rate of complications is desirable. Further research and randomized trials are required to increase our knowledge in this setting.

6 | LIMITATIONS

Our study had several limitations. First, is an observational study and the sample size was small and so should be interpreted with caution. We did not find a significant difference in mortality between CS and non-CS patients, which could be related to a lack of statistical power. A larger study with longer follow-up will be needed to clarify the effect of MitraClip in this scenario. Furthermore, we cannot exclude the presence of a selection bias in CS patients, in the sense that only those who responded to the medical therapy and cardiac support were those who received PMVR. Time form MI to PMVR was long and that means that even CS patients responded to the medical therapy in some way. This population can represent a better prognostic category and therefore our conclusions may not be applicable to all patients in CS with significant MR. Likewise, because of the small sample size and number of events, the multivariable analysis was limited. Thus, results should be considered hypothesis generating and not generalizable. Also, echocardiographic follow-up is lacking, so the effect on left ventricular remodeling has not been evaluated. However, our aim was to assess correlation within the clinical setting, not to show possible positive effects on left ventricular parameters. Likewise, number of patients with subvalvular apparatus rupture was small to draw definitive conclusions. Although if a successful repair can be achieved results seemed similar, larger series with these anatomies must be collected to assess the specific performance of MitraClip in this population. The shock status is a dynamic variable and we defined it at the time of MitraClip strategy decision. What we cannot ascertain is what was the SCAI classification at the beginning of the clinical course. Likewise, all patients were treated with MitraClip as a salvage strategy, but we cannot distinguish from the present study whether the patients were stable enough or with recurrent deterioration despite MCS support. Lastly, procedures were performed in centers that had high levels of experience with PMVR using MitraClip. Thus, our findings cannot be generalized to less experienced teams.

7 | CONCLUSION

Patients found to have significant MR during their index hospitalization for AMI had similar clinical outcomes with PMVR whether they presented in or out of cardiogenic shock, provided initial hemodynamic stabilization was first achieved before PMVR.

7.1 | Clinical perspective

7.1.1 | What is next?

Further research is warranted to confirm these results and to compare the percutaneous approach with conventional surgery.

7.1.2 | What is new?

PMVR with the MitraClip device may be a promising therapeutic strategy for patients with acute MR after AMI, with or without CS. This may represent a valid alternative for such patients.

7.1.3 | What is known?

Acute MR may develop following AMI, a condition associated with development of CS and high mortality. Until recently, conventional surgery was the only alternative, which is associated with significant mortality.

CONFLICT OF INTEREST

Rodrigo Estévez-Loureiro is consultant for Abbott Vascular and Boston Scientific. Dr. Taramasso is a consultant for Abbott Vascular, Boston Scientific, 4TECH, and CoreMedic; and has received speaker honoraria from Edwards Lifesciences. Dr. Denti has served as a consultant for Abbott Vascular, 4Tech, Neovasc, and InnovHeart; and has received honoraria from Abbott. Dabit Arzamendi is consultant for Abbott Vascular. Dr. Xavier Freixa is consultants for Abbott Vascular. Dr. Fam, has received speaker honoraria and travel or grant support from Edwards Lifesciences Francesco Maisano received Grant and/or Research Support from Abbott, Medtronic, Edwards Lifesciences, Biotronik, Boston Scientific Corporation, NVT, Terumo; receives Consulting fees, Honoraria from Abbott, Medtronic, Edwards Lifesciences, Swissvortex, Perifect, Xeltis, Transseptal solutions, Cardiovalve, Magenta; has Royalty Income/IP Rights Edwards Lifesciencesand is Shareholder of Cardiovalve, Cardiogard, Magenta, SwissVortex, Transseptalsolutions, 4Tech, Perifect. All other authors have reported that they have no relationships relevant to the contents of this article to disclose.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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