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REVIEW

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Transcatheter edge-to-edge mitral valve repair for post-myocardial infarction papillary muscle rupture and acute heart failure: A systematic review

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Abstract

Papillary muscle rupture (PMR) is a rare complication of acute myocardial infarction (AMI) associated with high mortality and morbidity. Surgery is the gold-standard treatment for these patients, but it is burdened by a high perioperative risk due to hemodynamic instability. Mitral transcatheter edge-to-edge repair (M-TEER) was reported to be safe and effective in unstable patients with significant mitral regurgitation. However, data in patients with post-AMI PMR are limited to a few case reports. In this review, we summarized all data available regarding percutaneous treatment of post-AMI PMR. These results show that M-TEER is safe and effective in this setting with low in-hospital mortality and complications and high rate of significant mitral regurgitation reduction.

KEYWORDS

Acute mitral regurgitation, acute myocardial infarction, mitral transcatheter edge-to-edge repair, papillary muscle rupture

1 | INTRODUCTION

Acute mitral regurgitation (MR) due to papillary muscle rupture (PMR) is a rare complication of acute myocardial infarction (AMI). Its prevalence, ranging from 0.05% to 0.26%,[1] has declined in the last decades because of improvement in revascularization strategies. However, in-hospital mortality of post-AMI MR remains extremely high, from 36% to 80%.[2,3]

Current guidelines recommend emergency surgical treatment of PMR.[4,5] However, many patients with PMR fail to receive surgery due to high or prohibitive surgical risk.[4,5] Indeed, early mortality after surgery for PMR is high as it ranges between 21% and 53%.[4–8]

Mitral transcatheter edge-to-edge valve repair (M-TEER) is currently indicated in selected heart failure (HF) patients with symptomatic and severe MR.[4,5,9–14] It was reported to be safe and effective also in patients with acute MR and/or hemodynamic instability.[15–20] However, evidence on its possible role in patients with acute MR secondary to post-AMI PMR is currently limited to a few case reports.

In this study, we reviewed available data about the clinical characteristics and outcomes of patients with post-AMI PMR undergoing M-TEER.

2 | METHODS

We searched for published articles in Medline/PubMed and Google Scholar from inception to February 22, 2023, using the following keywords: "TEER," "MitraClip," OR "PMVR" AND "papillary muscle rupture." We included studies fulfilling all of the following criteria: (a) reporting the use of M-TEER (i.e., MitraClip) in critically ill patients defined as with cardiogenic shock (CS), acute refractory pulmonary edema, vasoactive drug requirement, mechanical ventilation or circulatory support; (b) reporting post-AMI PMR as the main etiology of MR; (c) published case reports or case series. Duplicate publications and abstracts nonpublished and/or only presented at congresses were excluded.

Methodological quality appraisal was performed using a tool proposed by Murad et al. designed for case reports and series consisting of eight questions to evaluate selection, ascertainment, causality, and reporting (Supporting Information: Table 1).[21] Three of the eight questions were excluded as they were irrelevant or not feasible in regard to the study population and the outcome evaluated.

According to the Mitral Valve Academic Research Consortium (MVARC) definition, "acceptable" device success was defined as a reduction in MR of at least one grade with an absolute level of MR ≤ moderate (2+).[22] Procedural complications, vital status, and MR grade at follow-up were also reported when available.

Continuous variables are presented as mean ± standard deviation (SD) or median and interquartile range (IQR). Categoric data are presented as absolute numbers and/or percentages.

3 | RESULTS

Sixteen studies reporting the use of M-TEER in patients with acute HF caused by post-AMI PMR fulfilled our inclusion criteria (Figure 1). Among them, 17 were case reports and 1 was a case series including 5 patients (Figure 1 and Supporting Information: Table 2).[23–40] There were no registries or clinical trials identified.

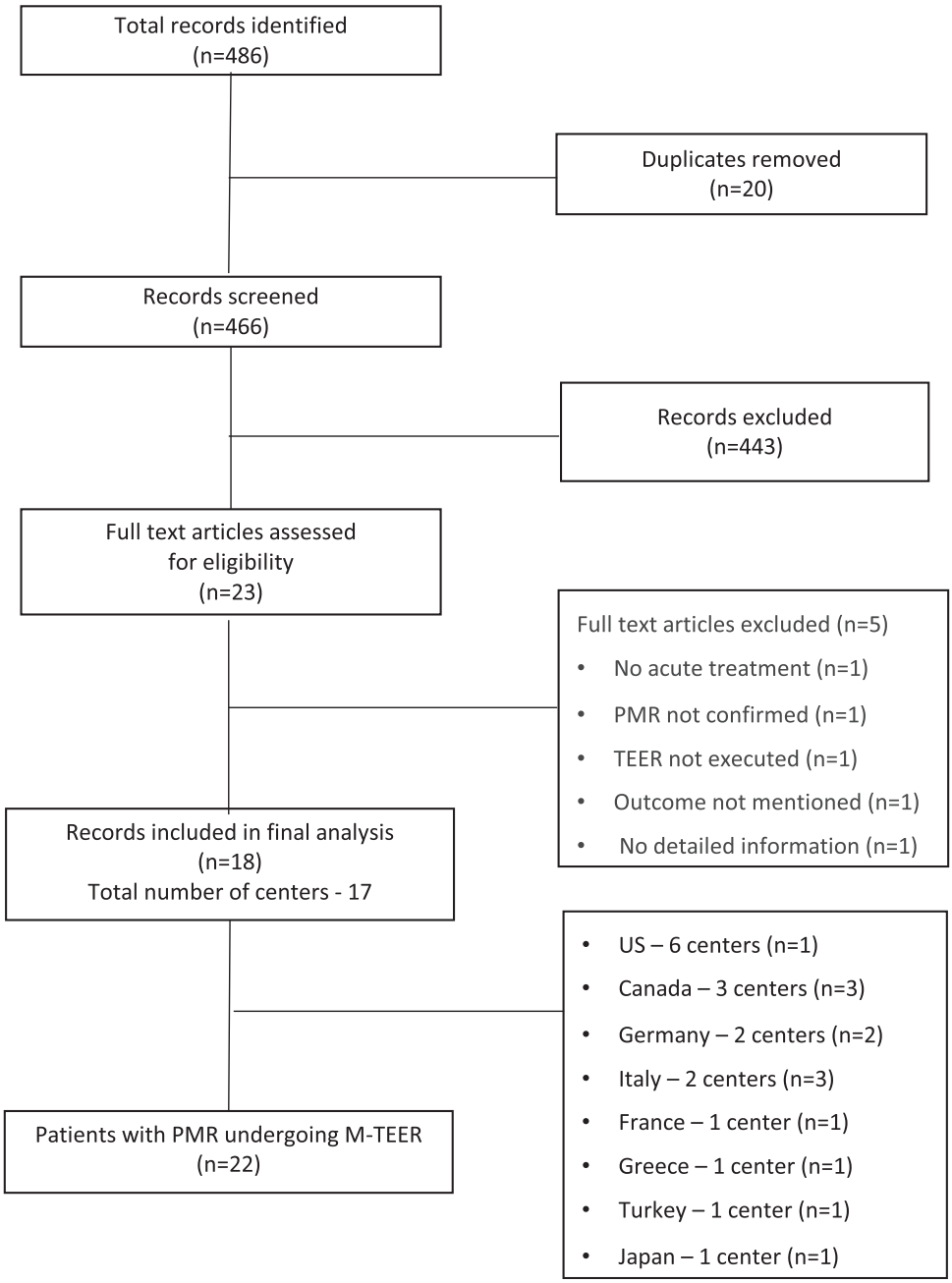

FIGURE 1 Study flow chart. M-TEER, transcatheter edge-to-edge mitral valve repair; PMR, papillary muscle rupture.

Baseline characteristics of the 22 patients finally included in the present analysis are reported in Table 1 and Figure 2. Mean age was 74 ± 11 years and 59.1% were males. An ST-elevation myocardial infarction (STEMI) was the most common cause of PMR (n = 17, 77.3%). Non-ST-elevation myocardial infarction (NSTEMI) was observed in five patients (22.7%). A complete rupture was noted in 12 patients (54.5%), whereas a partial rupture was observed in the remaining 10 cases (45.5%). The posteromedial papillary muscle was the most frequently involved (68.2%).

The most common clinical presentation was CS (86.4% of the cases). Temporary mechanical circulatory support (tMCS) was used in 21 out of 22 patients (95.5%). Intra-aortic balloon pump (IABP) was the most frequently used MCS (n = 19, 86.4%), followed by Impella (n = 3, 3.6%), veno-arterial (VA) extracorporeal membrane oxygenation (ECMO) (n = 2, 9.1%) and venous-venous (VV) ECMO (n = 1, 4.5%). Median time from admission to M-TEER was 1 day (IQR 0.3–7.0 days).

TABLE 1 Baseline characteristics.

Age—years, mean ± SD	74 ± 11
Male sex—no. (%)	13 (59.1%)
PMR etiology—no. (%)	– Ischemic 22 (100%)
Type of rupture—no. (%)	– Complete 12 (54.5%) – Partial 10 (45.5%)
PM involved—no. (%)	– Anterolateral 7 (31.8%%) – Posteromedial 15 (68.2%)
Acute coronary syndrome—no. (%)	– STEMI 17 (77.3%) – NSTEMI 5 (22.7%)
Clinical presentation—no. (%)	– Cardiogenic shock 19 (86.4%) – Pulmonary edema 3 (13.6%)
Culprit lesion—no. (%)	– Left circumflex artery 9 (40.9%) – Right artery 6 (27.3%) – Left main 1 (4.5%) – Other/unknown 6 (27.3%)
PCI performed—no. (%)	– Yes 14 (63.6%) – No 6 (27.3%) – Unknown 2 (9.1%)
Inotropes—no. (%)	– Yes 16 (72.7%) – No/unknown 6 (27.3%)
Need for MCS—no. (%)	– MCS 21 (95.5%) – No 1 (4.5%)
Type of MCS—no. (%)	– IABP 19 (86.4%) – VA-ECMO 2 (9.1%) – VV-ECMO 1 (4.5%) – Impella 3 (13.6%)
Need of mechanical ventilation—no (%)	– Invasive ventilation 13 (59.1%) – Noninvasive ventilation 2 (9.1%) – No/unknown 7 (31.8%)
Time from admission to MitraClip—days (n = 10)	3.3 (±3.9)

Abbreviations: MCS, mechanical circulatory support; NSTEMI, non-ST-elevation myocardial infarction; PM, papillary muscle; PMR, papillary muscle rupture; STEMI, ST-elevation myocardial infarction; VA-ECMO, veno-arterial extracorporeal membrane oxygenation; VV-ECMO, veno-venous extracorporeal membrane oxygenation.

Procedural characteristics and in-hospital outcomes are summarized in Table 2 and Figure 2. The MitraClip device was implanted in all cases and at least two clips were needed in 17 patients (77.3%). Among the 43 total MitraClip deployed, 27 (62.8%) were implanted between the A2-P2 scallops, while 5 (11.6%) between the A3-P3 scallop. Device success was achieved in all patients. MR degree was reduced from grade 4 (100%) to grades ≤1 or 2 in 81.8% and 18.2% of cases, respectively. The mean mitral valve (MV) gradient after the procedure was 3.7 ± 2.0 mmHg. In-hospital mortality occurred in four patients (18.2%). Mortality was unrelated to the device or procedure as caused by sepsis in two patients and HF in two patient.[28] The only nonfatal in-hospital complication was a cerebrovascular accident (minor hemorrhagic stroke).[39]

Follow-up was available for 14 of the 18 patients (77.8%) who survived to hospital discharge, with a median follow-up time of 2.5 months (IQR 1.0–6.0 months). All these 14 patients were alive at the reported follow-up. Information on residual MR was available for 11 patients (50%) and the MR severity at follow-up was grade ≤1 in 6 patients and grade 2 in 5 patients.

4 | DISCUSSION

Post-AMI acute PMR is a catastrophic condition commonly presenting with CS or pulmonary edema and requiring immediate intervention. Without surgical treatment, mortality as high as 80% has been reported.[2,3] Emergent care may include the need for vasoactive drugs, MCS, and respiratory support with invasive mechanical ventilation. MV surgery represents the standard-of-care for these patients and significantly improves their long-term survival, especially when combined with simultaneous coronary bypass surgery.[4,5 41,42] However, many patients with PMR are not treated with surgery due to very high or prohibitive surgical risk. In our systematic review of the literature, we summarized available evidence on percutaneous treatment of post-AMI PMR (i.e., M-TEER) as a possible alternative to surgery. Among the 22 patients included in this study, M-TEER was feasible, successfully performed with an "acceptable" device success in all cases, and resulted in postprocedural none/trace or mild MR in 18 patients (81.8%). In this high-risk population frequently presenting with CS (86.4% of patients), in-hospital mortality was 18.2% (four patients), and a periprocedural complication was reported in only one patient who experienced *a minor* hemorrhagic stroke.

Posteromedial PMR is far more common than anterolateral PMR since the anterolateral branch has a dual arterial blood supply from both the left anterior descending artery and the diagonal or marginal branch of the circumflex coronary artery, whereas the posteromedial papillary muscle has a single blood supply from the circumflex coronary artery or the right coronary artery, depending on

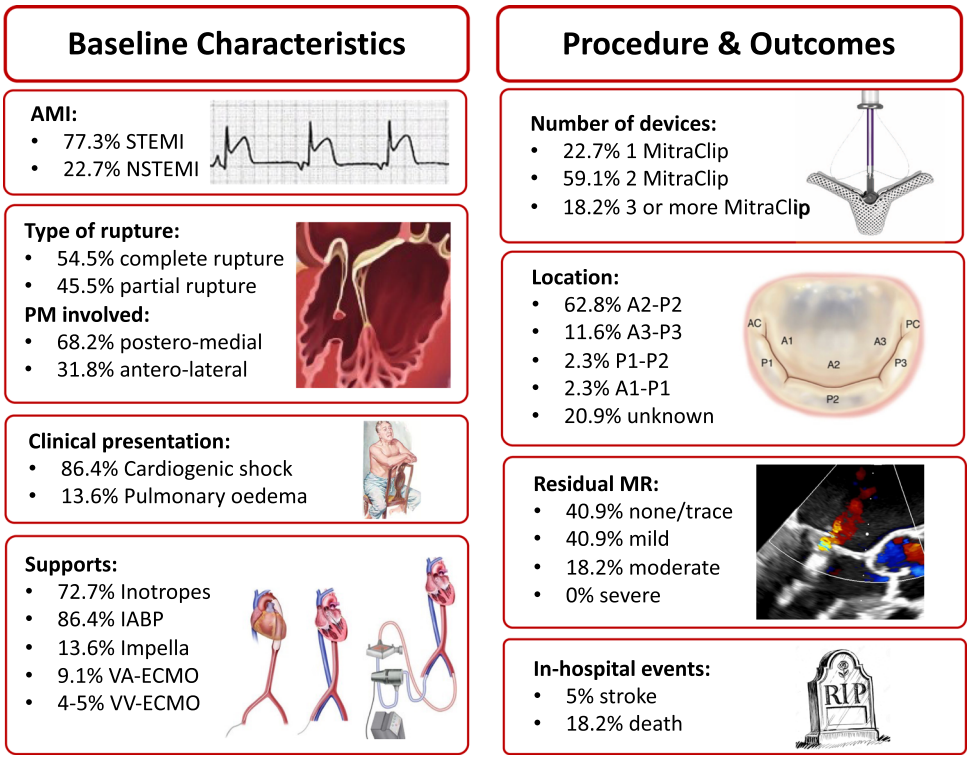

FIGURE 2 Patient presentation and TEER outcomes. AMI, acute myocardial infarction; IABP, intra-aortic baloon pump; MCS, mechanical circulatory support; M-TEER, transcatheter edge-to-edge mitral valve repair; NSTEMI, non-ST-elevation myocardial infarction; PMR, papillary muscle rupture; STEMI, ST-elevation myocardial infarction; VA-ECMO, veno-arterial extracorporeal membrane oxygenation; VV-ECMO, veno-venous extracorporeal membrane oxygenation. [Color figure can be viewed at wileyonlinelibrary.com]

dominance.[1] Consistently, in our systematic review, rupture involved mostly the posterior papillary muscle (68.2%).

Both patients with partial (45.5%) and complete (54.5%) PMR were included in our study. Partial PMR (occurring at one of the muscle heads) generally causes leaflet flail and pulmonary edema, while complete PMR causes flail of both the anterior and posterior leaflet and it is always associated with CS. PMR can be surgically treated with either MV repair or MV replacement. MV replacement is usually reserved for subjects with complete PMR or partial/incomplete PMR and compromised hemodynamic stability at surgery to reduce cardiopulmonary bypass, ischemic times, and related risks.[43–45] In a recent systematic review and meta-analysis on the surgical treatment of post-AMI PMR, complete PMR was associated with a more than twofold increased risk of operative mortality compared with partial or incomplete PMR, while MV repair was associated with a 67% decreased risk of mortality as compared to MV replacement. Overall early mortality was 21% and the most common cause of postoperative death was the development of a low cardiac output syndrome,[46] which is described also in other studies as a predictor of 30-day mortality after surgery.[46,47] Causes of decreased cardiac function following surgical MR surgery are the use of cardiopulmonary bypass, cardioplegic arrest, interruption of annular-chordal-papillary muscle continuity in nonvalve-sparing replacement, and afterload mismatch phenomenon. A closed-chest, off-pump repair with the MitraClip system may be associated with a lower risk of developing low cardiac output syndrome than previously reported with traditional surgery,[48] and may be particularly appealing in a very-high risk scenario with hemodynamic instability such as post-AMI PMR.

A few studies evaluated the outcomes of patients who developed acute MR after AMI and who received M-TEER, including patients with severe hemodynamic instability (e.g., CS).[15–20] The European Registry of MitraClip in Acute Mitral Regurgitation following an AMI (EREMMI) was the first multicenter registry reporting the safety and efficacy of MitraClip in patients with acute MR.[15] Jung et al. conducted a multicenter, collaborative, patient-level analysis on patients with CS and relevant MR treated with M-TEER. Successful device implantation was associated with decreased risk for mortality over the 1st-year follow-up. MR etiology was heterogeneous, but it was not mentioned whether patients with PMR were included in the analysis.[18] In the International REgistry MitraClip in AMI (IREMMI), patients who developed acute MR after AMI and who received M-TEER with the MitraClip device were stratified according to clinical presentation (CS vs. non-CS). No differences in outcomes were observed between the two groups. Six patients in the registry were reported to have partial or complete PMR, but specific data regarding these few patients were not showed.[19]

More recently, So et al. published a case series and a literature review including patients with CS due to acute MR and mechanical MV complications trated with TEER. Twelve patients were reported

TABLE 2 Procedural data and clinical outcomes

Clips implanted, mean ± SD	2.0 ± 0.7
Clips implanted—no. (%)	– One 5 (22.7%) – Two 13 (59.1%) – Three or more 4 (18.2%)
Type of Mitraclip	– XT 7 (31.8%) – Both 3 (13.6%) – NT 12 (54.5%)
MitraClip scallop—no. (%) (*n* clip = 43)	– A2-P2 27 (62.8%) – A3-P3 5 (11.6%) – P1-P2 1 (2.3%) – A1-P1 1 (2.3%) – Other/unknown 9 (20.9%)
Postprocedural MR	– None/trivial/trace 9 (40.9%) – Mild 9 (40.9%) – Moderate 4 (18.2%) – Severe 0 (%)
Postprocedural gradient—mmHg, mean ± SD (*n* = 15)	3.7 ± 2.0
Complications—no. (%)	– Stroke 1 (5%)
In-hospital death—no. (%)	– No death 18 (81.8%) – Death 4 (18.2%)
Cause of in-hospital death—no. (%)	– Sepsis 2 (50%) – HF 2 (50%)
Mean follow-up time—months, mean ± SD (*n* = 14)	4.5 ± 5.6
FU vital status—no. (%) (*n* = 18)	– No death 14 (77.8%) – FU not available 4 (22.2%)
FU MR—no. (%) (*n* = 11)	– None/trivial/trace 1 (9.1%) – Mild 5 (45.5%) – Moderate 5 (45.5%) – Severe 0 (0%)

Abbreviations: FU, follow-up; HF, heart failure; MR, mitral regurgitation.

to have partial or complete PMR; however, no specific outcomes stratified by or focused on PMR were revealed.[49]

Information regarding the use of novel devices (e.g., MitraClip G4 and Pascal P10) in the setting of ischemic PMR are limited. In our study, only four cases described the use of MitraClip G4.[28,31,32] It is reasonable to think that the newer devices will extend the possibility to better treat PMR given the larger device sizing and the chance to independently approximate anterior and posterior mitral leaflets.[50]

To our knowledge, this is the first analysis specifically focusing on the treatment of post-AMI PMR by means of M-TEER. From a technical perspective, M-TEER presents several challenging aspects in this context. MV area may be a limitation for M-TEER in patients with acute PMR, since the MV has not been adaptive enlarged. The reduced size of the left atrium significantly limits the height of the trans-septal puncture and the ability to easily reach a good trajectory toward the valve plane. The huge flail gap, the risk of papillary muscle impingement, and the high heart rate, may seriously complicate leaflet approximation. Nevertheless, in expert centers, this rescue procedure can be successfully performed. Moreover, in case of a suboptimal result, M-TEER can be considered as a bridge as it does not exclude the possibility to perform MV surgery, possibly replacement, after improvement of hemodynamic and clinical condition.[25]

A very high proportion of patients (95.5%) included in this study needed MCS. A case series of six patients suffering from acute MR from different etiologies, who received MCS with Impella CP during MitraClip implantation, was recently published.[51] Survival at discharge was 86%, suggesting that this strategy is feasible as a bridge to M-TEER and to obtain upfront hemodynamic stabilization.

Our findings are hypothesis-generating and suggest that MR reduction by means of M-TEER in critically ill patients with post-AMI PMR is feasible and might be effective in improving clinical outcomes. The long-term clinical benefits of emergent M-TEER in this setting remain to be established.

5 | LIMITATIONS

Several limitations need to be acknowledged. First, data come from observational reports and are thus susceptible to all inherent biases. The number of included patients is low, follow-up status is not reported for all patients, and clinical events beyond mortality are not described in all case reports and series. Moreover, completeness of cases' description as well as follow-up length varied a lot across studies included. Finally, the published cases are likely highly selected and may have better outcomes than nonpublished cases.

6 | CONCLUSIONS

Our analysis of the current literature shows that M-TEER is a safe and effective procedure for the treatment of post-AMI MR due PMR. The series analyzed reported an effective reduction of MR severity, relatively low in-hospital mortality and in-hospital complications rate. Dedicated studies are needed to confirm the role of M-TEER in this high-risk population and to assess long-term results.

CONFLICT OF INTEREST STATEMENT

Matteo Pagnesi received personal fees from Abbott Vascular, AstraZeneca, Boehringer Ingelheim, and Vifor Pharma. Andrea Montisci received speaker fees from Abiomed.Marco Metra received consulting honoraria for participation in steering committees or advisory boards or for speeches from Abbott Vascular, Amgen, AstraZeneca, Bayer, Edwards, Fresenius, Novartis, and

Servier. Marianna Adamo received speaker fees from Abbott vascular and Medtronic. Filippo Calì and Elisa Pezzola have no conflict of interest.

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SUPPORTING INFORMATION

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

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