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JACC FOCUS SEMINAR: MECHANICAL COMPLICATIONS OF ACUTE MYOCARDIAL INFARCTION, PART 1

JACC FOCUS SEMINAR

Management of Severe Mitral Regurgitation in Patients With Acute Myocardial Infarction

JACC Focus Seminar 2/5

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ABSTRACT

Severe acute mitral regurgitation after myocardial infarction includes partial and complete papillary muscle rupture or functional mitral regurgitation. Although its incidence is <1%, mitral regurgitation after acute myocardial infarction frequently causes hemodynamic instability, pulmonary edema, and cardiogenic shock. Medical management has the worst prognosis, and mortality has not changed in decades. Surgery represents the gold standard, but it is associated with high rates of morbidity and mortality. Recently, transcatheter interventions have opened a new door for management that may improve survival. Mechanical circulatory support restores vital organ perfusion and offers the opportunity for a steadier surgical repair. This review focuses on the diagnosis and the interventional management, both surgical and transcatheter, with a glance on future perspectives to enhance patient management and eventually decrease mortality. (J Am Coll Cardiol 2024;83:1799–1817) © 2024 the American College of Cardiology Foundation. Published by Elsevier. All rights reserved.

Mitral regurgitation (MR) is a frequent echocardiographic finding in patients developing a myocardial infarction (MI).[1] The true prevalence of this condition differs according to reperfusion strategy, diagnostic technique, and severity of presentation.[2-8] Recently, a large study documented mild MR as the most frequent (76%) form, followed by moderate (21%) and severe MR (3% of patients).[6] Risk factors for severe MR include age, female gender, heart failure, multivessel disease, and left ventricular dysfunction.[3,9-13] Even in patients undergoing primary PCI, moderate MR is present in 9.5% to 11.5% and severe MR in 0.7% to 2.8% of patients.[1,12] The development of severely symptomatic MR is potentially catastrophic.[14-16] This condition is mainly represented in the literature by the papillary muscle rupture (PMR). However, MR may also develop in a more "functional" phenotype, with serious clinical impairment.[17] This distinction is essential to understand the clinical presentation, prevalence, and treatment possibilities.

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ABBREVIATIONS AND ACRONYMS

AMI = acute myocardial infarction

CS = cardiogenic shock

ECMO = extracorporeal membrane oxygenation

LV = left ventricle/ventricular

MCS = mechanical cardiac support

MR = mitral regurgitation

MVR = mitral valve replacement

PMR = papillary muscle rupture

TEER = transcatheter edge-to-edge repair

MECHANISMS

MR WITH SUBVALVULAR APPARATUS RUPTURE. PMR is uncommon, with a prevalence around 0.05%.[18] The mortality rate has remained unchanged for decades, up to 42%.[18] The posteromedial muscle is more frequently affected, caused by the anatomical vasculature of this muscle.[19-21] PMRs usually occur in the first week after MI, more frequently in the first 24 hours after initial presentation.[22,23] PMR is more common in older women after inferoposterior MIs, with less extent of coronary disease and less diabetes.[22] PMR is a continuous spectrum that goes from papillary muscle elongation without rupture (**Figure 1**, Video 1); rupture of one of the heads of the PM (**Figure 2**, Video 2); and complete PMR (**Figure 3**, Video 3). Complete PMR induces torrential MR, pulmonary edema, and hemodynamic collapse, prompting emergent interventions. Partial rupture may be better tolerated, allowing time to stabilize the patient and select the most appropriate therapy. Russo et al[24] reported that almost 17% of patients were operated on beyond 30 days, which means they had been stabilized and had tolerated the recovery period.

MR WITHOUT SUBVALVULAR APPARATUS RUPTURE. Development of MR without subvalvular apparatus rupture (**Figure 4**, Video 4)—also known as "functional MR"—results from a combination of leaflet tethering and acute, regional left ventricular dilation.[14,25] This type of MR usually presents 1 week after the index MI.[22,23] Risk factors include advanced age, female patients, prior MI, multivessel disease, and recurrent ischemia.[22,26,27] Clinically, it is characterized by relapsing episodes of pulmonary edema and difficult medical management (poor drug tolerance). Functional MR can lead to cardiogenic shock (CS) during the acute or subacute phase.[28] This "malignant functional" MR accounts for almost 50% of cases, justifying early intervention.[5,29] Interestingly, there is a correlation between ischemic MR severity and myocardial viability, with viable myocardium reducing left ventricular (LV) remodeling and preventing development or worsening of MR.

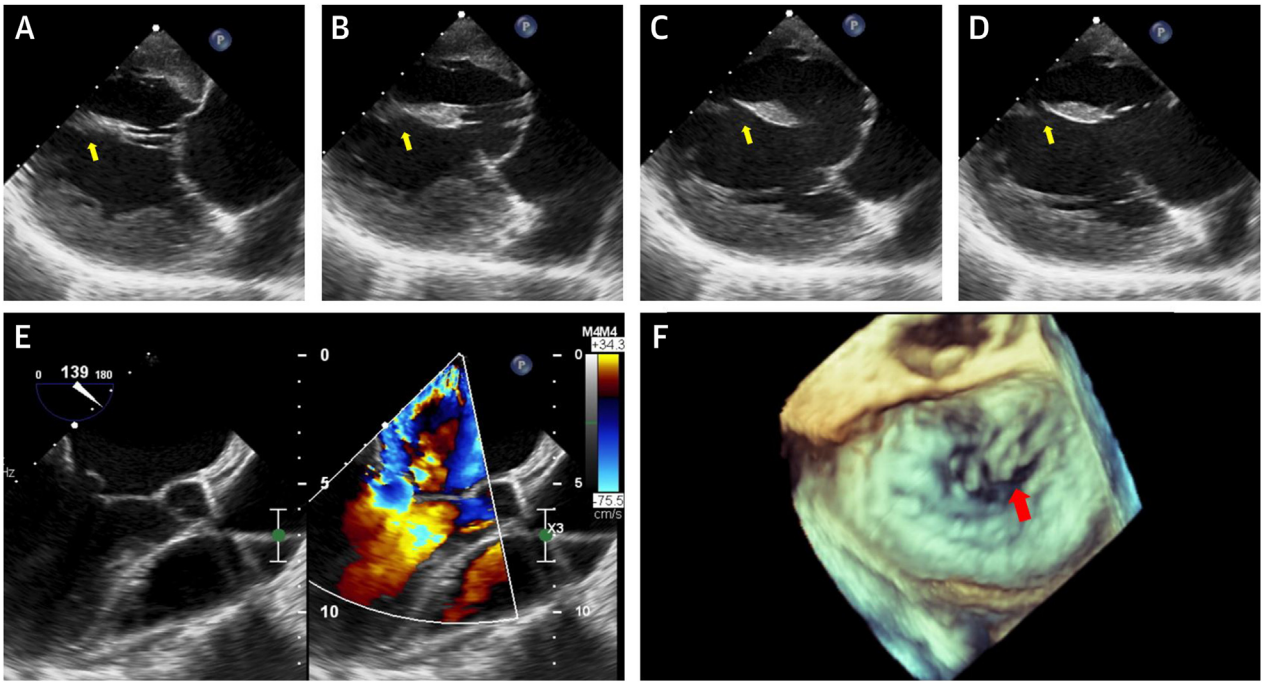
PATHOPHYSIOLOGY. The development of acute MR has a significant impact on hemodynamics. The regurgitant flow from the LV into a noncompliant left atrium results in sudden increase of left atrial pressure, leading to pulmonary edema. The LV may initially compensate to some extent, increasing stroke volume. However, the normal-sized LV in patients with acute MR cannot provide enough forward stroke volume to compensate for the reverse regurgitant volume into the left atrium. Reductions in forward flow decrease systemic arterial pressure leading to hypotension, low cardiac output, and CS.[30]

HIGHLIGHTS

- Severe MR developing early after MI is associated with increased risks of heart failure and mortality.
- Although surgical treatment can improve survival, the incidence of adverse events and mortality remain high.
- Early mechanical cardiac support and transcatheter repair techniques can expand treatment options to a broader population and potentially improve outcomes.

CLINICAL PRESENTATION. Special attention is warranted in late presenters or those with unsuccessful reperfusion (failure procedures or stent thrombosis). Patients with severe MR are typically symptomatic, developing heart failure.[31] However, the clinical spectrum will vary according to several factors. A clinical classification to risk-stratify patients from the initial medical contact is fundamental to streamline efforts and improve outcomes. A clinical classification is now available and facilitates consensus within the heart team (**Table 1**).[32] "Type 1" is the most severe presentation, leading to CS and pulmonary edema, or even cardiac arrest. "Type 2" includes patients with severe heart failure and pulmonary edema, but blood pressure is maintained (although cardiac index may still be decreased). "Type 3" represents a less severe form, characterized by episodes of pulmonary congestion and flash pulmonary edema. These 3 types will significantly affect patients' performance, which might warrant emergent intervention during the acute phase. "Type 4" includes patients with only mild to moderate symptoms of heart failure, despite severe MR. In these cases, the severity of symptoms is often related to the presence of preexisting conditions, such as chronic left atrial enlargement, or prior mitral valve disease. In some patients, mainly the elderly population with prior ischemic heart disease and LV dysfunction, a new coronary event might prompt a significant structural and functional deterioration of such a preexisting mitral pathology, leading to the development of severe MR and destabilizing the clinical condition, thereby warranting an intervention to address the valve dysfunction.

FIGURE 1 Transesophageal Echocardiography Showing Acute Mitral Regurgitation Caused by Partial Papillary Muscle Rupture



On the transgastric long-axis view (A-D, end-diastolic, mid-systolic, and early diastole, respectively) the partial solution of continuity (yellow arrow) over the papillary muscle can be noted. The systolic elongation of papillary muscle creates an anterior mitral leaflet prolapse (E, red arrow) with an eccentric mitral regurgitation jet directed to the posterior left atrial wall (F).

MEDICAL MANAGEMENT AND REVASCULARIZATION

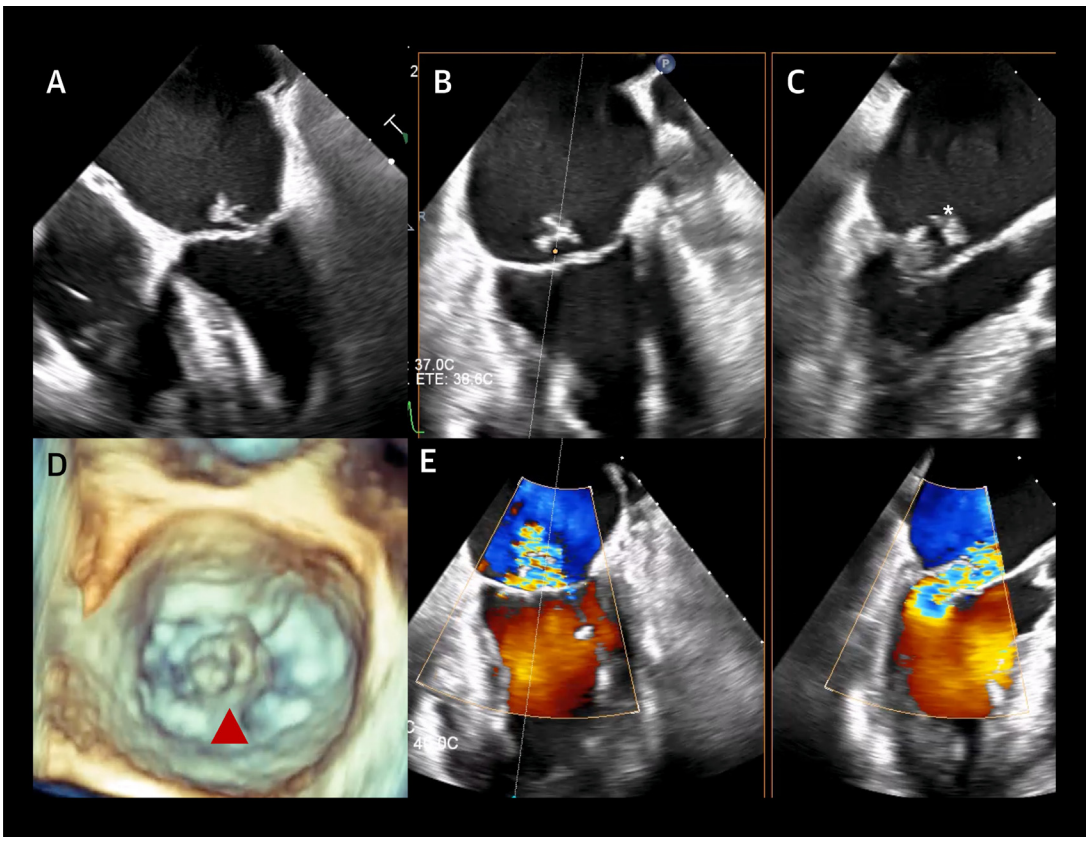
Immediate coronary reperfusion is the cornerstone in the prevention and treatment of severe MR.[5,33] In the absence of PMR, revascularization with primary PCI can significantly improve the degree of MR, and therefore should be the first line of treatment.[1,5] In fact, reperfusion can improve MR in up to 32% of patients. Shorter ischemic time and culprit vessel patency are associated with acute improvement of MR. Nevertheless, late presenters and those with unsuccessful reperfusion (and/or stent thrombosis) may require additional interventions.

Initially, medical management includes the relief of pulmonary congestion by diuretic agents and mechanical ventilation (including noninvasive ventilation or intubation as required).[34] Decrease in afterload with nitroprusside or nitroglycerin can reduce the regurgitation volume.[30,35] However, its use is limited by systemic hypotension and renal hypoperfusion. Vasoactive support might be required with norepinephrine or dopamine.[34] In case of low cardiac output, a positive inotropic agent should be added.[36] Acute deterioration or progression to CS requires mechanical circulatory support (MCS). This occurs in up to 70% of cases with PMR.[37] As such, the role of MCS is of great relevance, and will be specifically reviewed after surgical and percutaneous therapy.

IMAGING

Transthoracic echocardiography should be the first-line examination in post-MI patients with acute dyspnea. Transthoracic echocardiography allows for complete assessment of LV (ejection fraction, LV dimensions and assessment of wall motion abnormalities), mitral valve structure (annulus, leaflets, chordae and papillary muscles), and MR quantification. In technically limited cases, transesophageal echocardiography (TEE) may be required to establish the diagnosis and quantify severity.[38] Likewise, TEE is fundamental in patients selected for intervention. TEE allows for better evaluation, facilitating decision making between surgical or percutaneous. If

FIGURE 2 Transesophageal Echocardiography Showing Rupture of the Tip of Papillary Muscle



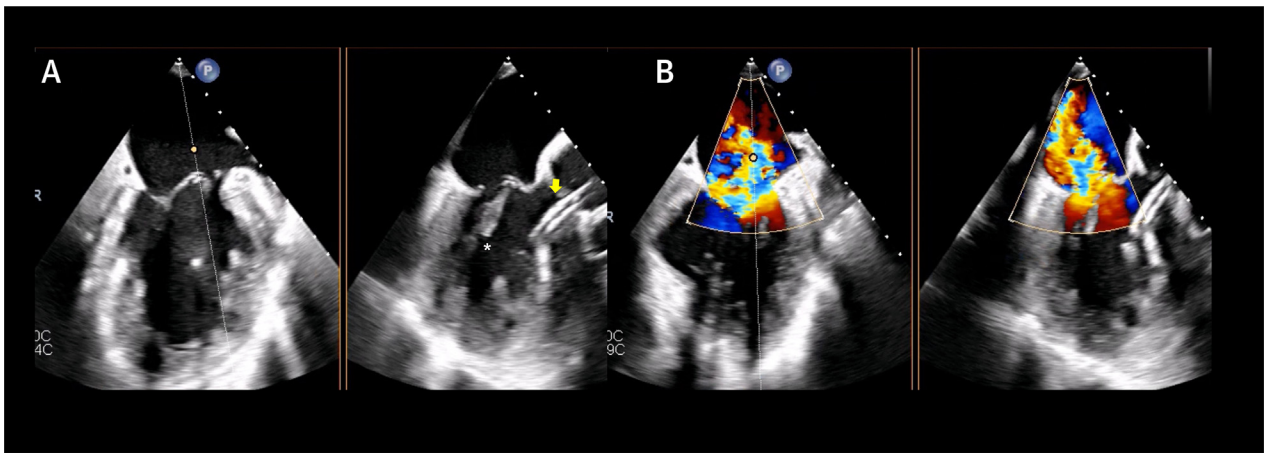
(A to C) 4-chamber, bicommissural, and left ventricular outflow tract; views, noting posterior leaflet flail with a small part of the papillary muscle (asterisk). (D) 3-dimensional en face view with the prolapsing segment (red arrowhead). (E) X-plane view with anteriorly directed mitral regurgitation jet.

transcatheter edge-to-edge repair (TEER) is selected, TEE is mandatory during the procedure.

An integrative approach including qualitative, semiquantitative, and quantitative parameters is recommended according to imaging guidelines.[39] However, some Doppler parameters are better to quantify chronic rather than acute MR. The combination of hypotension and high left atrium pressure decrease LV power and may lower the MR jet velocity across the mitral valve. Accordingly, color Doppler imaging often will not show a large turbulent flow disturbance, and thus, MR may be underestimated or not appreciated at all. A flail leaflet or ruptured papillary muscle, a hyperdynamic LV in a post-MI patient with pulmonary edema, or cardiogenic shock should be enough to substantiate the diagnosis, even if color Doppler does not show a large MR jet. Likewise, acute ischemic MR may be triggered by active or reversible myocardial ischemia and may disappear after reperfusion. Therefore, reassessment is advisable after revascularization.[14]

Contrary to PMR, acute "functional type" MR is caused by LV remodeling. The distortion between the LV and the mitral apparatus is best seen in the apical chamber views. Recently, Kimura et al,[40] using 3-dimensional echocardiography, observed that the mitral apparatus remains dynamic. As such, the most plausible mechanism in the "functional type" MR is not PM displacement but separation and excess angulation of PM, deforming the mitral valve. This is mainly related to the sudden-onset, regional wall motion abnormality without global LV remodeling.[40] The leaflets are essentially normal. Furthermore, a reduced leaflet area/annular ratio leading to a smaller coaptation index was also documented.[41] Abnormal leaflet adaptation can result in severe MR, despite relatively small leaflet tethering.[42] The mechanisms of post MI MR are shown in **Figure 5**.

FIGURE 3 Transesophageal Echocardiography Showing Complete Anterolateral Papillary Muscle Rupture

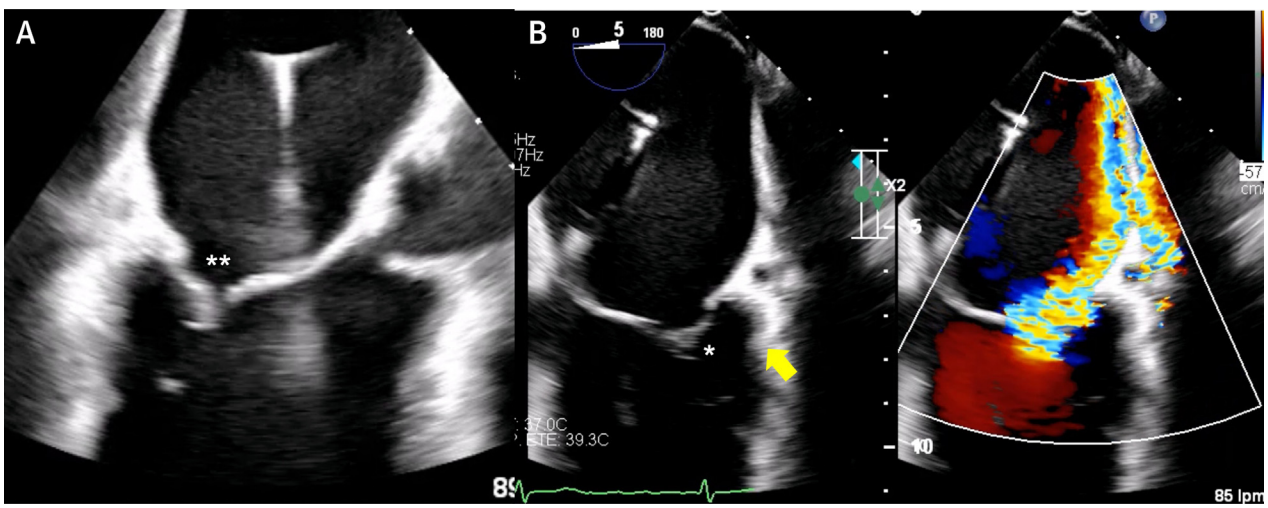


(A and B) X-plane views with the prolapse of the anterolateral commissure and the complete rupture of the muscle (asterisk). Note the hemodynamic compromise represented by mechanical cardiac support (Impella, yellow arrow). Resulting mitral regurgitation is torrential.

SURGICAL APPROACH

THE TIMING OF SURGERY. Surgical approach for ischemic functional MR is usually indicated by well-established factors: degree of MR, LV function/dimension, pulmonary artery systolic blood pressure, presence of atrial fibrillation, clinical symptoms, patient comorbidities, and response to medical therapy.[43] These aspects must be assessed by the heart team in terms of extent and potential changes, mainly deterioration, over time. Furthermore, the likelihood of mitral valve repair plays an additional critical role in the decision-making.[43] Functional ischemic MR may be present in some patients before the acute ischemic event. This situation is particularly common in elderly patients who may present with progressive ischemic functional MR with/without LV dysfunction, therefore requiring careful

FIGURE 4 Transesophageal Echocardiography of a Functional-Type Acute Mitral Regurgitation



(A and B) X-plane views demonstrating asymmetrical tethering with an eccentric and wide jet originating from centrolateral area (Video 4). **Gap between leaflets due to asymmetrical tethering. *Restricted posterior mitral leaflet. Yellow arrow indicates regional inferolateral wall motion abnormality.

TABLE 1 Clinical Classification of MR After MI

Type 1 • Cardiogenic shock: MAP <90 mm Hg + pulmonary edema • Elevated lactate levels • Requirement for vasoactive drugs and/or mechanical cardiac support • Requirement for urgent valvular intervention
Type 2 • Refractory pulmonary edema • MAP >90 mm Hg • Low output state (eg, oliguria) but normal lactate levels • Requirement for continuous intravenous diuretic agents • Requirement for urgent valvular intervention
Type 3 • MAP >90 mm Hg • Might be in low cardiac output state • Episodes of pulmonary edema • Intermittent intravenous diuretic agents • Valvular interventions
Type 4 • Mild-moderate HF • Oral diuretic agents • Typically treated medically, but late left ventricular remodeling may be unfavorable • Role of valve intervention uncertain

Adapted with permission from Shuvy et al,[32] from the IREMMI investigators.

HF = heart failure; MAP = mean arterial pressure; MI = myocardial infarction; MR = mitral regurgitation.

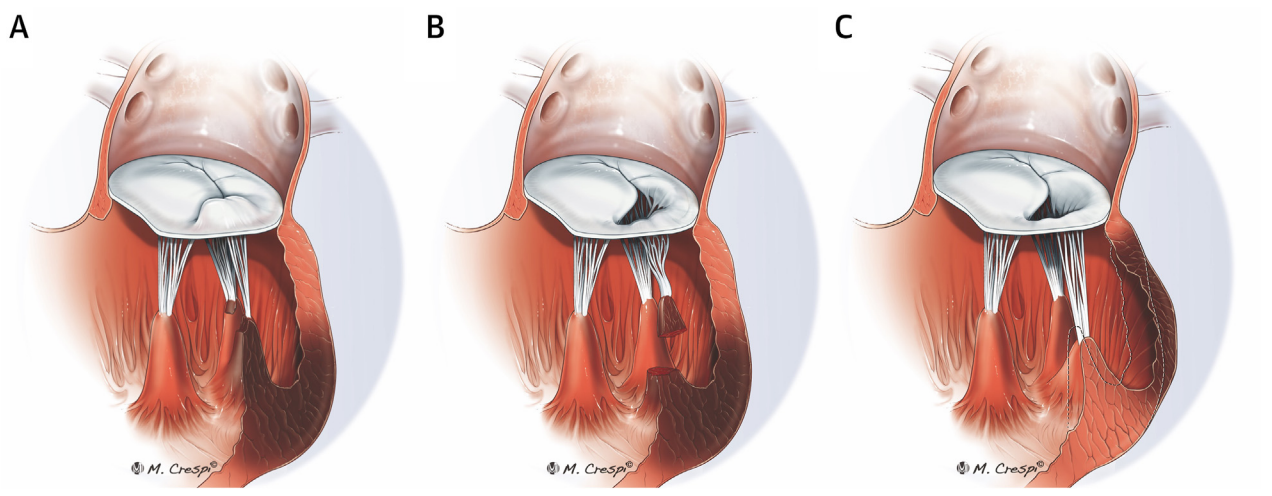
surveillance.[44] The absence of recurrent acute coronary events, however, does not preclude a progressive increase of MR, mainly because of further LV dilatation thereby leading to accentuation of mitral annular dilatation and mitral valve tethering caused by displaced papillary muscles, ultimately leading to the need of intervention.[44]

The timing and status of surgery markedly influence patient outcome, with early mortality higher than 20% in emergency indications, compared with lower than 4% in functional MR correction.[45,46] Indeed, severe MR caused by complete or partial PMR after MI usually warrants expedited mitral valve surgery (Video 5). Immediate surgical treatment remains at the forefront in the treatment of this entity. However, the timing of surgery is mostly determined by the hemodynamic status of the patient, with a reported median time to intervention of 7 days [24,47-51]

In other series,[49] more than 50% of surgical repair occurred within the first 2 days after MI. The 30-day mortality rate was 39%. Mortality predictors included low cardiac output, renal failure, and implementation of extracorporeal membrane oxygenation (ECMO). Of note, the time between acute myocardial infarction (AMI) and surgery showed no significant effects on survival.[49]

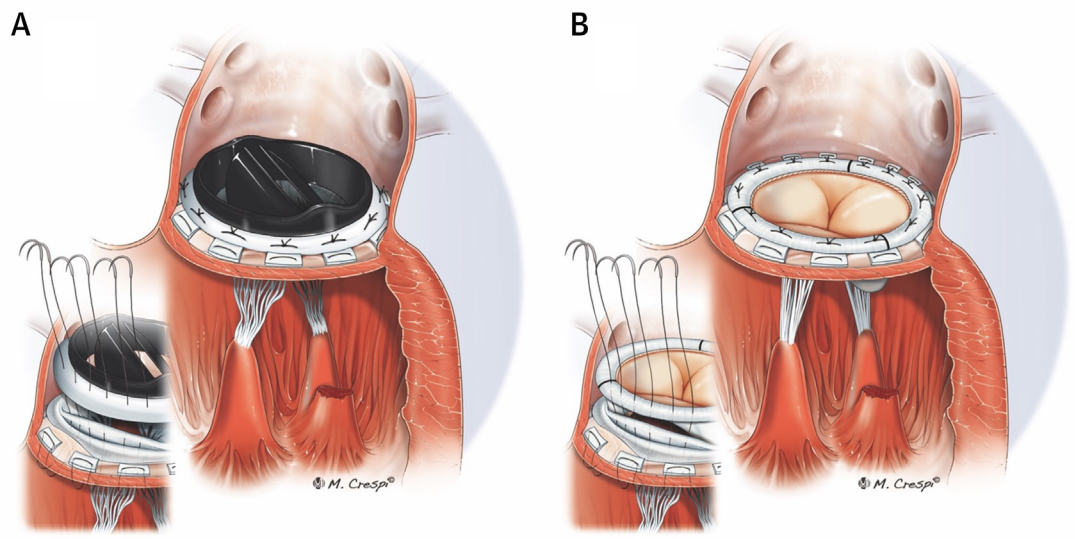
Kettner et al[50] showed that an early progression to CS and nonsurgical management were the only independent predictors of 30-day mortality. In their series, correction of acute MR was mostly performed with mitral valve replacement (MVR), and less frequently by papillary muscle repair.[50] Patients with CS underwent surgical intervention within a median of 1 day from onset of MR. In patients without CS, the operation was postponed for a median of 9 days.[50] Shorter time from onset of AMI to surgery was associated with better survival of patients with CS.[50]

FIGURE 5 Illustration Showing Mechanisms of Acute Mitral Regurgitation



After myocardial infarction (A) tip papillary muscle rupture. (B) Complete papillary muscle rupture. (C) Functional mitral regurgitation phenotype with posterior mitral leaflet restriction and local left ventricular remodeling.

FIGURE 6 Illustration Showing Mitral Valve Replacement in Papillary Muscle Rupture Setting



(A) Replacement with mechanical valve. (B) Replacement with biological valve. Both prosthesis implantation with preservation of the valve apparatus.

The role of mitral valve replacement. Randomized and observational multicenter trials comparing repair vs replacement in ischemic MR failed to show any difference in terms of LV remodeling or survival at 1 and 2 years from surgery, actually demonstrating a higher MR recurrence rate and cardiac-related hospital readmission in the repair group.[52-54]

In case of MVR, it is nowadays recognized the role of valvular and subvalvular apparatus, therefore, preserving mitral-ventricular continuity to prevent further postoperative LV dysfunction caused by mitral-ventricular decoupling.[46,48,55-57]

In the setting of acute MR caused by PMR, mortality rates with MVR remain high, but death without intervention can reach prohibitive rates of 80%.[43,45,46,51] These patients, however, typically undergo MVR in a critical state[24] with considerably high mortality rates, ranging from 12.5% to 39%.[24,43,45,46,51]

Russo et al[24] reported on 54 consecutive patients who underwent MVR for post-AMI PMR from 1980 through December 2000. Operative mortality was 18.5%. Five-year survival was 65%, and freedom from heart failure was 52%, similar to that of matched control subjects with AMI.

In a more contemporary cohort[56] from 2001 to 2019, the overall in-hospital mortality rate was 24.8%. Most patients underwent MVR (82.7%), mainly with bioprosthesis. Chordal sparing MVR is important, underscoring the importance of preservation of the subvalvular apparatus to improve long-term survival (Figure 6).[57]

The role of mitral valve repair. Mitral valve repair for secondary ischemic MR has been characterized by several reparative techniques, but none are completely satisfactory because of the well-known issue of addressing a normal valve apparatus, besides annular dilatation, in contrast to a ventricular mechanism of MR.[46,58] Indeed, besides the techniques focusing on the annular undersizing, mitral leaflet extension, or the edge-to-edge technique, all designed to enhance leaflet coaptation, papillary muscle approximation has been the only real and reproducible intervention acting on the actual mechanism of postischemic MR.[58] Furthermore, as mentioned, the lack of evidence coming from the randomized or multicenter studies[52-54] failed to demonstrate the superiority of mitral valve repair in such an MR setting, rather underlying the relevance and impact of recurrent MR after repair.[52-54] The current indications, however, still favor conservative surgical approach when sufficient expertise and likelihood of repair might be provided to the surgical candidate.[46,48,49,58,59]

In cases with complete PMR (as compared with partial), mitral valve repair is often not feasible

because of necrotic and friable infarcted tissue. Although mitral valve repair is not the preferred treatment strategy in patients with PMR,[46] some publications reported success with valve-sparing and reconstructive approaches.[46,48,49,58,59] A series of 24 patients[49] described successful mitral valve repair in almost one-third of patients. This was primarily achieved in cases of incomplete PMR. Bouma et al[60] also published a series of 9 patients with no in-hospital mortality, all with partial PMR and relatively low preoperative risk scores (only 1 patient with intra-aortic balloon pump). They reported a 90% mitral valve repair rate with 83% survival at 5 years.[60]

The preference for mitral valve repair when compared with MVR was higher in earlier studies, being reduced to 17% in the most recent cohorts.[59,61] This reflects the surgeons' preference for MVR. The mitral valve repair failure rates in the studies are variable and range from 4% to 50%.[29,47,49,62-64]

Interestingly, recent publications found no clear relationship between type of surgery and early mortality, although selection bias might have influenced these results.[56,64]

In patients with refractory CS, the use of bioprosthesis is strongly recommended.[46]

The surgical treatment of functional MR involves several reconstructive techniques, including annuloplasty, papillary muscle approximation, or edge-to-edge procedure, the so-called Alfieri's stitch (either para-commissural or central). However, these surgical procedures are more often applied in a chronic setting, although some exceptions apply.[46,59-61] **Figure 7** shows several mitral valve repair strategies in post-MI MR.

Of interest, no difference in mortality has been found between the 2 main mechanisms of post-MI MR in the surgical literature.[29]

The role of coronary artery bypass graft in the context of post-MI PMR. Russo et al[24] and Chevalier et al[29] showed that the performance of coronary artery bypass graft surgery was associated with lower operative mortality (OR: 0.18; 95% CI: 0.04-0.83; $P = 0.011$). Likewise, concomitant coronary bypass surgery was the only independent predictor of improved early survival.[56] Coronary bypass surgery will also ease cardiopulmonary bypass weaning, and potentially improve LV function.[29,30] However, other series have shown no effect of coronary surgery on survival.[61] Based on these observations, concomitant coronary bypass surgery is recommended following operators' considerations.

PERCUTANEOUS APPROACH

TRANSCATHETER INTERVENTIONS. Data supporting percutaneous therapy is limited but in progress. Percutaneous approach is growing because many patients are excluded for surgery. In the SHOCK (Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock) Trial Registry, only 38% of patients with acute MR were offered surgery.[16] Likewise, in a recent publication analyzing the presence of PMR in a large cohort of MI patients, only 57.5% of patients received surgical treatment.[37] This decision is influenced by age, comorbidities, and clinical stability. Even in surgical patients, early mortality, rate of transfusions, renal failure, and prolonged mechanical ventilation still remain high.[61,65] Therefore, a less-invasive approach to treat MR in post-MI patients is appealing to broaden the population receiving treatment.

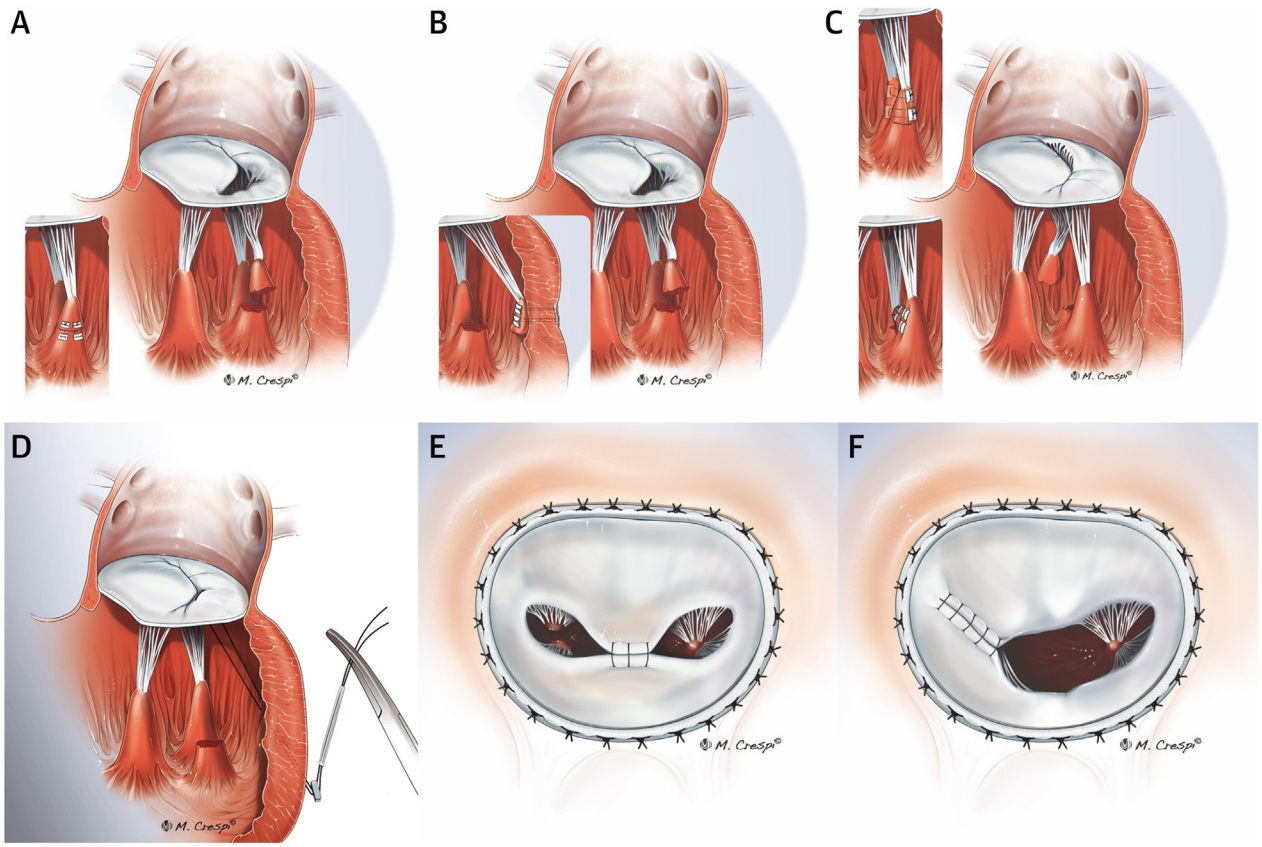
From all devices available, the TEER with the MitraClip system (Abbott Vascular) has the larger clinical experience. TEER with MitraClip is a safe and effective technique for reducing MR in high-risk patients for surgery. In chronic disease, TEER improves symptoms, quality of life, and prognosis in patients with functional and degenerative MR.[66-68] Lately, PASCAL has also shown a safe and effective performance compared with MitraClip in MR patients.[69,70] Likewise, transcatheter mitral valve replacement with different devices has shown promising results with a large proportion of MR elimination.[71]

Most importantly, because acute MR represents a large unmet need in the development of less invasive treatments, the use of transcatheter interventions in this scenario has grown significantly in the last years.

Papillary muscle rupture. Initially described as case reports,[72-77] it is now clear that PMR can be successfully treated percutaneously. Results show acute MR reduction and hemodynamic improvement. These initial reports refer to nonsurgical candidates, in whom TEER was offered as a "last resort" option. In fact, in all guidelines and recommendations,[30,43,78] the option for percutaneous therapy appears only in selected high-risk patients not suitable for surgery. However, given the high incidence of nonsurgical candidates, and the complexity of treating patients in CS with multiorgan failure, TEER may offer a valuable alternative in selected population.

The largest series of PMR treated by TEER has been recently presented.[79] All patients were turned down for surgery because of high surgical risk (median

FIGURE 7 Illustration Showing Techniques of Mitral Valve Repair in the Presence of Papillary Muscle Rupture



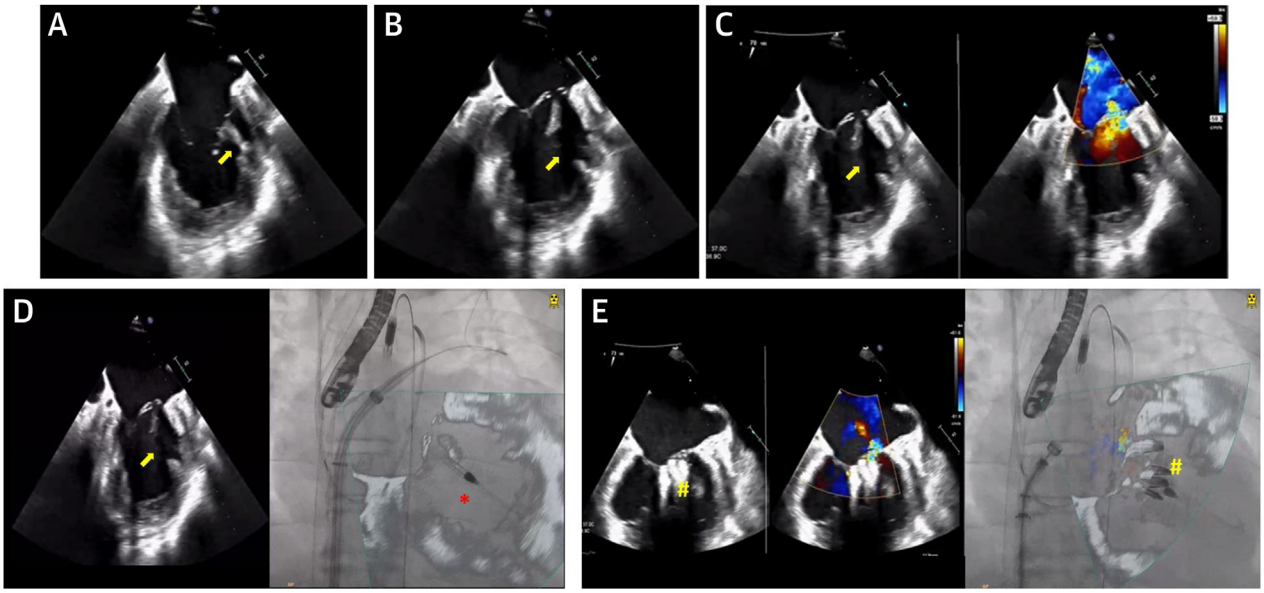
(A) Papillary muscle resuture; (B) reimplantation of papillary muscle into myocardium; (C) ruptured papillary muscle suture to the normal papillary muscle; (D) papillary muscle resection and leaflet suture to myocardial wall; (E) central Alfieri + annuloplasty ring; (F) para-commissural edge-to-edge repair technique.

EuroSCORE II 27%). All patients were on vasopressors, 90% were in CS, 83% were ventilated, and 74% were under mechanical support. Median LV ejection fraction was 45%. After a median 6 days post-MI, TEER success was 87%. The procedure results in rapid hemodynamic improvement. Significant left atrium V-wave reduction and decrease in pulmonary pressures were uniformly obtained. In-hospital mortality was 30%. Still high, but acceptable taking into consideration that patients were not surgical candidates. Interestingly, 22% of patients received elective, successful surgical mitral valve replacement at follow-up. This highlights the potential role of TEER as bridge-to-surgery, with a more stable or improved situation. An example of TEER in PMR is shown in **Figure 8** and Video 6.

These results were obtained mostly with the second MitraClip generation device.[80] It is expected that these results can even be enhanced with the current generation 4. This generation offers better leaflet grasping and continuous atrial pressure monitoring. Generation 4 reported excellent results (residual MR 0/1) in >90% at 30 days.[81]

Functional MR phenotype. Very promising results are now available for TEER in patients developing severe symptomatic "functional type" MR after AMI.[82] In a first publication, 44 patients with a high surgical risk (median EuroSCORE II 15.1%) were included between 2016 and 2018. Median time between MI and treatment was 18 days, reflecting multiple unsuccessful attempts to stabilize the condition with medical management. Patients were highly symptomatic, with 63.6% in NYHA functional class IV. Technical success was 86.6%. Mortality at 30 days was 9.1%. At 6 months, MR ≤2+ was noted in 72.5% and NYHA functional class I to II was observed in 75.9% of surviving patients.

FIGURE 8 Acute Mitral Regurgitation Caused by Complete Anterolateral PME Treated by Transcatheter Edge-to-Edge Repair



Complete papillary muscle rupture (yellow arrows) and severe mitral regurgitation originating from centrolateral scallops (A to C). Patient was in cardiogenic shock (note Impella in place, red star). Transcatheter edge-to-edge repair was carried out under transesophageal echocardiography and echo-fluoroscopy fusion imaging (D and E). After 4 MitraClip devices (yellow pound sign) MR was reduced to mild-to-moderate.

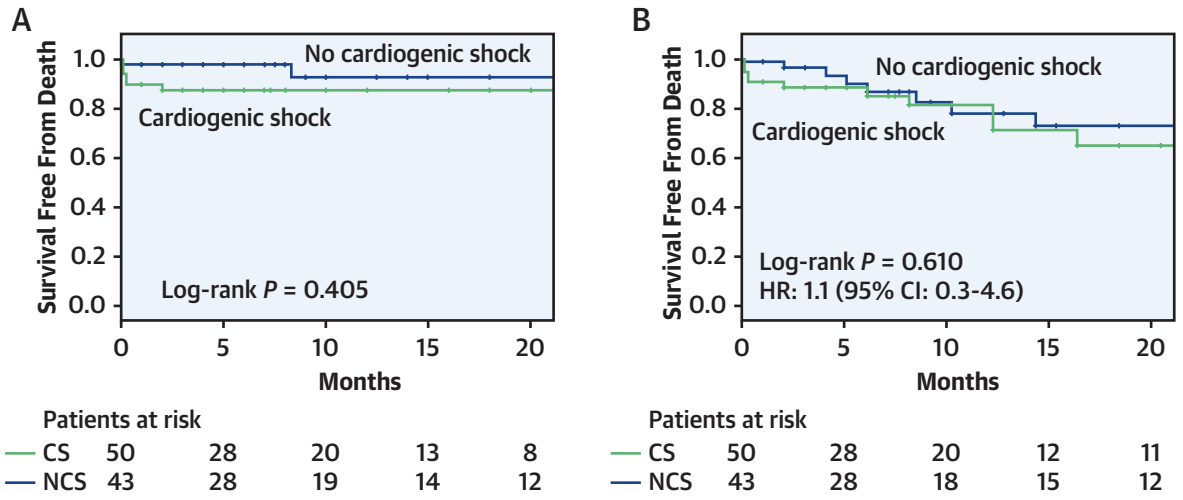
Subsequently, investigators assessed the role of TEER in patients with functional MR on CS. A cohort of 93 patients was studied, with refractory CS in 53%.[83] Two-thirds of CS patients were under support with intra-aortic balloon pump or Impella, and 12% under VA ECMO. Technical success was high and did not differ between patients with or without CS. The 30-day mortality was numerically higher in the CS group (10% CS vs 2.3% non-CS; $P = 0.212$). After median follow-up of 7 months, the combined event mortality/rehospitalization was similar (28% CS vs 25.6% non-CS; $P = 0.793$) and the MR reduction at 3 months was comparable (**Figure 9** and Video 7).

The most important predictor for survival was procedural success, independent of LV dysfunction.[84] These results were confirmed by other studies, supporting the role of TEER in CS patients.[85-87] Likewise, these patients are the paradigm of disproportionate MR, and therefore, high clinical benefit is expected if a successful result is obtained.[88] Local experience and heart team approach is essential to optimize patient selection and improve outcomes.

Finally, the most comprehensive study yet published compared conservative, surgical, and TEER therapy in the management of severe MR post-MI and included 471 patients MI from 21 institutions in the United States and Europe.[17] Patients with acute PMR receiving emergent therapy were excluded from the analysis. From the total group cohort, 56% were managed conservatively and 44% underwent interventions. From the interventional group cohort, 52% were treated with surgery and 48% with TEER. Patients managed medically had the worst outcomes. Patients managed with TEER were older and had higher morbidity burden. After propensity score adjustment, mortality at 1 year was higher in patients undergoing surgical correction when compared with those receiving TEER. This difference was driven by in-hospital mortality (16% vs 6%; $P = 0.03$), which was independent of the risk score profile of the patients (**Figure 10**). An example of functional type treatment by TEER is shown in **Figure 11**.

Potential advantages of a percutaneous approach. There are several potential advantages of a percutaneous approach of this condition. First, TEER induces an almost immediate hemodynamic improvement by relieving the amount of MR and increasing effective stroke volume. Simultaneously, a sudden decrease in left atrium and pulmonary artery pressures ameliorate pulmonary congestion, increasing cardiac output. These result in a faster recovery with the least tissue aggression possible.[89]

FIGURE 9 Effect of CS in Patients Undergoing Transcatheter Edge-to-Edge Repair for Acute Ischemic Mitral Regurgitation



(A) No difference between cardiogenic shock (CS) or non-CS patients on all-cause mortality. (B) No difference between groups regarding the combined endpoint of death/readmission for heart failure. Adapted with permission from Kar et al.[80]

Second, the extracorporeal, pump-related systemic inflammatory reaction is avoided. The release of free-radicals and associated microembolic phenomenon leading to postoperatory organ dysfunction[90,91] in patients with acute myocardial and lung damage are evaded.[92] In fact, patients with acute MR post-MI usually die from pulmonary complications.[23] This can easily be decreased by a fully percutaneous, off-pump procedure.

Third, TEER does not preclude a delayed cardiac surgery, as shown by Haberman.[79] In fact, the role of TEER as a bridge to a lesser risk surgery is appealing. And finally, compared with open heart surgery, TEER is associated with lower bleeding complications (just a venous access) in patients usually at high bleeding risk caused by antithrombotic therapy after MI or PCI, or in those under mechanical support with large bore-access catheters.[93]

All of these advantages might set a new paradigm in the management of these patients.[94]

Potential drawbacks of percutaneous approach and strength of the surgical procedure. Although initial results are promising, TEER in acute MR is associated with significant limitations that require careful analysis.

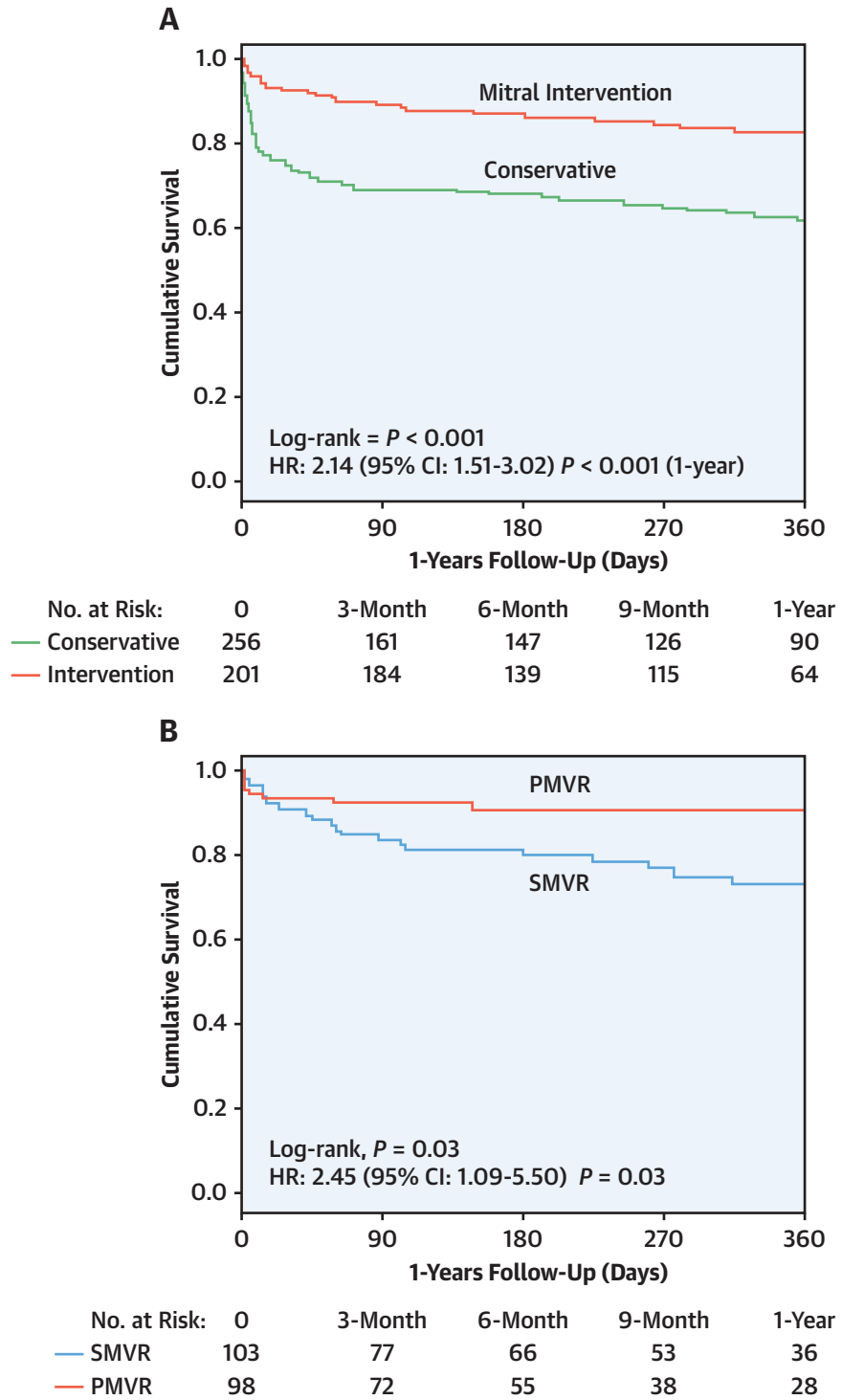
First, TEER in this setting is one of the most technically challenging procedures. The left atrium is small and noncompliant. Therefore, transeptal puncture and proper allocation of the TEER device over the valve is potentially complex and requires experience. Likewise, it is possible that a puncture outside fossa ovalis is required.

Second, flail segments can be large and wide, and commissural lesions are not uncommon. In those cases, it is advisable to take advantage of the new features of MitraClip generation 4 or PASCAL Ace,[95] which allow independent leaflet capture and leaflet optimization. With this new generation, almost all cases can be technically performed. In case of PMR, usually after multiple device deployment, the papillary muscle is stabilized avoiding further tissue tearing. Special attention is needed to not impinge the muscle with the device, avoid entanglement, or even complete PMR in those with a partial involvement.

Third, the clinical situation of the patient is also very demanding. Patients can be potentially unstable, under mechanical support, or even in cardiac arrest. TEER mandates accurate preprocedural investigation anatomical features to plan appropriate procedural strategy. Even in the presence of cardiocirculatory assistance, expeditious MR correction is required, making again surgery the preferred pathway.[96] Moreover, potential interactions between the device and intracardiac catheters must be avoided.[97] It is also advisable to reduce support after device implantation to evaluate mitral valve gradients.

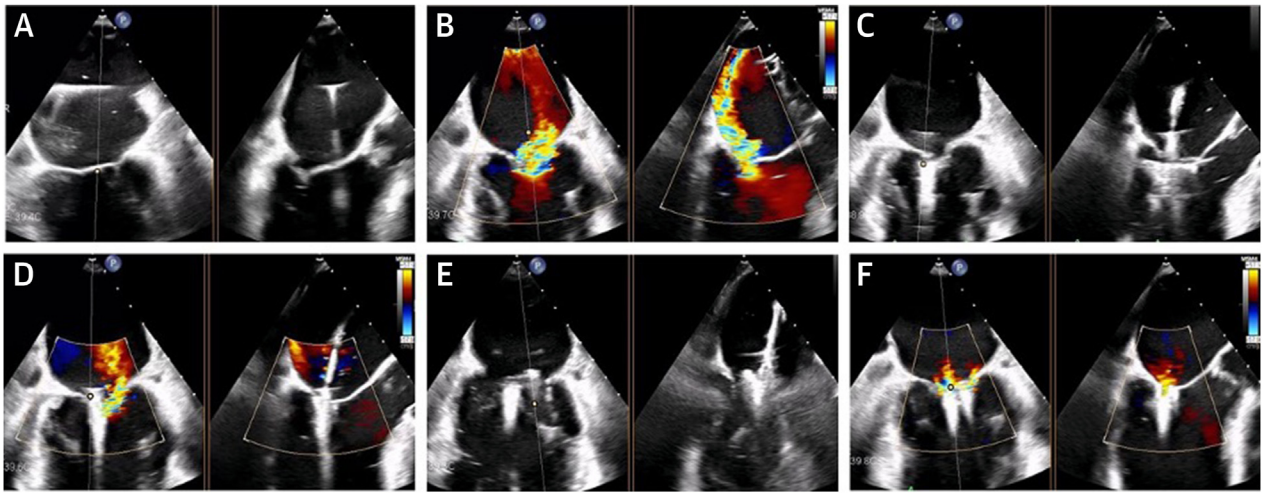
Fourth, initial results were obtained in cases performed at highly experienced centers in the use of

FIGURE 10 Survival Analysis of Post-Myocardial Infarction Mitral Regurgitation Patients With Different Management Strategies



(A) Significant increased mortality in patients managed conservatively. (B) A significant better survival in patients treated by TEER compared with those managed surgically. Adapted with permission from Haberman et al.[17] PMVR = percutaneous mitral valve repair; SMVR = surgical mitral valve replacement.

FIGURE 11 Acute Functional Type Mitral Regurgitation Treated by Transcatheter Edge-to-Edge Repair



(A and B) X-plane views demonstrating asymmetrical tethering with an eccentric and wide jet originating from centrolateral area. First device (MitraClip XTW) was implanted in central position (C), resulting in a moderate residual jet lateral to the clip (D). A second device (MitraClip NT) was implanted laterally (E) with trace mitral regurgitation as outcome and no significant transmitral gradient (F).

MitraClip. Thus, a TEER strategy cannot be generalized to less-experienced teams.

Finally, progressive LV remodeling will reduce the effective mitral valve competence reached during the original TEER.[96,98]

STUDY LIMITATIONS. The encouraging initial results with TEER are limited to retrospective, observational analyses of a small population. As such, selection bias cannot be excluded. Most of the patients who responded to medical therapy and cardiac support were those who received the therapy. This population can represent a better prognostic category, and therefore, this technique may not be applicable to all patients. However, this limitation may apply as well to surgical literature with only observational studies available, suffering from the same selection bias.[64]

Furthermore, as mentioned, long-term clinical and echocardiographic follow-up is limited. Ideally, the implementation of a properly designed and executed randomized trial should provide more reliable information. However, as in surgical literature, this trial is still lacking. Further research must be warranted to elucidate the best management options for this condition.

Most importantly, TEER likely precludes the possibility for mitral valve repair. Therefore, if it fails, MVR will almost certainly represent the expected procedure of these patients and is still the predominant first-line procedure in this population.

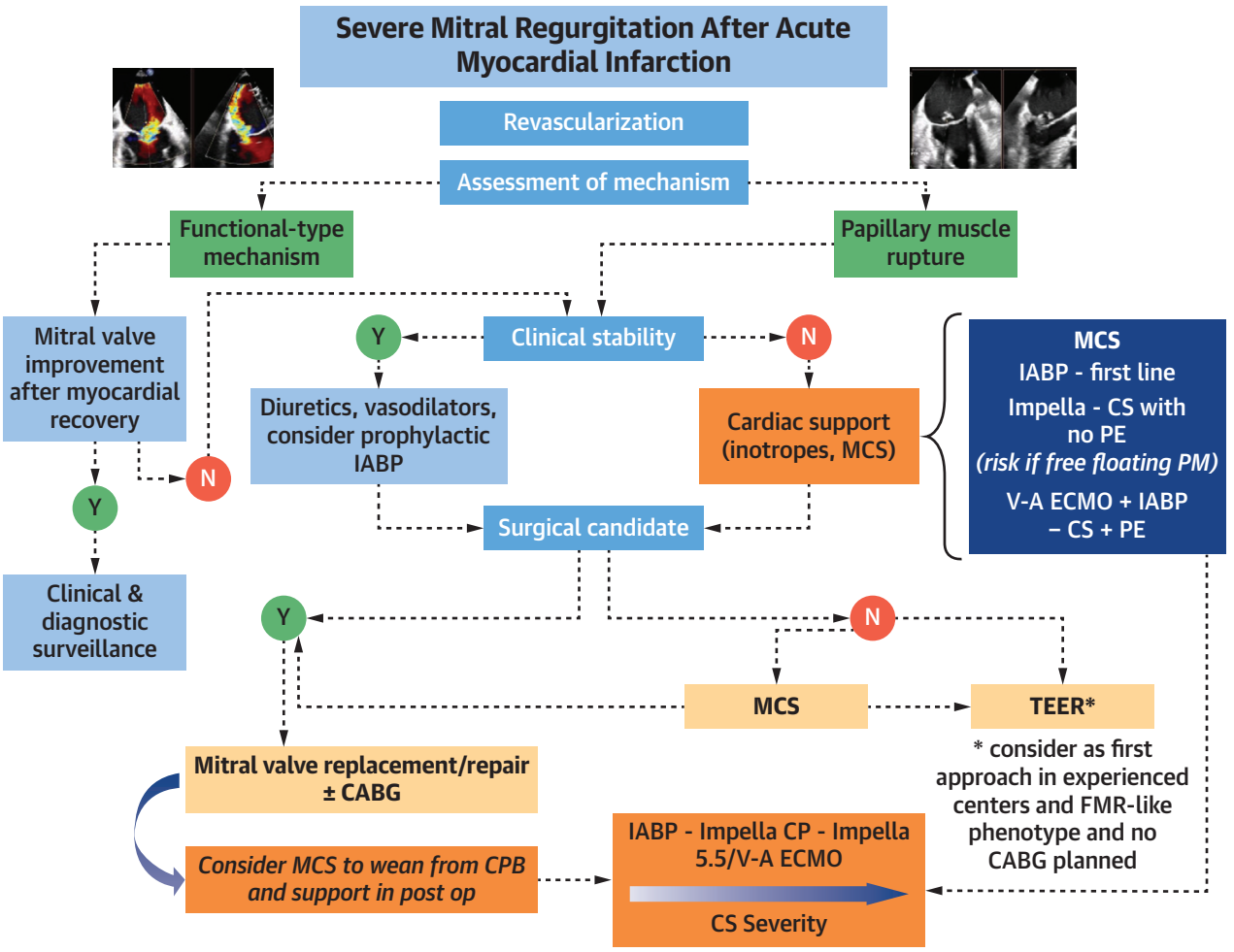
THE INCREASING ROLE OF MCS. As mentioned before, pre-emptive use of MCS in the presence of refractory CS can improve outcomes. This support will stabilize patients perioperatively.[99] Most importantly, MCS is crucial in many patients postoperatively. To emphasize this, the segment devoted to MCS was intentionally included after the segments devoted to therapy.

The initial data on MCS as a bridge to surgery was presented by Watkins et al[100] in 12 patients with deep cardiogenic shock. This strategy was associated with significant improvement in the most relevant hemodynamic and metabolic parameters. The benefit of MCS as bridge-to-surgery was also documented by Dobrilovic et al,[101] reducing operative risk and improving post-procedural outcome in CS patients.

Considering that the complications of CS can persist after therapy, postprocedural use of MCS may improve in-hospital survival in these patients, which has not changed in the last decades.[45,56]

Intra-aortic balloon pump still represents the first line of cardiocirculatory assistance in patients with acute MR post MI (**Central Illustration**). Intra-aortic balloon pump can improve LV forward flow, reduce myocardial workload, increase coronary perfusion, and reduce LV end-diastolic pressure. Therefore,

CENTRAL ILLUSTRATION Treatment of Severe Mitral Regurgitation After Acute Myocardial Infarction



Estévez-Loureiro R, et al. J Am Coll Cardiol. 2024;83(18):1799–1817.

Revascularization is crucial in the treatment of severe mitral regurgitation (see text). This figure drives the rational and therapeutic decision-making according to clinical stability and surgical candidacy. It also involves the emergent alternative for mechanical circulatory support, either before or after surgery if needed.
CABG = coronary artery bypass grafting; CPB = cardiopulmonary bypass; CS = cardiogenic shock; FMR = functional mitral regurgitation; IABP = intra-aortic balloon pump; MCS = mechanical circulatory support; PE = pulmonary edema; PM = papillary muscle; V-A ECMO = venoarterial extracorporeal membrane oxygenation; TEER = transcatheter edge-to-edge repair.

intra-aortic balloon pump is still recommended in the management of acute MR complicated by cardiogenic shock.[102] However, these patients frequently have refractory cardiocirculatory collapse and severe end-organ hypo-perfusion, making intra-aortic balloon pump assistance not sufficient. In these cases, more powerful MCSs should be considered (**Central Illustration**). Trans-aortic microaxial pumps, like Impella CP or Impella 5.5 (Abiomed), represent potential upgrades of assistance. Nonetheless, either form of Impella requires careful evaluation in the present of a floating papillary muscle, because it might be sucked in the device mechanism leading to sudden malfunction or even to embolization of cardiac debris. Impella represents a useful tool for intraoperative or perioperative support with dedicated LV assistance if no respiratory support is needed.

The more severe forms of CS might require further upgrade of assistance, with venoarterial extracorporeal life support (VA-ECMO) or TandemHeart, using a peripheral approach (**Central Illustration**). Such

devices may offer concomitant gas-exchange because of the presence of an oxygenator, which is extremely useful in the presence of severe pulmonary edema. The circuit uses a centrifugal pump such as the Centrimag (Thoratec), Rotaflow (Maquet), or TandemHeart (TandemLife) and a blood-gas exchange unit that includes a heat exchanger and a membrane oxygenator. As the blood transits through the membrane oxygenator, hemoglobin becomes fully saturated with oxygen and carbon dioxide is removed. The degree of oxygenation is determined by the flow rate and fraction of inspired oxygen. The circuit configuration permits the withdrawal and pumping of desaturated blood from the right atrium or a central vein, with nonpulsatile pump outflow directed toward the membrane oxygenator then guided via an outflow cannula to a systemic artery (eg, femoral or subclavian artery). Specifically, with VA-ECMO, LV afterload increases, as reflected by the increase in effective arterial elastance, a known component of LV afterload. This contributes to an increase in LV filling pressures. In patients with significantly reduced ejection fractions at baseline, VA-ECMO may cause an increase in wall stress and oxygen demand, which impedes myocardial recovery and may precipitate progressive pulmonary edema and acute lung injury. In these cases, strong consideration of biventricular mechanical support devices is mandatory. Concomitant use of VA-ECMO and Impella (ECMELLA) provides a synergistic approach to simultaneously reduce LV filling pressures and improve cardiac output. A large study in 2,427,315 patients with AMI reported PMR in 0.02% of patients. Of those, intra-aortic balloon pump was used in 71.2% of cases, Impella in 23.3%, and VA-ECMO in 5.5%.[37] The use of MCS decreased mortality and is encouraged in unstable patients to preserve or recover organ function before intervention. MCS can also improve survival within the peri-intervention period.

THE FUNDAMENTAL ROLE OF THE DEDICATED HEART TEAM. Case-by-case evaluation is mandatory to select the most appropriate approach in post-AMI MR. Surgery is still considered the first-line treatment of such a condition. However, in cases with "functional-type" MR or PMR in profound CS or in patients with significant comorbidities or even considered inoperable, TEER might offer an alternative for recovery or for bridging to a safer and lower-risk surgery.

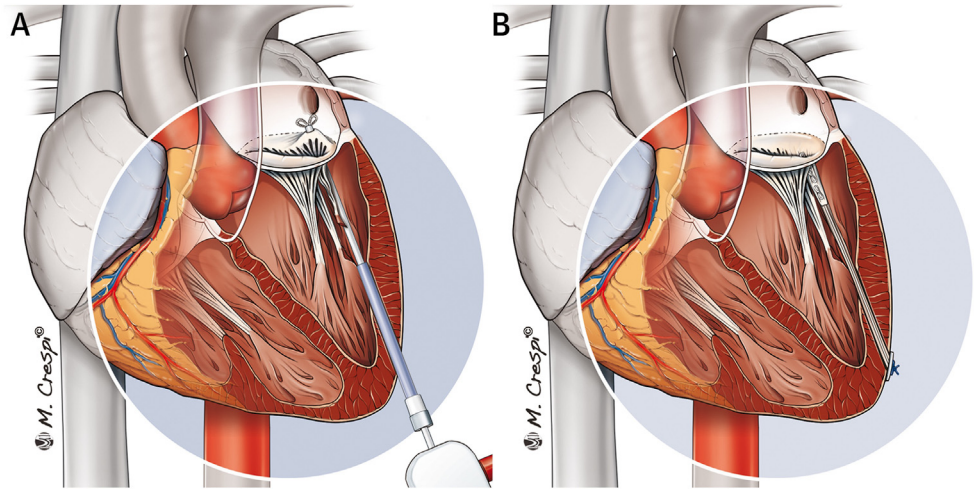
The dedicated heart team will need to assess the patient conditions and comorbidities. The heart team will appropriately define the mechanisms of post-AMI MR, describe the anatomical features, and evaluate the need and type of ancillary mechanical circulatory support. Furthermore, the heart team must evaluate the risk of the surgical approach, the feasibility and complexity of the TEER, and the periprocedural management, including potential complications. Most importantly, the heart team should delineate pathways to handle these complications after surgical or transcutaneous therapies. It is therefore understandable that a robust heart team, including intensivist, imaging, interventional, surgeon and heart failure specialists, will offer a better, multidisciplinary decision-making. It should not be underestimated that these patients, particularly the ones undergoing surgical procedures, are at high risk for further clinical deterioration, thereby requiring careful analysis and assessment of pros and cons. As mentioned, a prolonged use of preoperative mechanical circulatory support after the intervention might be required from the operating room or catheterization laboratory to the intensive care unit. The heart team should also consider the inherent aspects in the informed consent.[103]

FUTURE DEVELOPMENTS

SURGERY. Although TEER techniques have shown feasibility and promising results in selected patients with post-AMI PMR, surgery still remains at the frontline of valvular interventions in this scenario. The use of minimally invasive techniques, like transventricular off-pump mitral valve repair with artificial chordae,[104] have also been proposed in such a setting, thereby broadening the surgical options in terms of potential approaches (**Figure 12**). Considering the steady surgical mortality in the last 2 decades, a paradigm shift regarding procedural strategy and patient management is warranted. Percutaneous intervention will represent potential complementary procedures in high-risk or inoperable patients, or a bridge-to-surgery in other selected candidates. The critical game changer will be represented by enhanced modalities including the pre-emptive approach for MCS to preoperatively stabilize critically ill patients. Furthermore, MCS will reduce or prevent complications in the delicate perioperative phase of patients in cardiogenic shock or low cardiac output syndrome.

TRANSCATHETER APPROACH. Despite improvements in the transcatheter approach, there are multiple controversial issues. Studies show an average time of 20 days from MI to TEER. Considering that the

FIGURE 12 Acute MR Treated by Neochord Implantation



(A) Beating heart artificial chordae implantation in chordal or incomplete papillary muscle rupture. (B) Device implanted on prolapsing leaflet and attached to left ventricular apex.

procedure is associated with high technical success and rapid clinical recovery, earlier treatment could offer improved results. Furthermore, we only have information with the MitraClip device. Other devices like PASCAL are showing promising results.[71,95] As a nitinol-based constructed implant, PASCAL provides an easier tissue-device interaction. Furthermore, PASCAL has the possibility of elongation, an advantage to avoid device-induced, papillary muscle deterioration. Perhaps in the future a percutaneous valve replacement for urgent implantation will offer better results, similar to the ones seen in urgent TAVR for patients in CS for severe aortic stenosis.

CONCLUSIONS

Management of post-MI MR is a complex and challenging scenario. Recent advances in mechanical support and surgical and transcatheter techniques are intended to broaden the spectrum of patients eligible for successful therapy. Imaging plays a key role as a diagnostic tool and during interventional procedures. Pre-emptive MCS will improve results in both surgery and percutaneous repair. Surgery maintains its position as the first-line therapy. However, considering its favorable risk/benefit balance, TEER can potentially hold a prominent space in the immediate management of patients with MR post-MI in the near future. However, more in-depth studies of long-term effect and outcomes are needed. A dedicated and multidisciplinary heart team-based approach is essential to offer the best individualized and timely treatment.

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