Rupture of Papillary Muscle and Chordae Tendinae Complicating STEMI: A Call for Action

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Papillary muscle rupture (PMR) or chordae tendinae rupture (CTR) is a rare but lethal complication after ST elevation myocardial infarction (STEMI). Due to the rarity of this condition, there are limited studies defining its epidemiology and outcomes. This is a retrospective study from Nationwide Inpatient Sample database from 2002 to 2014 of patients with STEMI and PMR/CTR. Outcomes of interest were incidence of in-hospital mortality, cardiogenic shock (CS), utilization of mechanical circulatory support (MCS) devices and mitral valve procedures (MVPs) among patients with and without rupture. We also performed simulation using the cardiovascular model to better understand the hemodynamics of severe mitral regurgitation and effects of different medications and device therapy. We identified 1,888 patients with STEMI complicated with PMR/CTR. Most of the patients were >65 years of age (65.3%), male (63.6%), and white (82.3%). They had significantly higher incidence of CS, cardiac arrest, and utilization of MCS devices. In-hospital mortality was higher in patients with rupture (41% *vs.* 7.40%, $p < 0.001$) which remained unchanged over the study period. Hospitalization cost and length of stay was also higher in them. MVP and revascularization led to better survival rates (27.9% vs. 60.6%, adjusted OR: 0.14; 95% CI: 0.10–0.19; $p < 0.001$). Despite significant advancement in the revascularization strategy, PMR/CTR after STEMI continues to portend poor prognosis with high inpatient mortality. Cardiogenic shock is a common presentation and is associated with significantly inpatient mortality. Future studies are needed determine the best strategies to improve outcomes in patients with STEMI with PMR/CTR and CS. *ASAIO Journal* XXX; XX:00–00.

Key Words: ST elevation myocardial infarction, papillary muscle rupture, chordae tendinae rupture, cardiogenic shock, mechanical circulatory support devices

Acute ischemic mitral regurgitation (MR) is a known complication of ST elevation myocardial infarction (STEMI). It usually results from partial or complete papillary muscle rupture (PMR) or chordae tendinae rupture (CTR).[1–5] Advances in reperfusion techniques such as percutaneous coronary intervention (PCI) have resulted in significant decrease in the rates of mechanical complications of STEMI. The incidence of PMR/CTR in older studies was reported to be around 1–5% of acute myocardial infarction (AMI), but recent contemporary registries have reported incidence have declined to 0.25%.[1,2,6–8]

Acute MR from PMR/CTR is frequently associated with cardiogenic shock (CS) and massive pulmonary edema with poor short-term outcomes. Often, these patients require immediate hemodynamic support for incipient CS with the primary goal of increasing stroke volume and decreasing regurgitation. This can be achieved by using percutaneous mechanical circulatory support (MCS) devices, which also serve as a bridge to surgery.[9–12] The role of cardiac surgery has been heavily debated with conflicting evidence regarding the optimal approach and timing. Studies have reported that patients who underwent concomitant surgery of mitral valve replacement and coronary artery bypass graft (CABG) for PMR/CTR had good clinical outcomes.[4,5] Earlier nonrandomized trials advocated for immediate surgical intervention on acute MR in patients with acute shock resulting from mitral valve disruption.[13–15] In contrast, other studies have advocated for postponing the surgical intervention in hemodynamically stable patients to allow for the formation of fibrotic tissue.[6,11,16]

To our knowledge, nationwide large-scale data on in-patient mortality, clinical outcomes, incidence of CS and utilization of MCS devices in patients with STEMI complicated with PMR/CTR are lacking. We used a large US national inpatient sample (NIS) database to determine the incidence and clinical outcomes in STEMI patients with PMR/CTR.

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Methods

Data Source

This study was conducted using the NIS database of the Health Care Utilization Project sponsored by the Agency for Healthcare Research and Quality. Briefly, this nationally representative database is the largest all-payer inpatient database in the United States containing discharge data from a 20% stratified sample of hospitals and encounter-level information of hospital stays compiled in a uniform format with privacy protection of individual patients. Each year, more than 7 million hospital stays are sampled nationwide which, when weighted, estimates more than 35 million hospitalizations annually. The database protects patient confidentiality while providing useful information on each hospitalization, including patient demographic characteristics, hospital characteristics, discharge status, length of stay, expected payment source, severity, and comorbidity measures. Therefore, the use of the NIS data is exempted from an Institutional Review Board approval.

Study Population

The NIS was queried from 2002 to 2014 for all patients ≥18 years admitted with a primary diagnosis of STEMI using their respective International Classification of Diseases, 9th Revision (ICD-9) codes. We identified patients with PMR or CTR, incidence of CS, use of different MCS device and different mitral valve procedures (MVPs) using their respective ICD-9 code (Table 1, Supplemental Digital Content 1, http://links.lww.com/ASAIO/A562).[10,17,18]

Clinical Outcomes

The primary outcome of interest was all cause in-hospital mortality. We also looked for other outcomes such as the presence of CS, use of pressors and MCS device, MVP (both mitral valve repair and replacement), cost of hospitalization, and length of stay. The average length of stay was calculated only for patients who survived the hospitalization encounter. To calculate the cost of hospitalization, cost-to-charge ratio files were paired with the NIS data. Average cost of hospitalization was estimated by multiplying the total charge by the cost-to-charge ratio and computed in US dollars for each year.

Patient and Hospital Characteristics

Demographics included were age, sex, race, and median household income for patient's ZIP code. Hospital characteristics included hospital bed size, location/teaching status and hospital region. For disease severity, all elixhauser comorbidities were evaluated in each patient (Table 2, Supplemental Digital Content 2, http://links.lww.com/ASAIO/A562).

Cardiovascular Simulation

To better understand the hemodynamics of severe MR and effects of different medications and device therapy we used a previously validated cardiovascular model[19,20] to simulate severe mitral regurgitation with the effective orifice area of 0.78 cm^2 corresponding with a regurgitation fraction (RF) of 60%. Simulation were illustrated *via* pressure-volume loops of the left atrium and left ventricle. We then investigated four different forms of support: Intraaortic balloon pump (IABP), Impella (left ventricular-to-proximal aorta pumping), TandemHeart (left atrial-to-femoral artery pumping), and extracorporeal membrane oxygenation (ECMO) (right atrial-to-femoral artery pumping). Effects of drugs were also simulated by modifying left ventricle contractility (inotropes) or increasing systemic vascular resistance (vasopressors) or decreasing systemic vascular resistance (vasodilators).

Statistical Analysis

All patients with missing age, sex, or mortality data were excluded from the analysis. All categorical variables were compared using the Pearson chi square and one-way ANOVA for continuous variables to identify significant univariate associations. Categorical and continuous variables were reported as percentages and mean ± standard deviation, respectively. Intergroup differences in the outcomes were reported as percentages. Dichotomous outcomes were adjusted by modeling it in multivariate logistic regression model in the overall STEMI population. Within the PMR/CTR patient's cohort, predictors of mortality, CS, and use of MCS were computed using multivariate logistic regression model. All outcomes were reported as unadjusted odds ratio (OR) and adjusted OR (aOR) for the binary outcomes. The outcomes were adjusted for age at admission, sex, race, elixhauser comorbidities including diabetes, hypertension, smoking, percutaneous coronary intervention, mitral valve repair/replacement, cardiac arrest/ventricular fibrillation, bed size of hospital, location/teaching status of hospital, and region of hospital. Weighted data were used for all statistical analyses during IBM SPSS Statistics 24.0 (IBM Corp, Armonk, New York). Two-sided p value <0.05 was considered statistically significant for all analysis.

Results

Baseline Population/Hospital Characteristics

Between 2002 and 2014, there were 1,888 cases of STEMI that developed PMR or CTR, which amounted to 0.07% of all STEMI patients. **Table 1** shows the baseline characteristics among the study population. Patients with PMR/CTR were older (65–79 years: 44.9% *vs.* 29.8%, $p < 0.001$ and >80: 20.40% *vs.* 16.20%, $p < 0.001$). Mostly white and two-thirds were men. They were more likely to have a history of renal failure (11.6% *vs.* 7.2%, $p < 0.001$), anemia (12.4% *vs.* 9.7%, $p < 0.001$), and coagulation disorder (17.10% *vs.* 3.50%, $p < 0.001$). They had higher incidence of cardiac arrest (10.60% *vs.* 4.90%, $p < 0.001$) or CABG (44.60% *vs.* 8.40%, $p < 0.001$) but underwent less PCI (45.4% *vs.* 64.7%, $p < 0.001$).

Papillary muscle rupture/chordae tendinae rupture patients were less likely to have traditional cardiovascular risk factors like hypertension, alcohol abuse, smoking and obesity but had a higher incidence of valvular heart disease (5.6% *vs.* 0.2%, $p < 0.001$) (**Table 1**).

Primary and Secondary Outcomes

Table 2 shows that the in-hospital mortality was significantly higher in patients with *versus* without PMR/CTR (41%

Table 1. Baseline Characteristics of Patients with and Without Papillary or Chordae Rupture After STEMI

Patient level variables	No Papillary/Chordae rupture	Papillary/Chordae rupture	*p*
No. of cases, N	2,559,121	1,888	
Age (years)			<0.001
18–34	1.20%	0.50%	
35–49	15.30%	5.10%	
50–64	37.60%	29.00%	
65–79	29.80%	44.90%	
≥80	16.20%	20.40%	
Gender			0.01
Male	66.40%	63.60%	
Female	33.60%	36.40%	
Race			
White	79.10%	82.30%	<0.001
Black	7.40%	4.90%	
Hispanic	7.30%	4.40%	
Asian	2.20%	2.20%	
Native American	0.50%	1.20%	
Other	3.50%	5.00%	
Comorbidities			
Diabetes	25.6%	14.5%	<0.001
Anemia	9.70%	12.40%	<0.001
History of smoking	38.20%	22.90%	<0.001
Cardiac arrest	4.80%	10.60%	<0.001
Ventricular fibrillation	5.60%	5.60%	0.91
Alcohol abuse	2.90%	2.60%	0.34
Collagen vascular disease	1.8%	2.3%	0.07
Congestive heart failure	1.2%	4.7%	<0.001
Chronic obstructive pulmonary disease	15.4%	18.6%	
Coagulation disorder	3.50%	17.10%	<0.001
Drug abuse	2.0%	0.5%	<0.001
Hypertension	56.8%	41.2%	<0.001
Hypothyroidism	6.7%	5.6%	0.06
Liver disease	0.8%	0.5%	0.17
Fluid and electrolyte disorder	14.6%	37%	<0.001
Obesity	9.9%	6.8%	<0.001
Peripheral vascular disease	6.9%	7.8%	0.13
Acute renal failure	7.2%	11.6%	<0.001
History of valvular heart disease	0.2%	5.7%	<0.001
History of CABG	3.3%	1.5%	<0.001
Mechanical ventilation	8.5%	47.8%	<0.001
Type of MI			<0.001
Anterolateral	8.1%	5.8%	
Anterior	31.6%	7.7%	
Inferolateral	7%	10%	
Inferior-posterior	5.1%	11.7%	
Inferior	42.4%	50.3%	
Lateral	4.4%	10.7%	
Posterior	1.3%	3.9%	
Revascularization methods			
Fibrinolytic therapy	1.00%	0.50%	0.03
CABG	8.40%	44.60%	<0.001
PCI	64.70%	45.40%	<0.001
Type of stent			
Non-DES stent	25.90%	15.00%	<0.001
Drug-eluting stent	34.90%	19.20%	<0.001
Median household income category for patient's ZIP code (%)			0.01
0th–25th percentile	4.20%	6.30%	
26th–50th percentile	20.90%	13.90%	
51st–75th percentile	26.50%	36.80%	
76th–100th percentile	48.40%	43.10%	
Primary payer (%)			<0.001
Medicare	45.30%	59.30%	
Medicaid	6.10%	4.40%	
Private	36.90%	30.40%	
Self-pay	7.70%	3.10%	
Others	3.30%	2.30%	
Hospital characteristics			

(*Continued*)

Table 1. (*Continued*)

Patient level variables	No Papillary/Chordae rupture	Papillary/Chordae rupture	*p*
Hospital bed size (%)			<0.001
Small	8.90%	4.30%	
Medium	23.40%	23.30%	
Large	67.70%	72.40%	
Hospital location and teaching status (%)			<0.001
Rural	9.60%	5.10%	
Urban, nonteaching	42.40%	39.90%	
Urban, teaching	48.30%	55.00%	
Hospital region			<0.001
Northwest	18.40%	23.50%	
Midwest	23.30%	25.80%	
South	39.20%	27.40%	
West	19.00%	23.30%	
Disposition (%)			<0.001
Routine	67.20%	14.20%	
Transfer to short-term care	9.00%	10.00%	
SNF/ICF or another facility	8.40%	23.10%	
Home health care	7.30%	11.40%	
AMA	0.70%	0.00%	

AMA, against medical advice; ICF, intermediate care facility; CABG, coronary artery bypass graft; MI, PCI, percutaneous intervention; SNF, skilled nursing facility.

vs. 7.40%, $p < 0.001$) (**Figure 1**). In addition, PMR/CTR was associated with longer hospital stay (17 *vs.* 5 days, $p < 0.001$) and cost of hospitalization ($202,889 *vs.* $65,596, $p < 0.001$) compared with those without PMR/CTR (**Table 2**). Patients with PMR/CTR had significantly higher incidence of CS (73.50% *vs.* 8.80%; aOR: 7.44, 95% CI: 6.47–8.57, $p < 0.001$) and utilization of MCS devices (65.00% *vs.* 9.20%, aOR: 2.81, 95% CI: 2.46–3.20, $p < 0.001$). During our study period, IABP was the most commonly used MCS device in comparison to percutaneous ventricular assist devices (PVADs) or ECMO (Figures 1 and 2, Supplemental Digital Content 3, http://links.lww.com/ASAIO/A562). We also noted that CS was associated with significantly higher mortality in comparison to those without CS (45.5% *vs.* 28.4%; aOR: 4.98, 95% CI: 3.52–7.04, $p < 0.001$). Cardiogenic shock patients also had higher hospitalization, cost and length of stay as shown in **Table 3**.

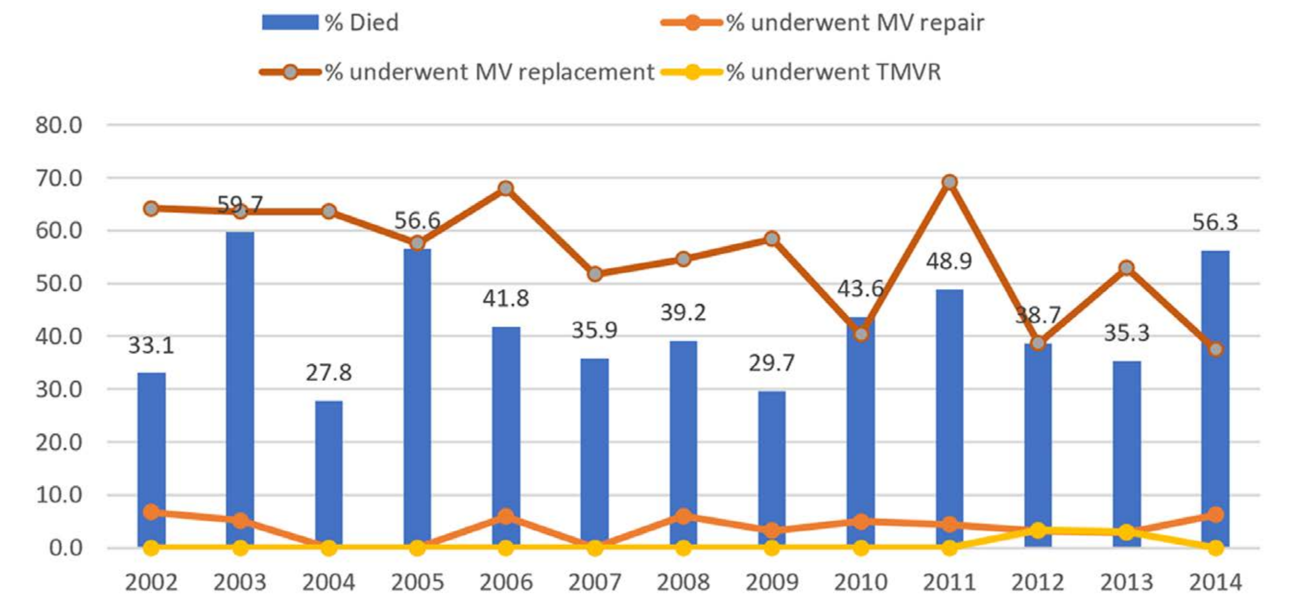
Sixty percent of patients with PMR/CTR underwent MVP and mitral valve replacement was the most common procedure among them (**Figure 1**). Table 3, Supplemental Digital Content 4, http://links.lww.com/ASAIO/A562 shows that those who underwent MVP had significantly lower rates of mortality as compared with those who did not undergo MVP (aOR: 0.14, 95% CI: 010–019, $p < 0.001$). Patients who underwent revascularization (CABG or PCI) with MVP had much better survival outcomes (Figure 2, Supplemental Digital Content 3, http://links.lww.com/ASAIO/A562). A total of 55.8% of patients

Table 2. Primary and Secondary Outcomes of In-hospital Mortality, Cardiogenic Shock, Mitral Valve Procedures, Mechanical Circulatory Device, Length of Hospital Stay and Cost of Hospitalization

Primary Outcomes					
Clinical Outcomes	No Papillary/Chord Rupture (n = 2,559,121)	Papillary/Chord Rupture (n = 1888)	Unadjusted OR	Adjusted OR*	*p*
In-hospital mortality	7.40%	41.00%	8.77 (8.0–9.61)	2.28 (2.02–2.58)	<0.001
Cardiogenic shock	8.80%	73.50%	28.89 (26.08–32.01)	7.44 (6.47–8.57)	<0.001
Cardiac arrest/ventricular fibrillation	8.2%	14.2%	1.86 (1.63–2.11)	1.26 (1.09–1.45)	0.002
Mitral valve procedures	0.30%	59.90%	—	—	<0.001
Vasopressor use	0.9%	5.2%	6.13 (5.01–7.51)	—	<0.001
Mechanical circulatory device	9.20%	65.00%	18.38 (16.72–20.21)	2.81(2.46–3.20)	<0.001
Type of mechanical circulatory support device used					
IABP	9.00%	93.20%	—	—	<0.001
PVAD	0.20%	2.60%	—	—	<0.001
ECMO	0.10%	2.90%	—	—	<0.001
Secondary outcomes					
Length of stay (in days)	5 (5.0–5.01)	17 (17.0–18.6)	—	—	<0.001
Cost of hospitalization (in dollars)	$65,596 (±47)	$202,889 (±4,403)	—	—	<0.001

*Adjusted for age at admission, sex, race, all Elixhauser comorbidities including diabetes, hypertension, smoking, percutaneous coronary intervention, mitral valve repair/replacement, cardiac arrest/ventricular fibrillation, bedsize of hospital, location/teaching status of hospital, and region of hospital.

ECMO, extracorporeal membrane oxygenation; IABP, intraaortic balloon pump; OR, odds ratio; PVAD, percutaneous ventricular assist device.



Solid vertical blue Bar represents the overall percentage of in-hospital mortality. Solid red dots represent the percentage of patients that underwent mitral valve replacement. Orange dots represents the percentage of patients that underwent mitral valve repair. Yellow dots represent the percentage of patients that underwent percutaneous transcatheter mitral valve repair.
MV: Mitral valve; TMVR: Transcatheter mitral valve repair.

Figure 1. Trend of in-patient mortality and mitral valve procedures.

underwent both revascularization and mitral valve procedure; of those patients, 30.7% had CABG with MVP, 10.3% underwent both CABG/PCI with MVP and 14.8% underwent PCI with MVP.

Predictors of Papillary Muscle rupture/Chordae Tendinae Rupture

Table 4 shows the multivariate logistic regression analysis to determine risk factors associated with increased rupture of papillary muscle and chordae tendinae: every 5 year increase in age was associated with 9% increased risk of PMR/CTR (aOR: 1.09, 95% CI: 1.07–1.12, $p < 0.001$). Compared with Caucasians, native Americans had a higher risk of PMR/CTR (aOR: 3.36, 95% CI: 2.09–5.38, $p < 0.001$). We also noted that patient with coagulopathy were associated with higher risk of PMR/CTR (aOR: 3.60, 95% CI; 3.17–4.09, $p < 0.001$). Patients with a history of heart failure and renal failure were also associated with significantly increased risk of rupture.

Predictors of In-hospital Mortality

Table 5 shows adjusted risk factors associated with increased inpatient mortality in STEMI-PMR/CTR patients. For every 5 year increase in age, there was a 9% increase in risk of inpatient mortality (aOR: 1.09, 95% CI: 1.07–1.12, $p < 0.001$). Female sex (aOR: 1.87, 95% CI: 1.44–2.41, $p < 0.001$), Hispanic (aOR: 7.05, 95% CI: 3.39–14.64, $p < 0.001$), and patients with coagulopathy (aOR: 1.48, 95% CI: 1.06–2.07) were associated with higher risk of in-hospital mortality. Among comorbidities, the presence of hypertension, smoking, those with cardiac arrest, and CS were associated with higher risk of in-hospital mortality.

Simulations of Severe Mitral Regurgitation with Different Medical Therapies and Mechanical Circulatory Support Devices

In comparison to a normal baseline condition, the presence of severe MR was associated with shortening of the isovolumetric contraction phase, increased stroke volume, and decreased systemic flow due to increase regurgitant flow to the left atrium (**Figure 2A**). Concomitantly, MR led to increases in pulmonary capillary wedge pressure (PCWP), left ventricle end-diastolic volume, and pressure as well as an increase in the left atrial volume.

Table 3. Clinical Outcomes of In-hospital Mortality, Length of Stay and Cost of Hospitalization in Patients with Papillary Muscle and Chordae Tendinae Rupture with and Without Cardiogenic Shock

Outcome	Cardiogenic Shock	No Cardiogenic Shock	Adjusted Odds Ratio*	*p*
Mortality	45.5%	28.4%	4.98 (3.52–7.04)	<0.001
Length of stay (in days)	18.6 (±0.4)	11.3 (±0.5)	—	<0.001
Cost of hospitalization (in US dollars)	2,23,360 (±5,271)	1,45,824 (±7,300)	—	<0.001

*Adjusted for age at admission, sex, race, all Elixhauser comorbidities, cardiac arrest, mitral valve repair, smoking, and hospital characteristics.

Table 4. Multivariate Predictors of Papillary Muscle and Chordae Tendinae Rupture in Patients Admitted with STEMI

Predictors	Adjusted Odds Ratio (95% CI)	*p*
Age (in 5 year increments)	1.09 (1.07–1.12)	<0.001
Female	0.95 (0.86–1.05)	0.34
Race		
White	Ref	
Black	0.67 (0.52–0.87)	0.003
Hispanic	0.66 (0.51–0.85)	0.002
Asian	0.83 (0.58–1.19)	0.31
Native American	3.36 (2.09–5.38)	<0.001
Others	1.39 (1.09–1.77)	0.006
Comorbidities		
Hypertension	0.54 (0.49–0.60)	<0.001
Diabetes	0.51 (0.44–0.58)	<0.001
Pulmonary circulation disorders	2.44 (1.25–4.77)	0.009
Congestive heart failure	2.16 (1.73–2.71)	<0.001
Anemia	0.84 (0.73–0.97)	0.02
Obesity	0.98 (0.81–1.18)	0.85
Renal failure	1.32 (1.13–1.53)	<0.001
Chronic pulmonary disease	1.07 (0.95–1.20)	0.23
Fluid and electrolyte disorder	2.58 (2.34–2.86)	<0.001
Coagulopathy	3.60 (3.17–4.09)	<0.001
Primary payer		
Medicare	Ref	
Medicaid	0.74 (0.58–0.96)	0.02
Private insurance	0.89 (0.78–1.02)	0.10
Location/teaching status		
Rural	Ref	
Urban, nonteaching	1.71 (1.39–2.13)	<0.001
Urban teaching	2.15 (1.74–2.66)	<0.001
Hospital region		
Northwest	Ref	
Midwest	0.86 (0.75–0.99)	0.04
South	0.57 (0.50–0.66)	<0.001
West	0.99 (0.86–1.14)	0.94

Variables adjusted for age at admission, sex, race, diabetes, anemia, hypertension, coagulopathy, fluid and electrolyte disorder, pulmonary circulation disorder, obesity, renal failure, chronic pulmonary disease, congestive heart failure, insurance status, hospital region, and bedsize of the hospital.

CI, confidence interval; STEMI, ST elevation myocardial infarction.

Inotropes and vasopressors worsened mitral RF, whereas vasodilators decreased regurgitation but decreased blood pressure (**Table 6** and **Figure 2B**). All MCS devices improved the forward aortic blood flow. However, the hemodynamic effects differed among the various devices (**Table 6** and **Figure 2C**). Intraaortic balloon pump provided minimal reductions of PCWP or RF. Among all devices, Impella 5.0 L/min provided the greatest degree of reductions in RF and PCWP with leftward shift of the left ventricle PV loops indicating significant unloading of the LV (*i.e.*, decreased end-diastolic volume and pressure). TandemHeart significantly decreased PCWP but, because of continuous reduction in LA pressure, resulted in a significant increase in RF. Extracorporeal membrane oxygenation resulted in worsening of PCWP owing to increased afterload pressure which also worsened RF. Using a combination of Impella with ECMO (ECPELLA) improved forward flow and decreased PCWP compared with ECMO alone (**Figure 2D**).

Discussion

Our study reports the largest nationwide analysis of patients that developed PMR and CTR after STEMI in the United States.

Table 5. Multivariate Predictors of Mortality in Patients with Papillary Muscle and Chordae Tendinae Rupture

Predictors	Adjusted Odds Ratio (95% CI)	*p*
Age (in 5 year increments)	1.09 (1.02–1.17)	0.01
Female	1.87 (1.44–2.41)	<0.001
Race		
White	Ref	
Black	0.69 (0.35–1.37)	0.29
Hispanic	7.05 (3.39–14.64)	<0.001
Asian	1.38 (0.51–3.70)	0.51
Native American	2.47 (0.75–8.10)	0.13
Others	0.95 (0.46–1.98)	0.90
Comorbidities		
Hypertension	1.33 (1.03–1.71)	0.02
Diabetes	0.22 (0.14–0.33)	<0.001
Smoking	1.43 (1.05–1.94)	0.02
Congestive heart failure	0.32 (0.17–0.59)	<0.001
Anemia	0.36 (0.24–0.54)	<0.001
Chronic pulmonary disease	0.71 (0.51–0.97)	0.03
History of coagulation disorder	1.48 (1.06–2.07)	0.01
Fluid and electrolyte disorder	1.28 (0.98–1.65)	0.06
Cardiac arrest	4.05 (2.69–6.10)	<0.001
Cardiogenic shock	3.09 (2.22–4.30)	<0.001
Procedures		
Revascularization	0.51 (0.37–0.71)	<0.001
Mitral valve procedure	0.14 (0.10–0.19)	<0.001
MCS device use	2.12 (1.56–2.88)	`<0.001
Primary payer		
Medicare	Ref	
Medicaid	0.42 (0.20–0.89)	0.02
Private insurance	0.38 (0.27–0.54)	<0.001
Location/teaching status		
Rural	Ref	
Urban, nonteaching	1.75 (1.0–3.07)	0.05
Urban teaching	1.36 (0.78–2.36)	0.27
Hospital bed size		
Small	Ref	
Medium	2.21 (1.16–4.21)	0.01
Large	2.47 (1.32–4.60)	0.005
Hospital region		
Northwest	Ref	
Midwest	2.11 (1.43–3.12)	<0.001
South	2.31 (1.62–3.29)	<0.001
West	1.14 (0.77–1.68)	0.50

Variable(s) adjusted for elective admission, sex, age, race, diabetes, anemia, cardiac arrest, smoking, congestive heart failure, chronic pulmonary disease, coagulopathy, hypertension, fluid and electrolyte disorders, cardiogenic shock, use of mechanical circulatory devices, elective admission, mitral valve interventions, revascularization, mitral valve interventions, primary expected payer, location/teaching status of hospital, bed size of hospital, and region of hospital.

CI, confidence interval; MCS, mechanical circulatory support.

The main findings from our analysis are 1) the in-hospital mortality in patients with PMR/CTR after STEMI remains significantly high (41% *vs.* 7.4%, $p < 0.001$); 2) sixty percent of the patients with CTR or PMR underwent MVP (either mitral valve replacement or repair) and had lower rate of mortality compared with those who did not undergo any MVP; and 3) patients that developed CTR or PMR after STEMI had extremely higher incidence of CS (73.5% *vs.* 8.8%, $p < 0.001$) and this was associated with a very high rate of MCS device usage for hemodynamic support (65% *vs.* 9.2%, $p < 0.001$).

The incidence of CTR/PMR decreased from 2002 to 2014, but in-patient mortality remained high and did not change over

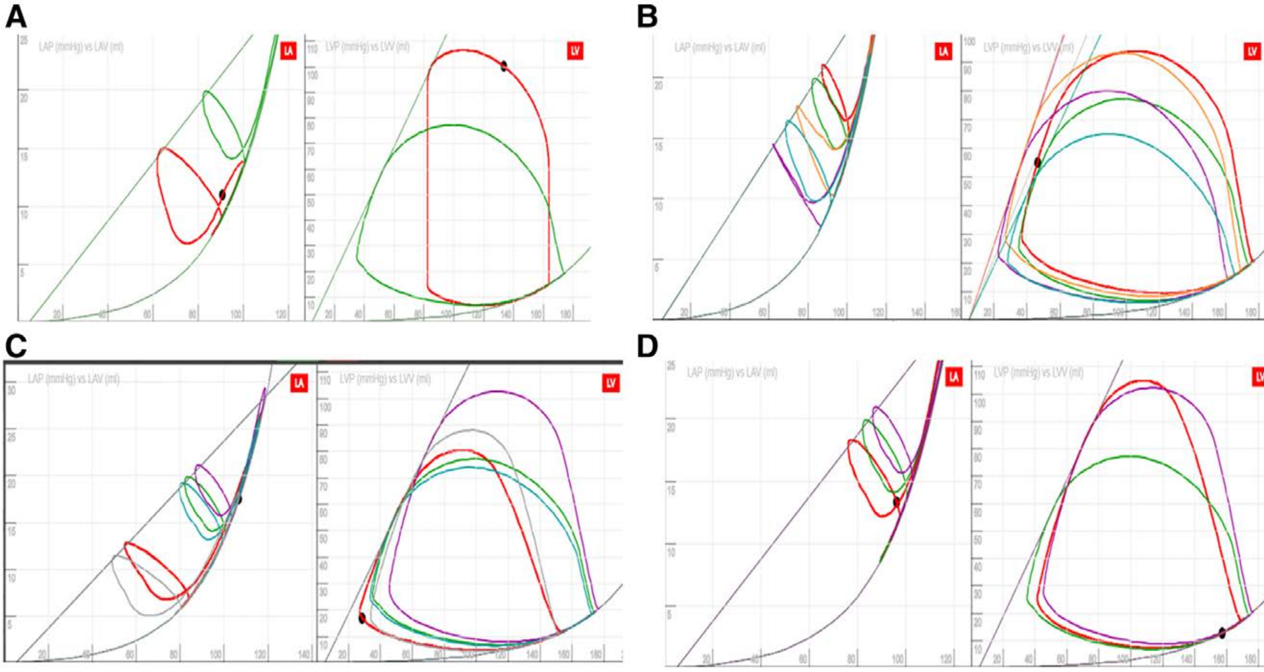


Figure 2. Demonstrates prototypical pressure-volume loops of the left atrium (LA) and left ventricle (LV) in patient with severe mitral regurgitation (MR). **A**: LA and LV pressure-volume loops without severe MR in red, and with severe MR (green) of with EROA of 0.78 cm^2. B: Demonstrates prototypical PV loops of the LA and LV in patient with severe MR with different medical therapy. Green loop is baseline (with severe MR). Other simulations as follows: with nonepinephrine 7.0 mcg/min (red); with dobutamine 7.5 mcg/kg/min (yellow); with Milrinone 0.5 mcg/kg/min (purple) *vs.* with nitroprusside 3.0 mcg/kg/min (blue). C: Comparison of prototypical pressure-volume loops of the LA and LV in a severe MR patient with different mechanical circulatory support (MCS) devices. Green loop is baseline with severe MR. Other simulations as follows: with IABP (blue); Impella 5.0 L/min (red); Tandem Heart (gray) and ECMO (purple). D; Comparison of prototypical pressure-volume loops of the LA and LV in severe MR (green) in patient with ECMO (purple) and ECMO + Impella 2.5 L/min (ECPELLA 2.5) (red). ECMO, extracorporeal membrane oxygenation.

this time period. Most patients presenting with PMR or CTR had inferior STEMI. This is because the posteromedial papillary muscle is more prone to rupture owing to its single vessel blood supply[3,21] as compared with the anterolateral papillary muscle with dual supply from both the left anterior descending artery and left circumflex artery; hence, the latter is more resistant to rupture because of infarction from a single vessel occlusion.[3] In addition to anatomic location, previous studies have demonstrated certain characteristics to be associated with increased risk of PMR/CTR. Qian *et al.*[22,23] reported that advanced age and renal dysfunction (eGFR ≤ 60 ml/min) were associated with increased rupture; we noted similar results as well.

As most of the patients at the time of presentation are hemodynamically unstable, they portend poor prognosis. There are currently no studies determining the risk factors associated with mortality in patients with PMR or CTR with STEMI. Certain baseline characteristics such increasing age, female

Table 6. Hemodynamic Impact of Various Medical Therapy and Mechanical Circulatory Support Devices on Severe Mitral Regurgitation

	Baseline	Severe MR	+Dobutamine (7.5 mcg/kg/min)	+Milrinone (0.5 mcg/kg/min)	+Nonepinephrine (7.0 mcg/min)	+Nitroprusside (3.0 mcg/kg/min)	IABP	Impella (5.0)	Tandem Heart	ECMO (5.0)	ECPELLA (2.5)
Flow (L/min)											
Aortic	6.0	3.8	5.4	5.2	3.6	4.3	4.0	0.5	0.9	1.8	0.4
MCS	N/A	N/A	N/A	N/A	N/A	N/A	N/A	4.9	4.8	4.7	7.0
Total body	6.0	3.8	5.4	5.2	3.6	4.3	4.0	5.4	5.7	6.5	7.4
Mitral regurgitation fraction (%)	N/A	60	58	56	66	55	59	53	87	80	74
Pressures (mm Hg)											
CVP	5	7	6	5	4	5	5	7	7	4	5
PA (mean)	16	23	27	22	25	19	22	18	17	23	21
PCWP	11	20	23	18	22	16	19	14	13	21	19
Aortic (mean)	88	56	68	55	69	42	58	75	80	89	100

CVP, central venous pressure; ECMO, extracorporeal membrane oxygenation; IABP, intraaortic balloon pump; MCS, mechanical circulatory support; PA, pulmonary artery; PCWP, pulmonary capillary wedge pressure.

gender, those with history of valvular heart disease or coagulation disorder, electrolyte abnormalities, and smoking were higher in patients with PMR/CTR. We also observed that the renal failure was higher in patients with PMR/CTR. However, it was not associated higher in-hospital mortality in patients with acute renal failure (45% *vs.* 45.9%; $p = 0.73$; with *vs.* without acute renal failure) or chronic kidney disease (45.5% *vs.* 42.3%; $p = 0.50$; those with *vs.* without chronic kidney disease).

A large number of patients with PMR present with CS and cardiac arrest, and are associated with significantly higher risk of mortality.[5] Cardiogenic shock in patients with PMR or CTR in AMI have bimodal distribution with most cases occurring in first 24 hours and about 85% developing CS during hospitalization.[24] Medical therapy involving judicious management of vasodilators and inotropes are essential but due to significant hypotension is usually not sufficient. On the other hand, vasopressor use can further exacerbate acute mitral regurgitation because of the increase in afterload (**Figure 2A**). Hence, early utilization of MCS devices is considered key for improving hemodynamics.[11,25–28]

As per the ACC guidelines on STEMI, it is considered class IIa indication (LOE B) to use IABP and class IIb indication (LOE C) to use an alternative left ventricular assist device in patients with refractory CS from any cause.[16] Among MCS devices, more than 90% of our cases underwent IABP placement (Figure 1, Supplemental Digital Content 3, http://links.lww.com/ASAIO/A562). Intraaortic balloon pump may decrease afterload and decrease myocardial oxygen demand and improve cardiac output, but its effects are modest and variable among patients (**Figure 2B**). Recently, PVAD devices such as Impella and TandemHeart have attracted more attention compared with IABP as the first choice.[29–33] However, there are limited case reports showing that the utilization of Impella improves cardiac output, reduces pulmonary edema in patients with acute MR.[26,28] Although the Impella approach provides the most LV unloading and reduction of MR, PMR/CTR is listed as contraindications for use of this device because it has not been specifically studied in PMR/CTR cases and because of the concern over the ingestion of ruptured muscle, chordae and leaflet material. TandemHeart has been used in patients with acute MR for stabilization before MVR; however, its placement requires transseptal puncture and dilatation which can delay initiation of circulatory support with increased risk of transseptal puncture in fully anticoagulated and unstable STEMI patient.[27] Furthermore, as shown in our simulation, the significant drop in LA pressures with TandemHeart can worsen RF, and this increase regurgitation can further damage the mitral valve apparatus (as shown in **Table 6**). This also has the potential to reduce LV pressure generation to the point where aortic valve may not open, resulting in aortic root stasis with the potential for aortic root thrombosis.[20] ECMO is a good option in patient with concomitant respiratory failure but if used alone can worsen pulmonary edema and regurgitation by increasing effective ventricular afterload as we demonstrated in our simulation (**Figure 2A**). Effective treatment of acute MR may require concomitant use of ECMO with Impella or IABP for afterload reduction.[25] The goal of the MCS device should be to decrease afterload, improve forward blood flow, and improve systemic blood pressure while decreasing left ventricular end-diastolic and pulmonary capillary pressures by decreasing the degree of MR.

Early and more aggressive application of short-term MCS device therapy has shown benefits in patients with postcardiotomy CS.[34,35] It is important to understand the hemodynamic role of each of these MCS devices for better selection for appropriate device therapy. This is especially important in patients with acute severe mitral regurgitation. Our simulations provide insight into the role of the hemodynamics of these devices. Extracorporeal membrane oxygenation is the most commonly used MCS devices in patients with postcardiotomy shock; however, as we demonstrated in our simulation model, it can worsen the severe mitral regurgitation in these patients and may need additional left ventricular unloading.

Emergent cardiac catheterization and early revascularization is the primary aim to improve outcomes and decrease mortality in these patients.[7,24,36] Acute severe MR because of PMR/CTR is usually associated with poor clinical outcomes and many of the patients require emergent mitral valve surgery. Despite significant advancement in the recent surgeries, patients who underwent emergent mitral valve replacement still continues to have high mortality of up to 20%.[37] According to the ACC guidelines in patients with STEMI undergoing surgical repair, it is a class I recommendations (LOE B) to undergo simultaneous CABG.[24] However, patients are often too unstable and at extremely high risk to undergo surgery. Studies have demonstrated that utilization of temporary MCS devices for initial stabilization before surgery can lead to significant improvement in CAGB-related survival rates.[16] In our study, we observed that 82% of STEMI-CS patients with PMR/CTR were stabilized with some type of MCS device. However, we noted that 67.4% survived and were discharged to home or another facility in comparison to 76.9% of the cases without MCS support. This difference can be present because patients requiring MCS devices might be more challenging to stabilize hemodynamically in comparison to those without MCS.

Recently transcatheter mitral valve repair (TMVR) such as Mitraclip (Abbott Vascular, Santa Clara, California) has shown a significant reduction in severity of mitral regurgitation in patients with heart failure and secondary mitral regurgitation.[38] However, the role of using TMVR in patients with acute myocardial infarction and acute mitral regurgitation is lacking. There have been a few case series demonstrating the use of Mitraclip in patients with AMI.[39] Mitraclip can especially be useful in selected cases in patients that are at a high risk for surgery. Further studies are needed to determine its role in this area.

Limitations

Several limitations of this study should be acknowledged. National Inpatient sample database follows a retrospective cross-sectional study design and one of the main limitations in this study is the inability to draw causality. Such administrative data lack clinical details related to demographics and therapies that are typically available in trials and registries. As with any large national registry database is subjected to coding errors. We were only able to comment on in-patient mortality and are unable to provide follow-up data of these patients. Moreover, the NIS does not provide objective vitals such as blood pressure and heart rate which are essential markers in assessing management of CS along with the absence of echocardiographic findings during the hospitalization. These limitations are counterbalanced by a larger sample size and absence of reporting bias which usually results from selective publications from specialized canters. Nevertheless, our study answered a lot of questions that could not be collected from larger clinical trials and single-center observational studies due to insufficient power.

Conclusion

Our study validates the notion that although outcomes have improved significantly for patients with acute MI, mortality from STEMI and PMR/CTR still continues to remain very high. Early revascularization strategy with either CABG or PCI along with MVP provides the best survival outcomes in these patients. The incidence of CS remains very high and it continues to carry extremely high mortality, length of stay, and cost of hospitalization. Early utilization of adequate temporary MCS device for hemodynamic stabilization may play a significant role in improving outcomes in these patients. Intraaortic balloon pump was the most commonly used device in our study which may not be sufficient to provide adequate support. Despite the high mortality, combined revascularization and mitral valve intervention is recommended however, better strategies are needed to tackle CS in patients with papillary and chordae rupture. Future studies are needed to determine effective combinations of pharmacologic and MCS device therapies to provide sufficient hemodynamic support and to improve outcomes in patients with acute MR and STEMI.

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