

NEW RESEARCH PAPERS

STRUCTURAL

Transcatheter Mitral Valve Repair in Cardiogenic Shock and Mitral Regurgitation



A Patient-Level, Multicenter Analysis

Richard G. Jung, BSc,^{a,b,*} Trevor Simard, MD,^{a,b,c,*} Christopher Kovach, MD, MSc,^{d,e} Kelsey Flint, MD,^{d,f} Creighton Don, MD,^e Pietro Di Santo, MD,^{a,c} Marianna Adamo, MD,^g Luca Branca, MD,^g Francesca Valentini, MD,^g Tomás Benito-González, MD,^h Felipe Fernández-Vázquez, MD, PhD,^h Rodrigo Estévez-Loureiro, MD, PhD,ⁱ Alessandra Berardini, MD,^j Nicolina Conti, MD,^j Claudio Rapezzi, MD,^{k,l} Elena Biagini, MD,^j Simon Parlow, MD,^{a,c} Risa Shorr, MLIS,^m Amos Levi, MD,^{a,c} Ana Manovel, MD,ⁿ Rosa Cardenal-Piris, MD,ⁿ Jose Diaz Fernandez, MD,ⁿ Mony Shuvy, MD,^o Dan Haberman, MD,^p Alessandra Sala, MD,^q Mohamad A. Alkhoul, MD,^r Claudia Marini, MD,^s Marta Bargagna, MD,^s Davide Schiavi, MSc,^t Paolo Denti, MD,^s Sinisa Markovic, MD,^u Nicola Buzzatti, MD,^s Vincent Chan, MD,^v Mark Hynes, MD,^w Thierry Mesana, MD, PhD,^v Marino Labinaz, MD,^{a,c} Federico Pappalardo, MD,^x Maurizio Taramasso, MD, PhD,^{s,y} Benjamin Hibbert, MD, PhD^{a,b,c}

ABSTRACT

OBJECTIVES The aim of this study was to evaluate the outcome of transcatheter mitral valve repair (TMVr) in patients with cardiogenic shock and significant mitral regurgitation (MR).

BACKGROUND Patients in cardiogenic shock with severe MR have a poor prognosis in the setting of conventional medical therapy. Because of its favorable safety profile, TMVr is being increasingly used as an acute therapy in this population, though its efficacy remains unknown.

METHODS A multicenter, collaborative, patient-level analysis was conducted. Patients with cardiogenic shock and moderate to severe (3+) or severe (4+) MR who were not surgical candidates were treated with TMVr. The primary outcome was in-hospital mortality. Secondary outcomes included 90-day mortality, heart failure (HF) hospitalization, and the combined event rate of 90-day mortality and HF hospitalization following dichotomization by TMVr device success.

RESULTS Between January 2011 and February 2019, 141 patients across 14 institutions met the inclusion criteria. In-hospital mortality occurred in 22 patients (15.6%), at 90 days in 38 patients (29.5%), and at one year in 55 patients (42.6%). Median length of hospital stay following TMVr was 10 days (interquartile range: 6 to 20 days). HF hospitalization occurred in 26 patients (18.4%) at a median of 73 days (interquartile range: 26 to 546 days). When stratified by TMVr procedural results, successful TMVr reduced rates of in-hospital mortality (hazard ratio [HR]: 0.36; 95% confidence interval [CI]: 0.13 to 0.98; $p = 0.04$), 90-day mortality (HR: 0.36; 95% CI: 0.16 to 0.78; $p = 0.01$), and the composite of 90-day mortality and HF hospitalization (HR: 0.41; 95% CI: 0.19 to 0.90; $p = 0.03$).

CONCLUSIONS TMVr may improve short- and intermediate-term mortality in high-risk patients with cardiogenic shock and moderate to severe MR. Randomized studies are needed to definitively establish MR as a therapeutic target in patients with cardiogenic shock. (J Am Coll Cardiol Intv 2021;14:1-11) © 2021 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**ABBREVIATIONS
AND ACRONYMS**

CI = confidence interval
HF = heart failure
HR = hazard ratio
IQR = interquartile range
LVEF = left ventricular ejection fraction
MCS = mechanical circulatory support
MR = mitral regurgitation
SCAI = Society for Cardiovascular Angiography and Interventions
TMVr = transcatheter mitral valve repair

Transcatheter mitral valve repair (TMVr) is an established therapy for patients with functional mitral regurgitation (MR) in the setting of heart failure (HF) or degenerative MR in patients at high or prohibitive surgical risk (1,2). Landmark trials, including EVEREST II (Endovascular Valve Edge-to-Edge Repair Study), COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation), and MITRA-FR (Percutaneous Repair with the MitraClip Device for Severe Functional/Secondary Mitral Regurgitation), examined TMVr in patients in stable condition with chronic MR on guideline-directed medical therapy, demonstrating an excellent procedural safety profile (1-4).

Moderate or greater MR is present in 5% to 10% of patients in cardiogenic shock (5,6). The role for TMVr in this setting remains unclear, particularly with the dynamic nature of functional MR in this setting. Importantly, these patients are often at prohibitive risk for surgical intervention and are not candidates for advanced mechanical circulatory support (MCS), representing a population presently without established therapies (7). The role of TMVr as an adjunct therapy in patients with cardiogenic shock remains poorly described (8). Recently, a number of small single-center studies have used TMVr in patients with concurrent MR and shock, supporting it as a safe and feasible alternative (7,9,10).

Herein, we performed a systematic review of the use of TMVr in patients with cardiogenic shock and

moderate to severe (3+) or severe (4+) MR to identify all reports. Given the relatively small cohort of patients in the identified studies, we performed an international, multicenter, patient-level analysis to evaluate the differences in: 1) short- and intermediate-term mortality; 2) length of hospital stay and readmission for HF exacerbation; and 3) comparison of clinical outcomes following TMVr stratified by device success (11).

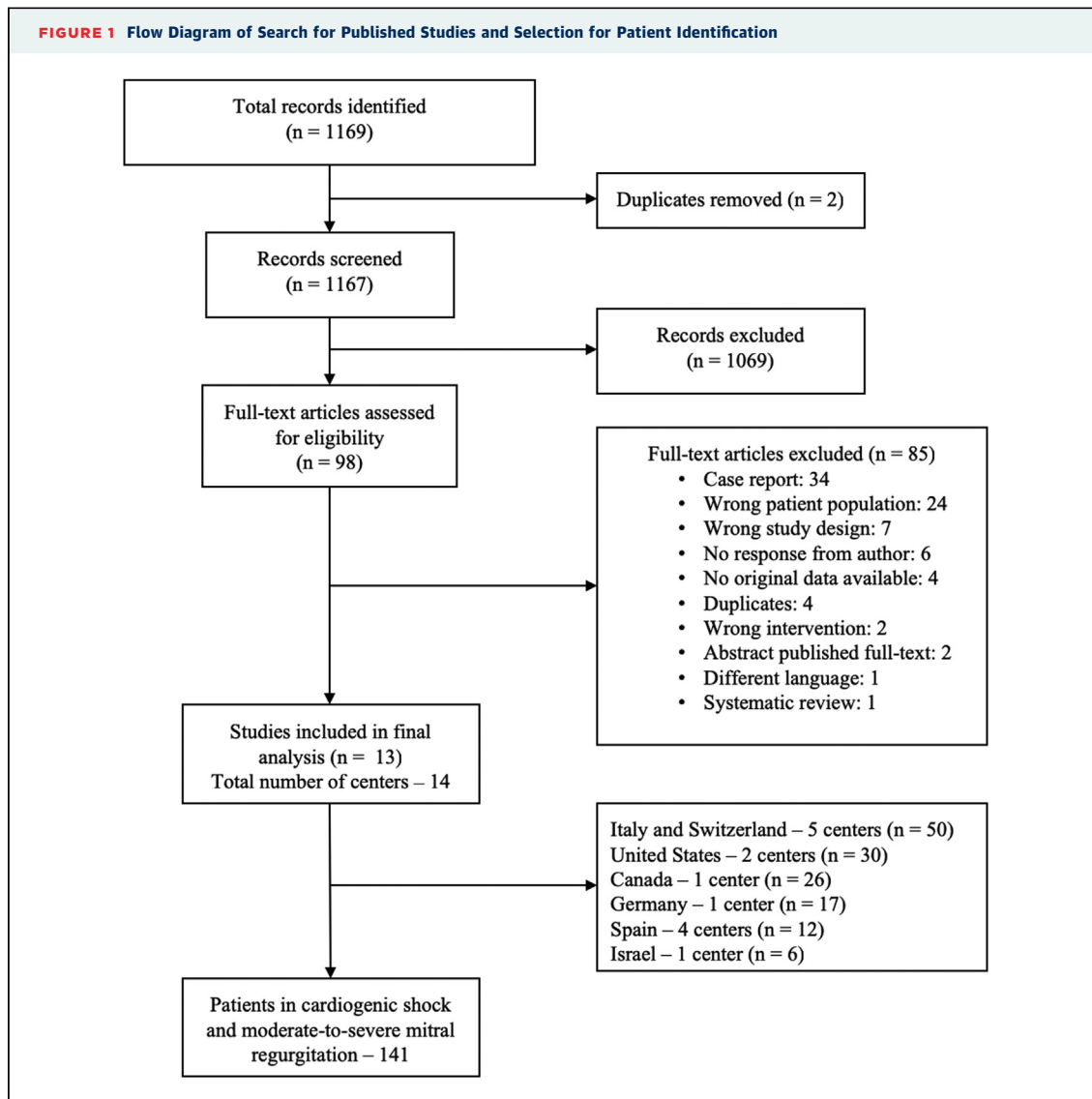
SEE PAGE 12

METHODS

The protocol was registered on September 2019 (PROSPERO: CRD42020151837) and was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. Each center's research and ethics committee approved its respective registry (7,8,10,12-23), and anonymized data were analyzed at the University of Ottawa Heart Institute.

SEARCH STRATEGY. The search for published studies was guided by a medical librarian using a combination of key terms and index headings such as "MitraClip", "(percutaneous or transcatheter or catheter-based or endovascular or trans-septal) and (MV repair or "edge-to-edge technique" or Alfieri technique or double-orifice technique)", and "cardiogenic shock" (Supplemental Table 1 for the full search strategy). The final search was conducted on September 13, 2019, in Embase and Embase Classic (1947 to present), Ovid MEDLINE (1946 to present), and the Cochrane Central Register

From the ^aCAPITAL Research Group, University of Ottawa Heart Institute, Ottawa, Ontario, Canada; ^bDepartment of Cellular and Molecular Medicine, University of Ottawa, Ottawa, Ontario, Canada; ^cDivision of Cardiology, University of Ottawa Heart Institute, Ottawa, Ontario, Canada; ^dDivision of Cardiology, University of Colorado School of Medicine, Aurora, Colorado; ^eDivision of Cardiology, University of Washington, Seattle, Washington, USA; ^fRocky Mountain Regional VA Medical Center, Medicine Services, Cardiology, Aurora, Colorado, USA; ^gCatheterization Laboratory, Cardiothoracic Department, Spedali Civili, Brescia, Italy; ^hDepartment of Cardiology, University Hospital of León, León, Spain; ⁱDepartment of Cardiology, Alvaro Cunqueiro Hospital, Vigo, Spain; ^jCardiology Unit, Cardio-Thoracic-Vascular Department, Sant'Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy; ^kCardiological Center, Universitario di Ferrara, University of Ferrara, Italy; ^lMaria Cecilia Hospital, GVM Care & Research, Cotignola, Italy; ^mUniversity of Ottawa Health Sciences Library, Ottawa, Ontario, Canada; ⁿJuan Ramon Jimenez University Hospital, Huelva, Spain; ^oCardiovascular Research Centre, Heart Institute, Hadassah-Hebrew University Medical Centre, Jerusalem, Israel; ^pHeart Center, Kaplan Medical Center, Hebrew University of Jerusalem, Jerusalem, Israel; ^qDepartment of Cardiovascular Anesthesia and Intensive Care, San Raffaele Scientific Institute, Milan, Italy; ^rDepartment of Cardiovascular Medicine, Mayo Clinic, Rochester, Minnesota, USA; ^sDepartment of Cardiac Surgery, San Raffaele Scientific Institute, Milan, Italy; ^tAlfieri Heart Foundation, Milan, Italy; ^uDepartment of Internal Medicine II, University of Ulm, Ulm, Germany; ^vDivision of Cardiac Surgery, University of Ottawa Heart Institute, Ottawa, Ontario, Canada; ^wDepartment of Anesthesiology, University of Ottawa Heart Institute, Ottawa, Ontario; ^xDepartment of Anesthesia and Intensive Care, IRCCS ISMETT, Palermo, Italy; and the ^yUniversity Heart Center Zurich, University Hospital of Zurich, Zurich, Switzerland. *Drs. Jung and Simard share first authorship. The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).



of Controlled Trials. Search results were exported to Endnote X9 (Thomson Reuters, New York, New York), and duplicates were removed using the program's duplicate identification feature.

Titles and abstracts were screened by two independent reviewers using Covidence (Melbourne, Australia). Eligible studies from screening were reviewed in full by two independent reviewers and were assessed for both inclusion and exclusion criteria. Corresponding investigators from the identified studies were contacted for the patient-level analysis.

INCLUSION AND EXCLUSION CRITERIA. We included case series, prospective, and retrospective studies reporting the use of the MitraClip or TMVr in critically ill patients (>18 years of age) defined as

Society for Cardiovascular Angiography and Interventions (SCAI) stage B to E cardiogenic shock (24) or requiring inotrope, ventilator, or MCS support. We excluded studies in children (<18 years of age), studies written in languages other than English, reviews, case reports, and animal studies. We also excluded studies that did not clearly define critically ill patients meeting the aforementioned criteria.

DATA EXTRACTION AND QUALITY ASSESSMENT.

All corresponding investigators with the appropriate patient populations were contacted to obtain patient-level information. Each center's ethics committees approved its respective registry, and anonymized data was transferred to the University of Ottawa Heart Institute for collation and analysis.

TABLE 1 Baseline Characteristics (n = 141)	
Age, yrs	68.9 ± 12.1
Male	78 (55.3)
BMI, kg/m ² (n = 112)	25.7 ± 5.1
BSA, m ² (n = 112)	1.9 ± 0.3
Coexisting conditions	
Hypertension	85 (60.3)
Dyslipidemia	76 (53.9)
Diabetes	57 (40.4)
Current smoker	46 (32.6)
Atrial fibrillation	63 (44.7)
CHADS ₂ score >2	79 (56.0)
Anemia	47 (33.3)
Related to HF	
History of HF	115 (81.6)
NYHA functional class (n = 135)	
II	5 (3.7)
III	32 (23.7)
IV	98 (72.6)
Hospitalization for HF within the previous year	92 (65.2)
Permanent pacemaker	46 (32.6)
NT-proBNP, pg/ml	6636.7 ± 8479.3
Related to CKD	
eGFR <60 ml/min	56 (39.7)
CRRT	6 (4.3)
Previous history	
Coronary artery disease	86 (61.0)
Percutaneous coronary intervention	62 (44.0)
PCI within the past 30 days	34 (24.1)
Myocardial infarction	76 (53.9)
Coronary artery bypass grafting	24 (17.0)
Cerebrovascular accident	14 (9.9)
STS risk score (n = 117)	16.1 ± 16.6
INTERMACS score (n = 88)	3.1 ± 1.0
SCAI cardiogenic shock class	
B	18 (12.8)
C	71 (50.4)
D	42 (29.8)
E	10 (7.1)
Lactate, mmol/l	3.5 ± 2.8
Intubated	51 (36.2)
Mechanical circulatory support	71 (50.4)
Mechanism of MR	
Functional	106 (75.2)
Degenerative	33 (23.4)
Both	2 (1.4)
Medication pre-MitraClip	
ASA	65 (46.1)
P2Y ₁₂ inhibitor	28 (19.9)
Anticoagulation	47 (33.3)
ACE inhibitor/ARB	49 (34.8)
Beta-blocker	77 (54.6)
Calcium-channel blocker	7 (5.0)
Mineralocorticoid receptor antagonist	46 (32.6)
Diuretic agent	119 (84.4)

Continued on the next page

The following characteristics were extracted for each patient: demographics and risk factors; MR mechanism; right heart catheterization measurements; presence of mechanical ventilator, inotrope,

vasopressor, or MCS support prior to TMVr; echocardiographic results pre- and post-TMVr; and procedural data (see [Supplemental Table 2](#) for data template). Outcomes including mortality, HF hospitalization cerebrovascular accident, length of hospital stay, and discontinuation of pharmacological support or MCS was collected at follow-up.

STATISTICAL ANALYSIS. Continuous variables are reported as mean ± SD or median (interquartile range [IQR]), and categorical variables are reported as proportions. Normally distributed continuous variables were compared using Student's *t*-test or paired *t*-test when applicable. Chi-square, Fisher exact, or McNemar tests were used to compare categorical variables.

The primary endpoint was in-hospital mortality following TMVr. Secondary outcomes were 90-day mortality, HF hospitalization and the combined event rate of 90-day mortality and HF hospitalization after stratification by device success (11). Acceptable device success was defined as a reduction of post-procedural MR by ≥1 grade prior to the procedure to an absolute level ≤2+ (11). The overall incidence of mortality and hospitalization for HF was generated using the Kaplan-Meier method. Changes in pre- and post-procedural MR grade were compared using the McNemar test after dichotomizing MR grades 1 and 2 and grades 3 and 4. Furthermore, pre- and post-procedural left ventricular ejection fraction (LVEF) was compared using a paired *t*-test, and simple linear regression was performed to evaluate the association between baseline and follow-up LVEF.

Device success and in-hospital and 90-day mortality and HF hospitalization event rates were estimated using the Kaplan-Meier method. Furthermore, hazard ratios (HRs) and two-sided 95% confidence intervals (CIs) with and without adjusting for age and sex to determine the association between device success and mortality or HF hospitalization were generated using a Cox proportional hazards model. Post hoc analysis was performed to evaluate differences in MR etiology (primary vs. secondary), reduced LVEF (<35%), acute versus chronic MR, and SCAI cardiogenic shock class to in-hospital mortality by the Cox proportional hazards model. All statistical analyses were conducted using SAS version 9.4 (SAS Institute, Cary, North Carolina). Statistical significance was defined as *p* < 0.05. All figures were generated using GraphPad Prism version 8 (GraphPad Software, La Jolla, California).

RESULTS

A total of 1,167 titles and abstracts were screened, and 98 full-text papers were reviewed for eligibility

TABLE 1 Continued

Hemodynamics pre-MitraClip	
Inotrope	111 (78.7)
Vasopressor	23 (16.3)
Heart rate, beats/min (n = 74)	86.3 ± 17.4
Systolic blood pressure, mm Hg (n = 62)	100.3 ± 18.5
Diastolic blood pressure, mm Hg (n = 62)	58.3 ± 12.4
Mean arterial pressure, mm Hg (n = 68)	74.4 ± 12.7
Pulmonary capillary wedge pressure, mm Hg (n = 55)	25.7 ± 8.3
Right atrial pressure, mm Hg (n = 44)	14.4 ± 7.7
Pulmonary artery systolic pressure, mm Hg (n = 58)	54.6 ± 15.5
Pulmonary artery diastolic pressure, mm Hg (n = 47)	25.9 ± 8.1
Pulmonary artery mean pressure, mm Hg (n = 56)	36.9 ± 10.1
Cardiac output, l/min (n = 46)	3.7 ± 1.4
Cardiac index, l/min/m ² (n = 55)	1.9 ± 0.7

Values are mean ± SD or n (%).

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; ASA = acetylsalicylic acid; BMI = body mass index; BSA = body surface area; CKD = chronic kidney disease; CRRT = continuous renal replacement therapy; eGFR = estimated glomerular filtration rate; HF = heart failure; MR = mitral regurgitation; NT-proBNP = N-terminal pro-brain natriuretic peptide; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; SCAI = Society for Cardiovascular Angiography and Interventions; STS = Society of Thoracic Surgeons.

(Figure 1). Eighty-five papers were excluded because they were case reports, the wrong patient population or intervention was studied, or there was a lack of response from the corresponding investigator and missing the outcome of interest. Ultimately, we identified 13 studies from 14 institutions involving a total of 141 patients in cardiogenic shock with moderate to severe MR (see Supplemental Table 3 for institutional-level contribution) (7,8,10,12-23).

PATIENT POPULATION. Between January 2011 and February 2019, 141 patients with cardiogenic shock and moderate to severe or severe MR who were deemed at prohibitive risk for surgical intervention underwent TMVr (Table 1) (24). The cohort's baseline characteristics reflected the critical nature of the patients, with a mean age of 68.9 years, 72.6% with baseline New York Heart Association functional class IV symptoms, 78.7% inotrope dependent, and 50.4% dependent on MCS despite medical optimization. The clinical status was reflected in the mean Society of Thoracic Surgeons risk score of 16.1 and INTERMACS score of 3.1. The mean LVEF was 33.8 ± 14.0%, and MR grade was 3+ in 15 patients (10.6%) and 4+ in 126 patients (89.4%). Furthermore, 71 patients (50.4%) had been classified with SCAI stage C cardiogenic shock, 42 patients (29.8%) with stage D cardiogenic shock, and 10 patients (7.1%) with stage E cardiogenic shock. Finally, the mean cardiac index of the entire cohort was 1.9 ± 0.7 l/min/m² (n = 55), the mean pulmonary capillary wedge pressure was

TABLE 2 Procedural Characteristics

Number of MitraClips used (n = 122)	1.0 (1.0-2.0)
Post-MitraClip trans-mitral gradient, mm Hg (n = 57)	4.4 ± 2.8
Procedural time, min (n = 75)	130.6 ± 79.7
Pre-procedural MR	
3	15 (10.6)
4	126 (89.4)
Post-procedural MR	
1 or 2	125 (88.7)
3 or 4	16 (11.3)

Values are median (interquartile range), mean ± SD, or n (%).
 MR = mitral regurgitation.

25.7 ± 8.3 mm Hg (n = 55), and the mean pulmonary artery pressure was 36.9 ± 10.1 mm Hg (n = 56).

All patients underwent TMVr, with a median time from admission of 11 days (IQR: 4 to 23 days), a median of 1.0 (IQR: 1.0 to 2.0) MitraClips implanted, and a mean procedural time of 130.6 ± 79.7 min (Table 2). Following TMVr, MR grade was 1 or 2+ in 125 patients (88.7%) and 3 or 4+ in 16 patients (11.3%). No procedural complications occurred during TMVr in this cohort.

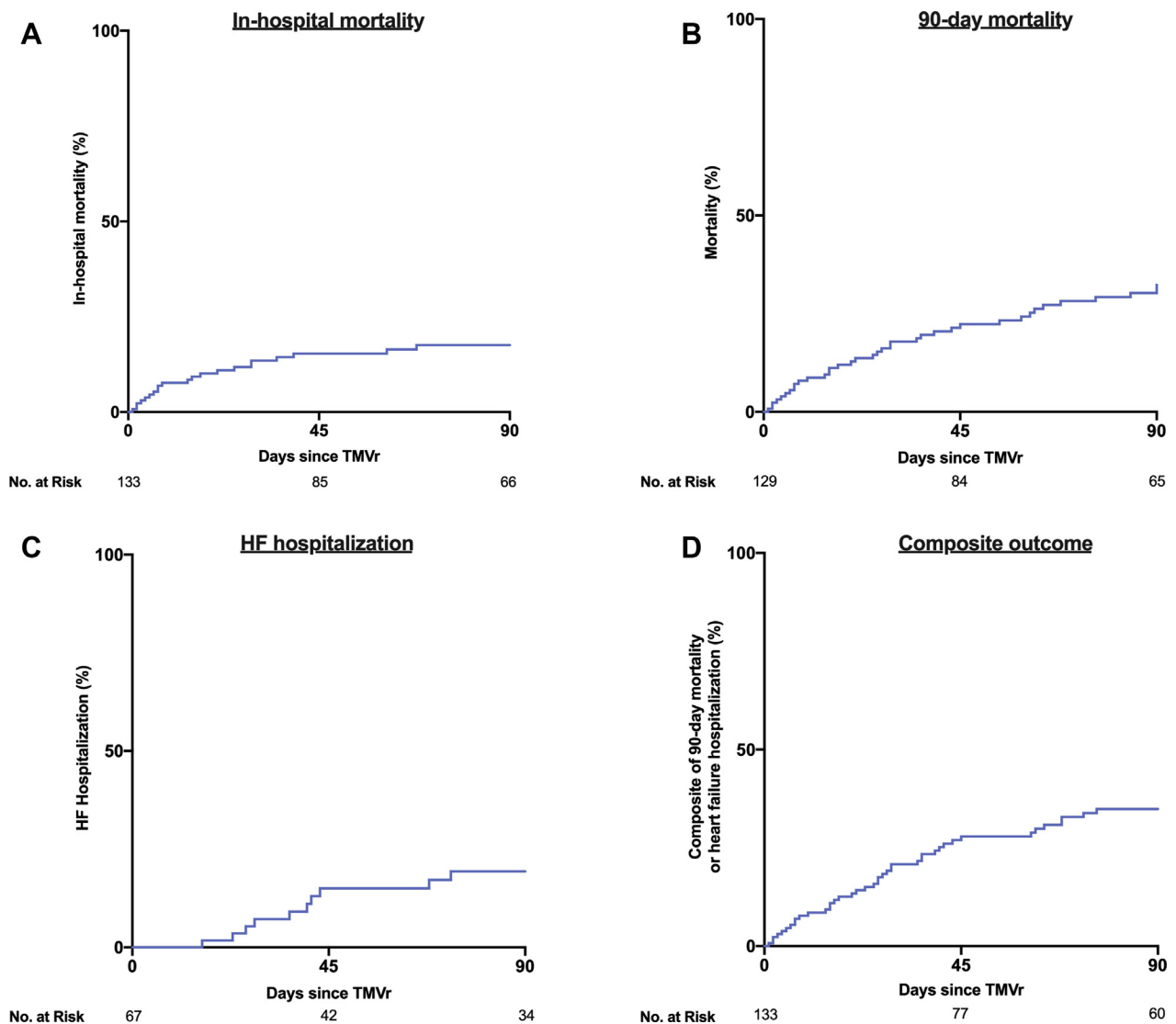
CLINICAL AND ECHOCARDIOGRAPHIC OUTCOMES.

Follow-up was complete in all patients, with a median duration of 93 days (IQR: 34.5 to 406.5 days). In-hospital death occurred in 22 patients (15.6%), 90-day mortality in 38 patients (29.5%), and 1-year mortality in 55 patients (42.6%) (Table 3, Figures 2A and 2B). Patients who died were older and more likely to have anemia, higher lactate levels, and higher Society of Thoracic Surgeons risk scores (Supplemental Table 4). The median length of stay in the hospital following the procedure was 10.0 days (IQR: 6.0 to 20.0 days), with a median duration of stay in the intensive care unit of 3.0 days post-implantation (IQR: 1.0 to 8.0 days). Hospital admission for HF following TMVr

TABLE 3 Clinical Outcomes

In-hospital	
Mortality (n = 141)	22 (15.6)
Duration of hospital stay, days (n = 138)	10.0 (6.0-20.0)
Duration of ICU stay, days (n = 103)	3.0 (1.0-8.0)
Inotrope dependence prior to discharge (n = 58)	13 (9.2)
Time to inotrope discontinuation, days	1.0 (0.0-6.0)
Follow-up	
90-day mortality (n = 129)	38 (29.5)
1-yr mortality (n = 129)	55 (42.6)
CHF admission (n = 141)	26 (18.4)
90-day composite outcome (n = 133)	41 (30.8)

Values are median (interquartile range) or n (%).
 CHF = congestive heart failure; ICU = intensive care unit.

FIGURE 2 Kaplan-Meier Curves Following TMVr in Patients With Cardiogenic Shock

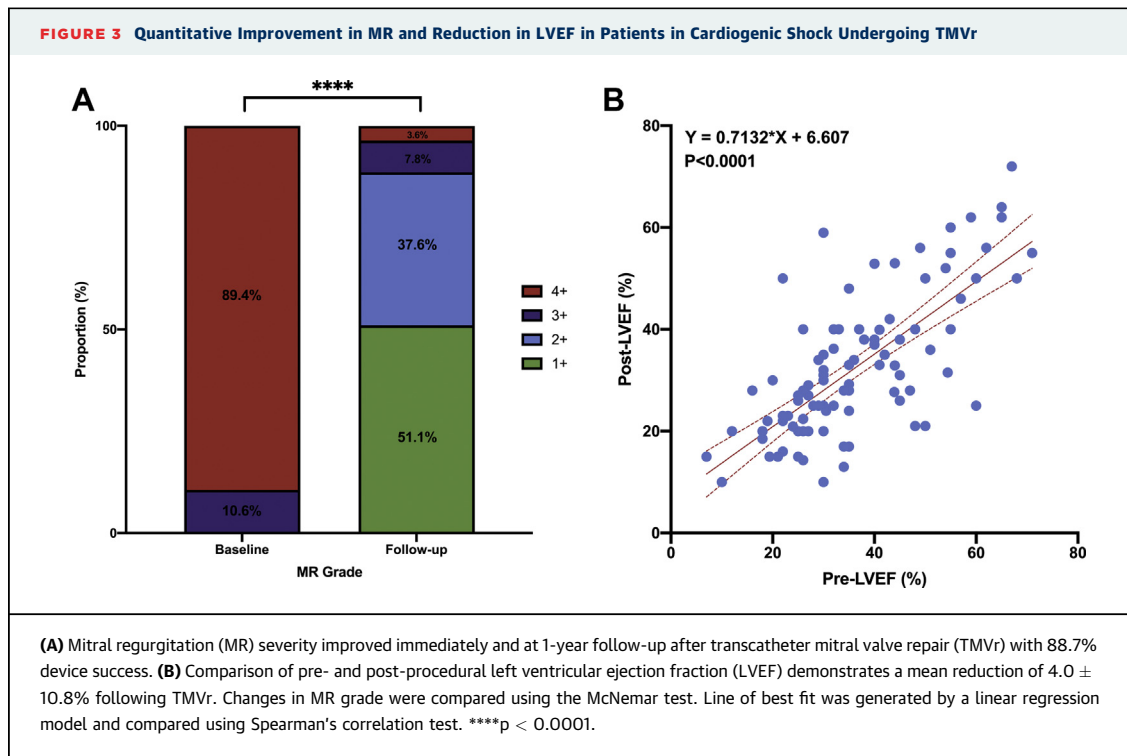
(A) In-hospital mortality occurred in 22 patients in cardiogenic shock (15.6%) following transcatheter mitral valve repair (TMVr). (B) 90-day mortality occurred in 38 patients in cardiogenic shock (29.5%) following TMVr. (C) Hospitalization for heart failure occurred in 26 patients in cardiogenic shock (18.4%) following TMVr. (D) The composite of 90-day mortality and heart failure (HF) hospitalization occurred 41 patients (30.8%) following TMVr.

was observed in 26 patients (18.4%), with a median of 73 days (IQR: 26 to 546 days) (Figure 2C). The composite of 90-day mortality and HF hospitalization occurred in 41 patients (30.8%) (Figure 2D).

All patients underwent post-procedural echocardiography, with a median time of 36 days (IQR: 4 to 399 days). MR grade pre- and post-TMVr was compared in a paired analysis demonstrating a significant reduction in MR grade ($p < 0.0001$) (Figure 3A). Pre- and post-procedural LVEF was

reduced following TMVr, with a mean difference of $3.7 \pm 10.4\%$ ($p = 0.0006$) (Supplemental Table 5, Figure 3B).

To assess the impact of MR reduction on survival, patients with device success were compared to those without device success. Acceptable device success was achieved in 125 patients (88.7%), defined as post-procedural change MR by ≥ 1 grade and an absolute grade of $\leq 2+$ on follow-up echocardiography, and 16 patients (11.3%) failed to achieve device success,



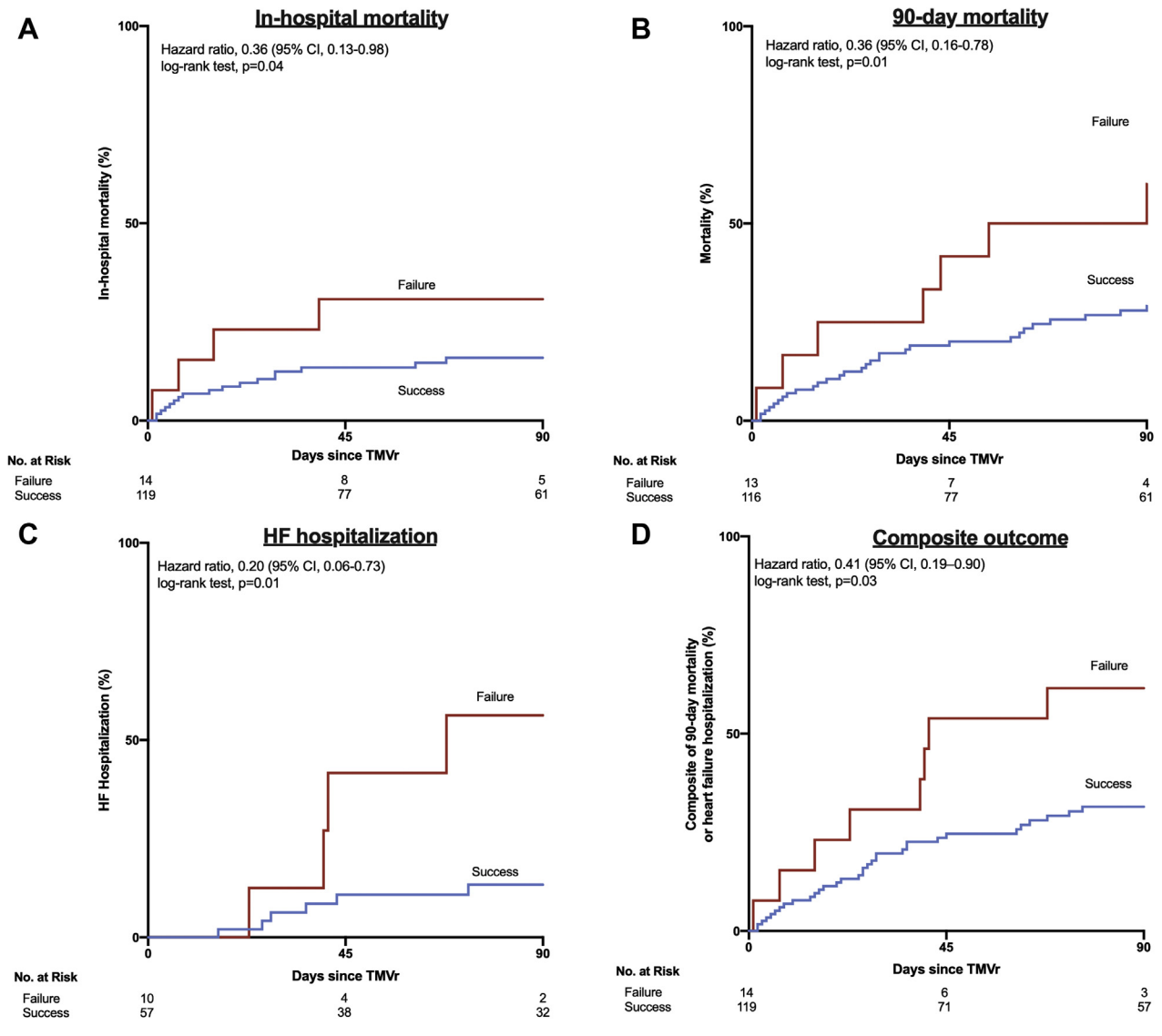
with no differences in baseline characteristics (Supplemental Table 6). Specifically, in patients in whom MR reduction was successful, there was lower in-hospital mortality (HR: 0.36; 95% CI: 0.13 to 0.98; p = 0.04) (Figure 4A, Supplemental Table 7). Device success was also associated with reduced rates of 90-day mortality (HR: 0.36; 95% CI: 0.16 to 0.78; p = 0.01) (Figure 4B) and 1-year mortality (HR: 0.46; 95% CI: 0.22 to 0.94; p = 0.03), and the association remained after adjusting for age and sex (Supplemental Table 7). Finally, device success was associated with lower rates of 90-day HF hospitalization following the procedure (HR: 0.20; 95% CI: 0.06 to 0.73; p = 0.01) (Figure 4C) and the composite of 90-day mortality and HF hospitalization (HR: 0.41; 95% CI: 0.19 to 0.90; p = 0.03) (Figure 4D). In-hospital mortality stratified by important subgroups, including baseline SCAI class, baseline LVEF, primary versus secondary, and acute versus chronic MR, are presented in Supplemental Figure 1.

DISCUSSION

In the present study, TMVr using the MitraClip system appears to be a viable therapeutic salvage strategy, demonstrating procedural safety and efficacy in MR reduction in patients with significant MR and cardiogenic shock. Although heterogenous in MR etiology, successful device implantation was

associated with decreased risk for mortality over the first year, supporting the hypothesis that MR reduction in the acute phase of shock may represent a therapeutic target addressable using a percutaneous approach (Central Illustration).

TMVr is known to reduce mortality and HF hospitalization; however, these benefits have been demonstrated only in patients in stable condition receiving guideline-directed medical therapy, excluding those who were at prohibitive surgical risk and in cardiogenic shock (1-3). Patients in cardiogenic shock with severe valvular disease represent a uniquely high-risk cohort with poor outcomes and limited therapies (7,25,26). Historically, in-hospital mortality in patients with severe MR from acute MI approaches 60% and remained at 40% following mitral valve surgery (5). In our cohort of patients with prohibitive surgical risk, we report an in-hospital mortality rate of 15.6%, with improved survival in those with device success. Indeed, in the setting of cardiogenic shock, increasing MR burden is associated with diminished survival, supporting a “dose effect” (27). Although our 1-year mortality in the total cohort was 50% (25,28,29), we further demonstrate that device success reduced 1-year mortality to 39.7% compared with 69.2% in those without device success, reflecting the high risk in baseline without MR treatment. Collectively, these observations suggest that the use of TMVr to reduce MR severity in

FIGURE 4 Kaplan-Meier Curves Following TMVr in Patients With Cardiogenic Shock Stratified by TMVr Device Success in MR

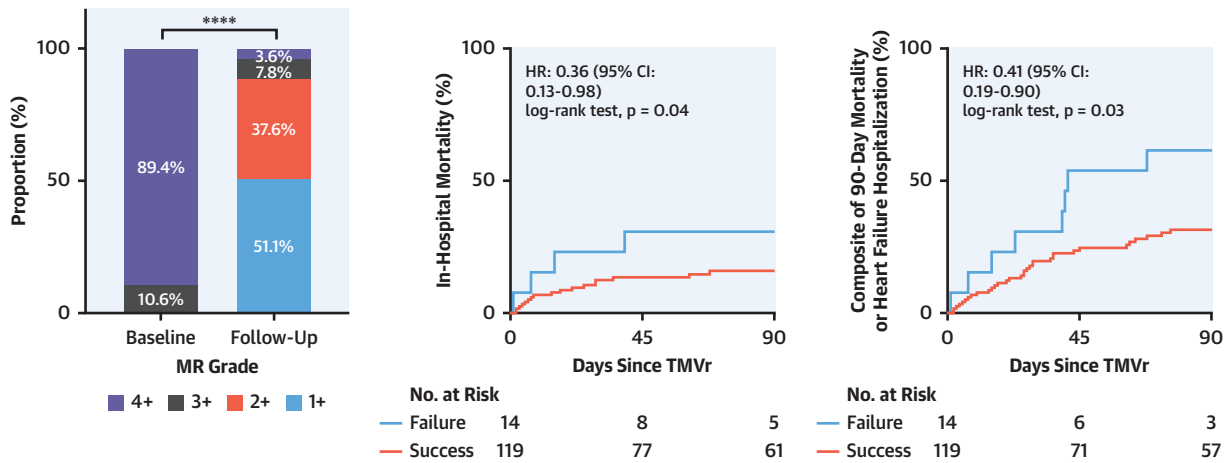
(A) Cumulative incidence of in-hospital mortality among patients who underwent transcatheter mitral valve repair (TMVr). Device success was associated with reduced rates of in-hospital mortality (hazard ratio [HR]: 0.36; 95% confidence interval [CI]: 0.13 to 0.98; $p = 0.04$). **(B)** Cumulative incidence of mortality at 90-day follow-up among patients who underwent TMVr. Patients with device success had reduced rates of 90-day mortality (HR: 0.36; 95% CI: 0.16 to 0.78; $p = 0.01$). **(C)** In patients with hospitalization for heart failure (HF) at 90-day follow-up among those who underwent TMVr, those with device success had a lower incidence of hospitalization for heart failure (HR: 0.20; 95% CI: 0.06 to 0.73; $p = 0.01$). **(D)** In patients with 90-day mortality and HF hospitalization at 90-day follow-up, device success was associated with a reduced cumulative event rate (HR: 0.41; 95% CI: 0.19 to 0.90; $p = 0.03$). Kaplan-Meier curves were generated and compared using the log-rank test, and HRs were evaluated using the Cox proportional hazards model. P values < 0.05 were considered to indicate statistical significance.

cardiogenic shock may translate to improved clinical outcomes.

Several considerations remain in selecting an optimal management strategy for patients with cardiogenic shock and significant MR. Currently, revascularization remains a cornerstone in the treatment of shock of ischemic etiology, and MCS is being

increasingly used up front in the management of these patients (30,31). Although one-half of the patients in our study had temporary MCS, with a majority receiving intra-aortic balloon pump support, all were deemed ineligible for escalation to durable support or transplantation at the time of TMVr (32). In the COAPT study, TMVr was associated with a 50%

CENTRAL ILLUSTRATION Impact of Successful Transcatheter Mitral Valve Repair on Clinical Outcomes in Patients With Cardiogenic Shock and Mitral Regurgitation



Jung, R.G. et al. *J Am Coll Cardiol Interv.* 2021;14(1):1-11.

Cumulative incidence of in-hospital mortality and composite of 90-day mortality and heart failure hospitalization among patients who underwent transcatheter mitral valve repair (TMVr) stratified by residual mitral regurgitation. **** indicates p < 0.0001. HR = hazard ratio; MR = mitral regurgitation.

reduction in the need for left ventricular assist device implantation (1). Although patients in the present study were deemed ineligible, in patients with cardiogenic shock and MR who are candidates for durable MCS, consideration for TMVr as either a bridge or adjunctive therapy may be reasonable. Moreover, MCS is reported to carry a 30% risk for complications including hemolysis, infection, and bleeding (30), while TMVr is a transvenous procedure with an exceptional safety profile, even in this high-risk cohort.

STUDY LIMITATIONS. First, the data are observational and are thus susceptible to all biases inherent to this study design.

Second, although reported outcomes following TMVr are encouraging, the lack of a comparison group who did not undergo intervention is notable. However, in the present study, the use of TMVr was a last-line salvage therapy, with ineligible patients typically receiving palliative care and dying in the hospital. Decisions to not treat these patients would reflect differences in baseline characteristics that could not be reasonably adjusted for.

Third, some hemodynamic parameters from right heart catheterization and echocardiographic data were missing from the cohort.

Finally, despite encompassing all available patient-level data on this cohort, the overall size remains small. Thus, although we were able to compare

outcomes between patients with and those without device success, more robust adjustment of the data was not possible.

CONCLUSIONS

In patients with cardiogenic shock with moderate to severe MR, TMVr is safe and technically feasible. Dedicated prospective studies are warranted, while TMVr may be considered in select patients pending the outcomes of larger clinical studies.

ACKNOWLEDGMENTS The authors thank all the collaborators and the CAPITAL Research Group for all their support and guidance for the completion of the project.

AUTHOR DISCLOSURES

Dr. Jung was funded by the Vanier CIHR Canada Graduate Scholarship. Dr. Benito-Gonzalez has received grants from Abbott Vascular, outside the submitted work. Dr. Estevez-Loureiro is a consultant for Abbott Vascular; and is a proctor for the MitraClip, outside the submitted work. Dr. Buzzatti has received personal fees from InnovHeart, outside the submitted work. Dr. Hibbert has received funding as a clinical trial investigator from Abbott, Boston Scientific, and Edwards Lifesciences, outside the submitted work. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr. Benjamin Hibbert, University of Ottawa Heart Institute, 40 Ruskin Street, H-4238, Ottawa, Ontario K1Y 4W7, Canada. E-mail: bhibbert@ottawaheart.ca.

PERSPECTIVES

WHAT IS KNOWN? Cardiogenic shock with severe MR is associated with poor outcomes with limited therapeutic options. Moderate or greater MR represents 5% to 10% of patients in cardiogenic shock, and these patients are often at prohibitive risk for surgical intervention and are not candidates for advanced MCS. The role of TMVr as an adjunct therapy in patients with cardiogenic shock remains poorly described.

WHAT IS NEW? The present study demonstrates that successful TMVr can be performed as a salvage therapy in

patients with no further options. Successful repair was associated with improved outcomes in this high-risk cohort and presents a novel therapeutic option in select patients.

WHAT IS NEXT? This study demonstrates the potential of TMVr as a salvage therapy, and prospective randomized studies are warranted to assess whether valvular intervention in those with cardiogenic shock and significant MR improves mortality in this high-risk cohort.

REFERENCES

- Stone GW, Lindenfeld J, Abraham WT, et al. Transcatheter mitral-valve repair in patients with heart failure. *N Engl J Med* 2018;379:2307-18.
- Feldman T, Foster E, Glower DD, et al. Percutaneous repair or surgery for mitral regurgitation. *N Engl J Med* 2011;364:1395-406.
- Obadia JF, Messika-Zeitoun D, Leurent G, et al. Percutaneous repair or medical treatment for secondary mitral regurgitation. *N Engl J Med* 2018;379:2297-306.
- Baumgartner H, Falk V, Bax JJ, et al. 2017 ESC/EACTS guidelines for the management of valvular heart disease. *Eur Heart J* 2017;38:2739-91.
- Thompson CR, Buller CE, Sleeper LA, et al. Cardiogenic shock due to acute severe mitral regurgitation complicating acute myocardial infarction: a report from the SHOCK trial registry. *J Am Coll Cardiol* 2000;36:1104-9.
- Thiele H, Ohman EM, Desch S, Eitel I, de Waha S. Management of cardiogenic shock. *Eur Heart J* 2015;36:1223-30.
- Flint K, Brieke A, Wiktor D, Carroll J. Percutaneous edge-to-edge mitral valve repair may rescue select patients in cardiogenic shock: findings from a single center case series. *Catheter Cardiovasc Interv* 2019;94:E82-7.
- Chan V, Messika-Zeitoun D, Labinaz M, et al. Percutaneous mitral repair as salvage therapy in patients with mitral regurgitation and refractory cardiogenic shock. *Circ Cardiovasc Interv* 2019;12:e008435.
- Pleger ST, Chorianopoulos E, Krumdordf U, Katus HA, Bekeredjian R. Percutaneous edge-to-edge repair of mitral regurgitation as a bail-out strategy in critically ill patients. *J Invas Cardiol* 2013;25:69-72.
- Turyan Medvedovsky A, Tonchev I, Tahiroglu I, et al. MitraClip therapy in critically ill patients with severe functional mitral regurgitation and refractory heart failure. *Struct Heart* 2019;3:296-301.
- Stone GW, Adams DH, Abraham WT, et al. Clinical trial design principles and endpoint definitions for transcatheter mitral valve repair and replacement: part 2: endpoint definitions: a consensus document from the Mitral Valve Academic Research Consortium. *J Am Coll Cardiol* 2015;66:308-21.
- Adamo M, Barbanti M, Curello S, et al. Effectiveness of MitraClip therapy in patients with refractory heart failure. *J Interv Cardiol* 2015;28:61-8.
- Adamo M, Curello S, Chiari E, et al. Percutaneous edge-to-edge mitral valve repair for the treatment of acute mitral regurgitation complicating myocardial infarction: A single centre experience. *J Int Cardiol* 2017;234:53-7.
- Di Prima AL, Covelto DR, Franco A, et al. Do patients undergoing MitraClip implantation require routine ICU admission? *J Cardiothorac Vasc Anesth* 2014;28:1479-83.
- Eliaz R, Turyan A, Beeri R, Shuvy M. Utilization of intra-aortic balloon pump to allow MitraClip procedure in patients with non-coapting mitral valve leaflets: a case series. *Eur Heart J Case Rep* 2019;3:ytz045.
- Estevez-Loureiro R, Arzamendi D, Freixa X, et al. Percutaneous mitral valve repair for acute mitral regurgitation after an acute myocardial infarction. *J Am Coll Cardiol* 2015;66:91-2.
- Kesler M, Seeger J, Wöhrle J, Rottbauer W, Markovic S. Intra-aortic balloon counterpulsation pump in heart failure patients during MitraClip implantation—a propensity-score matched analysis. *Catheter Cardiovasc Interv* 2018;92:1433-8.
- Samuel Del Castillo Garcia D, Carlos Minguito Carazo D, Tomas Benito Gonzalez D, et al. Outcomes following urgent percutaneous mitral valve repair: a single center observational study. *Eur Heart J Acute Cardiovasc Care* 2019;8 suppl 1:15-7.
- Taramasso M, Denti P, Cioni M, et al. Percutaneous mitral valve repair in high-risk patients: Single center experience. *EuroIntervention*, 2012. N:N188.
- Berardini A, Biagini E, Saia F, et al. Percutaneous mitral valve repair: the last chance for symptoms improvement in advanced refractory chronic heart failure? *J Int Cardiol* 2017;228:191-7.
- Buzzatti N, Taramasso M, Cioni M, et al. MitraClip therapy in idiopathic vs ischemic dilated cardiomyopathy, a single center experience. *J Am Coll Cardiol* 2013;1:B213.
- Haberman D, Taramasso M, Czarnecki A, et al. Salvage MitraClip in severe secondary mitral regurgitation complicating acute myocardial infarction: data from a multicentre international study. *Eur J Heart Fail* 2019;21:1161-4.
- Kovach CP, Bell S, Kataruka A, Reisman M, Don C. Outcomes of urgent/emergent transcatheter mitral valve repair (MitraClip): a single center experience. *Catheter Cardiovasc Interv*. 2020 Jun 26 [E-pub ahead of print].
- Baran DA, Grines CL, Bailey S, et al. SCAI clinical expert consensus statement on the classification of cardiogenic shock: this document was endorsed by the American College of Cardiology (ACC), the American Heart Association (AHA), the Society of Critical Care Medicine (SCCM), and the Society of Thoracic Surgeons (STS) in April 2019. *Catheter Cardiovasc Interv* 2019;94:29-37.
- Thiele H, Akin I, Sandri M, et al. PCI strategies in patients with acute myocardial infarction and cardiogenic shock. *N Engl J Med* 2017;377:2419-32.
- Sv Diepen, Katz JN, Albert NM, et al. Contemporary management of cardiogenic shock: a scientific statement from the American Heart Association. *Circulation* 2017;136:e232-68.
- Picard Michael H, Davidoff R, Sleeper Lynn A, et al. Echocardiographic predictors of survival and

response to early revascularization in cardiogenic shock. *Circulation* 2003;107:279-84.

28. Hochman JS, Sleeper LA, Webb JG, et al., for the SHOCK Investigators. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. *N Engl J Med* 1999;341:625-34.

29. Ouweneel DM, Eriksen E, Sjaw KD, et al. Percutaneous mechanical circulatory support versus intra-aortic balloon pump in cardiogenic shock after acute myocardial infarction. *J Am Coll Cardiol* 2017;69:278-87.

30. Russo JJ, Aleksova N, Pitcher I, et al. Left ventricular unloading during extracorporeal

membrane oxygenation in patients with cardiogenic shock. *J Am Coll Cardiol* 2019;73:654-62.

31. Tehrani BN, Truesdell AG, Sherwood MW, et al. Standardized team-based care for cardiogenic shock. *J Am Coll Cardiol* 2019;73:1659-69.

32. Estevez-Loureiro R, Adamo M, Arzamendi D, et al. Transcatheter mitral valve repair in patients with acute myocardial infarction: insights from the European Registry of MitraClip in Acute Mitral Regurgitation following an acute myocardial infarction (EREMMI). *EuroIntervention* 2020;15:1248-50.

KEY WORDS cardiogenic shock, mitral regurgitation, transcatheter mitral valve repair

APPENDIX For supplemental tables and a figure, please see the online version of this paper.



Go to <http://www.acc.org/jacc-journals-cme> to take the CME/MOC/ECME quiz for this article.