

Transcatheter edge-to-edge mitral valve repair in patients with acute decompensated heart failure due to severe mitral regurgitation

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Abstract

Background: *Transcatheter edge-to-edge mitral valve repair (TEER) has been established as a therapy for severe symptomatic mitral regurgitation (MR) in stable patients, and it has recently emerged as a reasonable option for acutely ill patients. The aim of this study was to evaluate the safety and efficacy of TEER in hospitalized patients with acute decompensated heart failure (HF) and severe MR that was deemed to play a major role in their deterioration.*

Methods: *We included 31 patients who underwent emergent TEER for MR $\geq 3+$ from 2012 to 2022 at Sheba Medical Center. Outcomes included procedural safety, procedural success, all-cause mortality, HF readmission, and functional improvement. Outcomes were evaluated at 3 months and at 1 year. Data were obtained retrospectively by chart review.*

Results: *Implantation of a TEER device was achieved in 97% of patients, and reduction in MR severity of at least two grades and final MR $\leq 2+$ at discharge was achieved in 74%. No intra-procedural mortality or life-threatening complications were noted. Mortality at 30 days was 23%. No excess mortality occurred beyond 6 months, with a total mortality of 41%. At 1 year all survivors had MR $\leq 2+$, all were free of HF hospitalizations, and 88% were at New York Heart Association class $\leq II$.*

Conclusions: *Mitral valve TEER for patients with acute decompensated HF and significant MR is safe, feasible, and achieves substantial reduction in MR severity. Despite high early mortality, procedural success is associated with good long-term clinical outcomes for patients surviving longer than 6 months. (Cardiol J)*

Key words: mitral valve, mitral regurgitation, acute decompensated heart failure, trans-catheter edge-to-edge repair, transcatheter edge-to-edge mitral valve repair

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Introduction

Heart failure (HF) is the leading diagnosis in hospitalized patients ≥ 65 years old, representing 1% to 2% of all hospital admissions [1, 2], and it is associated with increased mortality [3, 4]. Significant mitral regurgitation (MR) is prevalent among patients hospitalized for acute decompensated HF, and it is independently associated with excess 1-year mortality in those with left ventricular ejection fraction (LVEF) $< 50\%$ [5]. Owing to prohibitive surgical risk, therapeutic options are frequently limited for these critically ill hospitalized patients. Transcatheter edge-to-edge mitral valve repair (TEER) has been shown to be safe and effective in stable patients with severe MR who are at high surgical risk. Furthermore, data from large-scale clinical registries [6–9] and a large randomized clinical trial [10] suggest that TEER improves quality of life and reduces HF hospitalizations and mortality in patients with symptomatic MR. Nevertheless, data regarding the benefit of the procedure in critically ill patients are scarce, and the role of TEER as a salvage therapy in the acute setting has been described previously only by a limited number of case reports and case series [11–16]. The purpose of this study was to describe the outcomes and to evaluate the safety and efficacy of TEER in hospitalized patients with intractable HF and significant MR.

Methods

The study population included patients who underwent emergent TEER of the mitral valve from July 2012 to March 2022 at the Sheba Medical Center. All patients were hospitalized with acute decompensated HF (New York Heart Association [NYHA] class IV) resistant to intensive intravenous medical therapy and had MR $\geq 3+$ that was deemed to play a major role in their deterioration. The decision to proceed with TEER was based on lack of improvement despite maximal medical therapy, high- or prohibitive-surgical risk, and anatomic suitability for TEER. All patients were evaluated by the Heart Team, which included a non-interventional cardiologist, an interventional cardiologist, and a cardiothoracic surgeon. All procedures were performed under general anesthesia and with transesophageal echocardiography (TEE) and fluoroscopy guidance. Leaflet approximation was performed using MitraClip (Abbott, Menlo Park, CA, USA) or PASCAL (Edwards Lifesciences, Irvine, CA, USA) devices. We retrospectively

evaluated immediate, 3-month, and 1-year outcomes. All data were abstracted from patients' electronic medical records. Clinical, laboratory, echocardiographic, and electrocardiographic data were recorded at baseline and during follow-up. Acute procedural results were assessed by TEE at implantation and supplemented by transthoracic echocardiography before discharge. Safety was evaluated clinically, according to the occurrence of procedure-related adverse events. Mortality data were drawn from the national death registry. Descriptive statistics are used to report on the data. The study was approved by the local Ethics Committee and was conducted in accordance with the Declaration of Helsinki. Informed consent was provided by all subjects. Results are expressed as mean \pm standard deviation for continuous variables or as numbers (percentages) for categorical variables.

Procedure description

Venous access was obtained via the femoral vein followed by puncture of the trans-atrial septum. A steerable guide catheter, through which the device delivery system was introduced, was advanced into the left atrium and positioned over the mitral valve. The device was steered towards the origin of the regurgitation jet, and its arms were then opened and oriented perpendicular to the line of coaptation. The opened device was advanced through the mitral valve into the left ventricle (LV) and subsequently pulled back to grasp the leaflets, which produced a double orifice. Device position and presence of residual MR were evaluated with color flow Doppler. If the results were adequate, the device was locked and released from the delivery system. In patients with suboptimal MR reduction after initial device implantation, additional devices were implanted according to the operator's discretion.

Results

We included in the current study 31 hospitalized patients who underwent emergent TEER for severe MR and intractable HF. All patients had MR grade 3+ (10%) or 4+ (90%) at baseline. The etiology of MR (Fig. 1) was secondary in 28 (90%) patients, of whom 22 (79%) were ischemic (of these, 13 [59%] patients presented after recent myocardial infarction (MI) [mean 29 ± 20 days from event], 2 patients presented with partial rupture of papillary head and acute flail, and 9 [41%] had long-standing ischemic cardiomyopathy). Non-ischemic secondary MR was found in 6 (19%)

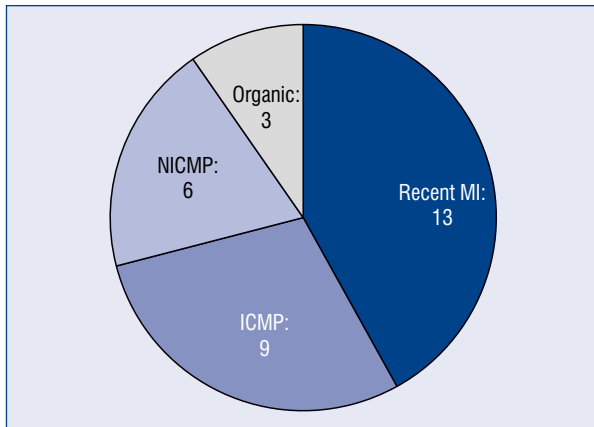


Figure 1. Etiology of mitral regurgitation; MI — myocardial infarction; ICMP — ischemic cardiomyopathy; NICMP — non-ischemic cardiomyopathy.

patients (5 with non-ischemic cardiomyopathy, 1 with annular dilatation secondary to long-standing atrial fibrillation). Primary MR with presence of prolapse and/or flail was found in 3 (10%) patients. Baseline characteristics are summarized in Table 1. The mean age was 73.5 ± 11 years and 32% were female. The indication for the procedure was intractable HF requiring intravenous (IV) therapy in patients with moderate to severe (3+) or severe (4+) MR that was considered to be etiologically significant in determining their clinical state. All patients were on high-dose (average 100 mg/day) IV furosemide, one-third were receiving IV vasodilators (nitroglycerin or nitroprusside), and two-thirds were receiving IV inotropes (dopamine, dobutamine, levosimendan, norepinephrine, or milrinone). In the days prior the procedure, 9 (29%) patients had been in cardiogenic shock (CS) and 20 (65%) were managed in the intensive care unit (ICU). During the 24 hours preceding TEER, 10 (32%) patients were receiving inotropic support, 4 (13%) were mechanically ventilated, and 1 (3%) had intra-aortic balloon pump.

Acute procedural outcomes and peri-procedural events

Implantation of a TEER device was achieved in 30/31 (97%) patients — 13 were implanted with a single device, 15 with two devices, and 2 patients with three devices. Acute procedural success, defined as a reduction in MR severity of at least two grades and final MR grade $\leq 2+$ at discharge, was achieved in 23 (74%) patients. In 3 patients the MR grade was reduced by one grade to MR

Table 1. Baseline characteristics.

Age [years]	73.5 ± 10.9
Male gender	21 (67.7%)
Body mass index [kg/m ²]	27.3 ± 4.3
Ischemic heart disease	25 (80.6%)
Past stroke or TIA	3 (9.7%)
Diabetes	17 (54.8%)
Atrial fibrillation:	
Paroxysmal	14 (45.2%)
Chronic	3 (9.7%)
Hyperlipidemia	22 (71.0%)
Hypertension	25 (80.6%)
Chronic kidney disease	18 (58.1%)
Smoking:	
Past	8 (25.8%)
Current	3 (9.7%)
Permanent pacemaker:	
Pacemaker	8 (25.8%)
CRT	3 (9.7%)
Cardiomyopathy:	
Ischemic	23 (74.2%)
Non-ischemic	6 (19.4%)
Past MI	26 (83.9%)
MI within 60 days prior to procedure	13 (41.9%)
Past PCI	20 (64.5%)
PCI within 60 days prior to procedure	9 (29.0%)
Past coronary artery bypass graft	11 (35.5%)
HF hospitalization within previous 1 year	
1 to 3 admissions	26 (83.9%)
4 to 6 admissions	5 (16.1%)
Hemoglobin [g/dL]	11.2 ± 2.6
Creatinine [mg/dL]	1.9 ± 1.1
Albumin [g/L]	32.0 ± 6.0
GFR [mL/min/1.73 m ²]	47.5 ± 26.8

All data are presented as means ± standard deviation or numbers (percentages, %) unless stated otherwise. CRT — cardiac resynchronization therapy; GFR — glomerular filtration rate; HF — heart failure; MI — myocardial infarction; PCI — percutaneous coronary intervention; TIA — transient ischemic attack

3+. Patients in whom procedural success was not achieved had higher mean effective regurgitant orifice area (EROA; 0.55 ± 0.36 vs. 0.43 ± 0.35 cm²), higher mean MR volume (65.4 ± 37.3 vs. 46.3 ± 23.2 mL), higher mean systolic pulmonary artery pressure (62.7 ± 22.5 vs. 57.9 ± 13.4 mmHg), and greater prevalence of severe LV dysfunction (62.5% vs. 26%) on baseline echocardiography. One patient developed mean transmitral gradient > 5 mmHg. An acute reduction in mean systolic

Table 2. Echocardiography before and after transcatheter edge-to-edge mitral valve repair (TEER).

	Baseline (n = 31)	Post-TEER (n = 31)	3 months (n = 14)	1 year (n = 9)
Mitral regurgitation severity:				
None	0 (0%)	2 (6.5%)	2 (14.3%)	1 (11.1%)
Mild	0 (0%)	10 (32.3%)	5 (35.7%)	3 (33.3%)
Moderate	0 (0%)	11 (35.5%)	5 (35.7%)	5 (55.6%)
Moderate-severe	3 (9.7%)	3 (9.7%)	1 (7.1%)	0 (0%)
Severe	28 (90.3%)	5 (16.1%)	1 (7.1%)	0 (0%)
Effective regurgitant orifice area [cm ²]	0.47 ± 0.35	0.27 ± 0.2	0.34 ± 0.43	0.26 ± 0.14
Mitral regurgitation volume [mL]	51.7 ± 28.6	31.4 ± 22.7	35.9 ± 37.5	31.3 ± 16.1
LV ejection fraction [%]	37.2 ± 13.4	37.0 ± 14.6	39.5 ± 13.1	43.9 ± 11.7
LV end-diastolic diameter [mm]	58.6 ± 9.9	57.8 ± 8.7	57.7 ± 8.8	54.4 ± 7.7
LV end-systolic diameter [mm]	46.7 ± 11.3	46.0 ± 11.6	45.5 ± 10.5	41.7 ± 7.2
Tricuspid regurgitation severity:				
Moderate	13/28 (46.4%)	5/29 (17.2%)	4 (28.6%)	2 (22.2%)
Moderate-severe	0/28 (0%)	2/29 (6.9%)	1 (7.1%)	0 (0%)
Severe	2/28 (7.1%)	3/29 (10.3%)	0 (0%)	0 (0%)
Systolic pulmonary arterial pressure [mmHg]	59.2 ± 16.1	48.6 ± 13.0	42.9 ± 13.1	41.4 ± 13.9
Tricuspid regurgitation systolic gradient [mmHg]	46.8 ± 15.3	37.6 ± 11.2	34.5 ± 12.0	32.6 ± 13.2
Left atrial volume index [mL/m ²]	63.4 ± 22.6	64.4 ± 19.1	57.4 ± 18.3	51.6 ± 20.6

All data are presented as means ± standard deviation or numbers (percentages, %) unless stated otherwise. LV — left ventricular

pulmonary artery pressure of 10.6 mmHg was noted after the procedure (Table 2), and a further decline was observed over the first year in patients for whom echocardiographic follow-up was available. No intra-procedural mortality was noted. Notable intra-procedural events occurred in 4 (13%) patients — hemodynamic instability in 2, access site bleeding requiring blood transfusion in 1, and suspected thrombus embolization in the left atrium without clinical sequelae in 1. Following the procedure, 8 (26%) patients remained mechanically ventilated (6 of them for more than 24 h) and 11 (36%) required inotropic support (8 of them for more than 24 h). During the early post-procedural period, 1 (3%) patient developed new CS, 3 (10%) developed septic shock, 4 (13%) patients had isolated acute kidney injury (AKI), and 6 (19%) patients required blood transfusion, 1 of them due to major upper gastrointestinal bleeding. A total of 19 (61%) patients required ICU care during their post-TEER hospitalization, with mean stay of 5.1 ± 4.0 days. Mean post-TEER hospitalization length was 10.6 ± 11.3 days.

Follow-up

Long-term mortality data were available for all patients. Estimates of the probability of survival

are shown in Figure 2. Mortality at 30 days was 23% (7/31 patients), with higher rates observed among patients in whom TEER failed (37.5%) than in those it succeeded (17%). All patients who died within 30 days of intervention had ischemic cardiomyopathy with a past medical history significant for MI, which was recent (within 60 days) in 5 (71%) of them. They were more likely to present with CS (57% deceased vs. 21% alive at 30 days) or MI (57% vs. 25%) during the month preceding the procedure, and to have lower mean albumin levels (26 ± 4 vs. 34 ± 6 g/L) and lower mean glomerular filtration rate (38 ± 22 vs. 50 ± 28 mL/min/1.73 m²) on pre-procedural evaluation. Furthermore, coronary artery disease with past percutaneous coronary intervention or coronary artery bypass graft, chronic kidney disease, diabetes mellitus, and smoking were more frequently observed in this patient group. Decreased 30-day survival was associated with higher rates of procedural failure (43% deceased vs. 21% alive) as well as major intra-procedural (43% deceased vs. 4% alive) and post-procedural (86% deceased vs. 12.5% alive) complications. Moreover, patients who died within 30 days were more likely to require ICU care, inotropic support, and mechanical ventilation within the 24 hours prior to or immediately following

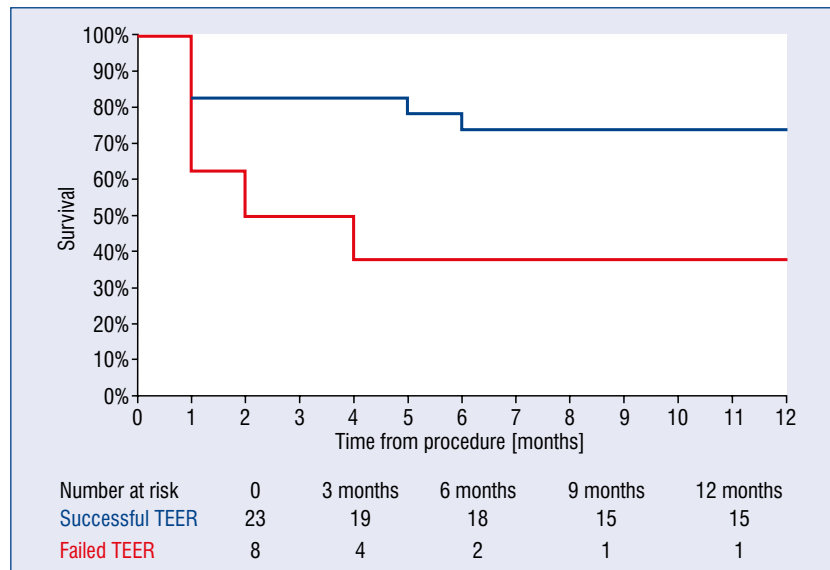


Figure 2. Kaplan–Meier estimates of 1-year survival stratified according to procedural outcome; TEER — transcatheter edge-to-edge repair.

the intervention. Pre-procedural CS and post-procedural AKI were associated with excess 30-day mortality (44% with vs. 14% without CS, 71% with vs. 8% without AKI). Survival at 3 months and 1 year was 74% (23/31 patients) and 59% (16/27 patients), respectively. Subgroups analysis according to procedural outcome demonstrated substantial differences between those who had successful compared to unsuccessful intervention (83% and 50% at 3 months, respectively, 71% and 17% at 1 year, respectively).

Echocardiography at 3 months (available for 14/23 patients) and 1 year (available for 9/16 patients) demonstrated durable reduction in regurgitation severity for all patients who underwent successful TEER. One patient had a mean trans-mitral gradient of 6 mmHg. While a notable improvement in EROA, regurgitant volume, systolic pulmonary artery pressure, and left atrial volume index was observed at 3 months and 1 year follow-up, there were only minor changes in LVEF, LV function, and LV dimensions. Echocardiographic parameters at baseline and follow-up are summarized in Table 2 and Figure 3.

NYHA class at baseline, 3-month, and 1-year follow-up is shown in Figure 4. At 3-month follow-up 82% of patients who underwent successful TEER were NYHA functional class I or II, 1 patient had been hospitalized for HF once, and 1 patient underwent implantation of a cardiac resynchronization therapy device. Two patients with residual severe MR underwent further

treatment (1 patient underwent LV assist device implantation; 1 had attempted redo-TEER, but due to partial rupture of the papillary head this was also unsuccessful, and she subsequently underwent successful surgical mitral valve replacement). At 1-year follow-up 87.5% of patients in whom intervention succeeded were NYHA functional class I or II, and all were free of HF hospitalizations.

Discussion

In the present study we report the outcomes of emergent TEER as a salvage therapy for severe MR in hospitalized patients who failed to improve despite maximal medical therapy. Our data suggest that the procedure is feasible and safe, and, although associated with high early mortality, it can provide good long-term outcomes to a significant proportion of critically ill patients.

All patients in our study were severely ill, hospitalized for HF decompensation, and on maximal intravenous drug therapy. Over half were treated within an ICU setting, one-third had been treated for CS during the index hospitalization, and a similar proportion were on intravenous inotropes at the time of the procedure. None of the patients were eligible for discharge due to intractable HF symptoms, and all were deemed to be at very high surgical risk.

Transcatheter edge-to-edge mitral valve repair has been established as a therapy for severe symptomatic MR in stable patients and is associated with a very low risk for peri-procedural adverse

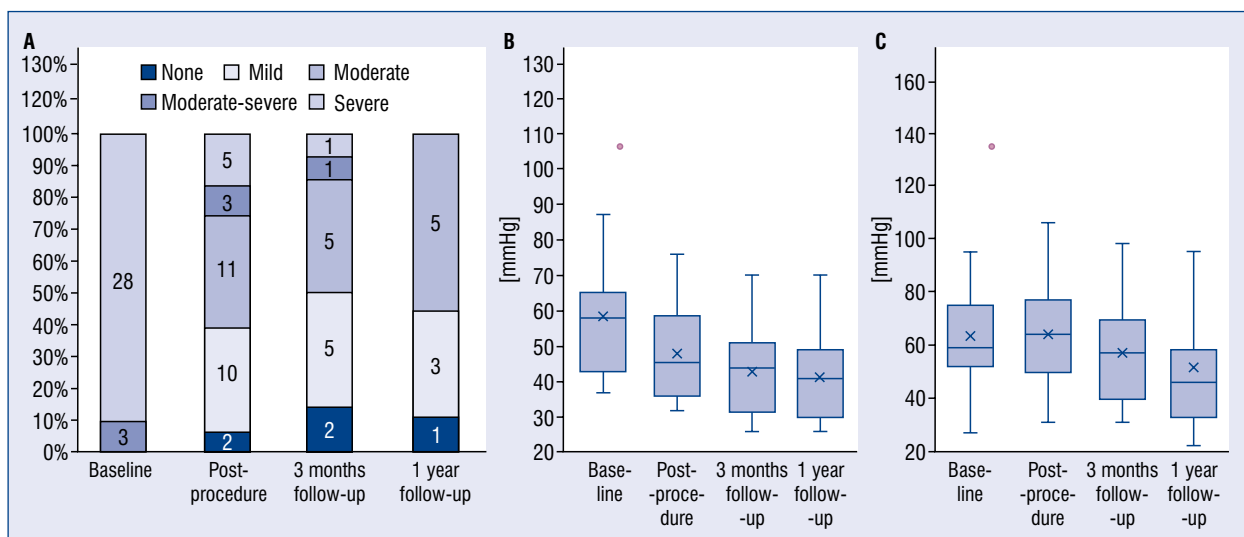


Figure 3. Echocardiographic data at baseline and follow-up; **A.** Mitral regurgitation grade; **B.** Systolic pulmonary arterial pressure; **C.** Left atrial volume index.

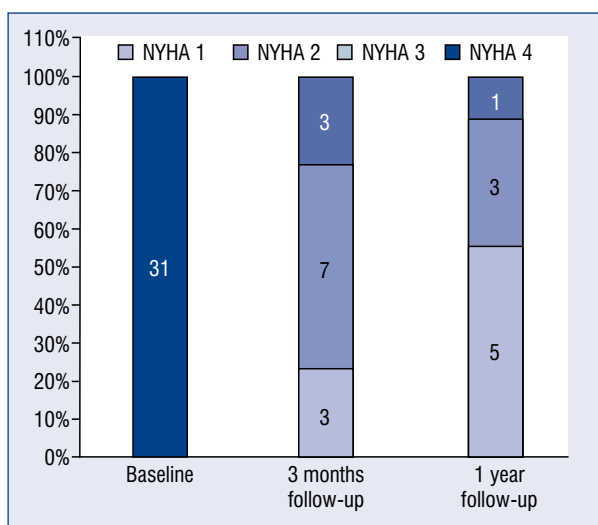


Figure 4. New York Heart Association (NYHA) classification at baseline and follow-up.

events. Indeed, the randomized EVEREST II trial demonstrated a superior safety profile compared with mitral valve surgery [17]. Two randomized trials and numerous large registries have corroborated these findings in higher-risk patients [7, 10, 18, 19]. Among the very sick patients undergoing TEER in our cohort, no patient died or suffered a life-threatening complication during or immediately following the procedure. Furthermore, none required urgent mitral valve surgery. However, the post-procedural course of these patients was much

more complex and dramatic than observed in stable patients: within the first 3 post-procedural days CS was noted in 4 patients, septic shock in 3, isolated AKI in 4, and 6 patients required blood transfusion. Two-thirds of patients were managed post-procedurally in the ICU. Prolonged (longer than 24 h) inotropic support and mechanical ventilation were noted in 8 and 6 patients, respectively. While there are limited data on peri-procedural events in other series in a similar setting [11, 13, 15, 16], the occurrence of major peri-procedural complications seems to be similar to those we describe [12–16].

Procedural success, defined as a reduction in MR severity of at least two grades and final MR grade $\leq 2+$ at discharge, was achieved in 74% of patients. Procedural failure was associated with higher pre-procedural mean EROA and mean MR volume. In fact, in our study mean EROA ($0.47 \pm 0.35 \text{ cm}^2$) and mean MR volume ($51.7 \pm 28.6 \text{ mL}$) were greater than those reported in a series of elective TEER [10, 18]. While procedural success in our cohort was similar to that reported in the historical EVEREST II trial [17], it was less than that reported in recent series of high-risk patients undergoing elective TEER, where success rates ranged from 91% to 97% [7, 9, 10, 18, 19]. Reported procedural success in series of acute TEER patients was higher than in our study. In a series similar to ours, in which the study population was fairly heterogeneous with regards to their clinical presentation, the success rate was 85% [14]. In patients presenting post MI, success rates ranged

from 88% to 95% [12, 15, 16], and in patients with CS the rates were higher, between 90% and 100% [11, 13, 16]. This probably reflects the patient selection and possible selection bias in retrospective multicenter registries, which may not have included all consecutive patients. We report here on all consecutive cases performed in our center over a period of 10 years. As such, our data may better reflect success rates attainable in acutely ill, non-selected patients in whom TEER is performed as a salvage therapy. MR $\leq 2+$ was observed in 86% of survivors at 3-month follow-up, which is consistent with other acute series reporting mid-term results. In these series, which focused on patients undergoing TEER after MI, 77% to 90.5% of patients had MR $\leq 2+$ at 3 months follow-up [15, 16]. Long-term reporting on MR grade is lacking for most series. At 1-year follow-up all survivors in our cohort had MR grade $\leq 2+$. In post-MI patients MR $\leq 2+$ was reported in 71% to 89% of patients, depending on LV function and MR type [12, 15].

Early mortality within 1 month following the procedure was high at 23%, which was due to intractable HF or complications of protracted hospitalization such as septic shock in 2 patients. This early mortality was higher than reported in elective TEER [7, 9, 10, 17–19], but similar to emergent mitral valve surgery [20], and likely reflects the severe nature of patients chosen for the procedure as 4 of 7 patients died despite a significant improvement in MR grade. Data regarding early mortality following acute TEER varies, with most studies reporting somewhat lower mortality rates. In post-MI patients, 30-day mortality did not exceed 10% [12, 16], and in patients with CS mortality ranged between 10% and 17% [11, 16]. In a series comparable to ours, which included patients undergoing urgent or emergent TEER, 30-day mortality was almost identical to ours, at 21% [14]. Additional excess mortality was noted between 1 and 6 months, with a total mortality of 41% at 6 months. However, mortality curves plateaued thereafter. Mortality at 1 year (41% of the entire cohort, 29% of patients who had successful intervention) was higher than seen in high-risk patients undergoing elective TEER (17–24%) [7, 9, 10, 18, 19], but similar to another series reporting long-term outcomes following acute TEER (42%) [11]. Procedural success was associated with increased early (83% of successful vs. 62.5% of failed TEER), mid-term (83% vs. 50%), and long-term (71% vs. 17%) survival. Furthermore,

all patients who experienced procedural failure and did not undergo further therapy died within 4 months of intervention. Although it is not possible to assume a causal relationship, there is a very positive association between procedural success and survival, which suggests that severe MR was probably a major contributor to the deteriorating clinical state of these patients, and that correction of MR may have played a part in the increased survival of those with procedural success.

In addition to lower mortality, patients with procedural success demonstrated significant clinical benefit, reflected by very low rates of HF hospitalizations and substantial improvement in functional status from baseline to 3-month and 1-year follow-up. Few data exist regarding the effect of acute TEER on quality of life. We report a readmission rate of 8% and NYHA class I or II in 77% of the cohort (82% of patients with successful procedure) at 3-month follow-up. Mid-term results following acute TEER were evaluated solely in a series assessing post-MI patients, reporting HF readmission rate of 13–23% and NYHA class I or II in 64–77% of patients [15, 16]. At 1-year follow-up all survivors in our cohort were free of HF hospitalizations and 88% were at NYHA class I or II.

Limitations of the study

The study has several limitations. This is a single-center, retrospective series, and as such suffers from all limitations inherent to such a design. Clinical and echocardiographic follow-up was not complete for all patients. However, mortality data were available for all patients. Moreover, our data do not enable us to assess optimal timing of TEER in these acutely ill patients. The major strength of our study is that it includes all consecutive patients who underwent TEER for intractable HF and severe MR and accurately reflects the outcome of these critically ill patients.

Conclusions

Mitral valve TEER for hospitalized patients with significant MR and intractable HF is safe and feasible, and it achieves a substantial reduction in MR severity. Despite high early mortality, procedural success is associated with good long-term clinical outcome for patients surviving longer than 6 months, thereby providing a therapeutic option for very high-risk sick patients with an otherwise poor prognosis. Further, larger-scale studies are needed to verify these results.

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Conflict of interest: None declared

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