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ORIGINAL RESEARCH

STRUCTURAL

Out-of-Hospital 30-Day Mortality After Mitral TEER

Insights From the STS/ACC TVT Registry

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ABSTRACT

BACKGROUND Transcatheter edge-to-edge repair of mitral valve (mTEER) is increasingly being adopted, with improved outcomes. However, it remains crucial to evaluate short-term out-of-hospital mortality to elucidate areas for further improvement.

OBJECTIVES The authors sought to evaluate incidence and predictors of out-of-hospital 30-day mortality after mTEER.

METHODS We used the Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry to identify patients who underwent mTEER between January 2014 and April 2023. Primary and secondary outcomes were 30-day out-of-hospital all-cause and cardiovascular mortality, respectively. Logistic regression and survival analysis models were used to identify factors associated with these outcomes.

RESULTS Of 61,139 patients who underwent mTEER, 1,813 (3.0%) died within 30 days of the procedure. Of these, 744 (41.0%) died out-of-hospital after discharge. Cardiovascular causes accounted for 63.4% of out-of-hospital mortality at 30 days. The median time from discharge to 30-day out-of-hospital all-cause mortality was 11 (Q1-Q3: 5-19) days. Older age, White race, non-Hispanic ethnicity, lower baseline hemoglobin, poor baseline health status, presentation as non–ST-segment elevation myocardial infarction, lower left ventricular ejection fraction, higher acuity presentation, in-hospital complications, ≥moderate residual mitral regurgitation, and lack of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers at discharge were independently associated with higher 30-day out-of-hospital all-cause and cardiovascular mortality.

CONCLUSIONS Although overall 30-day all-cause mortality after mTEER was low, 2 of 5 deaths occurred out-of-hospital after discharge. Multiple modifiable factors such as patient selection, guideline-directed medical therapy underutilization and procedural complications require optimization to mitigate out-of-hospital mortality after mTEER. (JACC Cardiovasc Interv. 2025;18:882-894) © 2025 by the American College of Cardiology Foundation.

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Mitral transcatheter edge-to-edge repair (mTEER) is being increasingly utilized for selected cases of degenerative or functional mitral regurgitation (MR) across the United States.[1] Improvements in device iterations and increased operator and institutional experience have been associated with the improved procedural success of mTEER.[2,3] A recent analysis of the Society of Thoracic Surgeons (STS)/American College of Cardiology (ACC) TVT (Transcatheter Valve Therapy) Registry demonstrated that in-hospital mortality after mTEER has improved from 2.9% in 2014 to 2.1% in 2022, with similar improvements in 30-day mortality (5.6% in 2014 to 4.2% in 2022).[1] However, despite a procedural success rate of >90% for mTEER in the United States, there remains a substantial proportion of patients who experience out-of-hospital mortality after discharge.[2-4] Factors associated with 30-day out-of-hospital mortality after mTEER remain unknown.[1,4] A prior study showed that approximately 30% of mortality within 30 days after transfemoral transcatheter aortic valve replacement occurred after discharge in the United States.[5] Similarly, with the increasing adoption of mTEER, it remains crucial to evaluate short-term out-of-hospital mortality to elucidate areas for further improvement. Therefore, the primary objective of this study was to evaluate out-of-hospital 30-day mortality after mTEER and to identify factors associated with this outcome.

ABBREVIATIONS AND ACRONYMS

ACC = American College of Cardiology

CV = cardiovascular

GDMT = guideline-directed medical therapy

KCCQ-OS = Kansas City Cardiomyopathy Questionnaire-Overall Summary

LV = left ventricular

MR = mitral regurgitation

mTEER = mitral valve transcatheter edge-to-edge repair

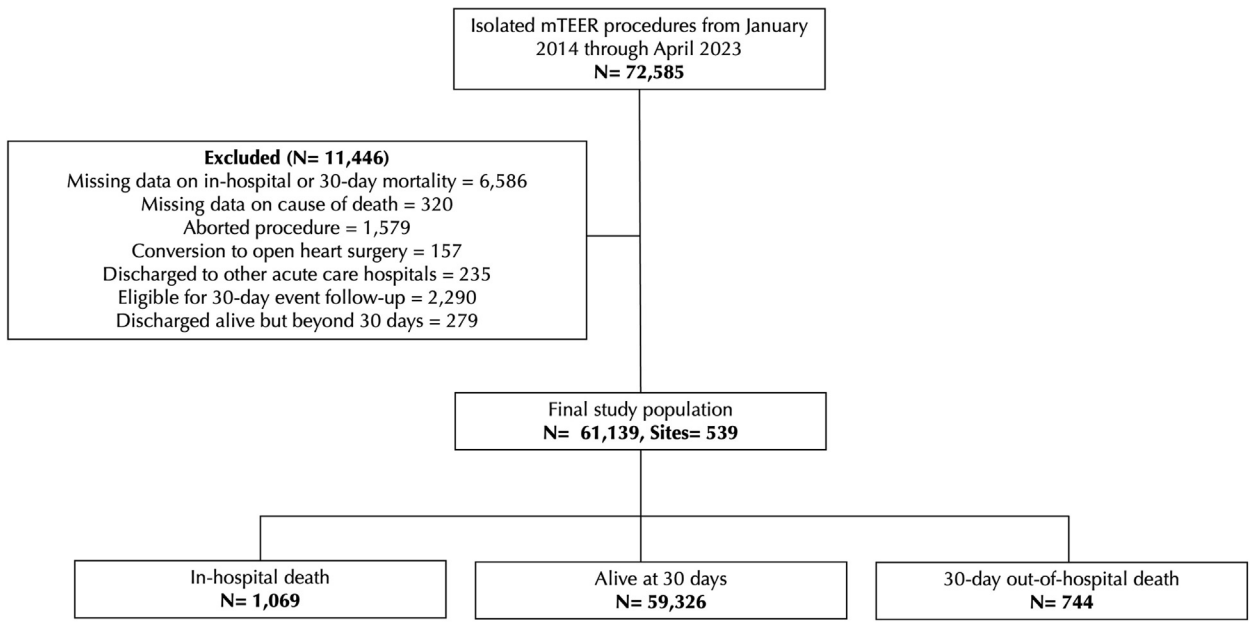
MV = mitral valve

STS = Society of Thoracic Surgeons

METHODS

DATA SOURCE. The TVT registry is a joint collaboration between the STS and the ACC to capture real-world data pertaining to all commercial cases of structural heart procedures including mTEER performed in the United States as mandated by the Centers for Medicare & Medicaid Services national coverage determination.[6,7] All consecutive mTEER cases

FIGURE 1 Study Population Selection Flowchart



Flowchart illustrates the selection of the final study cohort after applying the exclusion criteria. A 30-day follow-up period in the TVT (Transcatheter Valve Therapy) Registry is defined as 30 + 45 days, and therefore, procedure data within 75 days of data harvest were considered ineligible. mTEER = mitral valve transcatheter edge-to-edge repair.

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.

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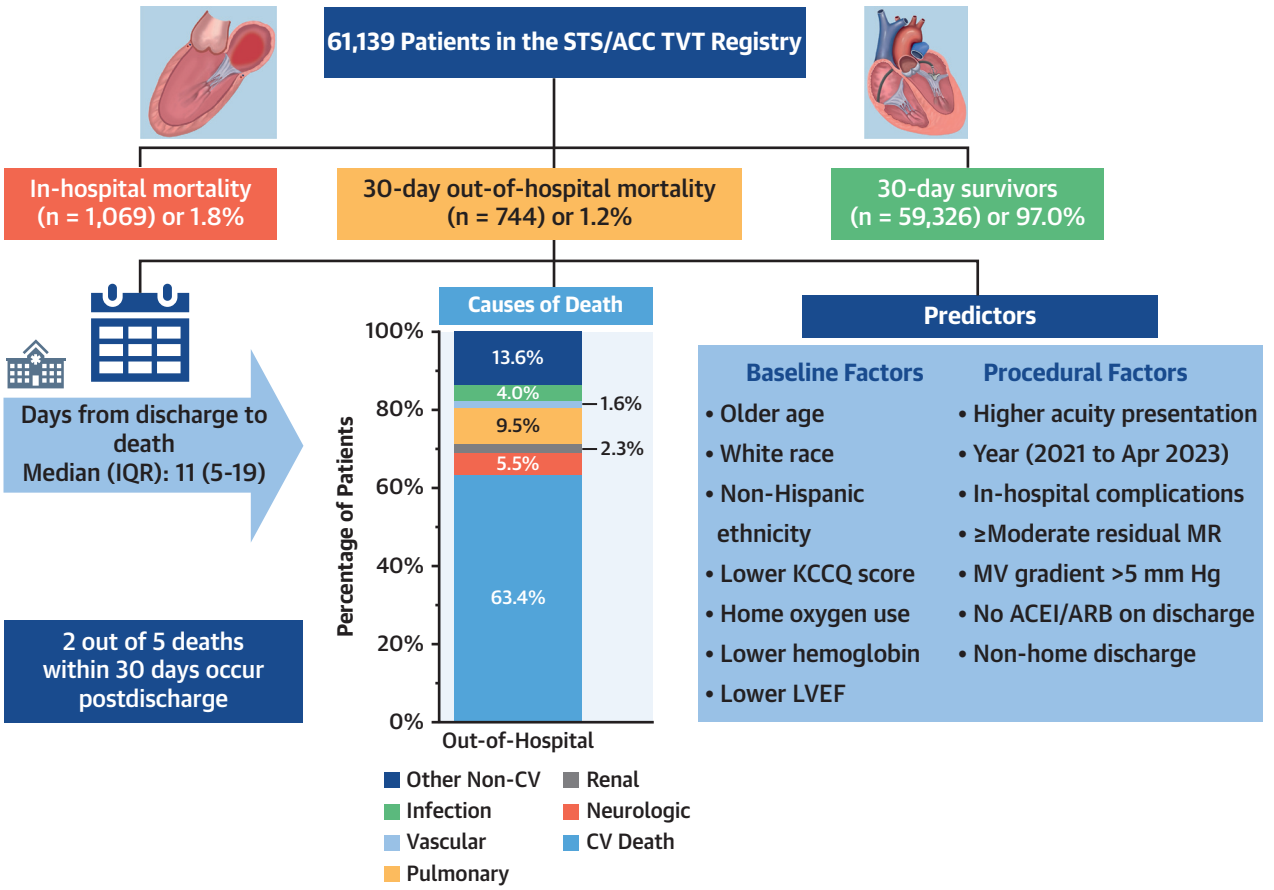
CENTRAL ILLUSTRATION **30-Day Out-of-Hospital Mortality After Mitral Transcatheter Edge-to-Edge Repair**



Bansal K, et al. JACC Cardiovasc Interv. 2025;18(7):882-894.

Of 61,139 patients included in the study, 1.2% developed out-of-hospital mortality at 30 days. Median time to death from discharge was 11 days (Q1-Q3: 5-19 days). Cardiovascular causes accounted for predominant cause of death (>60%) as depicted in the stacked bar graph. Several factors were independently associated with out-of-hospital mortality. ACC = American College of Cardiology; ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blockers; CV = cardiovascular; KCCQ = Kansas City Cardiomyopathy Questionnaire; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; MV = mitral valve; STS = Society of Thoracic Surgeons; TVT = Transcatheter Valve Therapy.

performed with available device platforms are required to be submitted to the registry for reimbursement by the Centers for Medicare & Medicaid Services, thereby virtually including all cases performed in the United States.[7] The registry collects detailed data including patient demographics, baseline characteristics, echocardiographic parameters, procedural information, functional status, quality of life, and in-hospital and mid-term outcomes (up to 1 year) using a standardized data collection form for the mTEER module and validated by the analytic center.[8] The registry undergoes random periodic audits of 10% of data elements for data quality and completeness by the National Cardiovascular Data Registry and the Duke Clinical Research Institute. To protect patient information, all research activities adhere strictly to the regulations outlined in the Common Rule (45 CFR §46).[9] Waiver of written informed consent, given the retrospective nature of the data, was granted by Advarra, which is designated as the central institutional review board for the TVT Registry. The Duke Institutional Review Board approved this study.

STUDY POPULATION. Consecutive patients who underwent mTEER between January 2014 and April 2023

TABLE 1 Baseline and Procedural Characteristics of mTEER Patients Stratified by 30-Day Vital Status

	30-Day Survivors (n = 59,326)	Out-of-Hospital 30-Day Mortality (n = 744)	*P* Value
Baseline characteristics			
Age, y	79 (72-85)	81 (74-86)	<0.001
Male	32,368 (54.6)	392 (52.7)	0.31
Race			0.04
White	50,882 (85.8)	670 (91.1)	
African American	5,464 (9.2)	53 (7.1)	
Asian	1,383 (2.3)	13 (1.7)	
American Indian/Alaskan Native	1,194 (0.3)	0 (0.4)	
Native Hawaiian/Pacific Islander	114 (0.2)	0 (0)	
Ethnicity, Hispanic/Latinx	3,458 (5.8)	26 (3.5)	0.01
Body surface area, m^2	1.9 (1.7-2.0)	1.8 (1.6-2.0)	<0.001
Pre-procedure creatinine, mg/dL	1.2 (0.9-1.6)	1.3 (1.0-1.9)	<0.001
Preprocedure hemoglobin, g/dL	12.2 (10.9-13.5)	10.9 (9.5-12.5)	<0.001
Baseline LV ejection fraction, %	53 (35-60)	50 (32-60)	0.002
Baseline KCCQ-OS score	41.7 (24.5-62.0)	27.6 (12.5-44.3)	<0.001
NYHA functional class within 2 wk			<0.001
I	1,261 (2.1)	6 (0.8)	
II	10,025 (16.9)	61 (8.2)	
III	37,029 (62.4)	402 (54.0)	
IV	10,420 (17.6)	270 (36.3)	
Current/recent smoker	4,117 (6.9)	50 (6.7)	0.82
Currently on dialysis	2,286 (3.9)	46 (6.2)	0.001
Hypertension	51,173 (86.3)	651 (87.5)	0.30
Diabetes	16,750 (28.2)	235 (31.6)	0.04
Atrial fibrillation/flutter	36,895 (62.2)	530 (71.2)	<0.001
Chronic lung disease	20,075 (33.8)	305 (41.0)	<0.001
Home oxygen	6,166 (10.4)	140 (18.8)	<0.001
Immunocompromised	4,281 (7.2)	56 (7.5)	0.73
Prior MI	15,262 (25.7)	212 (28.5)	0.09
Prior stroke/TIA	4,064 (6.9)	54 (7.3)	0.66
Peripheral artery disease	9,285 (15.7)	150 (20.2)	<0.001
Prior percutaneous coronary intervention	18,386 (31.0)	260 (34.9)	0.02
Prior coronary artery bypass graft	13,591 (22.9)	169 (22.7)	0.89
Carotid stenosis	5,593 (9.4)	92 (12.4)	0.006
Coronary artery disease			<0.001
No symptoms	30,384 (51.2)	357 (48.0)	
Symptoms unlikely to be ischemic	22,313 (37.6)	289 (38.8)	
Stable angina	2,274 (3.8)	21 (2.8)	
Unstable angina	920 (1.6)	12 (1.6)	
Acute non-ST-segment elevation MI	374 (0.6)	21 (2.8)	
Acute ST-segment elevation MI	103 (0.2)	4 (0.5)	
Left main stenosis ≥50%	3,482 (5.9)	44 (5.9)	0.77
Hostile chest	3,742 (6.3)	48 (6.5)	0.88
Porcelain aorta	488 (0.8)	6 (0.8)	0.96
Endocarditis	769 (1.3)	10 (1.3)	0.91
Prior permanent pacemaker	11,008 (18.6)	137 (18.4)	0.91
Prior implantable cardioverter-defibrillator	10,285 (17.3)	134 (18.0)	0.62
Prior aortic valve procedure(s)	5,418 (9.1)	82 (11.0)	0.08
Prior tricuspid valve procedure(s)	319 (0.5)	6 (0.8)	0.32
Echocardiographic characteristics			
MV mean gradient, mm Hg	2 (2-3)	3 (2-4)	<0.001
Mechanism of MR			0.29
Functional	12,145 (20.5)	167 (22.4)	
Degenerative	44,715 (75.4)	539 (72.4)	
Others	1,502 (2.5)	21 (2.8)	
Mitral stenosis	3,032 (5.1)	55 (7.4)	0.006
≥Moderate tricuspid regurgitation	28,492 (48.0)	434 (58.3)	<0.001
LV internal diastolic diameter, cm	5.3 (4.7-6.0)	5.3 (4.6-5.9)	0.84

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TABLE 1 Continued

	30-Day Survivors (n = 59,326)	Out-of-Hospital 30-Day Mortality (n = 744)	*P* Value
Procedural characteristics			
Procedural year			0.16
2014-2016	6,579 (11.1)	88 (1.8)	
2017-2019	20,483 (34.5)	232 (31.2)	
2020-April 2023	32,264 (54.4)	424 (57.0)	
Acuity status			<0.001
Elective	50,539 (85.2)	465 (62.5)	
Urgent	5,006 (8.4)	153 (20.6)	
Preprocedure shock, inotropes, or mechanical assist device	3,337 (5.6)	100 (13.4)	
Emergent/salvage or prior cardiac arrest within 24 h	444 (0.7)	26 (3.5)	
Annualized hospital mTEER volume	28.8 (18.8-40.7)	28.0 (18.2-40.6)	0.28
No. of successful clips deployed	1 (1-2)	1 (1-2)	<0.001
Postprocedural variables and complications			
Postprocedural ≥moderate residual MR	12,916 (21.8)	298 (40.0)	<0.001
Postprocedural MV mean gradient, mm Hg	4 (3-5)	5 (3-6)	<0.001
In-hospital/30-d VARC-3 major/life-threatening bleeding	436 (0.7)	60 (8.1)	<0.001
In-hospital blood transfusion	2,781 (4.7)	129 (17.3)	<0.001
In-hospital vascular access site complication	535 (0.9)	11 (1.5)	0.10
In-hospital stroke/TIA	301 (0.5)	18 (2.4)	<0.001
In-hospital MI	20 (0.0)	2 (0.3)	<0.001
In-hospital transseptal complication	113 (0.2)	5 (0.7)	0.003
In-hospital atrial septal defect closure	788 (1.3)	29 (3.9)	<0.001
In-hospital mitral leaflet or subvalvular injury	120 (0.2)	19 (2.6)	<0.001
In-hospital device-related complication	200 (0.3)	8 (1.1)	<0.001
In-hospital atrial fibrillation (new-onset)	635 (1.1)	24 (3.2)	<0.001
In-hospital cardiac arrest	193 (0.3)	12 (1.6)	<0.001
In-hospital MV reintervention	181 (0.3)	10 (1.3)	<0.001
Discharge information			
Discharge anticoagulant agents	31,507 (53.1)	360 (48.4)	<0.001
Discharge dual antiplatelet therapy, any	19,350 (32.6)	167 (22.4)	0.02
Discharge angiotensin-converting enzyme inhibitors/angiotensin receptor blockers	27,494 (46.3)	168 (22.6)	<0.001
Discharge beta-blockers	43,666 (73.6)	412 (55.4)	0.01
Discharged aldosterone antagonists	9,218 (15.5)	79 (10.6)	0.12
Discharge location			<0.001
Home	55,184 (93.0)	462 (62.1)	
Extended care/TCU/rehab	2,390 (4.0)	98 (13.2)	
Skilled nursing facility	1,495 (2.5)	68 (9.1)	
Hospice care	41 (0.1)	84 (11.3)	
Left against medical advice	48 (0.1)	3 (0.4)	
Other discharge location	163 (0.3)	29 (3.9)	

Values are median (Q1-Q3) or n (%).

KCCQ-OS = Kansas City Cardiomyopathy Questionnaire-Overall Summary; LV = left ventricular; MI = myocardial infarction; MR = mitral regurgitation; mTEER = mitral valve transcatheter edge-to-edge repair; MV = mitral valve; TCU = transitional care unit; TIA = transient ischemic attack; VARC = Valve Academic Research Consortium.

were included (Figure 1). We excluded patients who had missing in-hospital or 30-day vital status (n = 6,586), missing cause of death for in-hospital or 30-day mortality (n = 320), aborted procedure (n = 1,579), procedure converted to open heart surgery (n = 157), those discharged to other acute care hospitals (n = 235), those who were not eligible for 30-day event follow-up (n = 2,290), and those who were discharged alive but after 30 days of procedure (n = 279). This yielded a final study population of 61,139 patients at 539 sites across the United States. For this study, an aborted procedure was defined as the inability to deploy any device, and the procedure was aborted. Comparison of included vs excluded patients is summarized in Supplemental Table 1.

OUTCOMES. The primary outcome of interest was out-of-hospital all-cause mortality at 30 days. The secondary outcome was out-of-hospital cardiovascular (CV) mortality at 30 days. CV mortality included acute myocardial infarction, sudden cardiac death,

heart failure, stroke, CV procedure, CV hemorrhage, and other CV causes (Supplemental Table 2). All outcomes were site-reported, derived from the TVT registry data collection form, and classified in accordance with the Mitral Valve Academic Research Consortium criteria.[8,10]

STATISTICAL ANALYSIS. Demographic, clinical, periprocedural, and postdischarge characteristics were compared between patients who survived at 30 days and those who experienced out-of-hospital mortality, as well as between patients who died in-hospital vs those who died out-of-hospital within 30 days of mTEER. Categorical variables are presented as frequencies with percentages and were compared using the Pearson's chi-square test or Fisher exact test. Continuous variables are presented as median (Q1-Q3) and were compared using the Wilcoxon rank sum test. The timing of in-hospital and out-of-hospital mortality is presented as days from procedure and days from discharge to death, respectively. Causes of death for in-hospital and 30-day out-of-hospital mortality are presented as frequencies with percentages. Temporal trends in primary and secondary outcomes were examined using the Cochran-Armitage trend test.

Associations between prespecified factors and 30-day out-of-hospital all-cause mortality were examined using univariate and multivariable logistic regression models. For CV death, the association with prespecified factors was assessed using survival analysis with Fine-Gray's subdistribution hazard model to account for the competing risk of non-CV death. The clustering of patients within sites was accounted for using robust sandwich estimates of standard errors. The models included all variables listed in Supplemental Table 3 as covariates. Continuous variables were converted to categorical variables for the purpose of multivariable analysis. The results for out-of-hospital all-cause mortality are presented as ORs with corresponding 95% CIs and for out-of-hospital CV mortality are presented as HRs with corresponding 95% CIs.

Missing data for covariates were <5% for most variables except coronary artery disease (5.0%), baseline Kansas City Cardiomyopathy Questionnaire-Overall Summary (KCCQ-OS) score (12.7%), left main stenosis (13.4%), baseline mitral valve (MV) gradient (33.8%), left ventricular (LV) internal systolic dimension (12.4%), LV internal diastolic dimension (17.9%), postprocedure residual MR (7.1%), and postprocedure MV gradient (9.7%). Multiple imputation

TABLE 2 Baseline and Procedural Characteristics of mTEER Patients Stratified by In-Hospital Mortality vs 30-Day Out-of-Hospital Mortality

	In-Hospital Mortality (n = 1,069)	Out-of-Hospital Mortality at 30 Days (n = 744)	*P* Value
Baseline characteristics			
Age, y	79 (71-85)	81 (74-86)	<0.001
Male	558 (52.2)	392 (52.7)	0.84
Race			<0.001
White	894 (83.6)	670 (90.1)	
African American	80 (7.5)	53 (7.1)	
Asian	47 (4.4)	13 (1.7)	
American Indian/Alaskan Native	8 (0.7)	0 (0.0)	
Native Hawaiian/Pacific Islander	3 (0.3)	0 (0)	
Ethnicity, Hispanic/Latinx	90 (8.4)	26 (3.5)	<0.001
Body surface area, m^2	1.8 (1.6-2.0)	1.8 (1.6-2.0)	0.22
Preprocedure creatinine, mg/dL	1.5 (1.1-2.2)	1.3 (1.0-1.9)	<0.001
Preprocedure hemoglobin, g/dL	10.4 (8.9-12.1)	10.9 (9.5-12.5)	<0.001
Baseline LV ejection fraction, %	49 (32-60)	50 (32-60)	0.84
Baseline KCCQ-OS score	21.9 (7.8-38.5)	27.6 (12.5-44.3)	<0.001
NYHA functional class within 2 wk			<0.01
I	10 (0.9)	6 (0.8)	
II	63 (5.9)	61 (8.2)	
III	412 (38.5)	402 (54.0)	
IV	574 (53.7)	270 (36.3)	
Current/recent smoker	81 (7.6)	50 (6.7)	0.47
Currently on dialysis	124 (11.6)	46 (6.2)	<0.001
Hypertension	894 (83.6)	651 (87.5)	0.02
Diabetes	331 (31.0)	235 (31.6)	0.77
Atrial fibrillation/flutter	715 (66.9)	530 (71.2)	0.05
Chronic lung disease	408 (38.2)	305 (41.0)	0.24
Home oxygen	180 (16.8)	140 (18.8)	0.28
Immunocompromised	93 (8.7)	56 (7.5)	0.39
Prior MI	364 (34.1)	212 (28.5)	0.01
Prior stroke/TIA	64 (6.0)	54 (7.3)	0.28
Peripheral artery disease	208 (19.5)	150 (20.2)	0.73
Prior percutaneous coronary intervention	363 (34.0)	260 (34.9)	0.64
Prior coronary artery bypass graft	253 (23.7)	169 (22.7)	0.61
Carotid stenosis	95 (8.9)	92 (12.4)	0.02
Coronary artery disease			0.01
No symptoms	458 (42.8)	357 (48.0)	
Symptoms unlikely to be ischemic	379 (35.5)	289 (38.8)	
Stable angina	37 (3.5)	21 (2.8)	
Unstable angina	42 (3.9)	12 (1.6)	
Acute non-ST-segment elevation MI	67 (6.3)	21 (2.8)	
Acute ST-segment elevation MI	38 (3.6)	4 (0.5)	
Left main stenosis ≥50%	85 (8.0)	44 (5.9)	0.14
Hostile chest	70 (6.5)	48 (6.5)	0.93
Porcelain aorta	15 (1.4)	6 (0.8)	0.24
Endocarditis	17 (1.6)	10 (1.3)	0.67
Prior permanent pacemaker	180 (16.8)	137 (18.4)	0.40
Prior implantable cardioverter-defibrillator	203 (19.0)	134 (18.0)	0.61
Prior aortic valve procedure(s)	113 (10.6)	82 (11.0)	0.77
Prior tricuspid valve procedure(s)	3 (0.3)	6 (0.8)	0.12
Echocardiographic characteristics			
Mitral valve mean gradient, mm Hg	3 (2-4)	3 (2-4)	0.55
Mechanism of MR			0.92
Functional	240 (22.5)	167 (22.4)	
Degenerative	781 (73.1)	539 (72.4)	
Others	27 (2.5)	21 (2.8)	
Mitral stenosis	72 (6.7)	55 (7.4)	0.64
≥Moderate tricuspid regurgitation	621 (58.1)	434 (58.3)	0.74
LV internal diastolic diameter, cm	5.2 (4.5-5.9)	5.3 (4.6-5.9)	0.14

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TABLE 2 Continued

	In-Hospital Mortality (n = 1,069)	Out-of-Hospital Mortality at 30 Days (n = 744)	*P* Value
Procedural characteristics			
Procedural year			<0.001
2014-2016	150 (14.0)	88 (11.8)	
2017-2019	409 (38.3)	232 (31.2)	
2020-April 2023	510 (47.7)	424 (57.0)	
Acuity status			<0.001
Elective	432 (40.4)	465 (62.5)	
Urgent	188 (17.6)	153 (20.6)	
Preprocedure shock, inotropes, or mechanic assist device	288 (26.9)	100 (13.4)	
Emergent/salvage or prior cardiac arrest within 24 h	161 (15.1)	26 (3.5)	
Annualized hospital mTEER volume	27.1 (18.1-40.7)	28.0 (18.2-40.6)	0.81
No. of successful clips deployed	2 (1-2)	1 (1-2)	<0.001
Postprocedural variables and complications			
Postprocedural ≥moderate residual MR	482 (45.1)	298 (40.0)	<0.001
Postprocedural MV mean gradient	5 (3-7)	5 (3-6)	0.02
In-hospital/30-d VARC-3 major/life-threatening bleeding	146 (13.7)	60 (8.1)	<0.001
In-hospital blood transfusion	532 (49.8)	129 (17.3)	<0.001
In-hospital vascular access site complication	69 (6.5)	11 (1.5)	<0.001
In-hospital stroke/TIA	68 (6.4)	18 (2.4)	<0.001
In-hospital MI	13 (1.2)	2 (0.3)	0.03
In-hospital transseptal complication	20 (1.9)	5 (0.7)	0.03
In-hospital atrial septal defect closure	48 (4.5)	29 (3.9)	0.54
In-hospital mitral leaflet or subvalvular injury	54 (5.1)	19 (2.6)	<0.001
In-hospital device-related complication	37 (3.5)	8 (1.1)	0.001
In-hospital atrial fibrillation, new-onset	71 (6.6)	24 (3.2)	0.001
In-hospital cardiac arrest	336 (31.4)	12 (1.6)	<0.001
In-hospital MV reintervention	47 (4.4)	10 (1.3)	<0.001
Postprocedural mitral valve mean gradient	5 (3-7)	5 (3-6)	0.02

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with 10 imputed datasets was used to handle missing data for covariates. A sensitivity analysis was also performed evaluating the unadjusted OR for the primary outcome between imputed and complete case datasets to assess robustness of the results.

Results are presented in accordance with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines. All analyses were performed using SAS software version 9.4 (SAS Institute) at Duke Clinical Research Institute. A 2-tailed *P* value of <0.05 was considered statistically significant for all analyses.

RESULTS

PATIENT CHARACTERISTICS. The final study population included 61,139 patients who underwent isolated mTEER across 539 sites (Figure 1). Of these, 1,813 patients (3.0%) died in-hospital or out-of-hospital within 30 days. A total of 744 patients experienced the primary outcome of all-cause out-of-hospital mortality at 30 days, accounting for 41.0% of the overall 30-day mortality and 1.2% of the overall study cohort (Central Illustration). Of 12,552 patients who underwent mTEER for functional MR, 240 patients (1.9%) died in-hospital, and 167 patients (1.3%) died out-of-hospital within 30 days. Similarly, of 46,035 patients who underwent mTEER for degenerative MR, 781 patients (1.7%) died in-hospital, and 539 patients (1.2%) died out-of-hospital within 30 days.

Compared with patients who survived at 30 days, those who experienced out-of-hospital mortality were older, non-Hispanic, White, had higher baseline creatinine, lower baseline hemoglobin, and higher prevalence of current dialysis, chronic lung disease, home oxygen use, diabetes, history of atrial fibrillation/flutter, peripheral artery disease, carotid artery stenosis, and prior percutaneous coronary intervention (Table 1). They were also more symptomatic and had worse baseline functional status, as evidenced by higher NYHA functional class and lower KCCQ-OS scores, respectively. Patients who died out of hospital at 30 days also had lower LV ejection fraction, higher MV gradient, presence of mitral stenosis, higher grades of tricuspid regurgitation at baseline, and higher rates of nonelective procedures.

Postprocedural mean MV gradient, residual MR, and rates of in-hospital complications were significantly higher in patients who died out-of-hospital within 30 days compared with 30-day survivors. Procedural year and annualized hospital mTEER volume were not significantly different across both groups. Patients experiencing out-of-hospital mortality were less likely to be prescribed anticoagulant agents, antiplatelet agents, and guideline-directed medical therapy (GDMT) for heart failure (diuretic agents, beta-blockers, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers) at discharge, and were more likely to have non-home discharge.

Similar differences in demographics, comorbidities, echocardiographic and periprocedural characteristics, and discharge disposition were noted between 30-day survivors and those who died out-of-hospital due to CV causes (Supplemental Table 4).

We also compared patients who died in-hospital vs those who died out-of-hospital at 30 days. Patients who died in hospital were more likely to be younger, non-White, and Hispanic, had worse NYHA functional class and KCCQ score, higher baseline creatinine, lower baseline hemoglobin, higher prevalence of comorbidities, including dialysis dependence, prior

myocardial infarction, and higher acuity on presentation, and were from prior years (2014-2016) compared with those who died out-of-hospital within 30 days. There were no significant differences in baseline echocardiographic parameters, but higher rates of ≥moderate residual MR were noted in patients who died in-hospital despite having deployment of more clips during the procedure. In-hospital complication rates were high in both groups but significantly higher in patients who died in-hospital (Table 2).

CAUSES AND TIMING OF DEATH. For out-of-hospital all-cause mortality, the median time from discharge to mortality was 11 days (Q1-Q3: 5-19 days) (Figure 2). CV causes were the predominant reason for out-of-hospital mortality at 30 days (n = 472, 63.4%) (Figure 3). Median time to out-of-hospital CV mortality was 10 days (Q1-Q3: 4-18 days). Other causes of death were pulmonary (9.5%), neurological (5.5%), infection (4.0%), renal (2.3%), vascular (1.6%), and other non-CV causes (13.6%).

TEMPORAL TRENDS IN OUTCOMES. There was an overall numerical increase in 30-day out-of-hospital all-cause mortality, from 1.9% in 2014 to 22.8% in 2022 (P_{trend} = 0.10) (Supplemental Figure 1A), but it was not statistically significant. Similarly, out-of-hospital CV mortality increased from 1.9% in 2014 to 19.8% in 2022 (P_{trend} = 0.33), but it was not statistically significant (Supplemental Figure 1B).

PREDICTORS OF OUT-OF-HOSPITAL ALL-CAUSE AND CV MORTALITY AT 30 DAYS. Factors independently associated with 30-day out-of-hospital all-cause mortality were older age, White race, non-Hispanic ethnicity, lower body surface area, lower baseline hemoglobin, lower baseline KCCQ-OS score, home oxygen use, presentation as non-ST-segment elevation myocardial infarction, lower LV ejection fraction, recent procedural years (2021 to April 2023), higher acuity presentation, in-hospital complications (myocardial infarction, major/life-threatening bleeding, blood transfusions, device-related complications, atrial septal defect closure, mitral leaflet or subvalvular injury), deployment of >1 device, postprocedure MV gradient >5 mm Hg, postprocedure ≥moderate MR, lack of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers at discharge, and discharge to non-home location (Figure 4, Supplemental Table 5).

All aforementioned variables were also associated with out-of-hospital CV mortality at 30 days with minor differences as noted in Figure 4 and Supplemental Table 6.

TABLE 2 Continued

	In-Hospital Mortality (n = 1,069)	Out-of-Hospital Mortality at 30 Days (n = 744)	*P* Value
Discharge information			
Discharge anticoagulant agents	NA	360 (48.4)	NA
Discharge dual antiplatelet therapy, any	NA	167 (22.4)	NA
Discharge angiotensin-converting enzyme inhibitors/angiotensin receptor blockers	NA	168 (22.6)	NA
Discharge beta-blockers	NA	412 (55.4)	NA
Discharged aldosterone antagonist agents	NA	79 (10.6)	NA
Discharge location	NA		NA
Home		462 (62.1)	
Extended care/TCU/rehab		98 (13.2)	
Skilled nursing facility		68 (9.1)	
Hospice care		84 (11.3)	
Left against medical advice		3 (0.4)	
Other discharge location		29 (3.9)	
Death characteristics			
Death cause			<0.001
Cardiovascular death	738 (69.0)	472 (63.4)	
Neurological	36 (3.4)	41 (5.5)	
Renal	18 (1.7)	17 (2.3)	
Pulmonary	169 (15.8)	71 (9.5)	
Vascular	21 (2.0)	12 (1.6)	
Infection	56 (5.2)	30 (4.0)	
Other, noncardiovascular	31 (2.9)	101 (13.6)	
Days from procedure for in-hospital death	6 (3-11)	NA	-
Days from discharge for death at 30 days	NA	11 (5-19)	-

Values are median (Q1-Q3) or n (%).
NA = not applicable; other abbreviations as in Table 1.

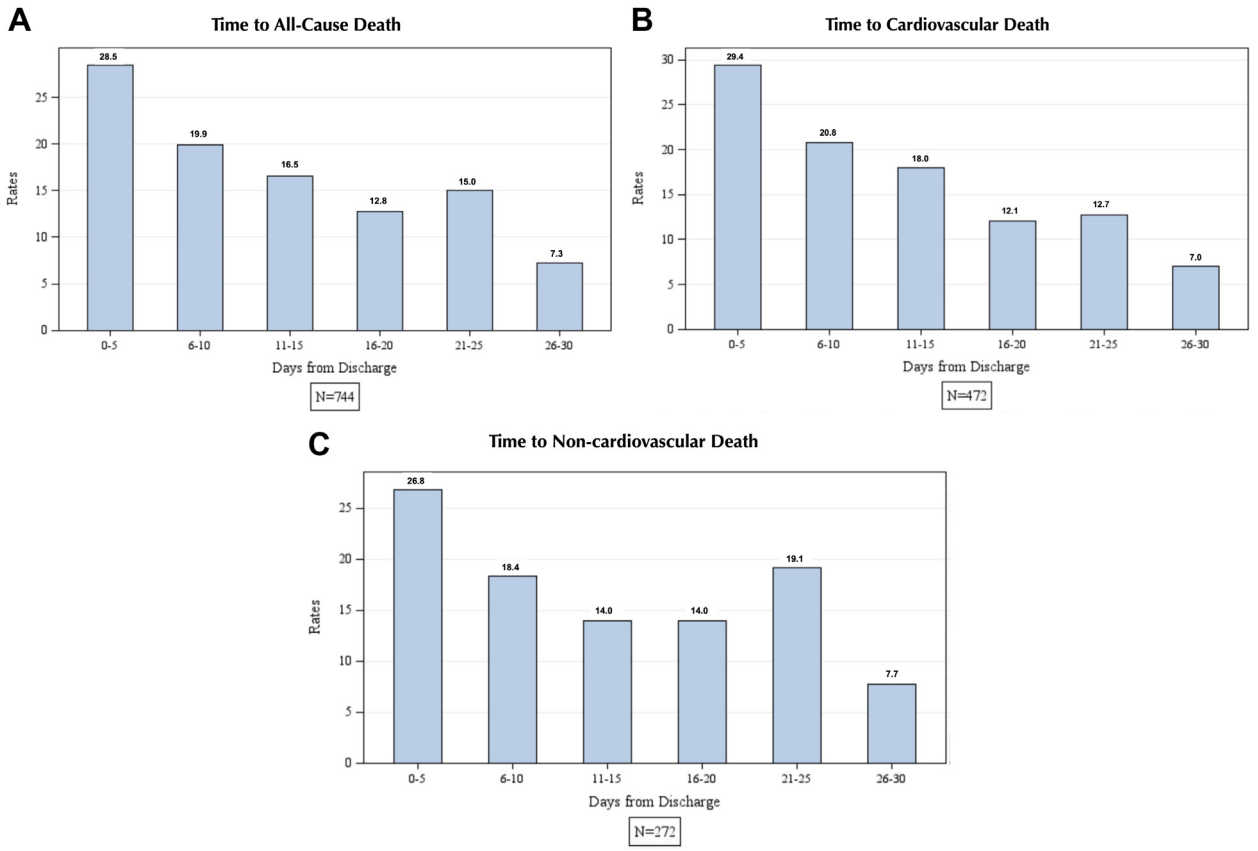
Sensitivity analysis with complete case dataset without imputation also showed similar results (Supplemental Table 7).

DISCUSSION

In this STS/ACC TVT Registry analysis of >60,000 patients who underwent mTEER, we report the following important findings: 1) 2 of every 5 deaths within 30 days of mTEER occurred out-of-hospital/postdischarge; 2) over 60% of 30-day out-of-hospital deaths were due to CV causes; 3) median time from discharge to out-of-hospital all-cause death was 11 days; and 4) several factors (demographics, comorbidities, echocardiographic and procedural characteristics, and in-hospital complications) were independently associated with out-of-hospital all-cause and CV mortality at 30 days.

Despite overall improvements in 30-day outcomes, cumulative 30-day mortality after mTEER remains around 3% to 4%.[1,4] We observed that 41% of these deaths occurred postdischarge, and the majority of out-of-hospital deaths were due to CV causes.

FIGURE 2 Timing of 30-Day Out-of-Hospital Mortality in Patients That Underwent mTEER



Histograms illustrate the timing of (A) all-cause, (B) cardiovascular, and (C) noncardiovascular 30-day out-of-hospital mortality since discharge from the index hospitalization. mTEER = mitral transcatheter edge-to-edge repair.

Mortality risk in the early postdischarge period (up to 30 days) after mTEER is distinct from in-hospital mortality, as noted by the differences in baseline characteristics and rates of in-hospital complications in these 2 groups in the current study. Our results are consistent with a prior meta-analysis of 15 studies, including 7,500 patients (enrolled between 2005 and 2016) that showed postdischarge 30-day mortality of 1.7%, with 71.5% of deaths due to cardiac causes.[4] We identified various modifiable risk factors independently associated with out-of-hospital all-cause and CV mortality in the early postprocedural period that will help better understand and mitigate these risks.

First, patient selection plays an essential role in its relation to out-of-hospital mortality after mTEER. In our study, patients experiencing out-of-hospital mortality had lower baseline KCCQ scores than survivors by an average of 15 points. Every 10-point increase in baseline KCCQ status was associated with 10% lower out-of-hospital all-cause and CV mortality. However, improving patient selection is more complex than just filtering out poor candidates. For instance, the presence of home oxygen use, baseline mitral stenosis, higher grades of tricuspid regurgitation, and rates of higher acuity procedures (eg, cardiogenic shock) were noted to be significantly higher in patients experiencing out-of-hospital mortality in our study. Although these patients were not well represented in the COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation; NCT01626079) trial, in clinical practice, they often do not have an alternative for managing MR. It is indeed noteworthy that more than

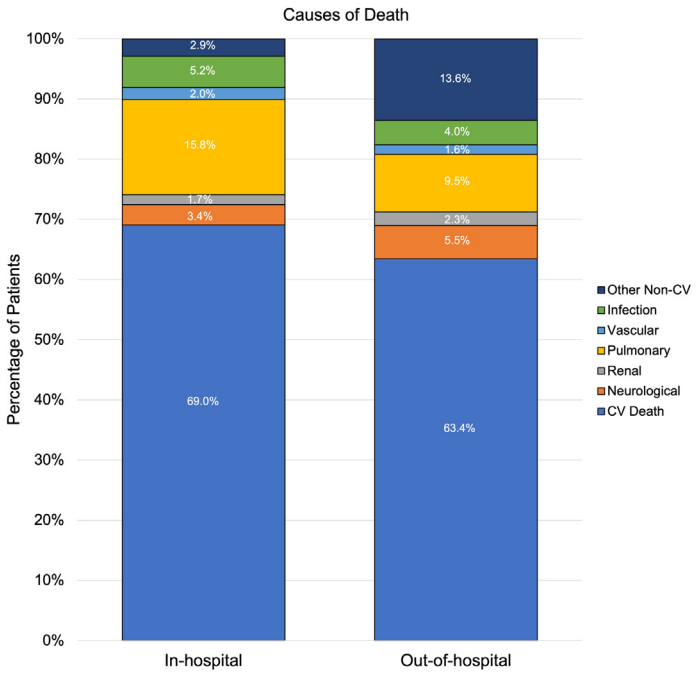
one-half of the patients who underwent mTEER for secondary MR between 2013 and 2020 in the United States would have been COAPT-ineligible.[11] We also did not find any relation between the etiology of MR and out-of-hospital mortality. Although mTEER for primary MR is approved for prohibitive surgical risk patients, it is more broadly approved across surgical risk for secondary MR. Multiple risk prediction tools for mortality have been developed using deep learning approaches, but the discrimination for these scores remains fair, at best.[12-14] The clinical utility of these scores for prognosticating and selecting optimal patients for mTEER needs further research.

Secondly, we also observed anemia as a potential modifiable risk factor that must be optimized before undergoing mTEER. Preprocedural anemia can be prevalent in up to one-half of patients undergoing mTEER and has been tied to poor outcomes.[1,15,16] We observed decreases in all-cause and CV mortality by 12% and 10%, respectively, with every unit (in mg/dL) increase in baseline hemoglobin. Almost one-half of the patients undergoing mTEER also have iron deficiency, which may contribute to anemia.[17] Clinical practice guidelines recommend intravenous iron infusions for iron-deficient patients with heart failure with reduced or mildly reduced ejection fraction to improve functional status and quality of life.[18] The utility of intravenous iron in treating iron deficiency anemia before mTEER to improve postprocedure outcomes needs further investigation.

Third, persistent MR after mTEER is an important prognostic factor. Achieving ≤2+ residual MR post-mTEER is associated with improved outcomes and provides an incremental benefit over GDMT.[19] On the other hand, GDMT up-titration is more tolerable in patients who have a significant reduction in MR after mTEER and is associated with reversal of LV remodeling and an additional 45% reduction in mortality or heart failure hospitalizations.[20,21] Specifically, renin-angiotensin-aldosterone system inhibitors are most likely to be titrated after mTEER due to improved blood pressure and increased cardiac output because of a reduction in MR that enhances the capacity to tolerate afterload reduction.[20,22] This may explain the findings in our analysis, which show a lack of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers at discharge to be independently associated with out-of-hospital mortality. However, in the event of an absence of a significant reduction in MR post-mTEER, the impact of optimal GDMT on long-term outcomes is maximal in such patients.[20] Despite having a Class 1 recommendation in the guidelines, pre- and post-mTEER GDMT prescription rates continue to be low in the real-world data from the TVT Registry, as less than one-fifth of the patients were on triple GDMT.[18,23] Increasing prescription rates and adherence to triple/quadruple GDMT and preferential use of sacubitril-valsartan over angiotensin-converting enzyme inhibitors/angiotensin receptor blockers are targets for intervention, given their demonstrated superiority for MR reduction and reduction in CV outcomes.[18,21,23,24] Close postdischarge follow-ups with the heart failure clinic, patient education, and electronic health record alerts are essential interventions to optimize GDMT in this vulnerable population.[25]

Lastly, as mTEER adoption grows to a sicker population, postprocedural complications such as major bleeding/blood transfusions, new-onset atrial fibrillation, higher grades of postprocedural residual MR, device-related complications, MV apparatus injury, and MV reinterventions may occur. These adverse events were shown to be associated with postdischarge 30-day mortality in our study. The higher prevalence of comorbidities that require anticoagulation and/or dual antiplatelet therapy, such as atrial fibrillation and coronary artery disease in

FIGURE 3 Causes of In-Hospital and 30-Day Out-of-Hospital Mortality in Patients That Underwent mTEER



The stacked bar graph depicts the breakdown by cause of in-hospital (A) and 30-day out-of-hospital (B) mortality. CV = cardiovascular; mTEER = mitral transcatheter edge-to-edge repair.

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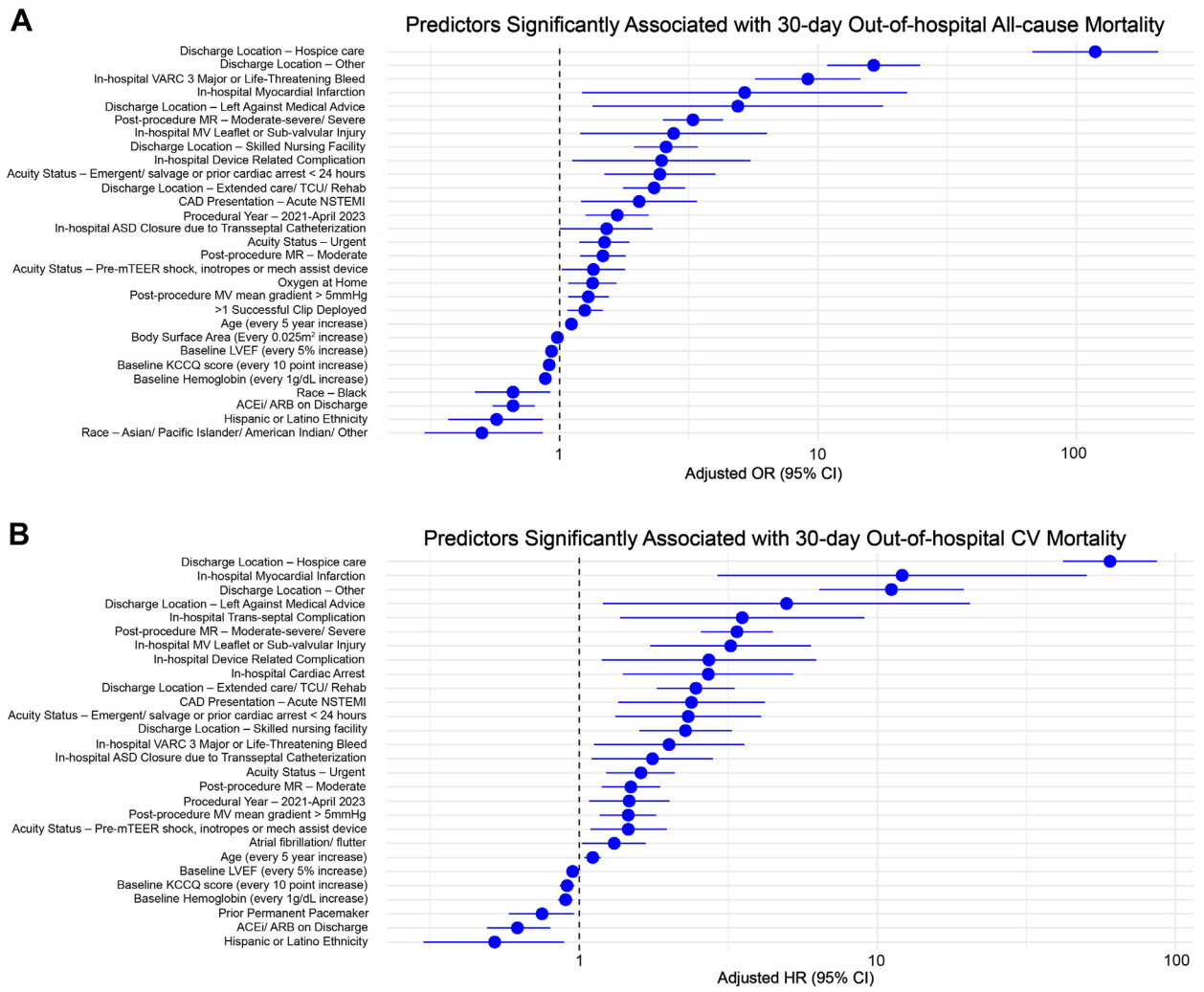
FIGURE 4 Factors Associated With 30-Day Out-of-Hospital Mortality After mTEER



Forest plots depict variables that were significantly associated with all-cause (A) and cardiovascular (B) out-of-hospital mortality after 30 days. ACEi = angiotensin-converting enzyme inhibitor; ARB = angiotensin II receptor blockers; ASD = atrial septal defect; CAD = coronary artery disease; KCCQ = Kansas City Cardiomyopathy Questionnaire; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; mTEER = mitral transcatheter edge-to-edge repair; MV = mitral valve; NSTEMI = non-ST-segment elevation myocardial infarction; TCU = transitional care unit; VARC = Valve Academic Research Consortium.

patients who experienced post-discharge mortality, may explain the higher risk of major bleeding. Previous studies found non-access site bleeding (eg, gastrointestinal, pericardial, genitourinary) as the predominant source despite the use of large-bore (24-F) venous access for mTEER.[26,27] Currently, no guidelines exist on the optimal antithrombotic therapy after mTEER, and there is wide variation in real-world practice.[28] Future studies on the optimal choice of antithrombotic therapy post-mTEER are needed to guide clinical practice and improve outcomes.

It is unclear whether these deaths within the early postdischarge period could have been prevented by a longer hospitalization. These patients were deemed safe to be discharged by physicians, though the patients were less likely to be discharged home. A significant proportion of patients who died out-of-hospital were transitioned to hospice care (11%) at

discharge, and 22% of patients were discharged to a skilled nursing/rehabilitation facility. This suggests that these patients were sick to begin with and potentially at higher risk of adverse outcomes given their multimorbidity and frailty.

STUDY LIMITATIONS. Certain limitations are noteworthy in the current study. There was a statistically significant difference in baseline variables of the included and excluded cohorts. Patients that were included compared with those who were excluded from the study had a higher prevalence of comorbidities, which may lead to selection bias. The observational nature of the data is subject to misclassification bias and residual confounding in the analytical models. Although mortality is adjudicated based on Mitral Valve Academic Research Consortium definitions, causes of death are site-adjudicated and subject to variation. However, periodic audits are performed for data completion and accuracy. Specific institutional practices and postprocedure care pathways could not be assessed in the study because of limitations of the dataset. Despite the benefit of sodium-glucose-cotransporter-2 inhibitors in heart failure, we were unable to determine their role as the information is currently not captured in the TVT registry.

CONCLUSIONS

All-cause mortality after mTEER was 3.0% at 30 days. Two of every 5 deaths within 30 days of mTEER occurred outside of the hospital/postdischarge, and over 60% of these deaths were due to CV causes. Multiple nonmodifiable and modifiable factors were independently associated with out-of-hospital mortality after mTEER. Future efforts should focus on improving patient selection, reducing procedural complications, and optimizing GDMT and postdischarge care to improve outcomes in this vulnerable population.

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PERSPECTIVES

WHAT IS KNOWN? There is growing adoption of mTEER with improvements in overall outcomes after the procedure. Approximately 2% to 3% of the patients die during the hospitalization after the procedure.

WHAT IS NEW? Two of every 5 deaths within 30 days of the procedure occurred postdischarge/outside of the hospital, and cardiovascular causes were the predominant cause of death (>60%). Several factors have been identified as being independently associated with out-of-hospital all-cause and cardiovascular mortality at 30 days.

WHAT IS NEXT? There are multiple modifiable factors, such as improving patient selection, reducing procedural complications, and optimizing GDMT, that can help improve outcomes in this vulnerable population.

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KEY WORDS mitral regurgitation, mortality, mTEER, transcatheter edge-to-edge repair, transcatheter mitral valve repair

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