

# Comparison of Outcomes of Transcatheter Mitral Valve Repair (MitraClip) in Patients <80 Years Versus ≥80 Years



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**The influence of age on outcomes of patients selected for transcatheter mitral valve repair (TMVR) remains largely unknown in the United States. This study sought to assess the outcomes of TMVR in highly aged patients (≥80 years). We queried the National Readmission Database from January 2014 to December 2016 for elective TMVR hospitalizations. Propensity-score matching was used to compare in-hospital and 30-day outcomes between highly aged patients and those less than 80 years. Of 6,025 (weighted national estimate) hospitalizations for TMVR, total of 3,368 included highly aged patients (mean age 85.3) and 2,657 included patients less than 80 years (mean age 69). In the Propensity-score matched cohort (age ≥ 80, n = 2,185; age <80, n = 2,197), highly aged patients had similar rates of in-hospital mortality (2.2% vs 1.6%; p = 0.22), ischemic stroke (0.5% vs 0.5%; p = 0.83), cardiac tamponade (0.2% vs 0.4%; p = 0.58), cardiogenic shock (1.2% vs 1.7%; p = 0.25), and acute myocardial infarction (0.6% vs 0.4%; p = 0.30), but higher rates of discharge to skilled nursing facility (9.7% vs 4.5%; p <0.001), all-cause 30-day readmissions (14.2% vs 10.5%; p <0.001), and heart failure-related 30-day readmissions (4.7% vs 3.0%; p = 0.006), compared with those less than 80 years. TMVR therapy is safe and is associated with low rates of in-hospital adverse events but higher rate of 30-day readmissions in highly aged patients compared with patients less than 80 years. Evidence-based interventions proven to be effective in reducing the burden of heart failure readmissions should be utilized in these patients to further improve outcomes. © 2020 Elsevier Inc. All rights reserved. (Am J Cardiol 2020;131:91–98)**

Transcatheter mitral valve repair (TMVR) with MitraClip has emerged as a novel treatment option in patients with severe mitral regurgitation (MR) who are considered at prohibitive risk of surgery.<sup>1–3</sup> Although TMVR has proven safety and efficacy in primary and secondary severe MR, fewer patients with age >80 years were included in the pivotal randomized controlled trials (RCTs). The average age of subjects enrolled in these RCTs was 69.7 years.<sup>1–3</sup> In comparison to the patient population included in these RCTs of TMVR, patients older than 80 years with severe MR are commonly encountered in real world clinical practice, and a large number of these patients will likely qualify for TMVR due to their prohibitive surgical risk. In the German TRAMI (TRANscatheter Mitral valve Interventions) registry, one fourth of patients were older than 80 years of age.<sup>4</sup> Similarly, data from the Society of Thoracic

Surgeons/American College of Cardiology Transcatheter Valve Therapy (TVT) registry showed that the median age of patients who underwent TMVR in the United States was 82 years.<sup>5</sup> Therefore, it is evident that TMVR is an important therapeutic option in highly aged patients with severe MR. However, scarce data exist on the influence of age on outcomes after TMVR therapy. The main objectives of our study were to determine in-hospital outcomes and readmission rates of highly aged (≥80 years) patients who underwent TMVR in the United States by utilizing a large national database.

## Methods

The National Readmission Database (NRD) was utilized to derive relevant patient information from January 1, 2014 to December 31, 2016. The NRD is a nationally representative sample of all age, all payer discharges from US nonfederal hospitals developed by the Agency for Health Care Research and Quality as part of the Health Care Cost and Utilization Project (HCUP).<sup>6</sup> For the year 2014, this database is composed of discharge-level hospitalization data from 22 states. For the year 2015 and 2016, the NRD includes data from 27 states. These states are geographically dispersed and represent 57.8% of the total US resident population and 56.6% of all US hospitalizations. Each patient record in the NRD contains information on the patient's diagnosis and procedures performed during the

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Funding: None.

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hospitalization, based on International Classification of Diseases, Ninth Revision-Clinical Modification (ICD-9-CM) and ICD-10-CM codes as well as Clinical Classification Software codes that group multiple ICD-9-CM and ICD-10-CM codes for facilitated analysis.

This study was deemed exempt by the Institutional Review Board of the University of Toledo Medical Center as the NRD is a publicly available database that contains deidentified patient information. We used the ICD-9-CM and ICD-10-CM procedure codes 35.97 and 02UG3JZ to identify all patients aged  $\geq 18$  years who underwent TMVR using MitraClip ( $n = 5,074$ , weighted national estimate = 9,571). We excluded nonelective admissions, hospitalizations with missing patient information and cases where another surgical or transcatheter valvular procedure was performed during the index hospitalization, leaving us with 6,025 patients for analysis (Figure 1).

Data on patient demographics, admission status, co-morbidities, hospital characteristics, and calendar year were extracted. The HCUP Clinical Classification Software, ICD-9-CM and ICD-10-CM codes used to define these variables were extracted from Elixhauser co-morbidity index as defined in HCUP database and additional covariates which are listed in Table 1 of the Supplement.<sup>7</sup>

The primary outcome of interest was in-hospital mortality. Secondary outcomes included ischemic stroke, hemorrhagic stroke, pericardial tamponade, cardiogenic shock, cardiac arrest, need for mechanical circulatory support (MCS), vasopressor use, infective endocarditis, need for mechanical ventilation, acute myocardial infarction (AMI [ST-Elevation Myocardial Infarction and Non-ST Elevation

Myocardial Infarction]), acute kidney injury (AKI), AKI requiring hemodialysis, vascular complications, need for blood transfusion and bleeding. The ICD-9-CM and ICD-10-CM codes used to identify these outcomes are listed in Table 1 in the Supplement. We also examined discharge disposition, length of stay (LOS), cost of hospitalization, all-cause 30-day readmissions and its predictors, heart failure (HF)-related 30-day readmission, median time to readmission for all-cause as well as HF-related 30-day readmissions, 30-day rates of stroke (ischemic and hemorrhagic), and 30-day mortality in those discharged alive after TMVR. In addition, primary causes of 30-day readmission for the highly aged cohort were identified. Readmissions were identified according to the methodology outlined by HCUP.<sup>8</sup> For the 30-day readmission analysis, we excluded patients who died during the index hospitalization and those with missing data on length of hospital stay to properly capture interval until readmission. For patients who had multiple readmissions within 30 days, only the first readmission was included. Furthermore, we excluded records of patients discharged in December of 2014, 2015, and 2016 because of unavailability of data on 30-day follow-up.

All statistical analyses were done using the weighted values of observations as provided by the NRD to measure national estimates. Baseline co-morbidities and in-hospital complications were compared using Mantel-Haenszel chi-square test for categorical variables and Student *t* testing was used to compare continuous variables. First, comparative outcome analysis was done without propensity score matching (PSM), then outcomes were analyzed with PSM to reduce selection bias and heterogeneity between the

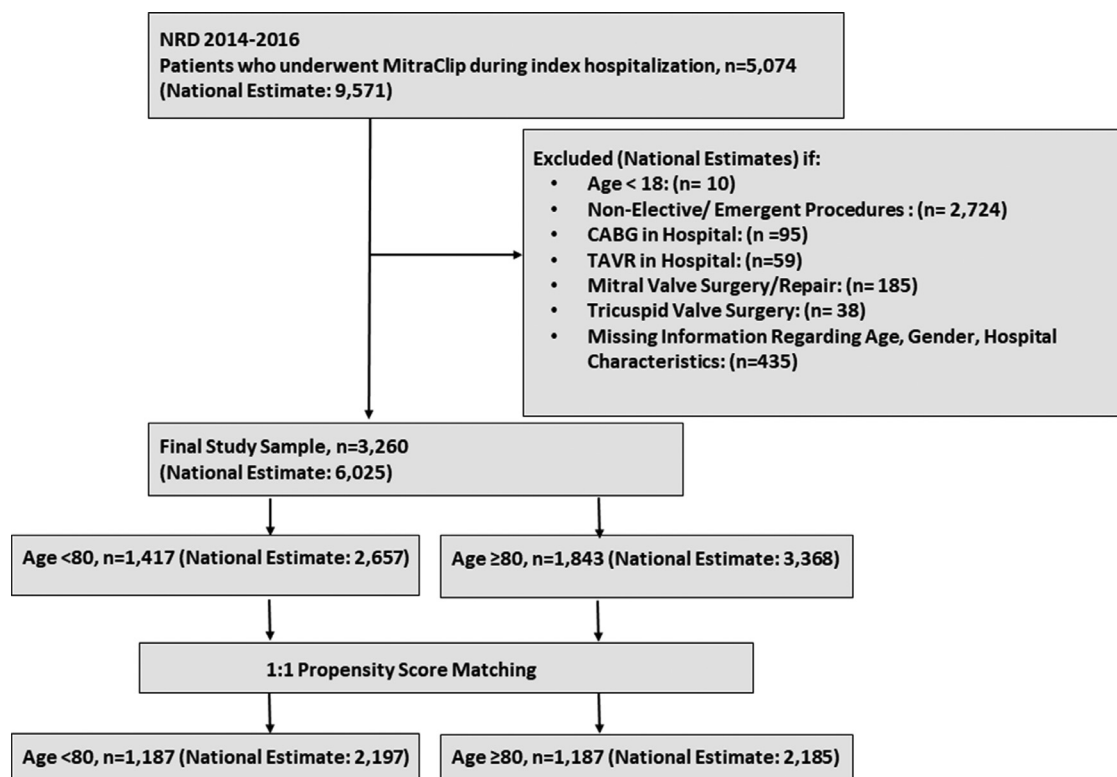


Figure 1. Study population selection flowchart. CABG = coronary artery bypass grafting; NRD = National Readmission Database; TAVR = transcatheter aortic valve replacement.

Table 1  
Baseline characteristics of patients who underwent transcatheter mitral valve repair in the unmatched cohort

Variables	Age (years)		p value
	<80 (N = 2,657)	≥80 (N = 3,368)	
Age (years), mean ± standard deviation	69 ± 9.5	85.3 ± 3.1	<0.001
Women	1197 (45.1%)	1674 (49.7%)	<0.001
Weekend admission	47 (1.8%)	57 (1.7%)	0.84
Weekday admission	2610 (98.2%)	3311 (98.3%)	0.84
Hypertension	1744 (65.6%)	2343 (69.6%)	0.001
Dyslipidemia	1412 (53.2%)	1888 (56%)	0.027
Smoker	1020 (38.4%)	899 (26.7%)	<0.001
Uncomplicated diabetes mellitus	560 (21.1%)	507 (15.0%)	<0.001
Complicated diabetes mellitus	220 (8.3%)	106 (3.1%)	<0.001
Hypothyroidism	398 (15.0%)	625 (18.6%)	<0.001
Body mass index ≥30 kg/m <sup>2</sup>	359 (13.5%)	143 (4.2%)	<0.001
Congestive heart failure	1891 (71.2%)	2539 (75.1%)	0.59
Coronary artery disease	1539 (57.9%)	1973 (58.6%)	0.61
Atrial fibrillation	1352 (50.9%)	2144 (63.7%)	<0.001
Healed myocardial infarction	334 (16.7%)	359 (107%)	<0.001
Cerebrovascular accident	192 (7.2%)	173 (5.1%)	0.001
Coronary artery bypass grafting	753 (28.3%)	704 (20.9%)	<0.001
Percutaneous coronary intervention	466 (17.5%)	623 (18.5%)	0.34
Peripheral arterial disease	379 (14.3%)	417 (12.4%)	0.032
Chronic renal failure	882 (33.2%)	1097 (32.6%)	0.61
Chronic liver disease	80 (3.0%)	25 (0.7%)	<0.001
Chronic lung disease	807 (30.4%)	648 (19.2%)	<0.001
Fluid and electrolyte imbalance	406 (15.3%)	367 (10.9%)	<0.001
Solid tumor	32 (1.2%)	18 (0.5%)	0.006
Alcohol abuse	45 (1.7%)	16 (0.5%)	<0.001
Metastatic cancer	12 (0.5%)	12 (0.4%)	0.68
Coagulopathy	250 (9.4%)	290 (8.6%)	0.29
Chronic blood loss anemia	12 (0.5%)	24 (0.7%)	0.23
Deficiency anemia	417 (15.7%)	543 (16.1%)	0.67
Teaching status of urban hospital			0.54
Metropolitan teaching	2420 (91.1%)	3011 (89.4%)	
Metropolitan-nonteaching	231 (8.7%)	353 (10.5%)	
Nonmetropolitan hospitals	6 (0.2%)	5 (0.1%)	
Hospital ownership			<0.001
Government, nonfederal	299 (11.3%)	263 (7.8%)	
Private, nonprofit	2138 (80.5%)	2844 (84.4%)	
Private, investor owned	219 (8.2%)	261 (7.1%)	
Hospital bed-size			0.38
Small bed-size	146 (5.5%)	212 (6.3%)	
Medium bed-size	434 (16.3%)	561 (16.7%)	
Large bed-size	2077 (78.2%)	2595 (77.0%)	
Hospital urban-rural designation			0.004
Large metropolitan	1818 (68.4%)	2307 (68.5%)	
Small metropolitan	833 (31.3%)	1057 (31.4%)	
Micropolitan	6 (0.2%)	5 (0.1%)	
Year (N %)			<0.001
2014 (N = 1,674%)	917 (54.8%)	757 (45.2%)	
2015 (N = 3,252%)	1552 (47.7%)	1700 (52.3%)	
2016 (N = 4,645%)	2037 (43.9%)	2608 (56.1%)	

groups. PSM were conditioned on baseline demographics, co-morbidities, and hospital characteristics as listed in Table 1. Nearest neighbor 1:1 variable ratio, parallel, balanced, propensity matching with a caliper width of 0.2 was used to create 2 well-matched groups for comparative analysis using multivariable logistic regression model (Figure 1 of the Supplement). In the PSM cohort, between group differences were reported with absolute mean difference (AMD), and statistical significance was set with AMD value of >0.1. To analyze time to 30-day readmissions,

Kaplan-Meier analysis was performed and statistical significance was evaluated using log-rank test. Hazard ratio and 95% confidence intervals (CIs) were generated using Cox proportional hazards regression model. Categorical variables were expressed as percentages and continuous variables as mean ± standard deviation or median (interquartile range) as appropriate. Odds ratios and 95% CIs used to report the results of comparative analysis. All p values were 2-sided, and statistical significance was set at <0.05. All statistical analyses were performed using RStudio software

(RStudio, Boston, MA) or IBM SPSS version 26 (IBM Corporation, Armonk, NY).

## Results

A total of 6,025 elective TMVR hospitalizations were included in the study, of which 2,657 (44%) included patients less than 80 years and 3,368 (56%) included highly aged patients. From 2014 to 2016, there was a significant increase in TMVR therapy in highly aged patients compared with patients less than 80 years (Table 1). In our unmatched cohort, highly aged patients were less likely to be female, had a lower prevalence of diabetes mellitus, obesity, known myocardial infarction, known coronary artery bypass grafting, known peripheral arterial disease, and

chronic lung and liver disease, compared with those less than 80 years.

PSM yielded 2,197 patients less than 80 years and 2,185 highly aged patients. The 2 groups were well balanced on all baseline characteristics (AMD <0.1; Table 2). In the PSM cohort, TMVR in highly aged patients had similar rates of in-hospital mortality, stroke, cardiac tamponade, vasopressor use, infective endocarditis, cardiogenic shock, cardiac arrest, AMI, bleeding, AKI requiring hemodialysis, but higher rates of AKI and lower rates of vascular complications, need for blood transfusion and MCS compared with those less than 80 years (Table 3). Highly aged patients were more likely to be discharged to a skilled nursing facility (SNF). In addition, LOS, hospital costs, 30-day rates of stroke and mortality were also similar in the 2 groups (Table 4).

Table 2  
Baseline characteristics of patients who underwent transcatheter mitral valve repair in the propensity-score matched cohort

Variables	Age (years)		Absolute mean difference
	<80 (N = 2,197)	≥80 (N = 2,185)	
Age (years), mean ± standard deviation	69.6 ± 9.4	85 ± 3.1	-
Women	1001 (45.5%)	972 (44.5%)	-0.0059
Hypertension	1442 (65.6%)	1473 (67.4%)	0.0076
Dyslipidemia	1611 (52.8%)	1188 (54.4%)	0.020
Smoker	785 (35.7%)	648 (29.7%)	-0.031
Uncomplicated diabetes mellitus	396 (18.0%)	372 (17.0%)	-0.015
Complicated diabetes mellitus	104 (4.7%)	100 (4.6%)	-0.0042
Hypothyroidism	3339 (15.4%)	397 (18.2%)	0.0286
Body mass index ≥30 kg/m <sup>2</sup> (%)	160 (7.3%)	142 (6.5%)	-0.0076
Congestive heart failure	1591 (72.4%)	1627 (74.5%)	0.019
Coronary artery disease	1227 (55.8%)	1285 (58.8%)	0.020
Atrial fibrillation	1194 (54.3%)	1269 (58.1%)	0.0371
Healed myocardial infarction	322 (14.7%)	278 (12.7%)	-0.0076
Cerebrovascular accident	143 (6.5%)	134 (6.1%)	-0.0025
Coronary artery bypass grafting	538 (24.5%)	520 (23.8%)	-0.0084
Percutaneous coronary intervention	371 (16.9%)	376 (17.2%)	0.0017
Peripheral arterial disease	314 (14.3%)	293 (13.4%)	-0.0010
Chronic renal failure	694 (31.6%)	703 (32.2%)	0.0034
Chronic liver disease	45 (2.0%)	24 (1.1%)	-0.0067
Chronic lung disease	571 (26.0%)	516 (23.6%)	-0.021
Fluid and electrolyte imbalance	274 (12.5%)	2719 (12.4%)	-0.0051
Solid tumor	21 (1.0%)	18 (0.8%)	-0.0008
Alcohol abuse	25 (1.1%)	16 (0.7%)	-0.000
Metastatic cancer	7 (0.3%)	10 (0.5%)	-0.0008
Coagulopathy	208 (9.5%)	217 (9.9%)	0.0034
Chronic blood loss anemia	12 (.5%)	22 (1.0%)	0.0051
Deficiency anemia	325 (14.8%)	342 (15.7%)	-0.0051
Teaching status of urban hospitals			-0.0011
Metropolitan-teaching	1994 (90.7%)	1928 (88.3%)	
Metropolitan-nonteaching	198 (9.0%)	254 (11.6%)	
No-metropolitan hospital	6 (0.3%)	2 (0.1%)	
Hospital ownership			0.026
Private, nonprofit	1764 (80.3%)	1827 (83.6%)	
Government, nonfederal	237 (10.8%)	189 (8.6%)	
Private, investor owned	196 (8.9%)	169 (7.7%)	
Bed-size of hospitals			-0.0371
Small bed size	132 (6.0%)	157 (7.2%)	
Medium bed size	336 (15.3%)	378 (17.3%)	
Large bed size	1730 (78.7%)	1650 (75.5%)	
Hospital urban-rural designation			-0.011
Large metropolitan	1489 (67.8%)	1453 (66.5%)	
Small metropolitan	702 (32.0%)	729 (33.4%)	
Nonmetropolitan	6 (0.3%)	0	

Table 3

In-hospital outcomes of patients who underwent transcatheter mitral valve repair in the unmatched and propensity score-matched cohort

Outcomes	Unmatched cohort				Propensity-score matched cohort			
	Age <80	Age ≥80	Odds ratio	p value	Age <80	Age ≥80	Odds ratio	p value
	(N = 2,657)	(N = 3,368)	(95% CI)		(N = 2,197)	(N = 2,185)	(95% CI)	
In-hospital mortality	38 (1.4%)	59 (1.8%)	1.22 (0.81-1.85)	0.35	36 (1.6%)	47 (2.2%)	1.32 (0.85-2.14)	0.22
Ischemic stroke	16 (0.6%)	15 (0.5%)	0.73 (0.36-1.49)	0.46	10 (0.5%)	11 (0.5%)	1.1 (0.46-2.60)	0.83
Hemorrhagic stroke	0	2 (0.1%)	-	0.507	-	-	-	-
Requirement of mechanical ventilation	117 (4.4%)	117 (3.5%)	0.78 (0.60-1.01%)	0.70	87 (4.0%)	93 (4.3%)	1.07 (0.80-1.45)	0.64
Mechanical circulatory support	52 (2.0%)	27 (0.8%)	0.40 (0.25-0.64%)	<0.001	48 (2.2%)	22 (1.0%)	0.45 (0.27-0.75)	0.002
Vasopressor use	33 (1.2%)	35 (1.0%)	0.83 (0.51-1.34%)	0.46	30 (1.4%)	30 (1.4%)	1.006 (0.60-1.67)	>0.99
Cardiogenic shock	42 (1.6%)	36 (1.1%)	0.67 (0.43-1.05%)	0.086	37 (1.7%)	27 (1.2%)	0.73 (0.44-1.20)	0.25
Cardiac tamponade	10 (0.4%)	12 (0.4%)	0.94 (0.40-2.19%)	>0.99	8 (0.4%)	2 (0.2%)	0.62 (0.20-1.92)	0.58
Cardiac arrest	24 (0.9%)	15 (0.4%)	0.49 (0.25-0.93%)	0.035	20 (0.9%)	10 (0.5%)	0.50 (0.23-1.07)	0.098
Acute myocardial infarction	11 (0.4%)	23 (0.6%)	1.65 (0.80-3.39%)	0.22	9 (0.4%)	14 (0.6%)	1.56 (0.67-3.63)	0.30
Infective endocarditis	5 (0.2%)	0	-	0.017	5 (0.2%)	0	-	0.062
Bleeding requiring transfusion	189 (7.1%)	152 (4.5%)	0.61 (0.49-0.76%)	<0.001	151 (6.9%)	113 (5.2%)	0.73 (0.57-0.95)	0.019
Bleeding	324 (12.2%)	346 (10.3%)	0.82 (0.70-0.96%)	0.021	264 (12.0%)	234 (10.7%)	0.87 (0.72-1.05)	0.18
Vascular complications	16 (0.6%)	3 (0.1%)	0.14 (0.04-0.50%)	0.001	16 (0.7%)	2 (0.1%)	0.12 (0.029-0.54)	0.001
Acute kidney injury	170 (6.4%)	249 (7.4%)	1.16 (0.95-1.42%)	0.13	137 (6.2%)	182 (8.3%)	1.36 (1.08-1.72)	0.009
Acute kidney injury requiring hemodialysis	4 (0.2%)	4 (0.1%)	0.78 (0.19-3.15%)	0.73	4 (0.2%)	4 (0.2%)	1.006 (0.25-4.02)	>0.99

Thirty-day all-cause readmissions and 30-day HF readmissions were higher in highly aged patients compared with those less than 80 years. (Table 4, Figure 2). Cardiac causes (51.6%) were the most frequent primary diagnoses associated with 30-day readmission in highly aged patients (Figure 3). HF (30%), gastrointestinal bleeding (6.8%), and arrhythmias (5.4%) were the top 3 causes of readmissions in highly aged patients.

On multivariable analysis before propensity matching, age ≥80 years (OR 1.29; 95% CI 1.08 to 1.55,  $p=0.004$ ), atrial fibrillation (OR 1.52; 95% CI 1.28 to 1.80,  $p<0.001$ ), anemia (OR 1.30; 95% CI 1.06 to 1.60,  $p=0.01$ ), chronic lung disease (OR 1.26; 95% CI 1.05 to 1.52,  $p=0.01$ ), lymphoma (OR 1.98; 95% CI 1.07 to 3.69,  $p=0.03$ ), and weight loss (OR 1.56; 95% CI 1.04 to 2.35,  $p=0.03$ ) were identified as independent predictors of 30-day readmission.

## Discussion

Our study investigated the influence of age on in-hospital and 30-day outcomes in patients who underwent elective

percutaneous TMVR, utilizing a large national database. The main findings are that: (1) MitraClip is frequently used in highly aged patients and its utilization increased during the study period; (2) the rates of In-hospital mortality, stroke, cardiac tamponade, cardiogenic shock, cardiac arrest, bleeding, and AKI requiring hemodialysis were similar, whereas rates of AKI were higher in highly aged patients, compared with those less than 80 years; (3) rates of vascular complications, blood transfusion, and MCS were higher in patients less than 80 years, compared with highly aged patients. However, patients less than 80 were sicker with higher burden of co-morbidities at baseline; (4) highly aged patients were more likely to be discharged to a SNF and had a higher rate of all-cause and HF-related 30-day readmissions.

Prior work using the German TRAMI registry revealed similar rates of death, stroke, pericardial effusion, vascular complications, but a higher rate of bleeding requiring transfusion in TMVR patients ≥76 years compared with those less than 76 years.<sup>9</sup> Our study used a higher age cutoff of 80 years and above, but showed similar results to the

Table 4

Cost of hospitalization, length of stay, discharge disposition, and 30-day outcomes in patients who underwent transcatheter mitral valve repair in the unmatched and propensity-score matched cohorts

Variables	Unmatched cohort				Propensity-score matched cohort			
	Age <80	Age ≥80	Odds ratio	p value	Age <80	Age ≥80	Odds ratio	p value
	(N = 2,657)	(N = 3,368)	(95% CI)		(N = 2,197)	(N = 2,185)	(95% CI)	
Cost of hospitalization (median & interquartile range) X \$10,000 USD	15.7 (11-22.5)	16.3 (11.4-22.5)	-	0.38	15.2 (10.8-22.3)	16.0 (11.3-22.5)	-	0.75
Length of stay (days), Median & interquartile range	2 (1-4)	2 (1-3)	-0.66 (-0.98 to -0.34)	<0.001	2 (1-4)	2 (1-3)	-0.39 (-0.80 to 0.02) <sup>†</sup>	0.062
Discharge to SNF*	137 (5.2%)	317 (9.4%)	1.91 (1.55-2.35)	<0.001	98 (4.5%)	211 (9.7%)	2.28 (1.78-2.93)	<0.001
30-day all-cause readmission*	262 (10.8%)	427 (13.8%)	1.32 (1.12-1.55)	0.001	207 (10.4%)	280 (14.2%)	1.42 (1.17-1.72)	<0.001
30-readmissions for heart failure*	76 (3.1%)	129 (4.2%)	1.34 (1.01-1.79)	0.045	60 (3.0%)	93 (4.7%)	1.59 (1.14-2.22)	0.006
30-day stroke*	14 (0.6%)	30 (1.0%)	1.68 (0.89-3.19)	0.127	7 (0.4%)	15 (0.8%)	2.17 (0.88-5.34)	0.091
30-day mortality*	19 (0.8%)	26 (0.8%)	1.07 (0.59-1.94)	0.81	11 (0.6%)	20 (1.0%)	1.84 (0.88-3.86)	0.107

\* Among those alive at discharge and readmitted to a hospital within the same state.

<sup>†</sup>  $\beta$  weights from linear regression.

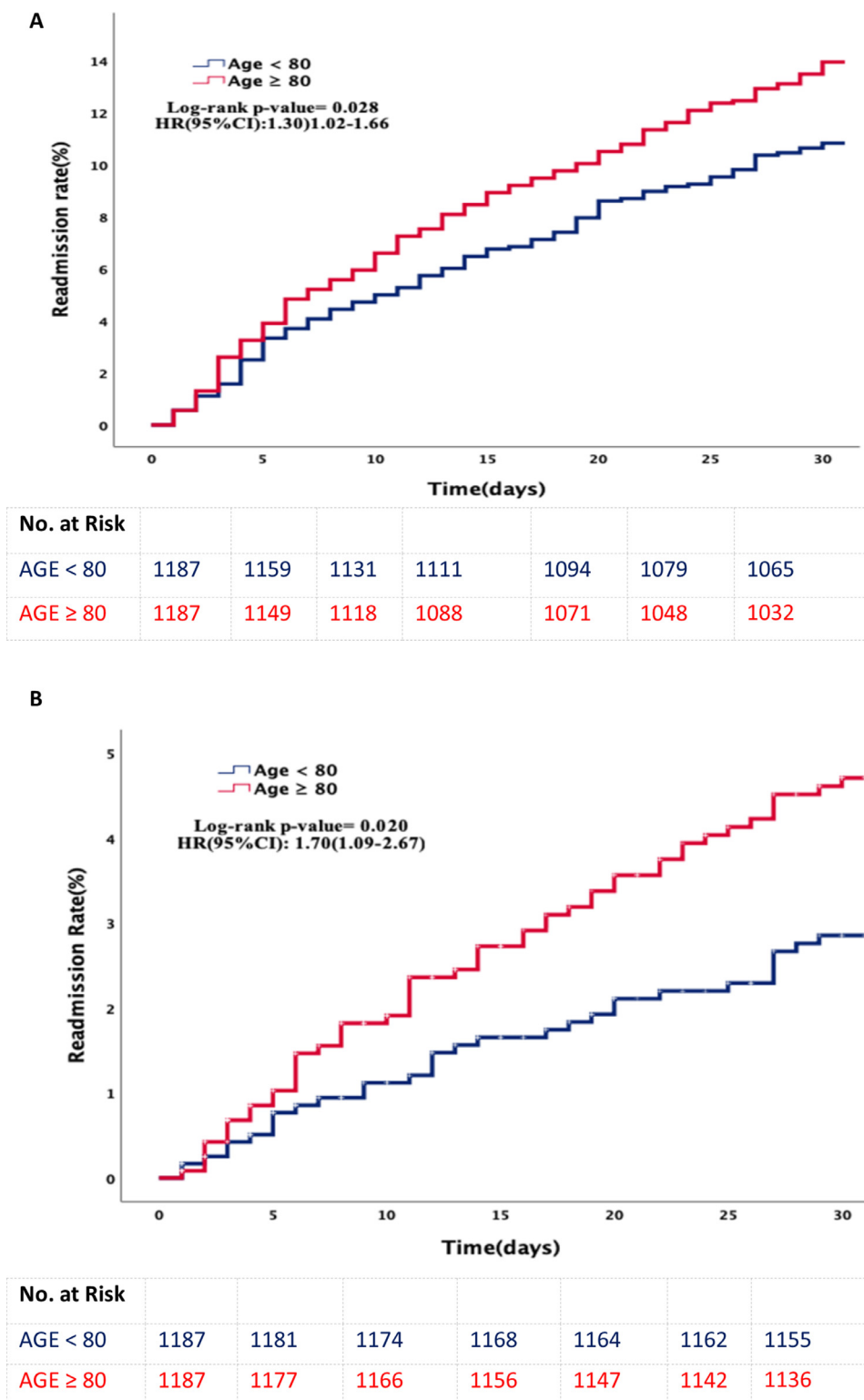


Figure 2. Kaplan-Meier curves for estimating rate of readmission in patients who were discharged alive and readmitted within 30 days. (A) All-cause readmissions; (B) Heart failure-related readmissions.

TRAMI registry data, except we found a lower rate of bleeding requiring transfusion in highly aged patients. Our study findings in highly aged patients are also consistent with the report from the TVT registry by Sorajja et al. which showed in hospital mortality of 2.7% and stroke rate

of 0.4%.<sup>5</sup> Advanced age is an independent factor associated with increased incidence of AKI, and higher rates of AKI associated mortality.<sup>10,11</sup> In addition, AKI after TMVR is associated with poor health status at 30 days, as assessed by the Kansas City Cardiomyopathy Questionnaire.<sup>12</sup> Our

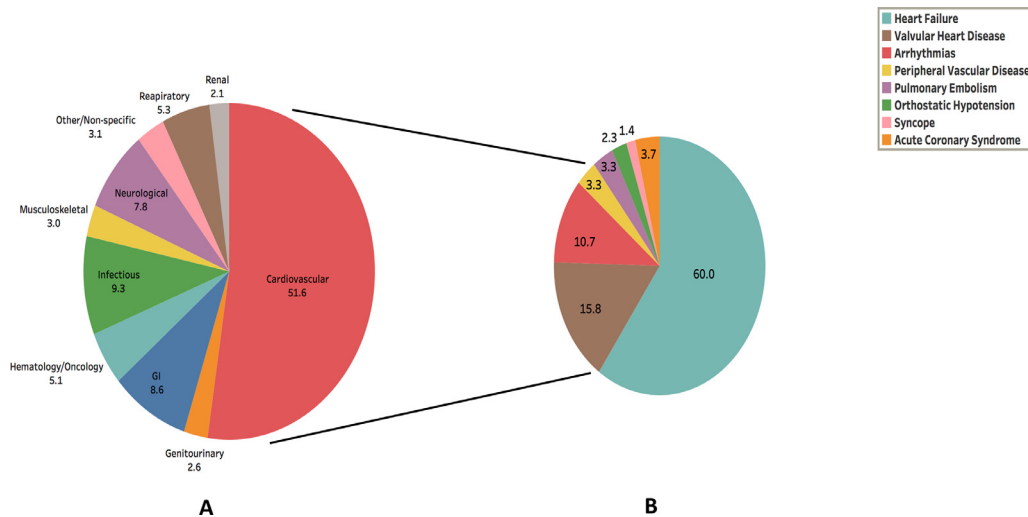


Figure 3. Causes of all-cause 30-day readmissions in highly aged transcatheter mitral valve repair therapy patients. (A) Noncardiac; (B) Cardiac. All numbers are n (%).

study showed higher rates of AKI in highly aged cohort, but the follow-up in our study was limited to 30 days, hence we cannot ascertain the influence of AKI on mid- and long-term outcomes.

Elderly patients are more commonly discharged to SNF after hospitalization in the United States.<sup>13,14</sup> SNF care accounts for over \$20 billion in Medicare costs annually.<sup>15</sup> Discharge to SNF is independently associated with elevated risk of death, readmission as well as higher health care cost.<sup>14,16,17</sup> Prior work utilizing NRD revealed that patients who underwent TMVR were less likely to be discharged to SNF compared with those patients who underwent surgical mitral valve repair (9% vs 12%).<sup>18</sup> We found that highly aged TMVR patients were more frequently discharged to SNF (9.4%), compared with those less than 80 years old (4.5%), and thus have identified a subgroup of TMVR patients at risk of adverse outcomes related to SNF discharge. Novel strategies that are proven to reduce readmissions, health care cost, and LOS at the SNF such as the Extension for Community Health Outcomes-Care Transitions videoconference program, that connects an interdisciplinary hospital-based team with clinicians at SNF may be beneficial in TMVR patients discharged to SNF.<sup>19</sup>

In a study of TMVR patients with a mean age of 76.7 years from the NRD, the 30-day all-cause readmission rate was 11.7%.<sup>20</sup> We found a higher 30-day all-cause readmission rate in the highly aged cohort (14.2%), but the rate of readmissions in patients under 80 in our study was quite similar to the rate reported in the previous study from NRD. Furthermore, we identified age  $\geq 80$ , atrial fibrillation, anemia, and chronic lung disease as independent predictors of 30-day readmission. Data from the TVT registry with a mean age of 82 years showed 4.9% readmission rate for HF in TMVR patients,<sup>5</sup> and we found a comparable 30-day readmission rate for HF in highly aged subjects. However, in the present study, the rate of 30-day readmission for HF was higher in highly aged subjects when compared with patients under 80 years of age (4.7% vs 3%, respectively).

There are several limitations of our study. First, despite PSM it is plausible that unobserved variables may have

influenced outcomes due to residual confounding. Second, the NRD is an administrative database relying on ICD-9-CM and ICD-10-CM codes, and is therefore vulnerable to miscoded and missing datasets. Nevertheless, multiple internal and external quality control measures are carried out to confirm that NRD datasets are valid and reliable.<sup>21</sup> Third, the NRD database lacks important clinical information such as the Society of Thoracic Surgeons risk score, New York Heart Association functional class, frailty, laboratory variables, medications used, MR severity and etiology, echocardiographic data, procedural characteristics such as site/number of clip implanted and post implant MR severity, and device related adverse events. In addition, the database lacks long-term follow-up and hence we are unable to ascertain the differences in quality of life measures between the 2 groups. Last, patients who are hospitalized in one state and readmitted to a hospital in another state would not have been captured in the NRD; however, we expect that to be uncommon in patients who underwent TMVR.

In a large, nationally representative cohort of patients who underwent TMVR, highly aged patients ( $\geq 80$  years) had similar in-hospital outcomes and 30-day mortality, but higher rates of 30-day all-cause and HF-related readmissions compared with those under 80 years of age. Evidence-based interventions proven to reduce the burden of HF-related readmissions should be utilized in these patients to further improve outcomes and quality of life. Future studies should focus on mid- and long-term outcomes of highly aged patients who underwent TMVR.

#### Authors' Contribution

Salik Nazir: conceptualization, methodology, formal analysis, writing – original draft preparation, visualization; Keerat Rai Ahuja: conceptualization, methodology, formal analysis, writing – original draft preparation, visualization; Hafeez Ul Hassan Virk: writing-original draft; Khalid Chngal: writing-Original draft; Ronak G. Soni: writing-review editing; Shashank Shekhar: methodology, validation;

Manpreet Kaur: methodology, validation; Najdat Bazarbashi: methodology, writing-review editing; P. Kasi Ramanathan: Writing – reviewing and editing; Rajesh Gupta: Writing – reviewing and editing, supervision, project administration.

## Disclosures

The authors declare that they have no known competing financial interests or personal relations that could have appeared to influence the work reported in this study.

## Supplementary materials

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.amjcard.2020.06.050>.

- Feldman T, Foster E, Glower DD, Glower DG, Kar S, Rinaldi MJ, Fail PS, Smalling RW, Siegel R, Rose GA, Engeron E, Loghin C, Trento A, Skipper ER, Fudge T, Letsou GV, Massaro JM, Mauri L, EVEREST II Investigators. Percutaneous repair or surgery for mitral regurgitation. *N Engl J Med* 2011;364:1395–1406.
- Stone GW, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM, Whisenant B, Grayburn PA, Rinaldi M, Kapadia SR, Rajagopal V, Sarembock IJ, Brieke A, Marx SO, Cohen DJ, Weissman NJ, Mack MJ, COAPT Investigators. Transcatheter mitral-valve repair in patients with heart failure. *N Engl J Med* 2018;379:2307–2318.
- Obadia J-F, Messika-Zeitoun D, Leurent G, Iung B, Bonnet G, Piriou N, Lefèvre T, Piot C, Rouleau F, Carrié D, Nejari M, Ohlmann P, Leclercq F, Saint Etienne C, Teiger E, Leroux L, Karam N, Michel N, Gilard M, Donal E, Trochu J-N, Cormier B, Armoiry X, Boutitie F, Mauco-Boulch D, Barnel C, Samson G, Guerin P, Vahanian A, Mewton N, MITRA-FR Investigators. Percutaneous repair or medical treatment for secondary mitral regurgitation. *N Engl J Med* 2018;379:2297–2306.
- Baldus S, Schillinger W, Franzen O, Bekerredjian R, Sievert H, Schofer J, Kuck K-H, Konorza T, Möllmann H, Hehrlein C, Ouarrak T, Senges J, Meinertz T, German Transcatheter Mitral Valve Interventions (TRAMI) investigators. MitraClip therapy in daily clinical practice: initial results from the German transcatheter mitral valve interventions (TRAMI) registry. *Eur J Heart Fail* 2012;14:1050–1055.
- Sorajja P, Vemulapalli S, Feldman T, Mack M, Holmes DR, Stebbins A, Kar S, Thourani V, Ailawadi G. Outcomes with transcatheter mitral valve repair in the United States: an STS/ACC TVT registry report. *J Am Coll Cardiol* 2017;70:2315–2327.
- Anon. The Hcup Nationwide Readmissions Database (NRD), 2010–2017. Available at: [https://www.hcup-us.ahrq.gov/db/nation/nrd/Introduction\\_NRD\\_2010-2017.jsp](https://www.hcup-us.ahrq.gov/db/nation/nrd/Introduction_NRD_2010-2017.jsp). Accessed January 24, 2020.
- Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* 1998;36:8–27.
- Anon. HCUP-US Methods Series. Available at: [https://www.hcup-us.ahrq.gov/reports/methods/methods\\_topic.jsp](https://www.hcup-us.ahrq.gov/reports/methods/methods_topic.jsp). Accessed January 24, 2020.
- Schillinger W, Hünlich M, Baldus S, Ouarrak T, Boekstegers P, Hink U, Butter C, Bekerredjian R, Plicht B, Sievert H, Schofer J, Senges J, Meinertz T, Hasenfu G. Acute outcomes after MitraClip therapy in highly aged patients: results from the German TRAnscatheter Mitral valve Interventions (TRAMI) Registry. *EuroIntervention* 2013;9:84–90.
- Yokota LG, Sampaio BM, Rocha EP, Balbi AL, Sousa Prado IR, Ponce D. Acute kidney injury in elderly patients: narrative review on incidence, risk factors, and mortality. *Int J Nephrol Renovasc Dis* 2018;11:217–224.
- Spieker M, Hellhammer K, Katsianos S, Wiora J, Zeus T, Horn P, Kelm M, Westenfeld R. Effect of acute kidney injury after percutaneous mitral valve repair on outcome. *Am J Cardiol* 2018;122:316–322.
- Arnold SV, Li Z, Vemulapalli S, Baron SJ, Mack MJ, Kosinski AS, Reynolds MR, Hermiller JB, Rumsfeld JS, Cohen DJ. Association of transcatheter mitral valve repair with quality of life outcomes at 30 days and 1 year: analysis of the transcatheter valve therapy registry. *JAMA Cardiol* 2018;3:1151–1159.
- WRITING GROUP MEMBERS, Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G, Ferguson TB, Ford E, Furie K, Gillespie C, Go A, Greenlund K, Haase N, Hailpern S, Ho PM, Howard V, Kissela B, Kittner S, Lackland D, Lisabeth L, Marelli A, McDermott MM, Meigs J, Mozaffarian D, Mussolino M, Nichol G, Roger VL, Rosamond W, Sacco R, Sorlie P, Roger VL, Stafford R, Thom T, Wasserthiel-Smolter S, Wong ND, Wylie-Rosett J, American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2010 update: a report from the American Heart Association. *Circulation* 2010;121:e46–e215.
- Hutt E, Frederickson E, Ecord M, Kramer AM. Associations among processes and outcomes of care for Medicare nursing home residents with acute heart failure. *J Am Med Dir Assoc* 2003;4:195–199.
- Anon. Medicare | CMS. Available at: <https://www.cms.gov/Medicare/Medicare>. Accessed February 1, 2020.
- Allen LA, Hernandez AF, Peterson ED, Curtis LH, Dai D, Masoudi FA, Bhatt DL, Heidenreich PA, Fonarow GC. Discharge to a skilled nursing facility and subsequent clinical outcomes among older patients hospitalized for heart failure. *Circ Heart Fail* 2011;4:293–300.
- Hakkarainen TW, Arbabi S, Willis MM, Davidson GH, Flum DR. Outcomes of patients discharged to skilled nursing facilities after acute care hospitalizations. *Ann Surg* 2016;263:280–285.
- Jogu HR, Arora S, Strassle PD, Patel C, Patil N, Venkatesh S, Alkhaimey H, Ramm CJ, Qamar A, Kim SM, Yeung M, Vavalle JP. Impact of age and comorbidities on the effect of transcatheter versus surgical mitral valve repair on inpatient outcomes. *Catheter Cardiovasc Interv* 2020;95:1195–1201.
- Moore AB, Krupp JE, Dufour AB, Sircar M, Travison TG, Abrams A, Farris G, Mattison MLP, Lipsitz LA. Improving transitions to post-acute care for elderly patients using a novel video-conferencing program: ECHO-care transitions. *Am J Med* 2017;130:1199–1204.
- Lima FV, Kolte D, Rofeberg V, Molino J, Zhang Z, Elmariah S, Aroon HD, Abbott JD, Ben Assa E, Khera S, Gordon PC, Inglessis I, Palacios IF. Thirty-day readmissions after transcatheter versus surgical mitral valve repair in high-risk patients with mitral regurgitation: analysis of the 2014–2015 Nationwide Readmissions Databases. *Catheter Cardiovasc Interv* 2019;1–11. <https://doi.org/10.1002/ccd.28647>.
- Anon. HCUP Quality Control Procedures. Available at: <https://www.hcup-us.ahrq.gov/db/quality.jsp>. Accessed December 8, 2019.