ORIGINAL RESEARCH

Role of Changing Procedural Characteristics Versus Changing Risk Profile in Age-Based Trends of Outcomes in Patients With Transfemoral Transcatheter Aortic Valve Replacement From 2012 to 2018: A Nationwide Analysis

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BACKGROUND: The trends in outcomes in patients who undergo transcatheter aortic valve replacement are well described in the literature. Some of these trends are driven by the decreasing risk profile of patients because of changing indications for transcatheter aortic valve replacement. We aimed to evaluate these trends in different age groups and quantify how much of these trends are driven by changes in procedural characteristics.

METHODS AND RESULTS: Using the National Inpatient Sample from 2012 to 2018, we identified 204,230 adult patients who underwent transfemoral aortic valve replacement. The study’s primary objective was to evaluate the changes in age-based trends in in-hospital mortality driven by changes in procedural characteristics over time. The secondary objectives were to evaluate similar trends in cardiac and noncardiac complications and resource use. Univariate and multivariate linear and logistic regression were used to obtain effect sizes. From 2012 to 2018, in-hospital mortality decreased from 1.8% to 0.79% in the age group 18 to 64 years, from 3.8% to 1.6% in the age group 65 to 80 years, and from 5.3% to 1.5% in the age group >80 years (P trend<0.01 for all age groups); these trends remained statistically significant on adjusted analysis except in patients aged 18 to 64 years. The other outcomes also showed variable trends over time. Length of stay, cost, and early discharge rates improved even after adjusting for comorbidities, which is likely attributable to improvement in procedural characteristics.

CONCLUSIONS: The changes in outcomes related to transcatheter aortic valve replacement are partly driven by changing patient risk profiles over time, but procedural characteristics have likely contributed to these trends in all age groups.

Key Words: procedural characteristics ■ TAVR ■ transcatheter aortic valve replacement ■ trends
Intermediate-risk, and low-risk patients using different valves and approaches. These trials led to its approval in high-risk, intermediate-risk, and low-risk patients. The primary objective of our study was to examine how outcomes have changed over time in different age groups and, with respect to the adjusted models, examine the extent to which these changes are driven by changes in patient characteristics versus changes in the procedural characteristics in patients who underwent transfemoral TAVR.

Nonstandard Abbreviations and Acronyms

| Abbreviation | Definition                  |
|--------------|-----------------------------|
| NIS          | National Inpatient Sample    |
| SAVR         | Surgical aortic valve replace |
| TAVR         | Transcatheter aortic valve replacement |

Outcomes

The outcome of interest was trends in complications and resource use after TAVR placement among the 3 age groups from the years 2012 to 2018. These outcomes included in-hospital mortality, acute myocardial infarction, cardiogenic shock, cardiac arrest, new pacemaker placement, acute renal failure, acute respiratory failure requiring mechanical ventilation,
## Table 1. Baseline Characteristics of Patients With Transfemoral Transcatheter Aortic Valve Replacement in All Age Groups From 2012 to 2018

| Age Group | 2012, n=280 | 2013, n=310 | 2014, n=330 | 2015, n=340 | 2016, n=350 | 2017, n=360 | 2018, n=370 | P value trend |
|-----------|-------------|-------------|-------------|-------------|-------------|-------------|-------------|--------------|
| Age 18–64 y, n=10495 | | | | | | | | |
| Women, % | 44.6 | 44.2 | 40.6 | 35.7 | 40.2 | 41.5 | 41.8 | 0.7 |
| Race and ethnicity, % | | | | | | | | 0.8 |
| White | 80 | 76.9 | 76.8 | 80.4 | 76.1 | 80.4 | 74 | |
| Black | 7.3 | 14.1 | 11.9 | 8.2 | 12.2 | 10.1 | 10.8 | |
| Hispanic | 9.1 | 3.8 | 7.3 | 5.7 | 5.5 | 5.3 | 10.3 | |
| Asian or Pacific Islander | 1.8 | 1.3 | 2.6 | 1.2 | 1.8 | 1.1 | 2.4 | |
| Native American | 0 | 0 | 0 | 0.4 | 0.9 | 0.4 | 0.6 | |
| Congestive heart failure, % | 57.1 | 66.3 | 71.3 | 70.7 | 74.6 | 75 | 75.1 | <0.01 |
| End-stage renal disease, % | 7.1 | 9.3 | 15 | 12 | 13.4 | 11.5 | 17.7 | <0.01 |
| Chronic lung disease, % | 17.9 | 34.9 | 32.5 | 35.3 | 35 | 36.9 | 31.4 | 0.6 |
| Chronic liver disease, % | 10.7 | 15.1 | 14.4 | 13.5 | 10.8 | 9.3 | 11.4 | 0.14 |
| Hypertension, % | 58.9 | 58.1 | 76.3 | 72.2 | 76.9 | 81.4 | 82 | <0.01 |
| Diabetes, % | 33.9 | 39.5 | 42.5 | 44.4 | 44.7 | 41.9 | 44.9 | 0.23 |
| Peripheral vascular disease, % | 19.6 | 24.4 | 25 | 28.9 | 22.2 | 20.1 | 19.4 | 0.02 |
| Obesity, % | 25 | 20.9 | 32.5 | 28.2 | 32.5 | 37.8 | 34.7 | <0.01 |
| Elective procedure, % | 66.1 | 67.4 | 69.4 | 67.7 | 72 | 71.3 | 72.2 | 0.13 |
| Elixhauser Comorbidity Index, mean±SE | 3.3±0.22 | 3.9±0.21 | 4.3±0.16 | 4.4±0.13 | 3.7±0.10 | 3.2±0.08 | 3.3±0.08 | <0.01 |

| Age 65–80 y, n=78580 | | | | | | | | |
| Women, % | 45.6 | 43.4 | 43.2 | 45.4 | 45.3 | 42.3 | 45.2 | 0.8 |
| Race and ethnicity, % | | | | | | | | 0.98 |
| White | 83.7 | 89.5 | 87.4 | 85.1 | 85.1 | 87 | 86 | |
| Black | 5.1 | 4.3 | 5.9 | 5.1 | 5.1 | 4.3 | 4.8 | |
| Hispanic | 3.5 | 1.6 | 3.8 | 5.1 | 5.2 | 4.7 | 5.7 | |
| Asian or Pacific Islander | 1.9 | 1.1 | 0.8 | 1.4 | 1.2 | 1.4 | 1.3 | |
| Native American | 0 | 0.2 | 0.2 | 0.2 | 0.3 | 0.4 | 0.3 | |
| Congestive heart failure, % | 71.1 | 69.9 | 76.3 | 74.2 | 73.4 | 72.7 | 72.7 | 0.7 |
| End-stage renal disease, % | 6.3 | 8.5 | 6.3 | 6.2 | 5.8 | 4.6 | 4.5 | <0.01 |
| Chronic lung disease, % | 44.1 | 43.8 | 40.3 | 38.1 | 36.8 | 35.1 | 33 | <0.01 |
| Chronic liver disease, % | 5.6 | 4 | 3.9 | 4.6 | 3.8 | 4 | 4.3 | 0.7 |
| Hypertension, % | 80.5 | 76.2 | 81.2 | 83.6 | 86.9 | 89.5 | 89.4 | <0.01 |
| Diabetes, % | 43.8 | 48.8 | 49.5 | 48.7 | 47 | 48.2 | 46 | 0.18 |
| Peripheral vascular disease, % | 30.9 | 29.1 | 29.5 | 28.6 | 27 | 24.2 | 22.1 | <0.01 |
| Obesity, % | 26.1 | 25 | 25.9 | 28.2 | 26 | 28.3 | 28.8 | 0.01 |
| Elective procedure, % | 75.2 | 77.8 | 78.4 | 78.4 | 78.6 | 82.5 | 82.8 | <0.01 |
| Elixhauser Comorbidity Index, mean±SE | 3.9±0.09 | 4.3±0.08 | 3.8±0.05 | 3.6±0.04 | 3±0.03 | 2.9±0.03 | <0.01 |

| Age >80 y, n=115255 | | | | | | | | |
| Women, % | 49.5 | 49.2 | 45.8 | 49.5 | 47.7 | 49.4 | 48.3 | 0.7 |
| Race and ethnicity, % | | | | | | | | 0.83 |
| White | 85.6 | 88.1 | 89.6 | 89.5 | 87.9 | 88.4 | 88.4 | |
| Black | 3.4 | 2.7 | 3.1 | 3.1 | 3.7 | 3.2 | 3 | |
| Hispanic | 3.5 | 3.6 | 2.9 | 4 | 4 | 4.5 | 5 | |
| Asian or Pacific Islander | 0.9 | 0.7 | 1.2 | 1 | 1.3 | 1.3 | 1.4 | |
| Native American | 0.4 | 0 | 0.1 | 0.1 | 0.1 | 0.3 | 0.2 | |
| Congestive heart failure, % | 73.7 | 73.7 | 77.5 | 73.4 | 71.8 | 74.5 | 72.77 | 0.24 |
| End-stage renal disease, % | 2.1 | 2.3 | 2.3 | 2.1 | 1.7 | 1.6 | 1.4 | <0.01 |
| Chronic lung disease, % | 29.1 | 28 | 25.8 | 26.4 | 24.9 | 22.8 | 22.8 | <0.01 |
| Chronic liver disease, % | 0.9 | 1.4 | 0.9 | 0.8 | 1.3 | 1.2 | 1.3 | 0.25 |
| Hypertension, % | 79.7 | 78.6 | 81.4 | 84.7 | 88.8 | 89.8 | 89.8 | <0.01 |
| Diabetes, % | 27.8 | 27.2 | 27 | 30.9 | 28.8 | 29.7 | 28.9 | 0.5 |
| Peripheral vascular disease, % | 30 | 26.6 | 27.8 | 26.5 | 25.1 | 24.8 | 22.9 | <0.01 |
| Obesity, % | 7.5 | 8.8 | 8.7 | 9.8 | 9.2 | 11 | 11.2 | <0.01 |
| Elective procedure, % | 74.7 | 78.6 | 75.9 | 79.7 | 79.7 | 82 | 82.9 | <0.01 |
| Elixhauser Comorbidity Index, mean±SE | 3.5±0.08 | 3.4±0.06 | 3.7±0.06 | 3.3±0.04 | 3.1±0.04 | 2.5±0.03 | 2.4±0.03 | <0.01 |
inflation-adjusted cost, length of stay, discharge rate within 24 hours, and discharge rate within 72 hours. Most of the complications were identified using ICD-9-CM and ICD-10-CM codes (Table S1). The variables for mortality, length of stay, and total charges are included in the NIS. Hospital charges represent the total charges billed by the hospital for the entire visit, not the actual cost of services. The Healthcare Cost and Utilization Project provides data on hospital-specific cost-to-charge ratios based on all-payer inpatient costs. This cost-related information is obtained from hospital accounting reports collected by the Centers for Medicare and Medicaid Services. Actual hospital cost was obtained by multiplying total hospital charges with the cost-to-charge ratio.12 We also used the Medical Expenditure Panel Survey to obtain inflation-adjusted cost estimates. The hospital-care price index was used to adjust hospital costs for inflation.13

**Statistical Analysis**

Baseline characteristics were compared using univariable linear and logistic regression, as shown in Table 1. P values <0.05 were considered to be statistically significant. Simple linear and logistic regression were used to analyze unadjusted coefficients and odds ratios (ORs) for outcomes, respectively.

Multivariable linear and logistic regression were used to obtain adjusted coefficients and odds ratios for outcomes, respectively. The variables used in the multivariate models included sex, race, hypertension, diabetes, congestive heart failure, chronic lung disease, chronic liver disease, end-stage renal disease, peripheral vascular disease, obesity, electiveness of the procedure, Elixhauser Comorbidity Index, and year. Year was included as a continuous covariate in the unadjusted and adjusted linear and logistic regression models to obtain unadjusted and adjusted coefficients and odds ratios of outcomes per year, respectively, along with the P value for trends. The data analysis for this article was generated using SAS software version 9.4 (SAS Institute, Cary, NC). Because of the complex sampling design of the NIS, survey procedures were used to account for stratification, clustering, and weighting to produce nationally representative estimates, standard errors, and P values.

**RESULTS**

The study sample included 204330 patients who underwent transfemoral TAVR from 2012 to 2018, of which 10495 patients were aged 18 to 64 years, 78580 were aged 65 to 80 years, and 115255 were aged >80 years. The baseline characteristics of all patients with TAVR stratified by different age groups are shown in Table 1. Among patients aged 18 to 64 years, the distribution of sex, race, elective procedures, and comorbidities, including diabetes, chronic lung disease, and chronic liver disease, did not change from 2012 to 2018. However, the comorbidity burden indicated by the Elixhauser Comorbidity Index and peripheral vascular disease significantly decreased over time. Hypertension, congestive heart failure, end-stage renal disease, and obesity significantly increased in this age group over time. Among patients aged 65 to 80 years as well as >80 years, the distribution of sex, race, congestive heart failure, chronic liver disease, and diabetes did not significantly change over time. However, Elixhauser Comorbidity Index condition count, end-stage renal disease, chronic lung disease, and peripheral vascular disease significantly decreased over time. Hypertension, obesity, and the number of elective procedures increased significantly over time.

The unadjusted and adjusted odds and coefficients of all outcomes per year are shown in Table 2. The unadjusted trend in in-hospital mortality from 2012 to 2018 is shown in Figure 1. In-hospital mortality significantly decreased in patients aged 18 to 64 years from 2012 to 2018 (1.79% to 0.93%; OR, 0.83; P<0.01), but this change was not significant when adjusted for sex, race, and comorbidities (adjusted OR [AOR], 0.95; P=0.48). In patients aged 65 to 80 years, in-hospital mortality decreased significantly from 3.8% to 1.1% (OR, 0.76; P<0.01), and there was a 13% statistically significant decrease in in-hospital mortality odds per year on adjusted analysis (AOR, 0.87; P<0.01). In patients aged >80 years, in-hospital mortality significantly decreased from 5.3% to 1.5% (OR, 0.79; P<0.01), and there was an 11% statistically significant decrease in in-hospital mortality odds per year on adjusted analysis (AOR, 0.89; P<0.01). The unadjusted trends in cardiac complications are shown in Figure 2. In patients aged 18 to 64 years, the rate of acute myocardial infarction (AMI) remained <4%, with no statistically significant change in odds in unadjusted (OR, 1.08; P=0.27) and adjusted (AOR, 1.15; P=0.09) models. In patients aged 65 to 80 years, the rate of AMI remained <4% as well, with no statistically significant change in odds over time, but there was a significant increase in odds of 9% per year seen on adjusted analysis (OR, 1; P=0.94; AOR, 1.09; P=0.04). In patients aged >80 years, the odds of AMI did not significantly change before and after adjustment (OR, 0.98; P=0.48; AOR, 1.04; P=0.2). The unadjusted pacemaker rates remained <14% in all age groups, with higher rates in elderly patients. The odds of new pacemaker placement did not significantly change over time in any age group in either unadjusted or adjusted models. The unadjusted rates of cardiogenic shock did not significantly change over time in patients aged 18 to 64 years but significantly decreased in patients aged 65 to 80 years from 3.2% to 2% (OR, 0.91; P<0.01) and in patients aged >80 years.
| Binary outcomes                        | Age 18–64y |                |                |                | Age 65–80y |                |                |                | Age >80y |                |                |                |
|---------------------------------------|------------|----------------|----------------|----------------|------------|----------------|----------------|----------------|----------|----------------|----------------|----------------|
|                                       | Unadjusted OR (95% CI) | P value trend | Adjusted OR (95% CI) | P value trend | Unadjusted OR (95% CI) | P value trend | Adjusted OR (95% CI) | P value trend | Unadjusted OR (95% CI) | P value trend | Adjusted OR (95% CI) | P value trend |
| Mortality                             | 0.83 (0.73 to 0.95) | <0.01          | 0.95 (0.81 to 1.0) | 0.48           | 0.76 (0.72 to 0.83) | <0.01          | 0.87 (0.80 to 0.94) | <0.01          | 0.79 (0.75 to 0.83) | <0.01          | 0.89 (0.84 to 0.94) | <0.01          |
| Acute renal failure                   | 0.94 (0.87 to 1.02) | 0.14           | 1.06 (0.97 to 1.16) | 0.19           | 0.87 (0.84 to 0.90) | <0.01          | 1.0 (0.97 to 1.04) | 0.75           | 0.88 (0.86 to 0.90) | <0.01          | 1.02 (0.99 to 1.02) | 0.14           |
| New pacemaker placement              | 0.98 (0.89 to 1.08) | 0.75           | 0.97 (0.88 to 1.08) | 0.64           | 0.98 (0.95 to 1.05) | 0.34           | 1.01 (0.97 to 1.05) | 0.6            | 0.98 (0.95 to 1.00) | 0.08           | 0.99 (0.97 to 1.02) | 0.86           |
| Acute stroke                          | 0.91 (0.73 to 1.14) | 0.4            | 0.96 (0.77 to 1.19) | 0.70           | 0.97 (0.90 to 1.04) | 0.4            | 1.1 (1.02 to 1.2)  | 0.01           | 0.95 (0.90 to 1.00) | 0.06           | 1.09 (1.02 to 1.16) | <0.01          |
| Bleeding requiring blood transfusion  | 0.76 (0.69 to 0.83) | <0.01          | 0.79 (0.71 to 0.88) | <0.01          | 0.71 (0.68 to 0.74) | <0.01          | 0.76 (0.73 to 0.8) | <0.01          | 0.70 (0.68 to 0.73) | <0.01          | 0.75 (0.73 to 0.79) | <0.01          |
| Acute myocardial infarction           | 1.08 (0.94 to 1.26) | 0.27           | 1.15 (0.98 to 1.4)  | 0.09           | 1.0 (0.92 to 1.08)  | 0.94           | 1.09 (1.002 to 1.19) | 0.04          | 0.98 (0.92 to 1.04) | 0.48           | 1.04 (0.97 to 1.11) | 0.2            |
| Acute respiratory failure requiring ventilator | 0.98 (0.88 to 1.10) | 0.78           | 1.1 (0.98 to 1.24)  | 0.11           | 0.96 (0.91 to 1.02) | 0.23           | 1.09 (1.02 to 1.16) | <0.01          | 0.95 (0.90 to 0.999) | 0.04           | 1.11 (1.04 to 1.17) | <0.01          |
| Cardiogenic shock                     | 1.04 (0.93 to 1.16) | 0.47           | 1.17 (1.04 to 1.23) | <0.01          | 0.91 (0.85 to 0.96) | <0.01          | 1.05 (0.97 to 1.12) | 0.2            | 0.89 (0.84 to 0.94) | <0.01          | 1.02 (0.95 to 1.08) | 0.6            |
| Cardiac arrest                        | 0.88 (0.78 to 1.009) | 0.07           | 0.93 (0.81 to 1.08) | 0.36           | 0.87 (0.81 to 0.92) | <0.01          | 0.95 (0.89 to 1.01) | 0.11           | 0.85 (0.81 to 0.89) | <0.01          | 0.94 (0.88 to 0.99) | 0.02           |
| Discharge within 24 h                 | 1.7 (1.5 to 1.9)  | <0.01          | 1.75 (1.5 to 1.98) | <0.01          | 1.9 (1.78 to 2)   | <0.01          | 1.78 (1.66 to 1.9)  | <0.01          | 1.94 (1.82 to 2)   | <0.01          | 1.80 (1.68 to 1.92) | <0.01          |
| Discharge with 72 h                   | 1.4 (1.3 to 1.5)  | <0.01          | 1.45 (1.34 to 1.56) | <0.01          | 1.6 (1.54 to 1.64) | <0.01          | 1.52 (1.46 to 1.58) | <0.01          | 1.6 (1.52 to 1.62) | <0.01          | 1.5 (1.45 to 1.55) | <0.01          |
| Continuous outcomes                   | Coefficient (95% CI) | P value trend | Adjusted coefficient (95% CI) | P value trend | Coefficient (95% CI) | P value trend | Adjusted coefficient (95% CI) | P value trend | Coefficient (95% CI) | P value trend | Adjusted coefficient (95% CI) | P value trend |
| Length of stay, d                     | −0.8 (−1 to −0.5)  | <0.01          | −0.5 (−0.7 to −0.3) | <0.01          | −0.8 (−0.9 to −0.8) | <0.01          | −0.46 (−0.5 to −0.4) | <0.01          | −0.8 (−0.8 to −0.7) | <0.01          | 0.4 (−0.5 to −0.4) | <0.01          |
| Inflation-adjusted cost in US dollars | −2785 (−4476 to −1093) | <0.01       | −1209 (−2730 to −312) | <0.01          | −2764 (−3258 to −2270) | <0.01          | −1333 (−1901 to −883) | <0.01          | −2595 (−3027 to −2163) | <0.01          | −1416 (−1864 to −967) | <0.01          |
from 3.7% to 1.8% (OR, 0.89; \( P < 0.01 \)). However, odds of cardiogenic shock showed a significant increase of 17% per year in patients aged 18 to 64 years (AOR, 1.17; \( P < 0.01 \)), with no significant change in other age groups on adjusted analysis. The odds of cardiac arrest did not significantly change over time in patients aged 18 to 64 years in either unadjusted or adjusted models. The odds of cardiac arrest significantly decreased in patients aged 65 to 80 years (OR, 0.87; \( P < 0.01 \)), but the results were not significant after adjustment. However,

**Figure 1.** Age-based trends in in-hospital mortality in patients who underwent transfemoral TAVR from 2012 to 2018. TAVR indicates transfemoral transcatheter aortic valve replacement.

**Figure 2.** Age-based trends in acute myocardial infarction (A), new pacemaker placement (B), cardiac arrest (C), and cardiogenic shock (D) in patients who underwent transfemoral TAVR from 2012 to 2018. TAVR indicates transfemoral transcatheter aortic valve replacement.
in patients aged >80 years, the odds decreased significantly in both unadjusted (OR, 0.85; \( P<0.01 \)) and adjusted (AOR, 0.94; \( P=0.02 \)) models.

The unadjusted trends in the rate of noncardiac complications are shown in Figure 3. The unadjusted and adjusted odds of acute kidney injury did not significantly change over time in patients aged 18 to 64 years. The unadjusted odds of acute kidney injury significantly decreased for other age groups, but this decrease was not significant after adjustment. Bleeding requiring transfusion decreased significantly in all age groups on both unadjusted and adjusted analyses (\( P<0.01 \) for all age groups for both unadjusted and adjusted models). The unadjusted and adjusted odds of acute ischemic stroke did not significantly change in patients aged <65 years. The unadjusted odds of acute ischemic stroke did not show any significant change in other age groups, but there was a significant increase in the odds of stroke after adjustment (\( P=0.01 \) for those aged \( \geq 65 \) and \( <80 \) years; \( P<0.01 \) for those aged \( >80 \) years). The odds of acute respiratory failure requiring mechanical ventilation did not significantly change over time in either unadjusted or adjusted analyses for patients aged 18 to 64 years. The unadjusted odds of acute respiratory failure requiring mechanical ventilation did not show a significant change in the patients aged \( \geq 65 \) and \( <80 \) years, but there was a significantly increasing trend over time in the adjusted model (\( P<0.01 \)). The odds of acute respiratory failure requiring mechanical ventilation showed a significantly increasing trend in patients aged >80 years on both unadjusted (\( P=0.04 \)) and adjusted (\( P<0.01 \)) analyses.

The unadjusted trends in resource use in patients with transfemoral TAVR from 2012 to 2018 are shown in Figure 4. The unadjusted length of stay significantly decreased from 10.8 to 8.4 days in patients aged 18 to 64 years, from 8.2 to 3.8 days in patients aged 65 to 80 years, and from 7.7 to 3.8 days in patients aged \( >80 \) years, and these results remained statistically significant after adjustment (\( P<0.01 \) for all age groups for both unadjusted and adjusted models). The unadjusted discharge rate within 24 hours significantly increased from 0% to 27% in patients aged 18 to 64 years, from 1.5% to 32.5% in patients aged 65 to 80 years, and from 1.67% to 28.6% in patients aged \( >80 \) years, and the results remain statistically significant on adjusted analysis (\( P<0.01 \) for all age groups for both unadjusted and adjusted models). The unadjusted discharge rate within 72 hours significantly increased from 16% to 67% in patients aged \( <65 \) years, from 18% to 73% in

Figure 3. Age-based trends in bleeding requiring blood transfusion (A), acute ischemic stroke (B), acute respiratory failure (C), and acute kidney injury (D) in patients who underwent transfemoral TAVR from 2012 to 2018. TAVR indicates transfemoral transcatheter aortic valve replacement.
patients aged ≥65 and ≤80 years, and from 16% to 72% in patients aged >80 years, and these results remained statistically significant after adjustment \((P<0.01\) for all age groups for both unadjusted and adjusted models). The inflation-adjusted cost also significantly decreased from $69,858 to $55,194 in patients aged <65 years, from $64,588 to $49,208 in patients aged ≥65 and ≤80 years, and $62,752 to $48,085 in patients aged >80 years, and these results remained statistically significant after adjustment \((P<0.01\) for all age groups for both unadjusted and adjusted models).

**DISCUSSION**

Our study showed a significantly decreasing trend in in-hospital mortality in unadjusted and adjusted analyses in all age groups except patients aged 18 to 64 years. Mortality showed no significant change over time in this age group in the adjusted analysis, whereas it decreased in the unadjusted analysis. On unadjusted and adjusted analysis, the trends in cardiac and non-cardiac complications were heterogeneous, with significant changes in some but not other complications in different age groups. Over time, length of stay and inflation-adjusted cost significantly decreased, and discharge rates within 24 and 72 hours significantly increased in both unadjusted and adjusted analyses. Our results suggest that change in indications of TAVR from high-risk populations to lower-risk populations has contributed to better outcomes, with few exceptions. However, changes in procedural characteristics also appear to have contributed to changes in outcomes.

The decreasing trend in mortality seen in our study cohort is consistent with other studies.\(^{14,15}\) We saw a significantly decreasing comorbidity burden in all age groups over time, because TAVR was initially indicated only for high-risk patients but, later on, was approved for intermediate-risk patients.\(^{16}\) Although TAVR was approved in 2019 for low-risk patients,\(^{17}\) that change will not be captured in these data, because it only extends until 2018. The odds of mortality showed a significantly decreasing trend in patients aged 65 to 80 and >80 years, even after adjustment for patient characteristics. This decrease in mortality is likely attributable to procedural characteristics, including better valves, smaller sheaths, improved quality of preoperative computed tomography imaging for procedural planning, and increased operator experience.\(^{18}\) However, these characteristics did not appear to significantly impact
in-hospital mortality outcomes in patients aged 18 to 64 years. The significant decrease in mortality in this age group seen on unadjusted analysis was no longer significant on adjusted analysis. One reason could be that in-hospital mortality was not as high in this age group even in 2012, when TAVR was indicated only in high-risk patients. The decreasing trend seen on unadjusted analysis was explained by the decreasing trend in risk profile in these patients over time; hence, there was no significant decrease in mortality seen in this age group on adjusted analysis.

AMI after TAVR, most commonly non–ST-segment–elevation myocardial infarction, has been described by previous studies. We did not see any significant change in odds of AMI even after adjustment in any age group except for patients aged 65 to 80 years, who had a significant increase in the odds of AMI over time in the adjusted analysis. The implications of this finding are unclear and would benefit from further study. Pacemaker placement rates were higher in elderly patients in our study. However, their odds did not change in any age group despite a decrease in the risk profile of patients and improvement in procedural characteristics over time. Previous studies have attributed the increasing pacemaker trend until 2015 and then decreasing trend thereafter, to procedural technique and valve changes over time. Our analysis focused on linear trends over time and did not identify this pattern. However, we did see variability in the rates of pacemaker placement throughout this period in all age groups, and the trends in those aged >80 years appear consistent with this pattern.

The unadjusted risk of post-TAVR cardiogenic shock did not show significant change over time in patients aged 18 to 64 years but showed a significantly increasing trend on adjusted analysis. Because the comorbidity burden has decreased over time, these trends may be attributed to changes in procedural characteristics. Severe aortic insufficiency after TAVR can lead to cardiogenic shock in these patients. Suicide left ventricle has also been described as sudden afterload reduction after TAVR resulting in hemodynamic collapse. Whether these complications were more common in the recent years in this age group needs to be studied. The unadjusted odds of cardiogenic shock showed a decreasing trend in patients aged 65 to 80 and >80 years, which is likely attributable to the decreasing risk profile of these patients over time, because this trend is no longer significant after adjustment for patient characteristics. The odds of cardiac arrest showed a nonsignificant trend in patients aged 18 to 64 years on both unadjusted and adjusted analyses. The odds of cardiac arrest after TAVR showed a decreasing trend on unadjusted analysis, but this trend was no longer significant when we accounted for comorbidities in patients aged 65 to 80 years on adjusted analysis. However, the decreasing trend is seen in patients aged >80 years on both unadjusted and adjusted analyses. Hence, improvement in procedural characteristics appears to have made a difference in this age group, likely because of increased vulnerability to these complications.

Similar variability was seen in noncardiac complications as well. The reduction in the length of stay and increase in discharge rate within 24 and 72 hours likely relate to the improvements in the procedure, because these findings were seen even after accounting for the decreasing risk profile in the adjusted analysis.

The inflation-adjusted cost decreased by about $15,000 in all age groups from 2012 to 2018. Although decreasing risk profile over time accounted for some of these decreasing costs, procedural factors, including better valves, smaller sheaths, improved quality of preoperative computed tomography imaging for procedural planning, and increased operator experience also likely contributed to these improvements. Reynolds et al evaluated the cost-effectiveness of TAVR using PARTNER A trial data and found that TAVR was of intermediate to high economic value compared with SAVR in high-risk patients, especially in patients with transfemoral TAVR. The incremental cost-effectiveness ratio for balloon expanding valve versus SAVR was $76,877 per quality-adjusted life-year. Further evaluation of self-expanding valve versus SAVR in high-risk populations showed an incremental cost-effectiveness ratio of $55,090 per quality-adjusted life-year overall and $52,897 per quality-adjusted life-year for patients who had transfemoral TAVR.

A study by Baron et al evaluated the hospital costs of intermediate-risk patients who received a SAPIEN XT valve in the PARTNER 2A trial and SAPIEN 3 valves in the SAPIEN-3 intermediate risk registry and found that TAVR was projected to be more cost-effective than SAVR in terms of higher quality-adjusted life expectancy and lower long-term follow-up costs. These cost savings were driven by the lower length of stay during the index hospitalization, lower rehospitalizations, and lower skilled-nursing facility and rehabilitation days. These benefits were only seen in patients with transfemoral access on stratified analysis. Furthermore, SAPIEN 3 valves used in the SAPIEN-3 intermediate risk registry were more cost-effective than earlier-generation SAPIEN XT valves used in the PARTNER 2A trial. These differences could again be likely attributable to the higher use of transfemoral access (88%) in the registry compared with the PARTNER 2A trial. Moreover, a recent meta-analysis by Tam et al evaluated the cost-effectiveness in low-risk patients who underwent balloon-expandable TAVR in the PARTNER 3 trial and self-expanding TAVR in the Evolute low-risk trial versus SAVR. The incremental cost-effectiveness ratio for balloon-expanding TAVR and self-expandable
TAVR against SAVR were $27,196 and $59,164, respectively.24 The improving trends in cost related to improvements in procedural safety over time seen in our study are also encouraging and will make TAVR even more cost-effective in the future.

Our study has several limitations. The NIS is an administrative database rather than a clinical database, relying on ICD coding to identify diagnoses. Different hospital coding practices could lead to misclassification bias because of inaccurate coding. The NIS does not have laboratory, medication, and imaging information, so these variables’ effects on outcomes cannot be studied in this database. Residual confounding is also possible. For example, the count of conditions from the Elixhauser Comorbidity Index only partially represents patient health status. We also conducted numerous statistical tests to assess many outcomes across subgroups, and some findings may have been attributable to chance.

Despite those limitations, this study has many strengths. To our knowledge, this is the first study to examine post-TAVR trends in outcomes and resource use stratified by age and quantify the effect of changes in procedural characteristics on these outcomes by accounting for the change in the risk profile of patients over time. In addition, the NIS is the largest all-payer database representing hospitals from all regions of the United States and hence is generalizable to the US population. The large sample size also increases power and minimizes the chances of type II error. Finally, the NIS has information on hospital charges and cost not available in many studies.

CONCLUSIONS
From 2012 to 2018, most outcomes of TAVR improved or at least did not worsen in analyses stratified by age groups, with and without adjustment for patient characteristics. Some improvements are explained by the decreasing risk profile of patients in all age groups, but others appear attributable to the improvement in procedural characteristics over time.

ARTICLE INFORMATION
Received May 14, 2022; accepted September 28, 2022.

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Sources of Funding
None.

Disclosures
None.

Supplemental Material
Table S1

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| Variables                                      | ICD-9 codes | ICD-10 codes                     |
|------------------------------------------------|-------------|---------------------------------|
| Transcatheter aortic valve replacement (TAVR) | **3505**    | '02RF372','02RF382','02RF3J2','02RF3K2' |
| Acute myocardial infarction                    | "4107","4100","4101","4102","4103","4104","4105","4106","4108","4109" | "I2101","I2102","I2109","I2111","I2119","I2121","I2129","I213","I214","I219","I21A1","I21A9","I220","I221","I222","I228","I229" |
| New pacemaker placement                        | "3780","3781","3782","3783","0050","0051" | "0JH6042","0JH6342","0JH8042","0JH8342","0JH6052","0JH6352","0JH8052","0JH8352","0JH6062","0JH6362","0JH8062","0JH8362","0JH6072","0JH6372","0JH8072","0JH8372","0JH6092","0JH6392","0JH8092","0JH8392","02HK3J2","02H66J2","02H69J2","02H60J2","02H60NZ","02H63J2","02H64NZ","02HKOJ2","02H64NZ","02HK3J2","02HK4NZ","02HK4NZ" |
| Cardiogenic shock                              | "78551"     | "R570","T8111X0","T8111XD","T8111XS" |
| Cardiac arrest                                 | "4275"      | "I462","I468","I469","I97120","I97121","I97170","I97711" |
| Acute renal failure                            | "5845","5846","5847","5848","5849" | 'N170','N171','N172','N178','N179' |
| Bleeding requiring blood transfusion           | "9900","9901","9902","9903","9904" | "30243N0","30243N1","30243P0","30243P1","30243H0","30243H1","30240N0","30240N1","30240P0","30240P1","30240H0","30240H1","30230H0","30230H1","30230N0","30230N1","30230P0","30230P1","30233N0","30233N1","30233P0","30233P1","30233H0","30233H1" |
| Acute ischemic stroke                          | "43301","43311","43321","43331","43381","43391","43401","43411","43491","436" | 'I6300', 'I63011', 'I63012', 'I63013', 'I63019', 'I6302', 'I63031', 'I63032', 'I63033', 'I63039', 'I6309', 'I6310', 'I6311', 'I6312', 'I63131', 'I63132', 'I63139', 'I6319', 'I6319', 'I6320', 'I6321', 'I63212', 'I63213', 'I63219', 'I6322', 'I63231', 'I63232', 'I63233', 'I63239', 'I6329', 'I6330', 'I63311', 'I63312', 'I63313', 'I63319', 'I63321', 'I63322', 'I63323', 'I63329', 'I6333', 'I63331', 'I63332', 'I63333', 'I63339', 'I63341', 'I63342', 'I63343', 'I63349', 'I6339', 'I6340', 'I6341', 'I63412', 'I63413', 'I63419', 'I63419', 'I63421', 'I63422', 'I63423', 'I63429', 'I63431', 'I63432', 'I63433', 'I63439', 'I63441', 'I63442', 'I63443', 'I63449', 'I6349', 'I6350', 'I63511', 'I63512', 'I63513', 'I63519', 'I63521', 'I63522', 'I63523', 'I63529', 'I63531', 'I63532', 'I63533', 'I63539', 'I63541', 'I63542', 'I63543', 'I63549', 'I6359', 'I6359' |
| Acute respiratory failure requiring mechanical ventilation | '9390', '9601', '9602', '9603', '9604', '9670', '9671', '9672', '09HN7BZ', '09HN8BZ', '0BH17EZ', '0BH18EZ', '0CHY7BZ', '0CHY8BZ', '0DH57BZ', '0DH58BZ', '5A09357', '5A09457', '5A09557', '5A1935Z', '5A1945Z', '5A19552', '1636', '16381', '16389', '1639' |