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Title: In-Hospital Outcomes of Transcatheter Aortic Valve Replacement in Patients with Mitral Valve Stenosis

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Abstract: Background: Little is known about the outcome of patients with MS undergoing transcatheter aortic valve replacement (TAVR). Therefore, we sought to evaluate the potential impact of MS on the outcome of patients who underwent TAVR using the US national cohort.

Method: Using weighted data from the National Inpatient Sample (NIS) database between 2011 and 2015, we identified patients who had undergone a TAVR as a primary procedure. Patients with MS diagnosis were compared to those without MS. Univariate and multivariate logistic regression analysis were performed for the outcomes of in-hospital mortality and post-procedural complications. Outcomes were also stratified by the type to TAVR (endovascular versus transapical).

Results: A total of 62,110 patients underwent TAVR (mean age  $81 \pm 8.72$ , 47.4% females, and 3.7% African Americans) and 887 patients had MS (1.43%). Patients with concomitant MS had higher in-hospital mortality (5.1% vs 3.5% adjusted Odds Ratio [aOR], 1.455; 95% confidence interval [CI], 1.059-2.001,  $P=0.021$ ), major adverse cardiac events (MACE) (9.0% vs 7.1% aOR, 1.297; 95% CI, 1.012-1.663,  $P=0.040$ ), major bleeding (16.3% vs 12.1% aOR, 1.303; 95% CI, 1.067-1.593,  $P=0.010$ ), cardiac complications (21.8% vs 16.0% aOR, 1.536; 95% CI, 1.300-1.815,  $P<0.001$ ) and acute myocardial infarction (AMI) (4.5% vs 2.8% aOR, 1.783; 95% CI, 1.249-2.545,  $P=0.007$ ) when compared with patients without MS.

Conclusion: Mitral stenosis is an independent risk factor for mortality and morbidity after TAVR procedure for patients with severe AS.

## **In-Hospital Outcomes of Transcatheter Aortic Valve Replacement in Patients with Mitral Valve Stenosis**

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**Keywords:** Transcatheter aortic valve replacement, mitral stenosis, Mortality.

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## **Abstract**

**Background:** Little is known about the outcome of patients with MS undergoing transcatheter aortic valve replacement (TAVR). Therefore, we sought to evaluate the potential impact of MS on the outcome of patients who underwent TAVR using the US national cohort.

**Method:** Using weighted data from the National Inpatient Sample (NIS) database between 2011 and 2015, we identified patients who had undergone a TAVR as a primary procedure. Patients with MS diagnosis were compared to those without MS. Univariate and multivariate logistic regression analysis were performed for the outcomes of in-hospital mortality and post-procedural complications. Outcomes were also stratified by the type to TAVR (endovascular versus transapical).

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**Conclusion:** Mitral stenosis is an independent risk factor for mortality and morbidity after TAVR procedure for patients with severe AS.

**Introduction:**

Transcatheter aortic valve replacement (TAVR) is now the standard of care for patients with severe aortic valve stenosis (AS) who are at high and intermediate risk for surgical aortic valve replacement (SAVR) <sup>1-5</sup>. The coexistence of mitral stenosis (MS) and aortic stenosis (AS) is far from being exceptional in SAVR. Current registries suggest a prevalence of 11.6% of mitral stenosis in patients undergoing TAVR <sup>6</sup>. In one study, 17% of patients referred for aortic valve replacement were found to have mitral stenosis <sup>7</sup> with double valve surgery associated with higher operative mortality and lower long-term survival rates compared with those undergoing isolated aortic valve replacement <sup>7,8</sup>. Furthermore, the risk of thromboembolism is higher in patients undergoing double valve replacement compared with patients undergoing isolated aortic valve replacement <sup>9</sup>.

The periprocedural hemodynamic effect of mitral stenosis in patients undergoing TAVR is not well understood. Although mitral regurgitation has been an established risk factor for increased morbidity and mortality in TAVR patients <sup>10,11</sup>, there is limited data regarding the outcome of TAVR patients with concomitant aortic stenosis and mitral stenosis. Many explanations have been proposed for the effect of MS on left ventricular (LV) hemodynamics including reduction in LV filling, reduction of LV compliance and diastolic dysfunction, increased afterload, and pulmonary hypertension <sup>12,13</sup> leading to potentially increased cardiovascular and overall morbidity and mortality. Furthermore, the presence of mitral annular calcification was associated with a higher overall and cardiac mortality, along with post-procedural morbidity <sup>14</sup>. Therefore, we sought to evaluate the impact of mitral stenosis on the in-hospital outcome of patients undergoing TAVR using the National Inpatient Sample (NIS).

**Method:**

### *Patient selection*

Using the NIS database from 2011 to 2015, we performed a retrospective analysis. The NIS is a publicly available identified database of hospital discharges in the United States, containing data from approximately 8 million hospital stays that were selected using a complex probability sampling design and the weighting scheme recommended by the Agency for Healthcare Research and Quality which is intended to represent all discharges from nonfederal hospitals. Each record includes one primary diagnosis and up to 24 secondary diagnoses from 2011 to 2014 and up to 29 secondary diagnoses from 2014 to 2015. After weighing the data, we identified 62,110 adult patients who had undergone TAVR as a primary procedure using the International Classification of Disease, Ninth Edition, Clinical Modification (ICD-9-CM) codes (35.05 and 35.06), out of which 887 patients with MS diagnosis (regardless of etiology) using the codes (394.0 and 396.0). Patients with concomitant mitral valve repair were excluded. Using the Clinical Classification Software codes provided by the Healthcare Cost and Utilization Project and the Elixhauser Comorbidity Index, comorbidities were appointed via ICD-9 codes. Supplemental table 1 identifies comorbidities from the Elixhauser comorbidity index, and ICD-9 codes used for other comorbidities and in-hospital outcomes. Institutional board review approval is not required as the NIS is a publicly available database.

### *Outcomes*

The primary outcome of the study was in-hospital mortality. The secondary outcomes were in-hospital complications which included hemorrhage requiring blood transfusion, vascular complications (injury to blood vessels, accidental puncture, injury to retroperitoneum, other vascular complications, vascular complications requiring surgery), cardiac complications (iatrogenic cardiac complications, hemopericardium, cardiac tamponade and pericardiocentesis), permanent pacemaker (PPM) implantation, conversion to open-heart

surgery, respiratory complications (post-procedural pneumothorax, post-procedural pulmonary edema, pulmonary collapse, prolonged mechanical ventilation >96 hours, tracheostomy), post-procedural stroke, and acute kidney injury (AKI). All procedure-related complications were identified using appropriate ICD-9- CM codes (Supplementary Table 1).

### *Statistical analysis*

The data was expressed as weighted mean values  $\pm$  standard deviation, and frequencies were denoted in percentages according to the presence or absence of MS. Independent t-tests were used for the comparison of continuous variables measurements, while chi-square test for categorical variables. Weighted values of patient level observations were generated to produce a nationally representative estimate of the entire US population of hospitalized patients. Univariable and multiple logistic regressions were used to study the association between the MS and the primary and secondary outcomes after TAVR. The regression models were adjusted for demographics (age, race and gender), urgency of TAVR (elective versus emergent), included Elixhauser comorbidities (other than valvular disorders), other relevant comorbidities (atrial fibrillation, smoking, carotid artery disease, coronary artery disease, prior stroke and dyslipidemia), TAVR access (endovascular or transapical), patient insurance, socioeconomic status and hospital characteristics. Linear regression models were used to assess the length of stay (LOS). Log transformation of LOS was used to adjust for positively skewed data. We performed a subgroup analysis by further stratifying patients for TAVR access for all outcomes. To further explore our findings, we performed multivariate logistic regression for the predictors of having MS in patients who underwent TAVR. For the trend analysis, Cochran-Armitage test was used to determine the presence of a linear trend in MS rates in patients who underwent TAVR during the studied years. P-value of less than 0.05 was considered statistically significant. SPSS version 25 software (IBM Corp, Armonk, NY) was used for all statistical analyses.

## **Results:**

### *Baseline Characteristics*

During the study period, a total of 62,110 patients underwent TAVR (mean age  $81 \pm 8.72$ , 47.4% females, and 3.7% African Americans). We identified 887 patients with MS (1.43%) and compared them with 61,233 (98.57%) patients without MS. Patients in the MS group were younger (79.10 vs 81.02,  $P < 0.001$ ) more females (65.6% vs 47.2%) and African American patients (7.9% vs 3.9%) ( $P < 0.001$  for both). Furthermore, the MS group had a lower burden of several comorbidities including hypertension (HTN), coronary artery disease (CAD), rheumatoid arthritis, psychosis and hyperlipidemia (HLD) ( $P < 0.001$ ). However, other comorbid conditions such as diabetes mellitus (DM), deficiency anemia, chronic pulmonary disease, hypothyroidism, fluid and electrolyte disorders, peripheral vascular disease (PAD) and pulmonary circulation disorders were more prevalent in the MS group. Baseline characteristics stratified by MS status is described in table 1.

In patients who underwent TAVR, and using multivariate logistic regression, female gender, African American race, complicated and uncomplicated diabetes mellitus, fluid and electrolyte disorders, peripheral vascular disease, pulmonary circulation disorders and renal failure were identified as predictors of having MS ( $P \leq 0.049$  for all). Female gender and pulmonary circulation disorders had the highest odds of having MS (OR, 2.178; 95% CI, 1.862-2.547,  $P < 0.001$ ), (OR, 2.319; 95% CI, 1.589-3.384,  $P < 0.001$ ), respectively (table 3). Younger patients were more likely to have MS (OR, 0.979; 95% CI, 0.971-0.988,  $P < 0.001$ ).

Using the Cochran-Armitage method, there was a statistically significant linear increase in the rate of MS patients undergoing TAVR from 1.0% to 1.6% between the years of 2011 and 2014 ( $P < 0.001$ ) (figure 3).

### *In-hospital Outcomes*

Following adjustment for baseline covariates, patients with MS had a statistically significant higher in-hospital mortality compared to the non-MS group after adjusting for patients' demographics, TAVR access, urgency, comorbidities, patient insurance, socioeconomic status and hospital characteristics (5.1% vs 3.5% adjusted Odds Ratio [aOR], 1.455; 95% confidence interval [CI], 1.059-2.001,  $P = 0.021$ ) (Figure 1). Furthermore, MS patients had a statistically significant higher major adverse cardiac events (MACE) (9.0% vs 7.1% aOR, 1.297; 95% CI, 1.012-1.663,  $P=0.040$ ), major bleeding (16.3% vs 12.1% aOR, 1.303; 95% CI, 1.067-1.593,  $P=0.010$ ), cardiac complications (21.8% vs 16.0% aOR, 1.536; 95% CI, 1.300-1.815,  $P<0.001$ ), and acute myocardial infarction (AMI) (4.5% vs 2.8% aOR, 1.783; 95% CI, 1.249-2.545,  $P=0.007$ ) when compared with non-MS patients. Interestingly, MS patients had statistically significant lower vascular complications when compared with non-MS patients (2.3% vs 3.7% aOR, 0.487; 95% CI, 0.308-0.768,  $P=0.002$ ) (figure 2). Risk-adjusted linear regression for length of stay demonstrated no statistically significant difference in length of stay between MS and non-MS groups ( $P=0.553$ ). The rates of PPM placement, respiratory complications, post-procedural stroke and conversion open heart surgery were comparable in both groups (Table 2).

Upon further stratifying the analysis by TAVR access, patients with MS undergoing endovascular TAVR had statistically significant higher in-hospital mortality (aOR 1.495; 95% CI, 1.016-2.095,  $P=0.041$ ), major bleeding (aOR 1.329; 95% CI, 1.072-1.593,  $P=0.009$ ), cardiac complications (aOR 1.462; 95% CI, 1.217-1.757,  $P < 0.001$ ), AMI (aOR 1.700; 95% CI, 1.156-2.502,  $P=0.007$ ). In addition, MS patients undergoing transapical TAVR had statistically significant higher cardiac complications (aOR 1.756; 95% CI, 1.1156-2.668,  $P=0.008$ ), respiratory complications (aOR 1.874; 95% CI, 1.254-2.801,  $P=0.002$ ) and acute kidney injury (aOR 3.769; 95% CI, 2.502-5.676,  $P < 0.001$ ) when compared with non-MS patients.



## **Discussion:**

In our national analysis of TAVI patients, we found that a small proportion (1.4%) to have mitral stenosis. The rates of mitral stenosis in this population with TAVR have been increasing over time from 1.0% to 1.6%. Furthermore, these patients with MS who undergo TAVR are more likely to be younger, female, African American and more likely to have diabetes mellitus, peripheral vascular disease, pulmonary circulation disorders and fluid and electrolyte disorder. Patients who underwent TAVR with MS had higher in-hospital mortality and adverse outcomes compared to patients without MS. These findings suggest that patients with MS who undergo TAVR are a high risk group, and measure for improving outcomes in this population is needed.

Patients who are referred for a TAVR procedure are often older and have more cardiovascular comorbidities. Although patients with MS were significantly younger compared to those without MS, they had higher rates of DM, chronic pulmonary disease, pulmonary circulation disorders, PAD, and deficiency anemia. The proposed mechanism for MS-induced LV dysfunction is due to myocardial inflammation that occurs in the acute phase of rheumatic fever, and the chronic hemodynamics changes triggered by change in preloading conditions <sup>12</sup>. Furthermore, MS has been frequently identified as a cause of elevated pulmonary artery pressure and pulmonary hypertension (PH) <sup>15</sup>. The changes in the LV preload and PH could explain the elevated risk of cardiac complications and mortality since PH is already known to be an independent risk factor for morbidity and mortality in TAVR patients, which is consistent with our findings <sup>16</sup>.

The recently published work by Jospeh et al. <sup>6</sup> has demonstrated a higher in-hospital mortality in patients with severe MS who underwent TAVR, which supports our findings. In addition, the 1-year mortality and the composite outcome of mortality, stroke, heart failure-related hospitalization and re-intervention of mitral disease were higher in both severe MS and non-severe MS patients who underwent TAVR. We have added to these findings by demonstrating a

higher MACE in MS patients compared with patients without MS. Interestingly, non-severe MS had no statistically significant difference in in-hospital mortality when compared with patients without MS.

In TAVR, the retrograde aortic approach has increased odds of left ventricular perforation causing pericardial effusions <sup>17,18</sup>. In our study, cardiac complications, including iatrogenic complications and cardiac tamponade, were significantly increased in MS patients compared with non-MS patients. Our population showed a rate of 21.8% in cardiac complications in those with MS compared to 16.0% in patients without MS. The increased risk of cardiac complications could be attributed to the LV dysfunction associated with MS <sup>12</sup>.

Our study showed that 4.5% of MS group suffered a post-procedural myocardial infarction compared with 2.8% in the non-MS group. Even after adjusting for potential cofounder, MS patients had almost 78% increased odds of AMI. Interestingly, previous literature had demonstrated the rate of AMI was comparable between MS and non-MS groups regardless of MS severity <sup>6</sup>.

Given our findings, we suggest a thorough pre-operative risk evaluation for MS patients requiring TAVR through hemodynamic evaluation. A possible expansion of hemodynamic assessment, especially in patients with clinical evidence of PH might improve the predictability of the procedural outcomes. The ACC/TAVI in-hospital mortality score has incorporated severe chronic pulmonary disease as predictor for worse outcomes in patients undergoing TAVR <sup>19</sup>. More studies are needed to further identify measures to minimize the procedural risk associated with this high risk population.

Our study has several limitations as it was a retrospective observational study, which poses a possible selection bias and unmeasured confounding factors. Moreover, the National Inpatient

Sample is an administrative database which could be subject to inaccurate coding and underreporting of comorbid diagnoses. In addition, data regarding the severity of mitral valve stenosis and other relevant echo parameters were missing. Furthermore, details of the TAVR procedure were not reported such as; the type of device used, anesthesia type and the amount of contrast used which pose possible confounding factors.

## **Conclusions**

Mitral stenosis patients had higher in-hospital mortality in patients undergoing TAVR with increased risk of major bleeding, cardiac complications and acute myocardial infarction. Based on these findings, we propose assessment of hemodynamics prior to TAVR procedure especially in patients with echocardiographic evidence for MS.

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TABLE 1. Baseline characteristics stratified by presence of MS.

| Variable                           | MS<br>(n=887) | No MS<br>(n=61,233) | P-Value |
|------------------------------------|---------------|---------------------|---------|
| <b>Age (mean±SD)</b>               | 79.10 ± 9.87  | 81.02 ± 8.70        | <0.001  |
| <b>Females, %</b>                  | 65.6          | 47.2                | <0.001  |
| <b>Race, %</b>                     |               |                     | <0.001  |
| White                              | 85.5          | 87.4                |         |
| Black                              | 7.9           | 3.9                 |         |
| Hispanic                           | 2.4           | 4.0                 |         |
| Asian or pacific islander          | 1.8           | 1.1                 |         |
| Native American                    | 0.0           | 0.2                 |         |
| Other                              | 2.4           | 3.4                 |         |
| <b>Elective hospitalization, %</b> | 75.0          | 76.6                | 0.599   |
| <b>Primary expected payer, %</b>   |               |                     | 0.012   |
| Medicare                           | 90.4          | 90.1                |         |
| Medicaid                           | 1.7           | 1.1                 |         |
| Private insurance                  | 7.3           | 7.0                 |         |
| Self-pay                           | 0.6           | 0.5                 |         |
| No Charge                          | 0.0           | 0.0                 |         |
| Other                              | 0.0           | 1.3                 |         |
| <b>Median household income, %</b>  |               |                     | 0.230   |
| 0 to 25 percentiles                | 21.0          | 19.9                |         |
| 26 to 50 percentiles               | 24.8          | 23.3                |         |
| 51 to 75 percentiles               | 25.9          | 28.8                |         |
| 76 to 100 percentiles              | 28.2          | 28.0                |         |
| <b>Bed size, %</b>                 |               |                     | 0.914   |
| Small                              | 4.5           | 4.8                 |         |
| Medium                             | 17.5          | 17.7                |         |
| Large                              | 78.9          | 77.5                |         |
| <b>Location/teaching status, %</b> |               |                     | 0.300   |
| Rural                              | 1.1           | 0.7                 |         |
| Urban nonteaching                  | 8.8           | 9.5                 |         |
| Urban teaching                     | 90.1          | 89.8                |         |
| <b>Hospital region, %</b>          |               |                     | <0.001  |
| Northeast                          | 21.3          | 25.4                |         |
| Midwest                            | 20.3          | 22.3                |         |
| South                              | 34.9          | 33.8                |         |
| West                               | 23.4          | 18.5                |         |
| <b>TAVR access</b>                 |               |                     |         |
| Endovascular access                | 1.2           | 84.3                | 0.076   |
| Transapical Access                 | 0.2           | 15.9                | 0.055   |
| <b>Comorbidities</b>               |               |                     |         |
| Hypertension, %                    | 74.6          | 80.5                | <0.001  |
| Diabetes, uncomplicated, %         | 34.9          | 29.2                | <0.001  |
| Diabetes, complicated, %           | 7.3           | 6.0                 | 0.107   |
| Hyperlipidemia, %                  | 55.7          | 65.4                | <0.001  |
| Smoking, %                         | 2.8           | 3.2                 | 0.486   |

|   |      |      |        |
|---|------|------|--------|
| Atrial fibrillation, %                            | 41.6 | 44.2 | 0.127  |
| Prior stroke, %                                   | 14.1 | 13.1 | 0.385  |
| Carotid disease, %                                | 6.8  | 7.4  | 0.446  |
| Coronary artery disease, %                        | 57.9 | 68.9 | <0.001 |
| Acquired immune deficiency, %                     | 0.0  | 0.0  | 0.703  |
| Alcohol Abuse, %                                  | 0.6  | 1.1  | 0.124  |
| Deficiency anemia, %                              | 30.1 | 24.8 | <0.001 |
| Rheumatoid arthritis/collagen vascular disease, % | 6.2  | 4.7  | 0.039  |
| Chronic blood loss anemia, %                      | 0.6  | 1.3  | 0.050  |
| Congestive heart failure, %                       | 9.6  | 8.4  | 0.205  |
| Chronic pulmonary disease, %                      | 36.6 | 33.0 | 0.024  |
| Coagulopathy, %                                   | 20.2 | 22.3 | 0.128  |
| Depression, %                                     | 9.0  | 7.5  | 0.080  |
| Drug abuse, %                                     | 0.6  | 0.3  | 0.161  |
| Hypothyroidism, %                                 | 25.8 | 20.3 | <0.001 |
| Liver disease, %                                  | 3.4  | 2.6  | 0.150  |
| Lymphoma, %                                       | 0.6  | 1.3  | 0.051  |
| Fluid and electrolyte disorders, %                | 30.4 | 25.1 | <0.001 |
| Metastatic cancer, %                              | 0.0  | 0.4  | 0.057  |
| Solid tumor without metastasis, %                 | 1.7  | 2.0  | 0.564  |
| Other neurological disorders, %                   | 6.8  | 6.3  | 0.604  |
| Obesity, %  | 16.9 | 14.7 | 0.069  |
| Paralysis, %                                      | 2.3  | 1.7  | 0.233  |
| Psychosis, %                                      | 0.6  | 1.8  | 0.007  |
| Renal Failure, %                                  | 38.3 | 35.7 | 0.117  |
| Peripheral arterial disease, %                    | 34.4 | 29.2 | 0.001  |
| Pulmonary circulation disorders, %                | 5.6  | 2.6  | <0.001 |
| Peptic ulcer excluding bleeding, %                | 0.0  | 0.0  | 0.641  |
| Weight loss                                       | 4.5  | 4.7  | 0.813  |

Abbreviations: MS – mitral stenosis; TAVR – transcatheter aortic valve replacement.



TABLE 2. In-hospital outcomes of mitral stenosis patients who underwent TAVR when compared with those without mitral stenosis.

| Outcome                                 | MS                | Non-MS   | UOR (95% CI) MS<br>(when compared<br>with no MS) | aOR (95% CI) MS<br>(when compared<br>with no MS) | Unadjusted<br>P-Value | Adjusted<br>P-Value |
|---|-------------------|----------|--|--|-----------------------|---------------------|
| <b>Overall (n)</b>                      | 887               | 61,233   |  |  |                       |                     |
| Endovascular (n)                        | 767               | 51,614   |  |  |                       |                     |
| Transapical (n)                         | 120               | 9,738    |  |  |                       |                     |
| <b>MACE</b>                             | 9.0%              | 7.1%     | 1.296 (1.028-1.634)                              | 1.297 (1.012-1.663)                              | 0.028                 | 0.040               |
| Endovascular                            | 8.5%              | 6.8%     | 1.264 (0.978-1.633)                              | 1.240 (0.940-1.637)                              | 0.073                 | 0.128               |
| Transapical                             | 12.5%             | 8.7%     | 1.507 (0.874-2.601)                              | 1.759 (0.994-3.111)                              | 0.140                 | 0.052               |
| <b>NACE</b>                             | 23.0%             | 19.7%    | 1.216 (1.039-1.424)                              | 1.090 (0.917-1.295)                              | 0.015                 | 0.330               |
| Endovascular                            | 23.4%             | 19.8%    | 1.233 (1.041-1.459)                              | 1.183 (0.993-1.410)                              | 0.015                 | 0.060               |
| Transapical                             | 20.8%             | 19.4%    | 1.094 (0.702-1.705)                              | 0.981 (0.615-1.564)                              | 0.702                 | 0.935               |
| <b>In-hospital mortality</b>            | 5.1%              | 3.5%     | 1.474 (1.088-1.995)                              | 1.455 (1.059-2.001)                              | 0.012                 | 0.021               |
| Endovascular                            | 4.6%              | 3.2%     | 1.444 (1.025-2.034)                              | 1.495 (1.016-2.095)                              | 0.035                 | 0.041               |
| Transapical                             | 8.3%              | 5.2%     | 1.666 (0.866-3.202)                              | 1.629 (0.809-3.277)                              | 0.126                 | 0.172               |
| <b>Length of stay (iQR), days</b>       | 5 (4-9)           | 5 (3-9)  |  |  |                       | 0.553               |
| Endovascular                            | 5 (4-8)           | 5 (3-8)  |  |  |                       | 0.389               |
| Transapical                             | 7.50 (5.25-13.50) | 7 (5-12) |  |  |                       | 0.573               |
| <b>Major Bleeding</b>                   | 16.3%             | 12.1%    | 1.404 (1.172-1.681)                              | 1.303 (1.067-1.593)                              | <0.001                | 0.010               |
| Endovascular                            | 16.8%             | 12.3%    | 1.443 (1.192-1.747)                              | 1.329 (1.072-1.684)                              | <0.001                | 0.009               |
| Transapical                             | 12.5%             | 11.5%    | 1.104 (0.640-1.903)                              | NA   | 0.723                 | NA                  |
| <b>Vascular complications</b>           | 2.3%              | 3.7%     | 0.601 (0.385-0.938)                              | 0.487 (0.308-0.768)                              | 0.025                 | 0.002               |
| Endovascular                            | 2.6%              | 3.9%     | 0.652 (0.417-1.019)                              | 0.515 (0.325-0.816)                              | 0.060                 | 0.005               |
| Transapical                             | 0.0%              | 2.4%     | NA   | NA   | NA                    | NA                  |
| <b>Cardiac complications</b>            | 21.8%             | 16.0%    | 1.461 (1.243-1.716)                              | 1.536 (1.300-1.815)                              | 0.082                 | <0.001              |
| Endovascular                            | 20.6%             | 15.8%    | 1.379 (1.155-1.645)                              | 1.462 (1.217-1.757)                              | <0.001                | <0.001              |
| Transapical                             | 29.2%             | 16.8%    | 2.042 (1.373-3.038)                              | 1.756 (1.156-2.668)                              | <0.001                | 0.008               |
| <b>AMI</b>                              | 4.5%              | 2.8%     | 1.669 (1.211-2.300)                              | 1.783 (1.249-2.545)                              | 0.002                 | 0.001               |
| Endovascular                            | 4.6%              | 2.8%     | 1.683 (1.194-2.372)                              | 1.700 (1.156-2.502)                              | 0.003                 | 0.007               |
| Transapical                             | 4.2%              | 2.7%     | 1.591 (0.644-3.929)                              | 2.203 (0.820-5.919)                              | 0.314                 | 0.117               |
| <b>Permanent pacemaker implantation</b> | 11.6%             | 10.4%    | 1.129 (0.918-1.389)                              | 1.219 (0.984-1.512)                              | 0.250                 | 0.070               |
| Endovascular                            | 12.1%             | 11.1%    | 1.100 (0.884-1.369)                              | 1.204 (0.960-1.511)                              | 0.392                 | 0.109               |
| Transapical                             | 8.3%              | 6.6%     | 1.297 (0.675-2.490)                              | 1.280 (0.652-2.516)                              | 0.435                 | 0.473               |
| <b>Open heart surgery</b>               | 2.8%              | 2.1%     | 1.379 (0.923-2.061)                              | 1.292 (0.858-1.946)                              | 0.116                 | 0.220               |
| Endovascular                            | 3.3%              | 2.1%     | 1.560 (1.043-2.335)                              | 1.497 (0.991-2.260)                              | 0.031                 | 0.055               |
| Transapical                             | 0.0%              | 1.8%     | NA   | NA   | <0.001                | NA                  |
| <b>Respiratory complications</b>        | 15.2%             | 12.2%    | 1.290 (1.073-1.552)                              | 1.172 (0.954-1.440)                              | 0.007                 | 0.131               |
| Endovascular                            | 12.4%             | 10.4%    | 1.218 (0.981-1.513)                              | 0.957 (0.747-1.226)                              | 0.074                 | 0.827               |
| Transapical                             | 33.3%             | 22.0%    | 1.777 (1.212-2.606)                              | 1.874 (1.254-2.801)                              | 0.003                 | 0.002               |
| <b>Post-procedural stroke</b>           | 1.1%              | 1.3%     | 0.864 (0.461-1.617)                              | 0.623 (0.302-1.287)                              | 0.647                 | 0.201               |
| Endovascular                            | 0.7%              | 1.3%     | 0.503 (0.208-1.217)                              | 0.412 (0.158-1.071)                              | 0.128                 | 0.069               |
| Transapical                             | 4.2%              | 1.4%     | 3.116 (1.252-7.753)                              | 1.612 (0.278-9.345)                              | 0.015                 | 0.594               |
| <b>Acute kidney injury</b>              | 20.3%             | 17.6%    | 1.194 (1.013-1.408)                              | 1.016 (0.836-1.235)                              | 0.035                 | 0.871               |
| Endovascular                            | 16.3%             | 16.3%    | 0.999 (0.824-1.212)                              | 0.705 (0.558-0.891)                              | 0.995                 | 0.003               |
| Transapical                             | 45.8%             | 24.2%    | 2.645 (1.842-3.799)                              | 3.769 (2.502-5.676)                              | <0.001                | <0.001              |

Abbreviations: AMI – acute myocardial infarction; aOR – adjusted odds ratio; IQR – interquartile range; MS– mitral stenosis; MACE – major adverse cardiovascular events; NACE – net adverse cardiovascular events; TAVR – transcatheter aortic valve replacement; uOR – unadjusted odds ratio. Unadjusted odds ratios are displayed given low event rate. NA indicates odds ratio could not be calculated due to an event rate of 0%

TABLE 3. The predictors of mitral stenosis in patients who underwent transcatheter aortic valve replacement.

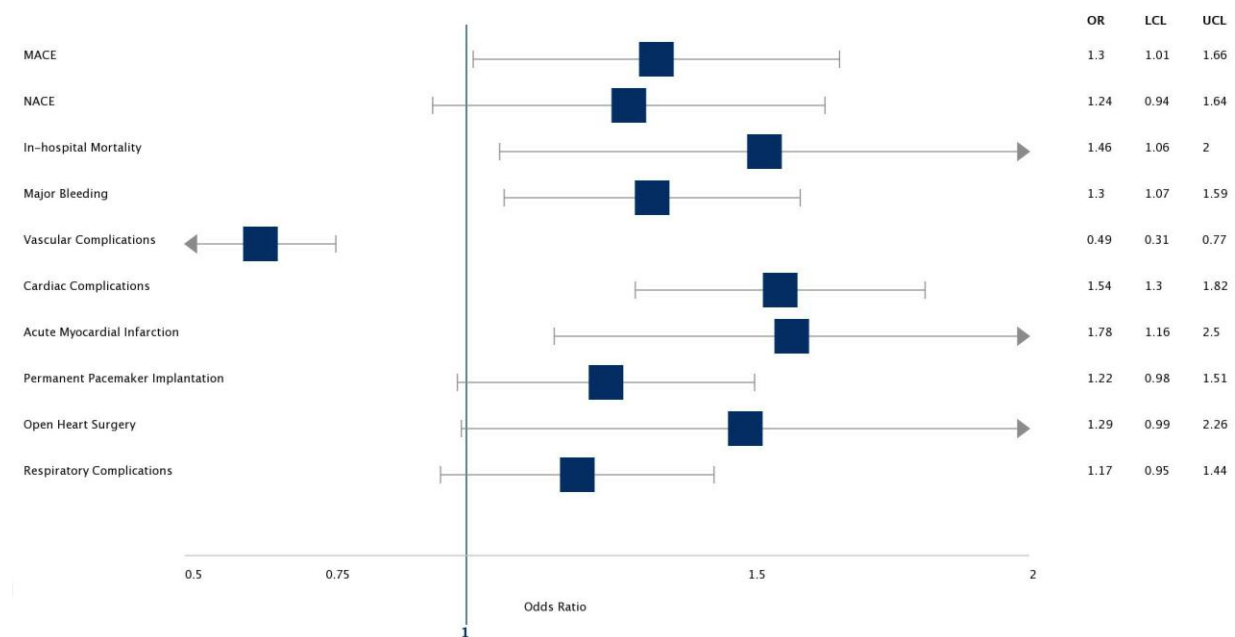
| Predictor                       | OR (95% CI)         | P-Value |
|---------------------------------|---------------------|---------|
| Age                             | 0.979 (0.971-0.988) | <0.001  |
| Female Gender                   | 2.178 (1.862-2.547) | <0.001  |
| African American Race           | 1.674 (1.277-2.197) | <0.001  |
| Uncomplicated Diabetes          | 1.375 (1.177-1.606) | <0.001  |
| Complicated Diabetes            | 1.325 (1.001-1.755) | 0.049   |
| Fluid and Electrolyte Disorders | 1.182 (1.011-1.383) | 0.036   |
| Peripheral Vascular Disease     | 1.395 (1.201-1.621) | <0.001  |
| Pulmonary Circulation Disorders | 2.319 (1.589-3.384) | <0.001  |
| Renal Failure                   | 1.205 (1.037-1.401) | 0.015   |

Abbreviations: OR– odds ratio; CI – confidence interval.

# Figure 1

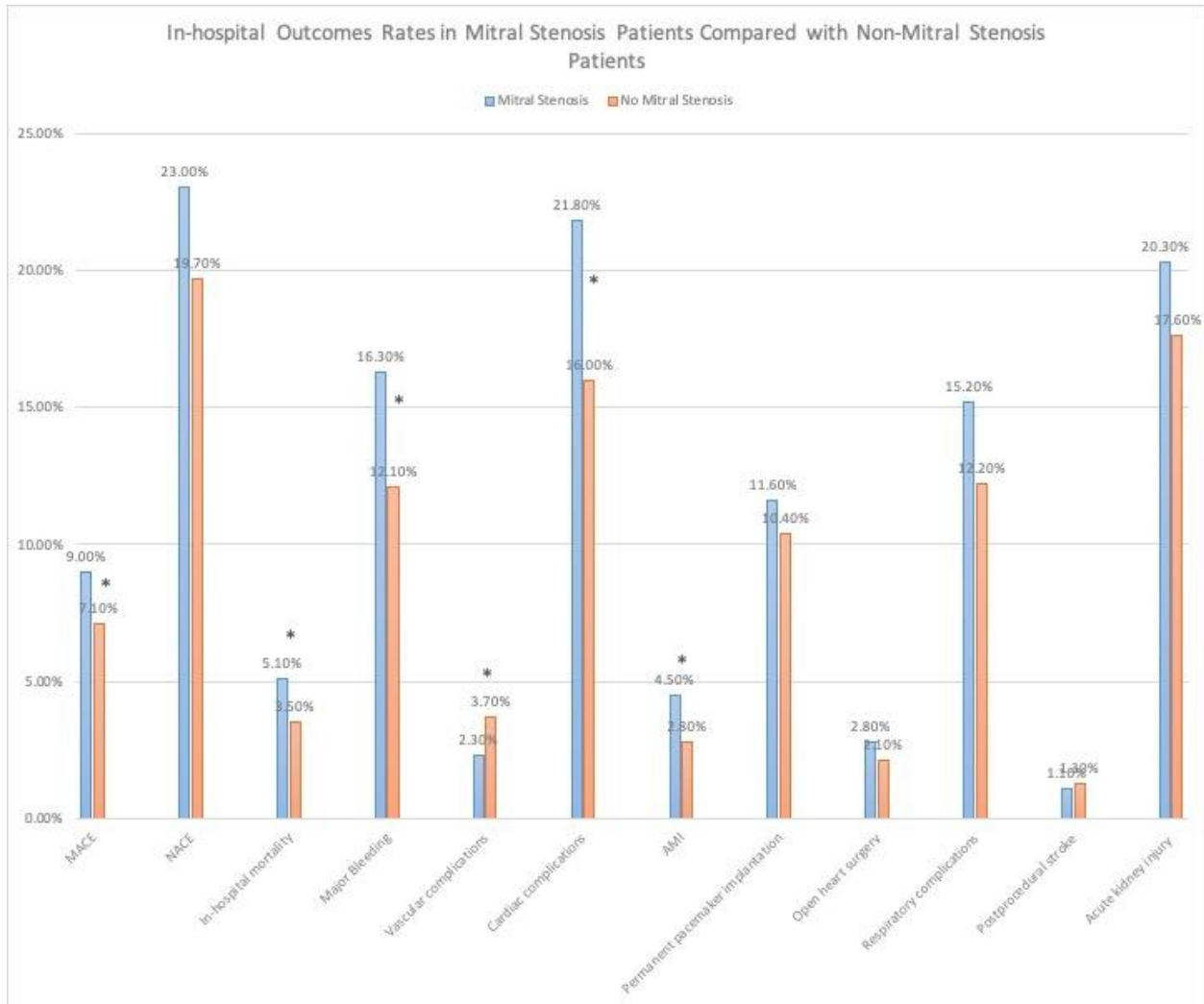
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Figure 1. Multivariate logistic regression of the outcomes of transcatheter aortic valve replacement in patients with mitral stenosis compared with those without mitral stenosis.



MACE – major adverse cardiovascular events; NACE – net adverse cardiovascular events; TAVR – transcatheter aortic valve replacement.

Figure 2. In-hospital outcomes rates in mitral Stenosis patients compared with non-mitral stenosis patients undergoing transcatheter aortic valve replacement.



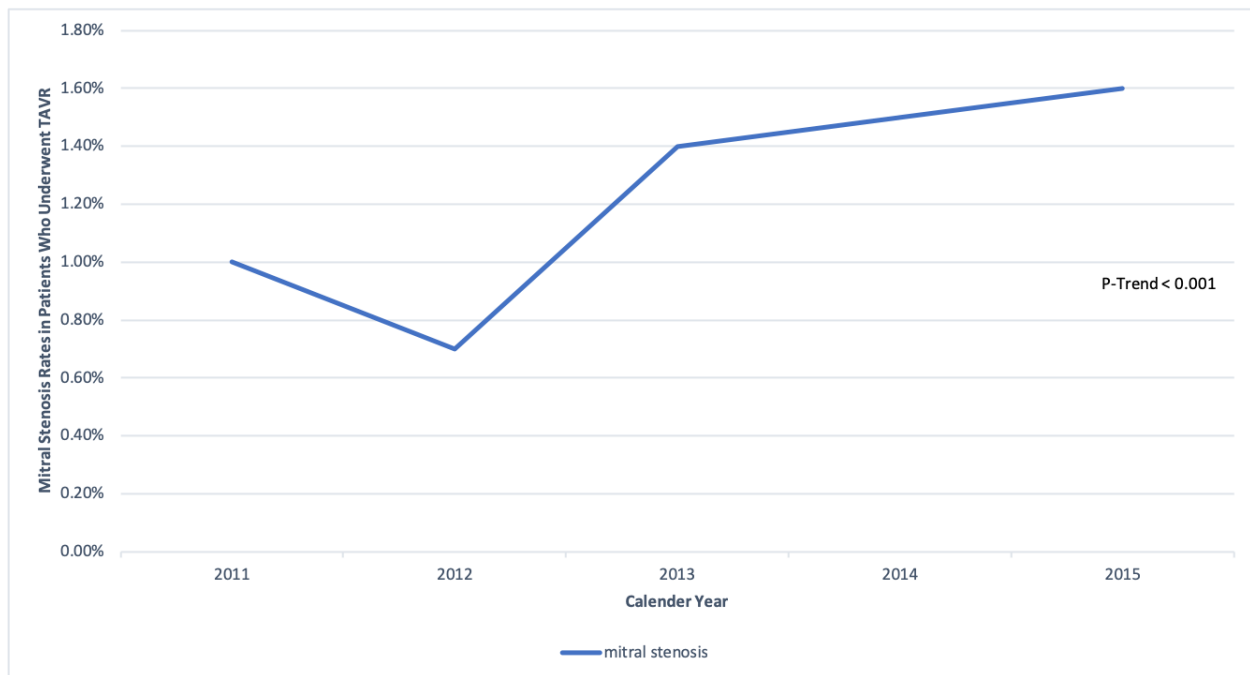
MACE – major adverse cardiovascular events; NACE – net adverse cardiovascular events; AMI – acute myocardial infarction.

\* Indicates statistical significance.

### Figure 3

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Figure 3. Trends in mitral stenosis rates in patients who underwent transcatheter aortic valve replacement.



TAVR – transcatheter aortic valve replacement.

**Electronic Supplementary Material (online publication only)**

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