
cTable 1. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Diagnoses Codes to Identify Patients With Heart Failure (HF), Stroke, and Myocardial Infarction (MI)
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This supplementary material has been provided by the authors to give readers additional information about their work.
**eTable 1. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) Diagnoses Codes to Identify Patients With Heart Failure (HF), Stroke, and Myocardial Infarction (MI)**

<table>
<thead>
<tr>
<th>Condition or procedure</th>
<th>ICD-9-CM Codes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Failure</td>
<td>398.x, 402.x1, 404.x1, 404.x3, 428.x</td>
</tr>
<tr>
<td>Stroke</td>
<td>433.x1, 434.x1, 997.02, 436, 437.1, 437.9, 430, 431, 432.x</td>
</tr>
<tr>
<td>MI</td>
<td>410.x0, 410.x1</td>
</tr>
</tbody>
</table>
**Table 2.** Postprocedural and In-Hospital Outcomes in Patients With Off-Label and On-Label TAVR Use

<table>
<thead>
<tr>
<th>Variable</th>
<th>Off-Label Use (N=2272)</th>
<th>On-Label Use (N=21575)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital death (%)</td>
<td>143 (6.3)</td>
<td>1011 (4.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Myocardial Infarction (%)</td>
<td>12 (0.5)</td>
<td>115 (0.5)</td>
<td>0.98</td>
</tr>
<tr>
<td>Transient Ischemic Attack (%)</td>
<td>12 (0.5)</td>
<td>49 (0.2)</td>
<td>0.007</td>
</tr>
<tr>
<td>Ischemic Stroke (%)</td>
<td>43 (1.9)</td>
<td>418 (1.9)</td>
<td>0.89</td>
</tr>
<tr>
<td>VARC Major Bleeding Event (%)</td>
<td>134 (5.9)</td>
<td>1514 (7.0)</td>
<td>0.06</td>
</tr>
<tr>
<td>Major Vascular Access Site Complication (%)</td>
<td>10 (0.4)</td>
<td>161 (0.7)</td>
<td>0.1</td>
</tr>
<tr>
<td>Cardiac Arrest (%)</td>
<td>149 (6.6)</td>
<td>1035 (4.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Permanent pacemaker (%)</td>
<td>115 (5.1)</td>
<td>1217 (5.6)</td>
<td>0.26</td>
</tr>
<tr>
<td>Device Migration (%)</td>
<td>4 (0.2)</td>
<td>77 (0.4)</td>
<td>0.16</td>
</tr>
<tr>
<td>Aortic Valve Reintervention (%)</td>
<td>12 (0.5)</td>
<td>70 (0.3)</td>
<td>0.11</td>
</tr>
<tr>
<td>Unplanned Other Cardiac Surgery or Intervention (%)</td>
<td>47 (2.1)</td>
<td>429 (2.0)</td>
<td>0.78</td>
</tr>
<tr>
<td>Incident Renal Failure (%)</td>
<td>227 (10.0)</td>
<td>1964 (9.1)</td>
<td>0.13</td>
</tr>
</tbody>
</table>

**Post procedure valvular parameters**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Off-Label Use (N=2272)</th>
<th>On-Label Use (N=21575)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residual Aortic Stenosis* (%)</td>
<td>134 (7.7)</td>
<td>1047 (6.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>AV Area* cm², Median (IQR)</td>
<td>1.7 (1.3-2.1)</td>
<td>1.7 (1.4-2.1)</td>
<td>0.26</td>
</tr>
<tr>
<td>AV Peak Doppler Velocity* (m/s), Median (IQR)</td>
<td>2.1 (1.8-2.5)</td>
<td>2 (1.7-2.4)</td>
<td>0.06</td>
</tr>
<tr>
<td>AV Mean Gradient* (mm Hg), Median (IQR)</td>
<td>10 (7-13)</td>
<td>9 (7-13)</td>
<td>0.007</td>
</tr>
<tr>
<td>Severe mitral regurgitation* (%)</td>
<td>162 (9.3)</td>
<td>144 (0.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Severe aortic regurgitation* (%)</td>
<td>15 (0.9)</td>
<td>40 (0.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Moderate/Severe Perivalvular leak** (%)</td>
<td>138 (12.4)</td>
<td>799 (7.6)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Assessed in patients who had a post-procedure echocardiogram.
** Assessed in patients with aortic regurgitation.
**eTable 3. Comparison of Baseline Characteristics Between Patients With CMS-Linked Data Available Versus Patients Without CMS-Linked Data Available**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients with CMS-linked data (N=15397)</th>
<th>Patient without CMS-linked data (N=8450)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Median (IQR), y</td>
<td>84 (79-88)</td>
<td>82 (75-87)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male</td>
<td>7643 (49.6)</td>
<td>4328 (51.2)</td>
<td>0.02</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>White</td>
<td>14664 (95.2)</td>
<td>7737 (91.6)</td>
<td></td>
</tr>
<tr>
<td>Black/African American</td>
<td>445 (2.9)</td>
<td>443 (5.2)</td>
<td></td>
</tr>
<tr>
<td>Insurance Payor</td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Private</td>
<td>9376 (60.9)</td>
<td>5704 (67.5)</td>
<td></td>
</tr>
<tr>
<td>Public</td>
<td>6021 (39.1)</td>
<td>2674 (31.6)</td>
<td></td>
</tr>
<tr>
<td>Prior PCI</td>
<td>5505 (35.8)</td>
<td>2976 (35.2)</td>
<td>0.37</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>4808 (31.2)</td>
<td>2708 (32.1)</td>
<td>0.18</td>
</tr>
<tr>
<td>Prior Aortic Valve Procedure</td>
<td>2431 (15.8)</td>
<td>1433 (17.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>Surgical AV repair or replacement*</td>
<td>269 (11.1)</td>
<td>248 (17.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Balloon aortic valvuloplasty*</td>
<td>2151 (88.5)</td>
<td>1182 (82.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TAVR*</td>
<td>38 (1.6)</td>
<td>22 (1.5)</td>
<td>0.96</td>
</tr>
<tr>
<td>Prior Stroke</td>
<td>1868 (12.1)</td>
<td>1049 (12.4)</td>
<td>0.53</td>
</tr>
<tr>
<td>Prior CEA/CAS</td>
<td>1166 (9.0)</td>
<td>624 (8.8)</td>
<td>0.65</td>
</tr>
<tr>
<td>Porcelain aorta</td>
<td>974 (6.3)</td>
<td>681 (8.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Peripheral Arterial Disease</td>
<td>4865 (31.6)</td>
<td>2654 (31.4)</td>
<td>0.74</td>
</tr>
<tr>
<td>Current/Recent Smoker</td>
<td>690 (4.5)</td>
<td>563 (6.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>13735 (89.2)</td>
<td>7471 (88.4)</td>
<td>0.07</td>
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<tr>
<td>Diabetes Mellitus</td>
<td>5410 (35.1)</td>
<td>3445 (40.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dialysis</td>
<td>593 (3.9)</td>
<td>383 (4.5)</td>
<td>0.01</td>
</tr>
<tr>
<td>Chronic Lung Disease - Severe</td>
<td>2055 (13.4)</td>
<td>1203 (14.2)</td>
<td>0.06</td>
</tr>
<tr>
<td>Prior MI</td>
<td>3818 (24.8)</td>
<td>2189 (25.9)</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>STS</td>
<td>2016</td>
<td>P-Value</td>
</tr>
<tr>
<td>--------------------------</td>
<td>------</td>
<td>--------</td>
<td>---------</td>
</tr>
<tr>
<td>NYHA Class III/IV within 2 weeks</td>
<td>12488 (81.1)</td>
<td>6945 (82.2)</td>
<td>0.005</td>
</tr>
<tr>
<td>Cardiogenic Shock w/in 24 Hours</td>
<td>69 (0.5)</td>
<td>49 (0.6)</td>
<td>0.17</td>
</tr>
<tr>
<td>Atrial Fibrillation/Flutter</td>
<td>6455 (41.9)</td>
<td>3271 (38.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>% Predicted Mortality (STS AV Replacement Mortality Model), Median (IQR)</td>
<td>7.0 (4.7-10.6)</td>
<td>6.4 (4.2-10.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Creatinine &gt; 2 mg/dL</td>
<td>1365 (8.9)</td>
<td>820 (9.7)</td>
<td>0.03</td>
</tr>
<tr>
<td>LVEF &lt; 30%</td>
<td>1047 (6.8)</td>
<td>639 (7.6)</td>
<td>0.02</td>
</tr>
<tr>
<td>Degenerative AV Disease</td>
<td>14566 (94.6)</td>
<td>7829 (92.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AV Mean Gradient (mm Hg) - Median (IQR)</td>
<td>43 (36-52)</td>
<td>43 (36-52)</td>
<td>0.32</td>
</tr>
<tr>
<td>Elective Procedure Status</td>
<td>13910 (90.3)</td>
<td>7575 (89.6)</td>
<td>0.06</td>
</tr>
<tr>
<td>Femoral Access Site</td>
<td>9266 (60.2)</td>
<td>5065 (59.9)</td>
<td>0.71</td>
</tr>
<tr>
<td>Device Success</td>
<td>14351 (93.2)</td>
<td>7809 (92.4)</td>
<td>0.0006</td>
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</tbody>
</table>

**Hospital Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>STS</th>
<th>2016</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital Location</td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Urban</td>
<td>11229 (72.9)</td>
<td>6414 (75.9)</td>
<td></td>
</tr>
<tr>
<td>Suburban</td>
<td>3399 (22.1)</td>
<td>1730 (20.5)</td>
<td></td>
</tr>
<tr>
<td>Rural</td>
<td>769 (5.0)</td>
<td>306 (3.6)</td>
<td></td>
</tr>
<tr>
<td>Hospital Type</td>
<td></td>
<td></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Private/Community</td>
<td>10032 (65.2)</td>
<td>5508 (65.2)</td>
<td></td>
</tr>
<tr>
<td>University</td>
<td>5151 (33.5)</td>
<td>2886 (34.2)</td>
<td></td>
</tr>
<tr>
<td>Government</td>
<td>214 (1.4)</td>
<td>56 (0.7)</td>
<td></td>
</tr>
<tr>
<td>Teaching Hospital</td>
<td>11137 (72.3)</td>
<td>6252 (74.0)</td>
<td>0.006</td>
</tr>
<tr>
<td>TAVR Volume, Median (IQR)</td>
<td>107 (70-170)</td>
<td>110 (69-170)</td>
<td>0.42</td>
</tr>
</tbody>
</table>

* Assessed in patients with prior aortic valve procedure.
**eTable 4.** Cumulative Incidence of 30-Day and 1-Year Adverse Cardiovascular Outcomes in Patients With Off-Label and On-Label TAVR Use

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Off-Label Use</th>
<th>On-Label Use</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Events</td>
<td>Rate, % (95% CI)</td>
<td>No. of Events</td>
</tr>
<tr>
<td>30 Day</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>119</td>
<td>8.5 (7.1-10.1)</td>
<td>855</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>81</td>
<td>5.8 (4.7-7.1)</td>
<td>606</td>
</tr>
<tr>
<td>Stroke</td>
<td>27</td>
<td>1.9 (1.3-2.8)</td>
<td>353</td>
</tr>
<tr>
<td>MI</td>
<td>14</td>
<td>1.0 (0.6-1.7)</td>
<td>105</td>
</tr>
<tr>
<td>1 Year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>315</td>
<td>25.6 (23.2-28.3)</td>
<td>2549</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>203</td>
<td>16.2 (14.2-18.4)</td>
<td>1718</td>
</tr>
<tr>
<td>Stroke</td>
<td>41</td>
<td>3.1 (2.3-4.2)</td>
<td>520</td>
</tr>
<tr>
<td>MI</td>
<td>29</td>
<td>2.5 (1.7-3.6)</td>
<td>245</td>
</tr>
</tbody>
</table>
eTable 5. Unadjusted Cumulative Adverse Cardiovascular Outcomes of Individual Off-Label Indications

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Only Severe MR (n=855)</th>
<th>Only Severe AR (n=736)</th>
<th>Only Bicuspid AV (n=384)</th>
<th>Only Moderate AS (n=155)</th>
<th>≥ 2 off-label indications (n=139)</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death, (%)</td>
<td>75 (8.8)</td>
<td>41 (5.6)</td>
<td>15 (3.9)</td>
<td>5 (3.2)</td>
<td>7 (5.0)</td>
</tr>
<tr>
<td>Ischemic Stroke, (%)</td>
<td>14 (1.6)</td>
<td>15 (2.1)</td>
<td>8 (2.1)</td>
<td>5 (3.2)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>VARC Major Bleeding Event, (%)</td>
<td>60 (7.2)</td>
<td>44 (6.2)</td>
<td>18 (4.8)</td>
<td>8 (5.2)</td>
<td>4 (3.0)</td>
</tr>
<tr>
<td>Cardiac Arrest, (%)</td>
<td>77 (9.0)</td>
<td>38 (5.2)</td>
<td>20 (5.2)</td>
<td>6 (3.9)</td>
<td>8 (5.8)</td>
</tr>
<tr>
<td>Permanent pacemaker, (%)</td>
<td>41 (4.8)</td>
<td>32 (4.4)</td>
<td>26 (6.8)</td>
<td>9 (5.8)</td>
<td>7 (5.1)</td>
</tr>
<tr>
<td>Incident Renal Failure, (%)</td>
<td>90 (10.8)</td>
<td>70 (9.8)</td>
<td>31 (8.2)</td>
<td>16 (10.3)</td>
<td>20 (15.0)</td>
</tr>
<tr>
<td>30 Day*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality, (%)</td>
<td>63 (11.0)</td>
<td>35 (7.8)</td>
<td>11 (5.6)</td>
<td>5 (4.8)</td>
<td>5 (6.3)</td>
</tr>
<tr>
<td>Heart Failure, (%)</td>
<td>40 (7.0)</td>
<td>23 (5.1)</td>
<td>6 (3.1)</td>
<td>8 (7.7)</td>
<td>4 (5.1)</td>
</tr>
<tr>
<td>Stroke, (%)</td>
<td>9 (1.6)</td>
<td>7 (1.6)</td>
<td>5 (2.6)</td>
<td>5 (4.8)</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td>MI, (%)</td>
<td>8 (1.4)</td>
<td>4 (0.9)</td>
<td>2 (1.0)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>1 Year*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality, (%)</td>
<td>152 (29.3)</td>
<td>94 (23.7)</td>
<td>37 (23.9)</td>
<td>16 (19.4)</td>
<td>16 (22.0)</td>
</tr>
<tr>
<td>Heart Failure, (%)</td>
<td>108 (20.7)</td>
<td>57 (13.9)</td>
<td>12 (7.4)</td>
<td>18 (20.4)</td>
<td>8 (11.3)</td>
</tr>
<tr>
<td>Stroke, (%)</td>
<td>17 (3.2)</td>
<td>9 (2.1)</td>
<td>6 (3.1)</td>
<td>6 (6.3)</td>
<td>3 (4.5)</td>
</tr>
<tr>
<td>MI, (%)</td>
<td>11 (2.1)</td>
<td>11 (3.0)</td>
<td>3 (1.6)</td>
<td>3 (5.1)</td>
<td>1 (1.3)</td>
</tr>
</tbody>
</table>

*30-day and 1-year outcomes were assessed in a CMS-linked subset (only severe MR: n=573; only severe AI: n=449; only bicuspid AV: n=196; only moderate AS: n=104; ≥ 2 off-label indications: n=79).
eTable 6. Association of Off-Label TAVR Use and Composite Adverse Cardiovascular Outcomes (Death, Heart Failure, MI, and Stroke) by Hospital Tertiles

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Level</th>
<th>Unadjusted</th>
<th>Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Hazard Ratio (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>30-Day Composite</td>
<td>Medium vs. Low</td>
<td>1.12 (0.97, 1.28)</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td>High vs. Low</td>
<td>1.16 (1.01, 1.34)</td>
<td>0.03</td>
</tr>
<tr>
<td>1-Year Composite</td>
<td>Medium vs. Low</td>
<td>1.03 (0.94, 1.13)</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>High vs. Low</td>
<td>1.05 (0.95, 1.15)</td>
<td>0.32</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex, body surface area, left ventricular ejection fraction, hemoglobin, platelet count, number of days from 11/1/2011 until procedure date, race, dialysis, left main stenosis &gt;=50%, proximal LAD stenosis &gt;= 70%, prior MI, endocarditis, prior stroke or TIA, carotid stenosis, PAD, tobacco abuse, diabetes, NYHA class IV, atrial fibrillation/flutter, conduction defect, severe chronic lung disease, home oxygen, hostile chest, porcelain aorta, access site (femoral vs. other), prior PCI, prior CABG, prior cardiac operations (2+ vs. 1 vs. 0), prior aortic valve procedure, prior non-aortic valve procedure, aortic stenosis etiology (degenerative vs. other), valve morphology (tricuspid vs. other), tricuspid regurgitation (moderate/severe vs. other), acuity (elective vs. urgent vs. shock or inotropes or assist device vs. emergency or salvage or cardiac arrest)
eFigure. Quarterly Trend in Off-Label TAVR Use

Quarterly Rate of Off-Label TAVR Use

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