Atrial Fibrillation Is Associated With Increased Mortality in Patients Undergoing Transcatheter Aortic Valve Replacement: Insights From the Placement of Aortic Transcatheter Valve (PARTNER) Trial

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Background—This study sought to evaluate the impact of atrial fibrillation (AF) on clinical outcomes in patients undergoing transcatheter aortic valve replacement.

Methods and Results—Data were evaluated in 1879 patients with baseline and discharge ECGs who underwent transcatheter aortic valve replacement in the Placement of AoRTic TraNsçatheter Valve (PARTNER) trial. A total of 1262 patients manifested sinus rhythm (SR) at baseline/SR at discharge, 113 SR baseline/AF discharge, and 470 AF baseline/AF discharge. Patients who converted from SR to AF by discharge had the highest rates of all-cause mortality at 30 days (P<0.0001 across all groups; 14.2% SR/AF versus 2.6% SR/SR; adjusted hazard ratio [HR]=3.41; P=0.0002) and over 2-fold difference at 1 year (P<0.0001 across all groups; 35.7% SR/AF versus 15.8% SR/SR; adjusted HR=2.14; P<0.0001). The presence of AF on baseline or discharge ECG was a predictor of 1-year mortality (adjusted HR=2.14 for SR/AF group and HR=1.88 for AF/AF groups; P<0.0001 for both groups versus SR/SR). For patients discharged in AF, those with lower ventricular response (ie, <90 bpm) experienced less 1-year all-cause mortality (HR=0.74; P=0.04).

Conclusions—After transcatheter aortic valve replacement, the presence of AF at discharge, and particularly, the conversion to AF by discharge and higher ventricular response are associated with increased mortality. These data underscore the deleterious impact of AF, as well as the need for targeted interventions to improve clinical outcomes, in patients undergoing transcatheter aortic valve replacement.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00530894.

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Key Words: aortic valve ◼ atrial fibrillation ◼ atrial flutter ◼ mortality ◼ transcatheter aortic valve replacement

Atrial fibrillation (AF) and atrial flutter are not only common clinical arrhythmias in the general population but are also associated complications of many cardiac procedures.1,2 AF is especially common in patients undergoing cardiac valve surgery and coronary artery bypass grafting,3-5 with 5% to 40% of all patients undergoing open cardiac surgery developing AF.6-8 The development of both preoperative and postoperative AF results to surgical aortic valve replacement (SA VR), postoperative AF associated complications of many cardiac procedures.1,2 AF is a known risk factor for mortality.9-14 Transcatheter aortic valve replacement (TAVR) has been shown to be an effective and less-invasive alternative to SAVR in elderly and high-risk patients.20-26 The development of AF after TAVR is common, ranging from 6% to 53% in prior reports.22,27,28 There are limited data on the association between AF and mortality in patients undergoing TAVR. Thus, the aims of this study are 2-fold: 1) to analyze the clinical impact of AF at 30 days and 1 year after TAVR and 2) to analyze the association...
WHAT IS KNOWN

- Patients undergoing transcatheter aortic valve replacement (TAVR) have relatively high rates of atrial fibrillation (AF).
- Studies in surgical aortic valve replacement patients have noted that the presence of AF is correlated with worsened outcomes, including higher mortality.
- A better understanding of the degree to which AF impacts on outcomes including mortality would have clinical utility.

WHAT THE STUDY ADDS

- For TAVR patients, the presence of AF at discharge, and especially the conversion to AF by discharge, is associated with increased mortality at 30-day and 1-year and repeat hospitalizations at 1-year.
- For those TAVR patients with AF, there is an association between higher ventricular rates >90 bpm and mortality.
- Patients with AF after TAVR also have higher rates of renal failure requiring dialysis and permanent pacemaker implantation.

between ventricular rate and mortality in AF patients after TAVR in the Placement of AoRTic TranScatheter Valve (PARTNER) trial.

Methods

Study Population

The design of the PARTNER trial has been previously described.21,22 Briefly, it enrolled patients with severe aortic stenosis who were deemed to be either high risk for SAVR (cohort A) or nonsurgical candidates (cohort B). Patients in cohort A were randomized to either SAVR or aortic valve replacement by the transfemoral or transapical approach. Patients in cohort B with adequate femoral access were randomized to transfemoral TAVR or standard medical therapy. After completion of the randomized trial enrollment, patients were enrolled in a continued access registry for either transapical or transfemoral TAVR. All patients who underwent TAVR had implantation of an Edwards SAPIEN valve (Edwards Lifesciences, Irvine, CA). The date of data extraction was February 2013.

Patients in the PARTNER trial had ECG, echocardiogram, and clinical evaluation performed at baseline, discharge, 30 days, 6 months, and 1 year post TAVR. Patients were included in this analysis only if they had undergone TAVR as part of either the randomized trial or the nonrandomized continued access registry and had baseline and discharge ECGs available for analysis.

The study was approved by the Institutional Review Board at each participating site, and all patients provided written informed consent.

End Points

All baseline, discharge, 30 days, 6 months, and 1 year ECG and echocardiograms were interpreted in independent core laboratories. AF was defined as AF or atrial flutter/tachycardia that was present on the baseline or discharge ECG. Patients were subdivided into 4 categories: patients with baseline sinus rhythm (SR) and discharge ECG showing SR, patients with baseline SR/discharge AF, patients with baseline AF/discharge AF, and patients with baseline AF/discharge SR. Clinical outcomes were then compared among the groups; the baseline AF/discharge SR group was not analyzed because of low number of patients in that group. Subgroup analyses were performed based on ventricular rate during AF (<90 versus ≥90 bpm) and TAVR type (transfemoral versus transapical).

The primary end point of this analysis was overall mortality. Secondary clinical end points included cardiovascular (CV) mortality, rehospitalization, stroke/transient ischemic attack (TIA), major bleeding, major vascular event, renal failure requiring dialysis, bradyarrhythmias requiring new pacemaker implantation, and change in 6-minute walk test distance result (meters), as described in the PARTNER trial protocol.21,22,29 All end points were measured at 30 days and 1 year. All adverse clinical events were adjudicated by an independent clinical events committee.

Statistical Analysis

All analysis was performed on the as-treated population, with results presented as median (25th–75th percentile) or percentages as appropriate. Continuous variables were compared across groups by the Kruskal–Wallis test, and categorical variables were compared using χ2 or Fisher exact test as appropriate. Event rates were reported as Kaplan–Meier estimates at 1 year and compared between groups using the log-rank test. Individual subgroup comparisons are presented if the overall P value for the comparison across the 3 groups is ≤0.05. To adjust for multiple comparisons, a Bonferroni corrected P value of 0.0167 is used to indicate statistical significance when summarizing pair wise comparisons. Mortality at 30 days and 1 year were modeled using Cox regression. The model included clinically relevant variables, such as age, sex, and Society of Thoracic Surgeons (STS) risk score along with bleeding requiring transfusion, bradyarrhythmia, requiring pacemaker implantation, myocardial infarction, renal failure requiring dialysis, and stroke, all defined by discharge. Because of the limited events at day 30, only the variables defined at discharge and STS risk score were included in the model. Landmark analysis was performed using 30 days as time = 0 to analyze the association between 30-day survival and 1-year mortality. Statistical analyses were performed using SAS software, versions 9.2 and 9.4 (SAS Institute, Cary, NC).

Results

Patient Population and Characteristics

The study population included 1879 patients from cohort A, cohort B, and the continued access registry of the PARTNER trial (Figure 1), 1097 of whom underwent transfemoral TAVR and 782 of whom underwent transapical TAVR. From this group, 1262 manifested SR at baseline/SR at discharge, 113 had SR baseline/AF discharge, 470 had AF baseline/AF discharge, and 34 had AF baseline/SR discharge. The latter group of 34 patients with AF baseline/SR discharge was not included in further analyses given their relatively low representation.

Baseline characteristics of each group are included in Table 1. Age ranged from 85 to 86 years across groups. STS score ranged from 10.5 to 11.1 and was highest in the baseline AF/discharge AF group. Notably, when compared with baseline SR/discharge SR patients, those patients with baseline AF/discharge AF were more likely to be male and had a higher STS score. Patients with baseline AF/discharge AF had higher rates of pulmonary hypertension and pacemakers compared with baseline SR/discharge SR patients. There were no significant differences among groups for body mass index, diabetes mellitus, hypertension, congestive heart failure, prior myocardial infarction, or stroke/TIA.

Baseline ECG and echocardiogram findings are in Table 2. Notable baseline ECG findings include significantly more first degree atrioventricular block in the baseline SR/discharge AF patients (versus the baseline SR/discharge SR patients). There
were no statistically significant differences in rates of inter-
ventricular conduction defect, right bundle branch block, or 
left bundle branch block. Baseline echocardiograms dem-
onstrated a significantly lower left ventricular ejection fraction in patients with baseline AF/discharge AF (55.0%) versus 
the baseline SR/discharge SR (57.5%) or the baseline SR/ 
discharge AF (58.6%) patients. Compared with the baseline 
SR/discharge SR patients, patients with baseline AF/discharge 
AF were also more likely to have at least moderate mitral 
regurgitation.

Clinical Outcomes
Thirty-day outcomes are listed in Table 3. Both all-cause mor-
tality (14.2%) and CV mortality (8.3%) were highest in the 
baseline SR/discharge AF group. There were no significant

 differences in other end points including rehospitalization, 
stroke/TIA, major bleeding, and major vascular complica-
tions. Requirement for permanent pacemaker placement was 
highest at 12.7% in the baseline SR/discharge AF group.

Patients discharged in AF had a longer length of stay than 
patients who presented and remained in SR by discharge (6 
versus 7 days, \( P = 0.0004 \) across all groups).

At 1 year, the percent of patients in AF for each group was 
SR/SR=5.2%, SR/AF=27.9%, AF/AF=79.8%, \( P < 0.0001 \) for 
all comparisons. One-year outcomes based on Kaplan–Meier 
analysis demonstrated significantly higher mortalities in the 
baseline SR/discharge AF (35.7%) group and the baseline AF/ 
discharge AF group (29.9%) compared with the baseline SR/
discharge SR group (15.8%; Figure 2). The baseline AF/dis-
charge AF group had the highest 1-year CV mortality (21%) 
and rehospitalization rate (26.7%), although the baseline SR/ 
discharge SR group had the lowest rates of all-cause mortality, 
CV mortality, and rehospitalization. In landmark analysis that 
including those patients surviving at 30 days, rhythm status 
remained a predictor of outcomes.

Secondary Outcomes
Thirty-day and 1-year outcomes are presented Tables 3 
and 4. Renal failure requiring dialysis and new pacemaker

Table 1. **Baseline Patient Characteristics**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>(a) Baseline SR/Discharge SR (n = 1262)</th>
<th>(b) Baseline SR/Discharge AF (n = 113)</th>
<th>(c) Baseline AF/Discharge AF (n = 470)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>85.3 (80.2, 89.2)</td>
<td>86.4 (80.5, 90.0)</td>
<td>86.1 (81.9, 89.3)</td>
<td>0.02</td>
</tr>
<tr>
<td>Male (%)</td>
<td>46.5</td>
<td>47.8</td>
<td>57.7</td>
<td>0.0002</td>
</tr>
<tr>
<td>STS score</td>
<td>10.5 (9.1, 12.4)</td>
<td>10.8 (9.7, 13.6)</td>
<td>11.1 (9.6, 13.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI</td>
<td>26.1 (22.7, 30.0)</td>
<td>26.3 (22.7, 30.8)</td>
<td>25.2 (22.5, 29.3)</td>
<td>0.21</td>
</tr>
<tr>
<td>NYHA (%)</td>
<td>0.22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class I–II</td>
<td>5.7</td>
<td>2.7</td>
<td>4.9</td>
<td></td>
</tr>
<tr>
<td>Class III</td>
<td>50.6</td>
<td>46.0</td>
<td>46.8</td>
<td></td>
</tr>
<tr>
<td>Class IV</td>
<td>43.7</td>
<td>51.3</td>
<td>48.2</td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>38.4</td>
<td>37.2</td>
<td>36.0</td>
<td>0.64</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>91.4</td>
<td>92.9</td>
<td>92.8</td>
<td>0.58</td>
</tr>
<tr>
<td>Prior MI (%)</td>
<td>26.8</td>
<td>22.3</td>
<td>23.1</td>
<td>0.21</td>
</tr>
<tr>
<td>Stroke/TIA (%)</td>
<td>26.5</td>
<td>17.4</td>
<td>26.7</td>
<td>0.11</td>
</tr>
<tr>
<td>Endocarditis (%)</td>
<td>0.5</td>
<td>1.8</td>
<td>0.2</td>
<td>0.10</td>
</tr>
<tr>
<td>Pulmonary hypertension (%)</td>
<td>36.2</td>
<td>37.4</td>
<td>47.8</td>
<td>0.0001</td>
</tr>
<tr>
<td>Permanent pacemaker (%)</td>
<td>8.5</td>
<td>13.3</td>
<td>17.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Liver disease (%)</td>
<td>2.4</td>
<td>1.8</td>
<td>3.2</td>
<td>0.54</td>
</tr>
<tr>
<td>COPD (%)</td>
<td>42.5</td>
<td>48.7</td>
<td>45.1</td>
<td>0.32</td>
</tr>
<tr>
<td>Rheumatic fever (%)</td>
<td>1.5</td>
<td>1.8</td>
<td>1.5</td>
<td>0.97</td>
</tr>
<tr>
<td>Renal disease (Cr ≥2%)</td>
<td>15.8</td>
<td>19.5</td>
<td>17.7</td>
<td>0.44</td>
</tr>
<tr>
<td>CHA2DS2VASC score</td>
<td>5.8±1.4</td>
<td>5.6±1.2</td>
<td>5.7±1.3</td>
<td>0.02</td>
</tr>
</tbody>
</table>

\( AF \) indicates atrial fibrillation; BMI, body mass index; \( CHA2DS2VASC \), congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, stroke/transient ischemic attack/thromboembolism, vascular disease, age 65–74 years, sexual category; \( COPD \), chronic obstructive pulmonary disease; \( MI \), myocardial infarction; NYHA, New York Heart Association; SR, sinus rhythm; STS, Society of Thoracic Surgeons; and TIA, transient ischemic attack.
Implantations were higher in the SR/AF group at both 30-day and 1-year. There was a nonsignificant trend for least improvement in 6-minute walk test distance in the SR/AF group at both 30-day and 1-year. Although rates of stroke/TIA and major bleeding were not significantly different among groups, there were trends for increased events in the baseline SR/discharge AF groups at both 30-day and 1-year.

Multivariable Analysis of Predictors of Mortality

Predictors of 30-day and 1-year mortality are listed in Tables 5 and 6. The development and maintenance of AF by discharge, as opposed to remaining in SR, was associated with higher 30-day mortality (hazard ratio [HR]=3.41 [1.78, 6.54]; \( P=0.0002 \)). The development of AF by discharge (SR/AF) and presenting and remaining in AF at discharge (AF/AF) were each associated with increased 1-year mortality (HR=2.14 [1.45, 3.10] and HR=1.88 [1.50, 2.36], respectively).

Effect of Ventricular Rate during AF on Outcomes

Those patients discharged in AF with lower ventricular response (ie, <90 bpm) experienced less 1-year all-cause mortality (HR= 0.74 [0.55, 0.99]; \( P=0.04 \)) and CV mortality (HR= 0.55, [0.38–0.79], \( P=0.0014 \)), compared with those patients with ventricular response ≥90 bpm (Figure 3). There was no statistically significant difference in left ventricular ejection fraction at either 30-day (53%) or 1-year (55%) between groups. When comparing patients discharged in AF

### Table 2. Baseline ECG/Echocardiographic Findings

<table>
<thead>
<tr>
<th>ECG/Echo Findings</th>
<th>(a) Baseline SR/Discharge AF (n=1262)</th>
<th>(b) Baseline SR/Discharge AF (n=113)</th>
<th>(c) Baseline AF/Discharge AF (n=470)</th>
<th>( P ) Value</th>
<th>All Groups (a) vs (b) (a) vs (c) (b) vs (c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (bpm)</td>
<td>72.0 (63.0, 81.0)</td>
<td>68.0 (62.0, 76.0)</td>
<td>75.5 (66.0, 86.0)</td>
<td>(&lt;0.0001 )</td>
<td>( 0.01 ) ( &lt;0.001 ) ( &lt;0.01 )</td>
</tr>
<tr>
<td>First degree atioventricular block (%)</td>
<td>19.2</td>
<td>27.1</td>
<td>...</td>
<td>(&lt;0.0001 )</td>
<td>0.05 ( ... ) ( ... )</td>
</tr>
<tr>
<td>IVCD (%)</td>
<td>5.2</td>
<td>5.6</td>
<td>5.8</td>
<td>0.88</td>
<td></td>
</tr>
<tr>
<td>LBBB (%)</td>
<td>9.7</td>
<td>7.5</td>
<td>7.0</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td>RBBB (%)</td>
<td>14.4</td>
<td>21.5</td>
<td>16.3</td>
<td>0.12</td>
<td></td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>57.5 (48.8, 60.0)</td>
<td>58.6 (50.1, 62.0)</td>
<td>55.0 (44.4, 60.0)</td>
<td>(&lt;0.0001 )</td>
<td>0.58 ( &lt;0.0001 ) 0.002</td>
</tr>
<tr>
<td>Mitral regurgitation (%)</td>
<td>None</td>
<td>4.2</td>
<td>1.8</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>Trace</td>
<td>28.5</td>
<td>31.8</td>
<td>16.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>49.3</td>
<td>41.8</td>
<td>55.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>15.6</td>
<td>21.8</td>
<td>22.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>2.5</td>
<td>2.7</td>
<td>3.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; IVCD, intraventricular conduction deficit; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; RBBB, right bundle branch block and SR, sinus rhythm.

### Table 3. Outcomes at 30 Days

<table>
<thead>
<tr>
<th>Outcome (%)</th>
<th>(a) Baseline SR/Discharge SR</th>
<th>(b) Baseline SR/Discharge AF</th>
<th>(c) Baseline AF/Discharge AF</th>
<th>( P ) Value</th>
<th>All Groups (a) vs (b) (a) vs (c) (b) vs (c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
<td>(&lt;0.0001 )</td>
<td>( &lt;0.001 ) 0.27 ( &lt;0.001 )</td>
</tr>
<tr>
<td>All-cause</td>
<td>2.6</td>
<td>14.2</td>
<td>3.6</td>
<td>( &lt;0.0001 )</td>
<td>( &lt;0.001 ) 0.27 ( &lt;0.001 )</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>1.6</td>
<td>8.3</td>
<td>2.8</td>
<td>( &lt;0.0001 )</td>
<td>( &lt;0.001 ) 0.11 ( 0.007 )</td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>5.3</td>
<td>5.8</td>
<td>7.2</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>3.9</td>
<td>7.4</td>
<td>3.2</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>7.3</td>
<td>9.9</td>
<td>7.9</td>
<td>0.58</td>
<td></td>
</tr>
<tr>
<td>Major vascular event</td>
<td>5.5</td>
<td>4.4</td>
<td>5.8</td>
<td>0.86</td>
<td></td>
</tr>
<tr>
<td>Renal failure requiring dialysis</td>
<td>1.5</td>
<td>6.3</td>
<td>3.2</td>
<td>0.001 ( 0.0003 ) 0.02 ( 0.13 )</td>
<td></td>
</tr>
<tr>
<td>New pacemaker</td>
<td>5.2</td>
<td>12.7</td>
<td>5.1</td>
<td>0.004 ( 0.001 ) 0.96 ( 0.004 )</td>
<td></td>
</tr>
<tr>
<td>LVEF</td>
<td>58.7 (50.0, 63.4)</td>
<td>59.1 (54.9, 62.6)</td>
<td>55.0 (49.2, 60.0)</td>
<td>0.0001</td>
<td>0.78 ( &lt;0.0001 ) 0.02</td>
</tr>
<tr>
<td>Change in 6MWTD (mean in meters)</td>
<td>21.8</td>
<td>-4.2</td>
<td>12.1</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>Length of stay in hospital after TAVR (d)</td>
<td>6.0 (4.0, 7.0)</td>
<td>7.0 (5.0, 8.0)</td>
<td>7.0 (5.0, 8.0)</td>
<td>0.0004</td>
<td>0.002 ( 0.005 ) ( 0.09 )</td>
</tr>
<tr>
<td>On aspirin</td>
<td>89.6</td>
<td>85.3</td>
<td>84.2</td>
<td>0.008 ( 0.19 ) 0.003 ( 0.80 )</td>
<td></td>
</tr>
<tr>
<td>On clopidogrel</td>
<td>58.6</td>
<td>30.9</td>
<td>27.5</td>
<td>(&lt;0.0001 )</td>
<td>( &lt;0.0001 ) ( &lt;0.0001 ) ( 0.51 )</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; LVEF, left ventricular ejection fraction; 6MWTD, 6-minute walk test distance; SR, sinus rhythm; TIA, transient ischemic attack; and TAVR, transcatheter aortic valve replacement.
by ventricular response <90 versus ≥90 bpm, there were no statistically significant differences in rates of pacemakers at baseline (17.5% for <90 bpm versus 23.3% for ≥90 bpm, P=0.09) or placement by discharge (7.4% for <90 bpm versus 5.0% for ≥90 bpm, P=0.22).

**Discussion**

This study is the largest published analysis of the adverse impact of AF after TAVR on clinical outcomes. The main findings are as follows: 1) patients discharged in AF after TAVR in the PARTNER Trial have increased 30-day and...
Atrial Fibrillation in PARTNER

1-year mortality, CV mortality, and 1-year repeat hospitalization, particularly in those patients who convert from SR to AF between admission and discharge; 2) patients with AF after TAVR and ventricular response >90 bpm have higher 1-year mortality than those with ventricular response ≤90 bpm; 3) patients with AF after TAVR also have higher rates of renal failure requiring dialysis, permanent pacemaker implantation, and a nonsignificant increase for stroke/TIA. In particular, there is an early divergence of the survival curves before 3 months, revealing that development of AF by discharge is associated with increased early mortality. These findings provide further evidence that the presence of AF at discharge, particularly if not present at baseline, is not a benign condition in TAVR patients.

Previous studies have shown that AF is generally associated with worse outcomes in many CV disease states, including poorer outcomes in SAVR. AF is also a known and relatively common complication of TAVR. Tanawuttiwat et al noted an incidence of new AF equal to 53% in a single-center, retrospective study of 231 consecutive patients undergoing transaortic TAVR and 14% after transfemoral TAVR. Possible precipitating factors include CV and overall physical status related to the aged patient population with aortic stenosis, such as atrial fibrosis and larger atrial size, and sequelae of the TAVR procedure itself. Although reports of clinical outcomes of AF after TAVR are limited, the absence of AF is associated with better left ventricular ejection fraction recovery and improved mitral regurgitation, whereas the presence of AF is associated with increased stroke risk and mortality.

The causes of increased mortality in AF patients remain unclear. Although increased thromboembolic risk is often implicated, this study demonstrated AF remained a predictor of mortality even after adjusting for several clinical comorbidities including stroke. Other possible factors besides stroke/TIA may include those associated with CV as well as overall functional status. With regard to CV status, this study noted that rapid ventricular response was associated with worse mortality outcomes for patients who developed AF by discharge, with possible reasons for the deleterious effects including reduced cardiac output and heart failure, including systolic as well as diastolic heart failure. Notably, left ventricular ejection fraction was worse in patients with AF/AF, and particularly, in patients discharged with AF and ventricular response ≥90 bpm, which suggests worsened CV status. These results argue for prospective studies analyzing the effect of more aggressive rate control on outcomes in such patients. With regard to the impact of permanent pacemaker implantation on patients undergoing TAVR, including those with AF, we found that mortality rates in those patients requiring pacemakers were increased more than 2-fold at 30 days. These results suggest that comorbidities associated with conduction abnormalities and pacemaker implantation may be causally related to increased mortality. For example, prior analysis has shown that implantation of new pacemakers is associated with higher rates of repeat hospitalization and mortality or repeat hospitalization at 1 year. Further studies examining the role of pacemaker implantation on mortality in patients undergoing TAVR are required.

Table 4. Outcomes at 1 Year (Based on Kaplan–Meier Analysis)

<table>
<thead>
<tr>
<th>Outcome (%)</th>
<th>Baseline SR/ Discharge SR</th>
<th>Baseline SR/ Discharge AF</th>
<th>Baseline AF/ Discharge AF</th>
<th>P Value</th>
<th>All Group</th>
<th>(a) vs (b)</th>
<th>(a) vs (c)</th>
<th>(b) vs (c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All-cause</td>
<td>15.8</td>
<td>35.7</td>
<td>29.9</td>
<td>&lt;0.0001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>9.0</td>
<td>20.6</td>
<td>21.0</td>
<td>&lt;0.0001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.91</td>
<td></td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>15.6</td>
<td>25.7</td>
<td>26.7</td>
<td>&lt;0.0001</td>
<td>0.01</td>
<td>&lt;0.001</td>
<td>0.84</td>
<td></td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>6.3</td>
<td>10.3</td>
<td>9.0</td>
<td>0.19</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major bleeding</td>
<td>11.5</td>
<td>16.0</td>
<td>16.6</td>
<td>0.03</td>
<td>0.18</td>
<td>0.15</td>
<td>0.96</td>
<td></td>
</tr>
<tr>
<td>Major vascular event</td>
<td>5.6</td>
<td>4.4</td>
<td>6.8</td>
<td>0.58</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal failure requiring dialysis</td>
<td>2.7</td>
<td>7.3</td>
<td>4.6</td>
<td>0.005</td>
<td>0.002</td>
<td>0.03</td>
<td>0.22</td>
<td></td>
</tr>
<tr>
<td>New pacemaker</td>
<td>6.8</td>
<td>16.3</td>
<td>7.0</td>
<td>0.001</td>
<td>0.0004</td>
<td>0.96</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>LVEF</td>
<td>60.0 (55.0, 64.3)</td>
<td>60.0 (55.0, 65.0)</td>
<td>55.6 (50.0, 61.0)</td>
<td>0.055</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in 6MWTD (mean, in meters)</td>
<td>33.1</td>
<td>8.0</td>
<td>38.3</td>
<td>0.32</td>
<td>0.002</td>
<td>&lt;0.0001</td>
<td>0.89</td>
<td></td>
</tr>
<tr>
<td>On aspirin</td>
<td>86.6</td>
<td>71.4</td>
<td>72.3</td>
<td>&lt;0.0001</td>
<td>0.39</td>
<td>&lt;0.0001</td>
<td>0.055</td>
<td></td>
</tr>
<tr>
<td>On clopidogrel</td>
<td>32.9</td>
<td>27.3</td>
<td>16.3</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; CI, confidence interval; MI, myocardial infarction; SR, sinus rhythm; and STS, Society of Thoracic Surgeons.

Table 5. Multivariable Predictors of 30-Day Mortality

<table>
<thead>
<tr>
<th>Death</th>
<th>P Value</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradycardiac event requiring pacemaker</td>
<td>0.0301</td>
<td>2.57 (1.10–6.03)</td>
</tr>
<tr>
<td>Bleeding event requiring transfusion</td>
<td>&lt;0.0001</td>
<td>3.97 (2.04–7.70)</td>
</tr>
<tr>
<td>MI</td>
<td>0.0104</td>
<td>4.62 (1.43–14.88)</td>
</tr>
<tr>
<td>Renal failure (dialysis required)</td>
<td>&lt;0.0001</td>
<td>8.82 (4.13–18.84)</td>
</tr>
<tr>
<td>STS risk score</td>
<td>0.0139</td>
<td>1.05 (1.01–1.09)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.0216</td>
<td>2.99 (1.17–7.62)</td>
</tr>
<tr>
<td>Baseline SR/discharge AF (vs baseline SR/discharge SR)</td>
<td>0.0002</td>
<td>3.41 (1.78–6.54)</td>
</tr>
</tbody>
</table>

AF indicates atrial fibrillation; CI, confidence interval; MI, myocardial infarction; SR, sinus rhythm; and STS, Society of Thoracic Surgeons.
With regard to overall functional status, several markers were worse in the AF groups, including decreased 6-minute walk test distance, especially in those patients with ventricular rates > 90 bpm, higher rates of renal failure, and bradyarrhythmias requiring pacemakers. These results suggest that physical vitality is reduced in AF patients after TAVR when compared with patients who were in SR at discharge, a hypothesis-generating observation. Further studies of newer-generation TAVRs and techniques are warranted to explore the association between TAVR and procedure type, development of AF, and clinical outcomes.

Frequency of cardiac rhythm monitoring may account for the difference between this study and others reporting stroke and mortality in AF patients after TAVR, as rhythm status in this study was determined with baseline and discharge ECGs. For example, Amat-Santos et al\textsuperscript{31} noted no statistically significant difference in mortality with new-onset AF, which occurred in $31\%$ of patients. However, all patients were on continuous cardiac monitors, and all but 1 patient experienced spontaneous, electric, or chemical cardioversion to SR during the hospitalization. Greater than $70\%$ of patients experienced AF for <24 hours. Thus, patients in this trial would be less likely to be discharged in AF and possessed different characteristics from those in the present analysis, who were in AF at discharge and likely shouldered a larger AF burden. In another smaller, single-center trial of 389 total patients undergoing TAVR, Stortecky et al\textsuperscript{34} noted increased mortality in 131 AF patients with TAVR (the majority of which were Medtronic CoreValves), most of whom had preexisting AF. Our results differ in noting the highest mortality occurred in patients with baseline SR/discharge AF, findings which may be related to the different burden of AF between study populations.

### Clinical and Research Implications

AF is a comorbidity in patients undergoing TAVR that is associated with worse overall outcomes, including mortality. Patients who develop AF by discharge form a problematic group not only with regard to anticoagulation (eg, whether to anticoagulate and which medication to use) but also with regard to decisions regarding rate-control and rhythm-control strategies. Although $\beta$-blockers, amiodarone, and other drug options have shown some promise in treating postoperative AF\textsuperscript{36–38}, it remains unclear the extent to which these are useful agents in managing TAVR patients.

The maintenance of SR suggests a protective effect in patients undergoing TAVR. Further research should be directed toward determining the extent to which AF-targeted therapy in patients undergoing TAVR can improve outcomes with strategies including refinement of anticoagulant therapy, rate-control, antiarrhythmic agents, and cardioversion.\textsuperscript{17,18}

### Study Limitations

This study was a post hoc analysis of a prospective trial with adjudication of ECG and clinical outcome data, and ECGs were analyzed at discrete time points: baseline, discharge, and 1 year. Continuous cardiac rhythm monitoring was not available for this study. Thus, patients with a change in rhythm status or rate between admission and discharge, such as those who developed new-onset AF during hospitalization and subsequently converted to SR before discharge, were not included in the group of patients analyzed as having developed AF. Similarly, patients who may have developed AF after discharge were not included in the AF cohort. In addition, this study does not include details regarding history of AF or flutter in any of the patients, nor does it include details of antiarrhythmic or anticoagulant treatment while in the hospital or after discharge. Finally, although adjustments for several covariates were made, the potential for unmeasured confounders exists.

### Conclusions

After TAVR, the presence of AF at discharge, and especially the conversion to AF with ventricular rates >90 bpm, is associated with an increase in early and late all-cause and CV mortality. Although it is evident that AF is associated with an increase in mortality in patients who undergo TAVR, it remains unclear whether effective treatment of AF rhythm or rate could reduce this increase in mortality. AF patients undergoing TAVR should be further studied for strategies that can improve clinical outcomes.

### Disclosures

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References


Atrial Fibrillation Is Associated With Increased Mortality in Patients Undergoing Transcatheter Aortic Valve Replacement: Insights From the Placement of Aortic Transcatheter Valve (PARTNER) Trial


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房颤与接受经导管主动脉瓣置换术患者死亡率增高相关
来自 PARTNER 试验的见解

心房颤动（atrial fibrillation，AF）与心房扑动不仅是一种普通的心脏疾病，更与许多心脏手术密切相关，在接受了心脏瓣膜手术和冠状动脉旁路移植术的患者中，房颤尤为多见，在所有接受了心脏开胸手术的患者中，有5%-40%的患者会发生房颤。而术前或术后房颤，都可能增加患者的死亡率。

目前已知，术后房颤是导致接受外科主动脉瓣置换术（SAVR）患者死亡的风险因素，而接受了与 SAVR 同样有效，但侵袭性更小的经导管主动脉瓣置换术（TAVR）后发生房颤，是否也会增加患者死亡率的数据还十分有限。本次研究的目的就是要评估房颤对接受经导管主动脉瓣置换患者临床预后的影响。

在 PARTNER（the Placement of Aortic Transcatheter Valve）试验中，共纳入了 1879 例需接受经导管主动脉瓣置换的患者，分别在他们入院和出院时进行心电图（ECG）检测。其中 1262 例患者入院 ECG 与出院 ECG 均表现为窦性心律（sinus rhythm，SR），113 例患者入院 ECG 为 SR，出院 ECG 为 AF，470 例患者入院 ECG 与出院 ECG 均为 AF。随访发现，ECG 由 SR 转为 AF 组的患者，出院后 30 天全因死亡率最高（各组死亡率不全相同，p < 0.0001；14.2% SR/AF vs. 2.6% SR/SR；校正 HR = 3.41；p = 0.0002），1 年内全因死亡率增加超过 2 倍（各组死亡率不全相同，p<0.0001；35.7% SR/AF vs. 15.8% SR/SR；校正 HR=2.14；p < 0.0001）。入院或出院 ECG 表现为 AF 可作为预测 1 年死亡率的指标（SR/AF 校正 HR = 2.14；AF/AF 校正 HR = 1.88；两组与 SR/SR 组不同，p < 0.0001）。出院 ECG 为 AF 而心室率较低（如：< 9bpm）的患者 1 年死亡率也较低（HR = 0.74；P = 0.04）。

经导管主动脉瓣置换术后出院 ECG 表现为 AF，特别是由 SR 转变为 AF 并伴较高心室率的患者与死亡率增高相关。以上数据表明 AF 的不利影响，急需靶向干预以改善经导管主动脉瓣置换术患者的临床预后。