# Frequency of and Prognostic Significance of Atrial Fibrillation in Patients Undergoing Transcatheter Aortic Valve Implantation

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**The prognostic implications of preexisting atrial fibrillation (AF) and new-onset AF (NOAF) in transcatheter aortic valve implantation (TAVI) remain uncertain. This study assesses the epidemiology of AF in patients treated with TAVI and evaluates their outcomes according to the presence of preexisting AF or NOAF. A retrospective analysis of 708 patients undergoing TAVI from 2 heart hospitals was performed. Patients were divided into 3 study groups: sinus rhythm (n = 423), preexisting AF (n = 219), and NOAF (n = 66). Primary outcomes of interest were all-cause death and stroke both at 30-day and at 1-year follow-up. Preexisting AF was present in 30.9% of our study population, whereas NOAF was observed in 9.3% of patients after TAVI. AF and NOAF patients showed a higher rate of 1-year all-cause mortality compared with patients in sinus rhythm (14.6% vs 6.5% for preexisting AF and 16.3% vs 6.5% for NOAF, p = 0.007). No differences in 30-day mortality were observed between groups. In patients with AF (either preexisting and new-onset), those discharged with single antiplatelet therapy displayed higher mortality rates at 1 year (42.9% vs 11.7%, p = 0.006). Preexisting AF remained an independent predictor of mortality at 1-year follow-up (hazard ratio [HR] 2.34, 95% CI 1.22 to 4.48, p = 0.010). Independent predictors of NOAF were transapical and transaortic approach as well as balloon postdilatation (HR 3.48, 95% CI 1.66 to 7.29, p = 0.001; HR 5.08, 95% CI 2.08 to 12.39, p <0.001; HR 2.76, 95% CI 1.25 to 6.08, p = 0.012, respectively). In conclusion, preexisting AF is common in patients undergoing TAVI and is associated with a twofold increased risk of 1-year mortality. This negative effect is most pronounced in patients discharged with single antiplatelet therapy compared with other antithrombotic regimens.**  **(Am J Cardiol 2016;118:1527−1532)**

Transcatheter aortic valve implantation (TAVI) is an established treatment for patients with aortic stenosis (AS) who are inoperable or at high risk for surgery.[1,2] A substantial proportion of patients who are scheduled for TAVI are noted to have atrial fibrillation (AF) at the time of the screening for eligibility for TAVI.[3] Indeed, AF and AS coexist with a prevalence that varies from 16% to 40%.[4] Moreover, new-onset AF (NOAF) is a frequent finding in the postoperative period after TAVI, with an incidence ranging from 0.7% to 31.9%.[5] Population-based studies indicate an increased risk of stroke and systemic embolism as well as impaired long-term survival of subjects with AF compared with those with normal sinus rhythm (SR).[6] In the general population, AF is estimated to increase the risk of death 1.5-fold in men and 1.9-fold in women.[7] AF is a well-established predictor of adverse outcomes in patients with AS, and several previous studies demonstrated increased risk for mortality related to AF in patients undergoing open-chest valve surgery.[8,9] Similarly, NOAF is associated with overall and late mortality after coronary artery bypass graft, perioperative complications, and 30-day mortality and cerebrovascular events (CVE) in patients with postmyocardial infarction.[10] However, data on the prevalence and impact of preexisting AF or NOAF in the setting of TAVI are scant and limited to retrospective studies that have specifically focused on this issue.[11−15] In the present study, we sought to evaluate the epidemiology, predictors, management, and prognostic implications of AF, either preexisting or new-onset, in patients who underwent TAVI.

## Methods

Data were collected on consecutive patients with severe, symptomatic AS undergoing TAVI at Baylor Heart and Vascular Hospital (Dallas, Texas) and the Heart Hospital Baylor Plano (Plano, Texas) from January 2012 to August 2015. Baseline demographics, procedural data, and clinical outcomes were retrospectively collected and analyzed. For

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See page 1531 for disclosure information.

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Table 1
Characteristics of the study population

| Variable | All patients (n=708) | Sinus Rhythm (n=423) | Pre-existing AF (n=219) | New-Onset AF (n=66) | p |
|---|---|---|---|---|---|
| Baseline characteristics | | | | | |
| Age (years), mean ± SD | 81.9±7.8 | 80.9±8.3 | 83.4±6.6 | 83.1±7.7 | 0.001 |
| Men | 341 (54.4%) | 231 (54.6%) | 128 (58.4%) | 28 (42.4%) | 0.072 |
| Body Mass Index (kg/m$^2$), median (IQR) | 27.9±12.9 | 28.4±15.9 | 26.8±5.9 | 28.9±8.1 | ns |
| Hypertension | 574 (82.2%) | 352 (84.0%) | 167 (78.0%) | 56 (84.8%) | ns |
| Hyperlipidemia | 481 (69.6%) | 293 (70.9%) | 150 (70.1%) | 39 (60.0%) | ns |
| Diabetes | 265 (40.1%) | 165 (42.0%) | 74 (36.3%) | 26 (40.0%) | ns |
| Chronic kidney disease | 345 (49.6%) | 207 (50.0%) | 109 (50.2%) | 29 (43.9%) | ns |
| End stage renal disease | 22 (3.5%) | 13 (3.5%) | 7 (3.6%) | 2 (3.1%) | ns |
| Coronary artery disease | 475 (68.2%) | 291 (70.3%) | 140 (64.2%) | 44 (67.7%) | ns |
| Peripheral arterial disease | 225 (34.0%) | 140 (35.4%) | 65 (32.0%) | 20 (31.7%) | ns |
| COPD | 132 (20.8%) | 81 (21.4%) | 36 (18.5%) | 15 (23.8%) | ns |
| Previous CABG/PCI | 296 (44.6%) | 176 (44.1%) | 91 (45.3%) | 29 (45.3%) | ns |
| Previous CVE | 124 (19.5%) | 60 (16.1%) | 54 (26.7%) | 10 (15.9%) | 0.007 |
| Echocardiographic findings | | | | | |
| Left ventricle ejection fraction (%), mean ± SD | 54.6±13.0 | 55.0±13.1 | 53.3±13.1 | 55.7±12.7 | ns |
| Stroke Volume indexed (ml/m$^2$), mean ± SD | 37.6±12.0 | 38.6±12.3 | 34.8±11.4 | 40.8±10.3 | <0.0001 |
| Aortic valve mean gradient (mmHg), mean ± SD | 44.1±13.6 | 44.4±13.5 | 43.3±14.1 | 44.8±12.6 | ns |
| Aortic valve area (cm$^2$), mean ± SD | 0.68±0.18 | 0.69±0.18 | 0.66±0.18 | 0.61±0.18 | 0.054 |
| Procedural characteristics | | | | | |
| Type of Valve | | | | | ns |
| Balloon-expandable | 451 (63.8%) | 264 (62.4%) | 142 (64.8%) | 46 (69.7%) | ns |
| Self-expandable | 256 (36.2%) | 159 (37.6%) | 77 (35.2%) | 20 (30.3%) | ns |
| Approach | | | | | <0.0001 |
| Trans-femoral | 610 (86.3%) | 376 (88.9%) | 192 (87.7%) | 43 (65.2%) | |
| Trans-apical | 65 (9.2%) | 33 (7.8%) | 17 (7.8%) | 15 (22.7%) | |
| Trans-aortic | 28 (4.0%) | 11 (2.6%) | 10 (4.6%) | 7 (10.6%) | |
| Subclavian | 4 (0.6%) | 3 (0.7%) | 0 (0.0%) | 1 (1.5%) | |
| Post-operative Drugs | | | | | <0.0001 |
| DAPT | 426 (61.0%) | 315(75.2%) | 77 (35.8%) | 34 (53.1%) | |
| OAT | 133 (19.1%) | 25 (6.0%) | 92 (42.8%) | 16 (25.0%) | |
| DAPT+OAT | 40 (5.7%) | 4 (1.0%) | 28 (13.0%) | 8 (12.5%) | |
| Single antiplatelet therapy | 99 (14.2%) | 75 (17.9%) | 18 (8.4%) | 6 (9.4%) | |

AF = atrial fibrillation; CABG = coronary aortic bypass graft; COPD = chronic obstructive pulmonary disease; CVE = cerebrovascular events; DAPT = double antiplatelet therapy; IQR = interquartile range; NOAF = new-onset atrial fibrillation; OAT = oral anticoagulant therapy; PCI = percutaneous coronary intervention; SD = standard deviation.

the purpose of the current analysis, data from both medical centers were pooled, and a joint database was created. The study was approved by the Baylor Institutional Review Board.

Preexisting AF was diagnosed based on clinical history and/or on a 12-lead electrocardiogram performed before TAVI. NOAF was defined as any episode of AF occurring within 30 days after TAVI in a patient with no previous known AF, lasting long enough to be recorded on a 12-lead electrocardiogram or at least 30 seconds on a rhythm strip.[11,16,17] All study end points were defined according to Valve Academic Research Consortium definitions.[18] The primary outcomes of interest were all-cause death and stroke both at 30-day and at 1-year follow-up. Secondary measures included in-hospital mortality and minor, major, and life-threatening bleedings.

Continuous variables are summarized as mean ± SD or as medians and interquartile range as appropriate and were compared using the Student *t* test or Mann−Whitney rank-sum test. Categorical variables were compared using the chi-square or the Fisher's exact test. Binary logistic regression was used for the prediction of NOAF and 1-year all-cause mortality in the whole population as well as in patients with AF, respectively, as dependent variables, whereas baseline variables of clinical interest and/or satisfaction of the entry criterion of $p < 0.05$ in the univariable analysis were used as explanatory variables. Survival curves were constructed using Kaplan−Meier estimates, whereas comparisons relied on the log-rank test. A 2-sided alpha level of 0.05 was used for all superiority testing. All statistical analyses were performed using SPSS (version 19) statistical software (SPSS, Inc., Chicago, Illinois).

## Results

The study population consisted of 708 patients who underwent TAVI, divided in 3 study groups: patients in SR up to 30 days after TAVI and without any history of AF (n = 423), patients with preexisting AF (n = 219), and patients with NOAF (n = 66). The baseline characteristics, echocardiographic, and procedural data of these groups are

Table 2
Clinical outcomes

| Variable | All patients (n=708) | Sinus Rhythm (n=423) | Pre-existing AF (n=219) | New-Onset AF (n=66) | p |
|---|---|---|---|---|---|
| In-hospital mortality | 11 (1.6%) | 5 (1.2%) | 5 (2.3%) | 1 (1.5%) | 0.564 |
| Bleeding | | | | | 0.666 |
| Minor | 45 (6.4%) | 23 (5.5%) | 18 (8.2%) | 4 (6.1%) | |
| Major and life-threatening | 10 (1.4%) | 7 (1.7%) | 2 (0.9%) | 1 (1.5%) | |
| 30-day outcomes | | | | | |
| Stroke/TIA | 17 (2.4%) | 9 (2.1%) | 5 (2.3%) | 3 (4.5%) | 0.486 |
| All-cause mortality | 21 (3.0%) | 9 (2.1%) | 10 (4.6%) | 2 (3.0%) | 0.225 |
| 1-year outcomes | | | | | |
| Stroke/TIA | 24 (4.6%) | 12 (3.9%) | 7 (4.3%) | 5 (10.2%) | 0.147 |
| All-cause mortality | 51 (9.9%) | 20 (6.5%) | 23 (14.6%) | 8 (16.3%) | 0.007 |

AF = atrial fibrillation; TIA = transient ischemic attack.

Table 3
Stratified analysis according to discharge therapy in patients with atrial fibrillation for all-cause mortality at 1 year

| Variable | n | Event | HR, 95% CI | p |
|---|---|---|---|---|
| Single Anti-Platelet Therapy | 14 | 6 (42.9%) | reference | - |
| Multiple anti-thrombotic therapy | 188 | 22 (11.7%) | 0.18 (0.06-0.56) | 0.003 |
| DAPT | 84 | 11 (13.1%) | 0.20 (0.06-0.69) | 0.011 |
| OAT | 74 | 6 (8.1%) | 0.12 (0.03-0.45) | 0.002 |
| DAPT+OAT | 30 | 5 (16.7%) | 0.27 (0.06-1.11) | 0.070 |

CI = confidence interval; DAPT = double antiplatelet therapy; HR = hazard ratio; OAT = oral anticoagulant therapy.

Table 4
Stratified analysis according to type of atrial fibrillation for all-cause mortality at 1 year

| Rhythm | n | Event | HR, 95% CI | p |
|---|---|---|---|---|
| Sinus Rhythm | 306 | 20 (6.5%) | reference | |
| Permanent AF | 147 | 21 (14.3%) | 2.38 (1.25-4.55) | 0.009 |
| Persistent AF | 1 | 0 | - | |
| Paroxysmal AF | 5 | 0 | - | |
| Atrial Flutter | 5 | 2 (40.0%) | 9.53 (1.50-60.37) | 0.017 |
| NOAF | 49 | 8 (16.3%) | 2.79 (1.15-6.75) | 0.023 |

AF = atrial fibrillation; CI = confidence interval; HR = hazard ratio; NOAF = new-onset atrial fibrillation.

listed in Table 1. The observed prevalence of preexisting AF (paroxysmal, persistent, or permanent) in our study population was 30.9%. Patients with preexisting AF displayed a higher prevalence of previous CVE, had a lower stroke volume index (SVi), and were significantly older than patients in SR. NOAF was observed in 66 patients (9.3%). A significantly higher incidence of NOAF was observed in patients treated using the transapical, transaortic, or other approaches compared with those treated using the transfemoral approach (23.1%, 28.6%, and 25.0% vs 7.2%, respectively; p <0.001).

Clinical outcomes are described in Table 2. Patients with preexisting AF and patients with NOAF showed a higher rate of 1-year all-cause mortality compared with patients in SR (14.6% vs 6.5% for preexisting AF and 16.3% vs 6.5% for NOAF, p = 0.007, Table 2). In-hospital and 30-day mortality rates, 30-day and 1-year stroke/transient ischemic attack rate and bleeding were similar between groups (Table 2). When looking at patients with AF, those discharged with single antiplatelet therapy displayed higher mortality rates at 1 year compared with patients treated with dual antiplatelet therapy or anticoagulants (42.9% vs 11.7%, p = 0.011; Table 3). Table 4 reports number of events and hazard ratio (HR; 95% CI) for each type of AF; permanent AF, atrial flutter, and NOAF were associated with a significantly higher rate of 1-year all-cause mortality (HR 2.38, 95% CI 1.25 to 4.55, p = 0.009; HR 9.53, 95% CI 1.50 to 60.37, p = 0.017; HR 2.79, 95% CI 1.15 to 6.75, p = 0.023, respectively). The event-free survival curves at 1 year of patients treated by TAVI according to the presence of AF (either preexisting and new-onset) are shown in Figure 1. Overall, patients with AF (either preexisting or new-onset) had worse outcomes compared with those in SR in terms of all-cause mortality (log-rank = 0.008; Figure 1). Survival curves of patients with AF (either preexisiting or new-onset) according to the antithrombotic discharge regimen are shown in Figure 1. AF patients discharged with single antiplatelet therapy displayed the worst survival at 1-year follow-up (log-rank = 0.003; Figure 1).

Predictors of 1-year all-cause mortality are reported in Table 5. In the total population, male gender and preexisting AF are both independent predictors of mortality at 1-year follow-up (HR 2.05, 95% CI 1.07 to 3.90, p = 0.029; HR 2.34, 95% CI 1.22 to 4.48, p = 0.010, respectively). Moreover, the use of a transfemoral approach showed a significant protective role on mortality at 1 year (HR 0.34, 95% CI 0.16 to 0.73, p = 0.006). Table 5 reports the multivariable analysis for 1-year all-cause mortality in patients with AF as well. As shown, single antiplatelet therapy and a transfemoral approach remained the only independent predictors of 1-year mortality in patients with AF (HR 4.25, 95% CI 1.17 to 15.4, p = 0.028; HR 0.28, 95% CI 0.10 to 0.78, p = 0.015, respectively).

Predictors of the incidence of NOAF are reported in Table 6. The use of transapical and transaortic approach as well as balloon postdilatation resulted as independent predictors of NOAF (HR 3.48, 95% CI 1.66 to 7.29, p = 0.001; HR 5.08, 95% CI 2.08 to 12.39, p <0.001; HR 2.76, 95% CI 1.25 to 6.08, p = 0.012, respectively).

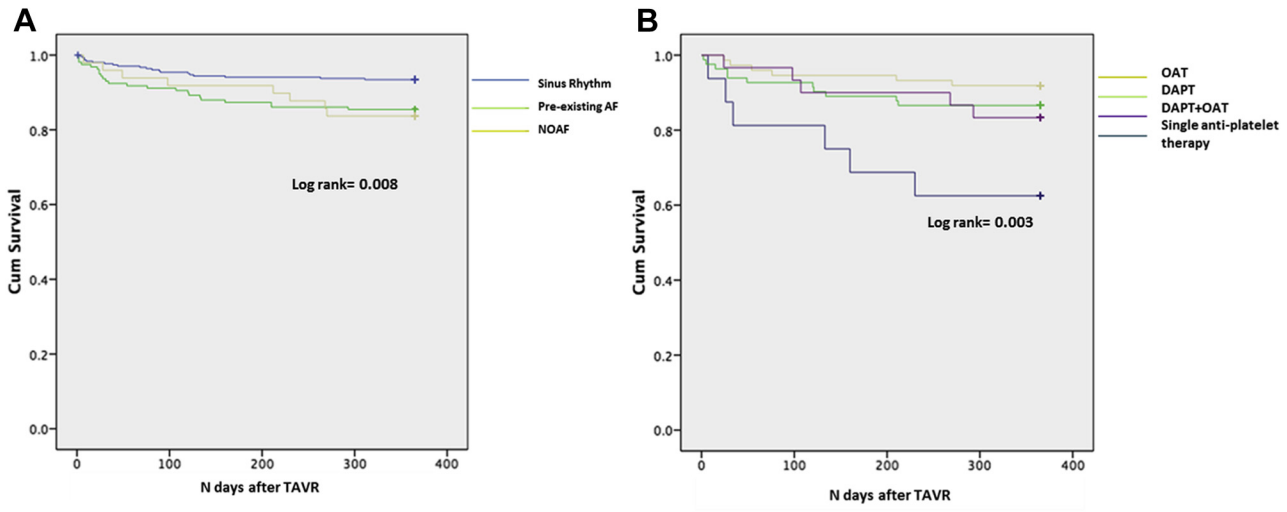


Figure 1. Kaplan–Meier survival curves. *(A)* 1-year survival according to group rhythm. *(B)* 1-year survival according to the discharge antithrombotic therapy in patients with AF.

Table 5
Predictors of all-cause mortality at 1 year in the total population and in the atrial fibrillation patients

| Variable | Multivariate Analysis | |
|---|---|---|
| | HR (95% CI) | p |
| All Patients | | |
| Male sex | 2.05 (1.07-3.90) | **0.029** |
| Chronic kidney disease | 1.79 (0.97-3.30) | 0.060 |
| Pre-existing Atrial Fibrillation | 2.34 (1.22-4.48) | **0.010** |
| New-Onset Atrial Fibrillation | 2.15 (0.82-5.64) | 0.119 |
| Atrial fibrillation patients | | |
| Age | 1.00 (0.94-1.07) | 0.923 |
| LVEF | 1.02 (0.98-1.06) | 0.328 |
| *For each 1 unit increase* | | |
| Thrombocytopenia | 0.99 (0.98-1.00) | 0.212 |
| *For each 1 unit increase* | | |
| Single Anti-Platelet Therapy | 4.25 (1.17-15.4) | **0.028** |
| Trans-femoral Approach | 0.28 (0.10-0.78) | **0.015** |
| Trans-femoral Approach | 0.34 (0.16-0.73) | **0.006** |

Statistically significant values are shown in bold type.
CI = confidence interval; HR = hazard ratio.

Table 6
Predictors of new-onset atrial fibrillation

| | Multivariate Analysis | |
|---|---|---|
| | HR (95% CI) | p |
| Age | 1.03 (0.99-1.07) | 0.105 |
| Body Mass Index (kg/m$^2$) | 1.01 (0.99-1.02) | 0.190 |
| *For each 1 unit increase* | | |
| Stroke Volume Indexed (ml/m$^2$) | 1.02 (0.99-1.04) | 0.057 |
| *For each 1 unit increase* | | |
| Self-expandable Valve | 2.07 (0.93-4.58) | 0.074 |
| Balloon post-dilatation | 2.76 (1.25-6.08) | **0.012** |
| Trans-apical Approach | 3.48 (1.66-7.29) | **0.001** |
| Trans-Aortic Approach | 5.08 (2.08-12.39) | **<0.001** |
| Trans-Subclavian | 6.00 (0.48-74.87) | 0.164 |

CI = confidence interval; HR = hazard ratio.

## Discussion

The present study adds to the current knowledge that (1) preexisting AF is a common condition among high-risk elderly patients undergoing TAVI, with a prevalence of 30.9% in this patient population; (2) preexisting AF is associated with a significantly increased risk of all-cause mortality at 1-year follow-up, whereas it does not seem to represent a risk factor for 30-day all-cause mortality or for short- and long-term stroke; (3) NOAF occurred in 9.3% of patients after TAVI, with a particularly higher incidence in those treated with a transapical or transaortic approach and with a balloon postdilatation; NOAF, however, was not an independent predictor of mortality in our cohort; and (4) Patients with AF discharged with single antiplatelet therapy post-TAVI have worse 1-year survival compared with other antithrombotic regimens.

AF has a high prevalence in patients with severe AS. It is well established that AF is a major predictor of death, stroke, and congestive heart failure in cardiac surgery.[6] Unfortunately, only a few conflicting small studies have assessed the epidemiology and clinical impact of AF in TAVI-treated patients.[19] Indeed, in 2 small series of patients undergoing TAVI, Nuis et al[13] and Amat-Santos et al[11] observed a significant direct correlation between NOAF and stroke only. Conversely, Yankelson et al[14] and Barbash et al[12] found that preexisting AF, but not NOAF, increased the rate of mortality and stroke at 1 year. Finally, Stortecky et al[5] and Nombela-Franco et al[3] found that both NOAF and preexisting AF increased the risk for ischemic cardiac and cerebrovascular events at follow-up. A recent meta-analysis, including these studies, concluded that AF was associated with a significantly increased risk of all-cause mortality at long-term follow-up, whereas NOAF was associated with increased risk of stroke.[20] An updated version of this meta-analysis identified NOAF as linked to higher mortality rates both at 30-day and 1-year post-TAVI.[21] Similarly, a recent report from the SOURCE XT (SAPIEN XT Aortic Bioprosthesis Multi-Region Outcome

Registry) registry concluded that the presence of either preexisting or NOAF increased all-cause and cardiac mortality and bleeding events and that NOAF was associated with increased stroke rates at long-term follow-up. However, therapy data were not reported.[15]

Our study confirms the observations about preexisting AF and all-cause mortality. Similarly, our study corroborates a link between NOAF and stroke reported by previous reports.[11,22,23] We found, indeed, that the event rate trended higher, although not significantly, in patients with NOAF at short- and long-term follow-up. In contrast, in our cohort, patients with preexisting AF did not experience a higher incidence of new CVE, compared with patients in SR. First, it is possible that patients with AF were treated more aggressively with antithrombotic drugs, thus lowering the risk of stroke; second, it is important to underline that patients undergoing TAVI are already at increased risk for stroke. Moreover, we cannot exclude an underestimation of AF rate or some overlap between the NOAF and preexisting AF groups because of the limited sensitivity of the methods used in clinical practice to assess AF. In our cohort, systematic 72-hour continuous post-TAVR electrocardiographic monitoring was not routinely performed.

The association between transapical access and NOAF has been already reported and has been previously attributed to epicardial and pericardial injury, similar to that occurring in cardiac surgery.[24] This supports the current paradigm that transfemoral access provides the best outcomes and is the favored approach.[25,26] The continued reduction in delivery size now allows transfemoral access in greater than 90% of patients.[27] Balloon postdilation is an another independent procedural predictor of NOAF observed in this study, as well in other previous reports.[15] However, we found no association of NOAF with the presence of moderate/severe postprocedural paravalvular leak, perhaps because moderate/severe paravalvular leak is less common with new generation devices.[25]

The results of this study show that the patients with the worst survival after TAVI are those in AF (either preexisting or new-onset) that have been discharged with single antiplatelet therapy. Despite the belief that there was a contraindication to DAPT or oral anticoagulant therapy (such as thrombocytopenia, fall risk, high bleeding risk, and so on), patients with AF discharged on single antiplatelet therapy had the worst outcome of any of the groups. Even after adjusting for potential cofounders being discharged with single antiplatelet therapy remained an independent predictor of mortality (Table 6). This raises the question of whether this patient population would benefit from a more aggressive antithrombotic therapy despite the higher risk profile. Data from prospective studies or registries are needed to assess and compare alternative treatment strategies and regimens to reduce the risk of mortality. Of note, this result came from a small number of patients and should therefore be considered as hypothesis generating. Moreover, the study design (retrospective and observational) carries all the limitations inherent to such an investigation.

## Disclosures

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1. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S; PARTNER Trial Investigators. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. *N Engl J Med* 2010;363:1597−1607.
2. Smith CR, Leon MB, Mack MJ, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Williams M, Dewey T, Kapadia S, Babaliaros V, Thourani VH, Corso P, Pichard AD, Bavaria JE, Herrmann HC, Akin JJ, Anderson WN, Wang D, Pocock SJ; PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med* 2011;364:2187−2198.
3. Nombela-Franco L, Webb JG, de Jaegere PP, Toggweiler S, Nuis RJ, Dager AE, Amat-Santos IJ, Cheung A, Ye J, Binder RK, van der Boon RM, Van Mieghem N, Benitez LM, Perez S, Lopez J, San Roman JA, Doyle D, Delarochelliere R, Urena M, Leipsic J, Dumont E, Rodes-Cabau J. Timing, predictive factors, and prognostic value of cerebrovascular events in a large cohort of patients undergoing transcatheter aortic valve implantation. *Circulation* 2012;126:3041−3053.
4. Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV, Singer DE. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the anticoagulation and risk factors in atrial fibrillation (atria) study. *JAMA* 2001;285:2370−2375.
5. Stortecky S, Windecker S, Pilgrim T, Heg D, Buellesfeld L, Khattab AA, Huber C, Gloekler S, Nietlispach F, Mattle H, Juni P, Wenaweser P. Cerebrovascular accidents complicating transcatheter aortic valve implantation: frequency, timing and impact on outcomes. *EuroIntervention* 2012;8:62−70.
6. Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. *Circulation* 1998;98:946−952.
7. Miyasaka Y, Barnes ME, Bailey KR, Cha SS, Gersh BJ, Seward JB, Tsang TS. Mortality trends in patients diagnosed with first atrial fibrillation: a 21-year community-based study. *J Am Coll Cardiol* 2007;49:986−992.
8. Jorgensen TH, Thygesen JB, Thyregod HG, Svendsen JH, Sondergaard L. New-onset atrial fibrillation after surgical aortic valve replacement and transcatheter aortic valve implantation: a concise review. *J Invasive Cardiol* 2015;27:41−47.
9. Filardo G, Hamilton C, Hamman B, Hebeler RF Jr, Adams J, Grayburn P. New-onset postoperative atrial fibrillation and long-term survival after aortic valve replacement surgery. *Ann Thorac Surg* 2010;90:474−479.
10. Mariscalco G, Klersy C, Zanobini M, Banach M, Ferrarese S, Borsani P, Cantore C, Biglioli P, Sala A. Atrial fibrillation after isolated coronary surgery affects late survival. *Circulation* 2008;118:1612−1618.
11. Amat-Santos IJ, Rodes-Cabau J, Urena M, DeLarochelliere R, Doyle D, Bagur R, Villeneuve J, Cote M, Nombela-Franco L, Philippon F, Pibarot P, Dumont E. Incidence, predictive factors, and prognostic value of new-onset atrial fibrillation following transcatheter aortic valve implantation. *J Am Coll Cardiol* 2012;59:178−188.
12. Barbash IM, Minha S, Ben-Dor I, Dvir D, Torguson R, Aly M, Bond E, Satler LF, Pichard AD, Waksman R. Predictors and clinical implications of atrial fibrillation in patients with severe aortic stenosis undergoing transcatheter aortic valve implantation. *Catheter Cardiovasc Interv* 2015;85:468−477.
13. Nuis RJ, Van Mieghem NM, Schultz CJ, Moelker A, van der Boon RM, van Geuns RJ, van der Lugt A, Serruys PW, Rodes-Cabau J,

van Domburg RT, Koudstaal PJ, de Jaegere PP. Frequency and causes of stroke during or after transcatheter aortic valve implantation. *Am J Cardiol* 2012;109:1637−1643.
14. Yankelson L, Steinvil A, Gershovitz L, Leshem-Rubinow E, Furer A, Viskin S, Keren G, Banai S, Finkelstein A. Atrial fibrillation, stroke, and mortality rates after transcatheter aortic valve implantation. *Am J Cardiol* 2014;114:1861−1866.
15. Tarantini G, Mojoli M, Windecker S, Wendler O, Lefevre T, Saia F, Walther T, Rubino P, Bartorelli AL, Napodano M, D'Onofrio A, Gerosa G, Iliceto S, Vahanian A. Prevalence and impact of atrial fibrillation in patients with severe aortic stenosis undergoing transcatheter aortic valve replacement: an analysis from the source xt prospective multicenter registry. *JACC Cardiovasc Interv* 2016;9:937−946.
16. Wann LS, Curtis AB, January CT, Ellenbogen KA, Lowe JE, Estes NA 3rd, Page RL, Ezekowitz MD, Slotwiner DJ, Jackman WM, Stevenson WG, Tracy CM, Fuster V, Ryden LE, Cannom DS, Le Heuzey JY, Crijns HJ, Lowe JE, Curtis AB, Olsson SB, Ellenbogen KA, Prystowsky EN, Halperin JL, Tamargo JL, Kay GN, Wann LS, Jacobs AK, Anderson JL, Albert N, Hochman JS, Buller CE, Kushner FG, Creager MA, Ohman EM, Ettinger SM, Stevenson WG, Guyton RA, Tarkington LG, Halperin JL, Yancy CW; ACCF/AHA/HRS. 2011 ACCF/AHA/HRS focused update on the management of patients with atrial fibrillation (updating the 2006 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol* 2011;57:223−242.
17. Kappetein AP, Head SJ, Genereux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA, Hahn RT, Kirtane AJ, Krucoff MW, Kodali S, Mack MJ, Mehran R, Rodes-Cabau J, Vranckx P, Webb JG, Windecker S, Serruys PW, Leon MB; Valve Academic Research Consortium-2. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *EuroIntervention* 2012;8:782−795.
18. Leon MB, Piazza N, Nikolsky E, Blackstone EH, Cutlip DE, Kappetein AP, Krucoff MW, Mack M, Mehran R, Miller C, Morel MA, Petersen J, Popma JJ, Takkenberg JJ, Vahanian A, van Es GA, Vranckx P, Webb JG, Windecker S, Serruys PW. Standardized endpoint definitions for transcatheter aortic valve implantation clinical trials: a consensus report from the valve academic research consortium. *J Am Coll Cardiol* 2011;57:253−269.
19. Gargiulo G, Sannino A, Capodanno D, Barbanti M, Buccheri S, Perrino C, Capranzano P, Indolfi C, Trimarco B, Tamburino C, Esposito G. Transcatheter aortic valve implantation versus surgical aortic valve replacement: a systematic review and meta-analysis. *Ann Intern Med* 2016;165:334−344.
20. Sannino A, Gargiulo G, Schiattarella GG, Perrino C, Stabile E, Losi MA, Galderisi M, Izzo R, de Simone G, Trimarco B, Esposito G. A meta-analysis of the impact of pre-existing and new-onset atrial fibrillation on clinical outcomes in patients undergoing transcatheter aortic valve implantation. *EuroIntervention* 2015;11 [Epub ahead of print].
21. Gargiulo G, Capodanno D, Sannino A, Barbanti M, Perrino C, Capranzano P, Stabile E, Indolfi C, Trimarco B, Tamburino C, Esposito G. New-onset atrial fibrillation and increased mortality after transcatheter aortic valve implantation: a causal or spurious association? *Int J Cardiol* 2016;203:264−266.
22. Motloch LJ, Reda S, Rottlaender D, Khatib R, Muller-Ehmsen J, Seck C, Strauch J, Madershahian N, Erdmann E, Wahlers T, Hoppe UC. Postprocedural atrial fibrillation after transcatheter aortic valve implantation versus surgical aortic valve replacement. *Ann Thorac Surg* 2012;93:124−131.
23. Chopard R, Teiger E, Meneveau N, Chocron S, Gilard M, Laskar M, Eltchaninoff H, Iung B, Leprince P, Chevreul K, Prat A, Lievre M, Leguerrier A, Donzeau-Gouge P, Fajadet J, Mouillet G, Schiele F; FRANCE-2 Investigators. Baseline characteristics and prognostic implications of pre-existing and new-onset atrial fibrillation after transcatheter aortic valve implantation: results from the France-2 registry. *JACC Cardiovasc Interv* 2015;8:1346−1355.
24. Tanawuttiwat T, O'Neill BP, Cohen MG, Chinthakanan O, Heldman AW, Martinez CA, Alfonso CE, Mitrani RD, Macon CJ, Carrillo RG, Williams DB, O'Neill WW, Myerburg RJ. New-onset atrial fibrillation after aortic valve replacement: comparison of transfemoral, transapical, transaortic, and surgical approaches. *J Am Coll Cardiol* 2014;63:1510−1519.
25. Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, Thourani VH, Tuzcu EM, Miller DC, Herrmann HC, Doshi D, Cohen DJ, Pichard AD, Kapadia S, Dewey T, Babaliaros V, Szeto WY, Williams MR, Kereiakes D, Zajarias A, Greason KL, Whisenant BK, Hodson RW, Moses JW, Trento A, Brown DL, Fearon WF, Pibarot P, Hahn RT, Jaber WA, Anderson WN, Alu MC, Webb JG; PARTNER 2 Investigators. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2016;374:1609−1620.
26. Blackstone EH, Suri RM, Rajeswaran J, Babaliaros V, Douglas PS, Fearon WF, Miller DC, Hahn RT, Kapadia S, Kirtane AJ, Kodali SK, Mack M, Szeto WY, Thourani VH, Tuzcu EM, Williams MR, Akin JJ, Leon MB, Svensson LG. Propensity-matched comparisons of clinical outcomes after transapical or transfemoral transcatheter aortic valve replacement: a placement of aortic transcatheter valves (partner)-I trial substudy. *Circulation* 2015;131:1989−2000.
27. Kodali S, Thourani VH, White J, Malaisrie SC, Lim S, Greason KL, Williams M, Guerrero M, Eisenhauer AC, Kapadia S, Kereiakes DJ, Herrmann HC, Babaliaros V, Szeto WY, Hahn RT, Pibarot P, Weissman NJ, Leipsic J, Blanke P, Whisenant BK, Suri RM, Makkar RR, Ayele GM, Svensson LG, Webb JG, Mack MJ, Smith CR, Leon MB. Early clinical and echocardiographic outcomes after Sapien 3 transcatheter aortic valve replacement in inoperable, high-risk and intermediate-risk patients with aortic stenosis. *Eur Heart J* 2016;37:2252−2262.