Clinical Investigation

Impact of Atrial Fibrillation Type on Outcomes of Transcatheter Aortic Valve Replacement for Aortic Stenosis: A Single-Center Analysis

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Abstract

Background: Atrial fibrillation (AF) is a recognized risk factor for mortality after transcatheter aortic valve replacement for severe aortic stenosis, but the impact of different types of AF on clinical outcomes remains unclear.

Methods: This retrospective study included 982 patients divided into 3 groups: no AF, paroxysmal AF, and nonparoxysmal AF (persistent or permanent). Clinical outcomes were analyzed using inverse probability weighting and multivariate models.

Results: There were 610, 211, and 161 patients in the no-AF, paroxysmal AF, and nonparoxysmal AF groups, respectively. For the entire cohort, the mean (SD) age was 82 (7.7) years, and the periprocedural, 1-year, and 5-year mortality rates were 2.0%, 12%, and 50%, respectively. After inverse probability weighting, the periprocedural mortality rate was higher in the nonparoxysmal AF group than in the no-AF group (odds ratio, 4.71 [95% CI, 1.24-17.9]). During 5 years of follow-up (median [IQR], 22 [0-69] months), all-cause mortality was higher in the nonparoxysmal AF group than in the no-AF group (hazard ratio [HR], 1.56 [95% CI, 1.14-2.14]; *P* = .006). The paroxysmal AF group was not associated with worse clinical outcomes than the no-AF group (HR, 1.02 [95% CI, 0.81-1.49]) for all-cause mortality. Stroke rates were comparable among the 3 groups. Multivariate analysis also showed increased all-cause mortality in the nonparoxysmal AF group compared with the no-AF group (adjusted HR, 1.43 [95% CI, 1.06-1.93]; *P* = .018), while all-cause mortality was comparable between the paroxysmal AF and no-AF groups (adjusted HR, 1.00 [95% CI, 0.75-1.33]).

Conclusion: In patients undergoing transcatheter aortic valve replacement for severe aortic stenosis, having nonparoxysmal AF was associated with a higher risk of periprocedural and all-cause mortality compared with having no AF. Paroxysmal AF showed no such association.

Keywords: Transcatheter aortic valve replacement; atrial fibrillation; aortic valve

Introduction

Atrial fibrillation (AF) is 1 of the most common cardiac arrhythmias, particularly in older patients and patients with heart failure (HF), and it is associated with an increased risk of stroke, HF, and mortality.[1,2] Transcatheter aortic valve replacement (TAVR) is a well-established treatment option for patients with symptomatic severe aortic stenosis (AS) that is considered surgically inoperable or who are considered intermediate

to high risk.[3-5] Patients with AS who are candidates for TAVR tend to be older and also have HF, and AF is a common condition in these cohorts. According to the Society of Thoracic Surgeons (STS)/American College of Cardiology Transcatheter Valve Therapies Registry, approximately 40% of patients undergoing TAVR for AS had a history of AF.[6] Atrial fibrillation is of concern in patients with AS because AS causes increased left ventricular end-diastolic pressure, resulting in poor left ventricular filling, which is exacerbated by AF because of the lack of atrial contraction. In fact, AF is a well-established risk factor for mortality, even after successful TAVR.[7-9] Little is known, however, about whether clinical outcomes differ between patients with different types of AF.[10,11] The sharing of important cardiovascular risk factors between AS and AF further complicates any direct comparison of their effects. To address these complexities, the current study aims to evaluate both early and late outcomes after TAVR by AF type using an inverse probability weighting (IPW) method to adjust for confounding.

Patients and Methods

This retrospective observational study reviewed the data of patients who underwent TAVR for severe AS at a participating institution. From January 2018 to September 2022, a total of 1,099 TAVR procedures was performed. Of the patients who underwent surgery, 982 qualified for inclusion in the current study. Patients who underwent valve-in-valve TAVR for a failed bioprosthesis (n = 114) were excluded, as were patients in whose cases the procedure was aborted because of the unsuccessful delivery of a transcatheter heart valve or in which TAVR was converted to surgical AVR (n = 3). The observational period for this study extended through September 30, 2023.

Patients were classified into 3 groups based on their diagnosed type of AF: (1) no AF, (2) paroxysmal AF, and (3) nonparoxysmal AF (persistent or permanent). The primary end point was all-cause mortality, and other outcomes of interest included periprocedural outcomes, all incidents of stroke, a composite of all-cause mortality or stroke, rehospitalization for HF, and overt bleeding. Definitions, terminology, and reported outcomes were consistent with the STS/American College of Cardiology Transcatheter Valve Therapies Registry and the Valve Academic Research Consortium 3 criteria.[12] The decision to perform a TAVR procedure was made by a

Key Points

- Patients with paroxysmal and non-paroxysmal AF accounted for 21% and 16%, respectively, of patients undergoing TAVR in this cohort.
- Nonparoxysmal AF was associated with a higher risk of periprocedural and all-cause mortality compared with not having AF. In contrast, paroxysmal AF showed no such association.
- Risk stratification has traditionally been based on the presence or absence of AF; however, this study suggests the importance of stratification by AF type when assessing risk and prognosis for TAVR.

Abbreviations

AF, atrial fibrillation
AS, aortic stenosis
HF, heart failure
IPW, inverse probability weighting
STS, Society of Thoracic Surgeons
TAVR, transcatheter aortic valve replacement

Supplementary Materials

For supplemental materials please see the online version of this paper.

dedicated heart team, primarily based on the patient's age and surgical risk according to the STS Predicted Risk of Mortality as well as on patient anatomy and patient-specific factors such as frailty. The choice of balloon-expanding or self-expanding valve for TAVR was generally not based on the presence or absence of AF but on several other factors, such as the presence of coronary artery disease and the anatomy of the aortic root complex, including annular size and valve/root calcification. For example, self-expanding valves are preferred for patients with small aortic annuli, while balloon-expandable valves are preferred in patients with coronary artery disease because they allow better access to the coronary ostium after TAVR. The general strategy for antithrombotic therapy after TAVR at the corresponding institution is as follows: double antiplatelet therapy for 4 weeks and single antiplatelet therapy thereafter in patients without AF; oral anticoagulation therapy and single antiplatelet therapy in patients with AF. This strategy, however, is individualized according to factors such as the risk of thrombosis or bleeding, the presence of coronary artery disease, the patient's history of deep vein thrombosis, left atrial appendage closure, and recent percutaneous coronary intervention. For follow-up, beginning from post-TAVR day 0 (time = 0), patients were censored at their last recorded contact,

whether at the corresponding hospital, their primary clinic, or by telephone. Follow-up event information was collected accordingly, with the observation period for each patient concluding upon their reaching the primary end point. The study protocol was approved by the Main Line Hospitals Institutional Review Board (45CFR164.512). Individual patient consent was waived because of the retrospective nature of the study.

Statistical Analysis

Continuous values are presented as mean (SD) unless otherwise noted. The distribution of these variables was assessed using the Shapiro-Wilk test. For variables with a normal distribution, the t test was used for 2-group comparisons, and analysis of variance was used for 3-group comparisons. For non-normal distributions, the Wilcoxon rank sum test was used for 2-group comparisons, and the Kruskal-Wallis test was used for analyses involving 3 groups. Categorical values are reported as numbers (percentages) or percentages, and the χ^2 test or Fisher exact test was used to compare groups, as appropriate. When statistically significant differences were observed among the 3 groups, post hoc tests with the Bonferroni correction were used to determine specific group differences. Inverse probability weighting was employed to estimate the average treatment effect while controlling for confounding variables. Propensity scores were calculated using a generalized

TABLE I. Baseline and Procedural Characteristics Before and After IPW

	Before IPW				After IPW			
	No AF (n = 610)	Paroxysmal AF (n = 211)	Nonparoxysmal AF (n = 161)[a]	P value	No AF (effective sample size, n = 571)	Paroxysmal AF (effective sample size, n = 172)	Nonparoxysmal AF (effective sample size, n = 100)[a]	P value
Baseline characteristics								
Age, mean (SD), y	81 (7.8)	82 (7.3)[b]	82 (7.4)[b]	.002	81 (7.8)	82 (7.1)	82 (7.1)	.10
Male sex, No. (%)	317 (52)	108 (51)	126 (65)	<.001	49	53	59	.17
Female sex, No. (%)	293 (48)	103 (49)	56 (35)[b,c]	<.001	51	47	41	.17
Body surface area, mean (SD), m²	1.89 (0.28)	1.88 (0.29)	1.97 (0.30)[b,c]	.04	1.89 (0.28)	1.91 (0.29)	1.95 (0.28)	.01
Body mass index, mean (SD)	28 (6.2)	27 (6.6)	28 (6.4)	.32	28 (6.3)	28 (6.2)	28 (6.2)	.80
New York Heart Association class III or IV, No. (%)	276 (45)	137 (65)[b]	103 (64)[b]	<.001	49	59	55	.10
STS score, mean (SD)	4.1 (3.4)	5.6 (4.1)[b]	5.5 (3.5)[b]	<.001	4.5 (3.7)	5.0 (3.7)	4.9 (3.4)	.19
Diabetes, No. (%)	194 (32)	78 (37)	57 (35)	.33	33	33	31	.93
Chronic obstructive pulmonary disease, No. (%)	113 (19)	47 (22)	32 (20)	.49	19	21	20	.94
Creatinine ≥2 mg/dL, No. (%)	73 (12)	36 (17)	16 (9.9)	.08	13	14	9.2	.45
Dialysis, No. (%)	22 (3.6)	11 (5.2)	6 (3.7)	.58	4.6	3.1	3.4	.54
Prior stroke, No. (%)	69 (11)	27 (13)	26 (16)	.25	11	13	16	.32
Peripheral artery disease, No. (%)	137 (22)	52 (25)	41 (25)	.65	25	21	28	.42
Prior percutaneous coronary intervention, No. (%)	221 (36)	84 (40)	60 (37)	.65	38	40	39	.89

Continued

TABLE I. Baseline and Procedural Characteristics Before and After IPW, Continued

	Before IPW				After IPW			
	No AF (n = 610)	Paroxysmal AF (n = 211)	Nonparoxysmal AF (n = 161)[a]	*P* value	No AF (effective sample size, n = 571)	Paroxysmal AF (effective sample size, n = 172)	Nonparoxysmal AF (effective sample size, n = 100)[a]	*P* value
Prior coronary artery bypass graft, No. (%)	86 (14)	39 (18)	45 (28)[b]	.001	16	18	21	.35
Prior pacemaker or defibrillator, No. (%)	57 (9.3)	39 (18)[b]	43 (27)[b]	<.001	12	18	19	.047
Hemoglobin, mean (SD), g/dL	12.3 (1.8)	11.6 (2.0)[b]	12.1 (2.0)	<.001	12.2 (1.9)	12.0 (2.0)	12.2 (1.9)	.70
Albumin, mean (SD), g/dL	3.7 (0.4)	3.6 (0.5)[b]	3.6 (0.4)[b]	<.001	3.7 (0.4)	3.7 (0.5)	3.7 (0.4)	.29
Brain-type natriuretic peptide, mean (SD), pg/mL	423 (675)	723 (909)[b]	561 (502)[b]	<.001	505 (746)	545 (717)	533 (572)	.75
Left ventricular ejection fraction, mean (SD), %	61 (12)	57 (16)[b]	55 (14)[b]	<.001	59 (13)	59 (13)	58 (14)	.62
Aortic valve area, mean (SD), cm^2	0.77 (0.22)	0.73 (0.19)	0.70 (0.16)	.54	0.76 (0.22)	0.74 (0.17)	0.72 (0.17)	.08
Mean pressure gradient, mean (SD), mm Hg	44 (13)	43 (13)	37 (12)[b,c]	<.001	43 (13)	42 (12)	40 (12)	.11
Mitral valve regurgitation of at least a moderate intensity, No. (%)	65 (11)	33 (16)	33 (20)[b]	.002	12	13	15	.65
Tricuspid valve regurgitation of at least a moderate intensity, No. (%)	43 (7.0)	34 (16)[b]	54 (34)[b,c]	<.001	11	13	18	.03
Bicuspid aortic valve, No. (%)	17 (2.8)	3 (1.4)	4 (2.5)	.58	2.4	1.3	2.4	.59
Procedural characteristics								
Nonelective procedure, No. (%)	44 (7.2)	30 (14)[b]	14 (8.7)	.009	9.1	10	6.7	.43
Transfemoral access, No. (%)	555 (91)	190 (90)	151 (93)	.42	90	91	96	.09
Self-expanding valve, No. (%)[d]	293 (48)	96 (45)	61 (38)	.07	48	44	38	.16

AF, atrial fibrillation; IPW, inverse probability weighting; STS, Society of Thoracic Surgeons.

SI conversion factor: To convert from mg/dL to μmol/L, multiply by 76.25. To convert from g/dL to g/L, multiply by 10. To convert from pg/mL to ng/L, multiply by 1.

[a] Persistent or chronic AF.

[b] Significant difference from no-AF group with post hoc test (*P* < .0167).

[c] Significant difference from paroxysmal AF group with post hoc test (*P* < .0167).

[d] Evolut R, PRO, PRO+, and FX valves (Medtronic) vs balloon-expandable valve (SAPIEN 3 Ultra [Edwards Lifesciences]).

boosted model with 10,000 trees, a shrinkage parameter of 0.01, and a minimum of 10 observations per node. The model included the covariates listed in Table I. Weights were derived from the propensity scores using the *twang* package in R (R Foundation for Statistical Computing). These weights were then applied to the data to balance the distribution of the covariates between groups. The goodness of fit of the variables was assessed using the absolute standardized mean difference, with values less than 0.1 indicating an ideal fit and values of 0.1 to 0.2 indicating an acceptable fit. Logistic regression analysis was used to calculate odds ratios and 95% CIs for periprocedural outcomes by AF type. New permanent pacemaker implantation was not included in the logistic regression analysis after IPW because of the challenges associated with excluding patients with prior pacemaker or defibrillator implantation from the cohort after IPW. Kaplan-Meier curves were constructed to estimate event-free rates for the outcomes of interest, and Cox proportional hazards models were used to assess the effect of AF type on all-cause mortality, stroke, and a composite of all-cause mortality or stroke. In addition, forward-selection multivariate models were used to assess predictors of all-cause mortality and the composite outcome. Predictors of periprocedural outcomes and stroke were not assessed by multivariate analysis because of the expected small number of events. In addition to the following prespecified variables—AF type, age, sex, New York Heart Association classification, and STS Predicted Risk of Mortality scores—variables with a statistically significant association ($P < .05$) with each outcome in the univariate analysis were included in the multivariate analysis. For patients with missing data for certain variables (albumin, n = 7; brain-type natriuretic peptide, n = 23; aortic valve area, n = 2), the median value or the most frequent value was imputed for multivariate analyses and propensity-score estimation. All *P* values were 2 sided, and a 5% level was considered statistically significant. All analyses were conducted using R, version 4.2.3, software.

Results

Baseline Patient Characteristics

Baseline and procedural characteristics before and after IPW are shown in Table I. Of the 982 patients in this study, there were 610 patients (62%), 211 patients (21%), and 161 patients (16%) in the no-AF, paroxysmal AF,

and nonparoxysmal AF groups, respectively. The mean (SD) age of the entire cohort was 82 (7.7) years. Before IPW, patients in the paroxysmal and nonparoxysmal AF groups were older, had higher rates of New York Heart Association class III and IV disease, had undergone pacemaker or defibrillator implantation, and experienced moderate or greater tricuspid valve regurgitation. They also had higher STS Predicted Risk of Mortality scores and brain-type natriuretic peptide levels as well as lower albumin levels and left ventricular ejection fractions than the no-AF group. In addition, patients in the nonparoxysmal AF group were more likely to be male and had a greater body surface area and a lower transaortic mean pressure gradient compared with patients in the other 2 groups. The mean (SD) annulus cardiac size was 24.5 (2.6) mm in the no-AF group, 25.1 (2.7) mm in the paroxysmal AF group, and 25.7 (2.8) mm in the nonparoxysmal AF group ($P < .01$). Because all the continuous variables analyzed had non-normal distributions, nonparametric analyses were used to compare the groups. Four and 6 patients had a history of left atrial appendage closure in the paroxysmal and nonparoxysmal AF groups, respectively. After IPW, similar baseline and procedural characteristics were observed, and most variables achieved ideal to acceptable balance among the 3 groups, with several variables showing mild imbalance, including body surface area, aortic valve area, mean pressure gradient, and prevalence of moderate or greater tricuspid valve regurgitation (Table I and Supplemental Table I). The absolute standardized mean difference with love plots is shown in Supplemental Figure 1.

During the study period, the Sapien 3 Ultra valve (Edwards Lifesciences) was used for balloon-expandable valves. For self-expanding valves, the Evolut R, Evolut PRO, Evolut PRO+, and Evolut FX valves (Medtronic) were used; the Evolut R valve was used in only 1 patient in this cohort.

Periprocedural Outcomes

The overall periprocedural mortality rate was 2.0%, and periprocedural outcomes are summarized in Supplemental Table II. Results of logistic regression analyses for the periprocedural outcomes by AF type are shown in Table II. After IPW, nonparoxysmal AF was significantly associated with a high periprocedural mortality rate compared with not having AF, with an odds ratio of 4.71 (95% CI, 1.24-17.9), whereas paroxysmal AF did not show a statistically significant difference. Other major complications were comparable among groups.

TABLE II. Periprocedural Outcomes Before and After IPW

| Variable | Paroxysmal AF vs no AF | | Nonparoxysmal AF[a] vs no AF | |
| | Odds ratio or standardized mean difference (95% CI) | | Odds ratio or standardized mean difference (95% CI) | |
	Crude	After IPW	Crude	After IPW
Periprocedural mortality	2.95 (0.91-9.52)	3.39 (0.97-11.8)	5.26 (1.80-16.2)[b]	4.71 (1.24-17.9)[b]
Major cardiac structural complication	2.34 (0.57-8.92)	2.70 (0.72-10.2)	1.52 (0.22-7.13)	2.31 (0.44-12.1)
Major vascular complication	1.32 (0.41-3.70)	1.97 (0.77-5.10)	1.03 (0.23-3.36)	0.47 (0.06-3.66)
Acute stroke	0.89 (0.25-2.54)	0.50 (0.11-2.26)	0.58 (0.09-2.12)	0.43 (0.06-3.35)
Acute kidney injury stage ≥2	0.57 (0.13-1.76)	0.44 (0.10-1.93)	1.01 (0.29-2.83)	1.15 (0.33-4.03)
New permanent pacemaker implantation[c]	1.28 (0.80-2.00)	NA	1.19 (0.68-2.00)	NA
Transaortic mean pressure gradient, mm Hg[c]	−0.71 (−1.47 to 0.05)	−0.30 (−1.10 to 0.49)	−2.22 (−3.07 to −1.38)[b]	−1.57 (−2.45 to −0.71)[b]
Transaortic mean pressure gradient ≥ 20 mm Hg[c]	0.67 (0.28-1.40)	0.79 (0.34-1.84)	0.11 (0.01-0.49)[b]	0.19 (0.03-1.40)
Prosthesis-patient mismatch of at least moderate intensity	1.04 (0.73-1.46)	0.99 (0.65-1.51)	1.34 (0.92-1.93)	1.06 (0.63-1.77)
Aortic valve regurgitation of at least moderate intensity[c]	2.97 (1.01-8.77)	1.92 (0.55-6.63)	1.08 (0.16-4.53)	0.81 (0.10-6.69)
STS risk score, mean (SD)	9.1 (5.5)	6.4 (4.5)	6.3 (3.2)	6.0 (3.7)

AF, atrial fibrillation; IPW, inverse probability weighting; NA, not applicable.

[a] Persistent or chronic AF.

[b] $P < .05$.

[c] Thirty-day data or in-hospital data if 30-day data were not available.

A lower postoperative mean pressure gradient was observed in patients with nonparoxysmal AF compared with patients without AF.

Late Outcomes

The median (IQR) follow-up period was 22 (0-69) months, and the Kaplan-Meier estimated 1-year and 5-year overall mortality rates were 12% and 50%, respectively. In addition, the incidence of stroke in the entire cohort was 2.2% at 1 year and 6.5% at 5 years. Antithrombotic therapy at discharge in each group is shown in Supplemental Table III. In summary, 61% of patients with paroxysmal AF and 86% of patients with nonparoxysmal AF were receiving oral anticoagulants at discharge. During follow-up after TAVR, 8 patients with paroxysmal AF and 5 patients with nonparoxysmal AF underwent left atrial appendage closure. Figure 1 shows Kaplan-Meier curves for the late outcomes of interest comparing the 3 groups, and Table III and Supplemental Table IV show the results of Cox proportional hazards regression analyses for the late outcomes. Nonparoxysmal AF was associated with an increased risk of all-cause mortality and a composite of all-cause mortality or stroke compared with not having AF, with hazard ratios of 1.56 (95% CI, 1.14-2.14) and 1.54 (95% CI, 1.14-2.09), respectively, after IPW. Although a crude analysis showed an increased risk of all-cause mortality and the composite outcome in the patients with paroxysmal AF compared with patients without AF, the differences after IPW were not statistically significant. Consistent findings were observed in the multivariate analyses; nonparoxysmal AF was an independent predictor of all-cause mortality and the composite outcome compared with not having AF, but paroxysmal AF was
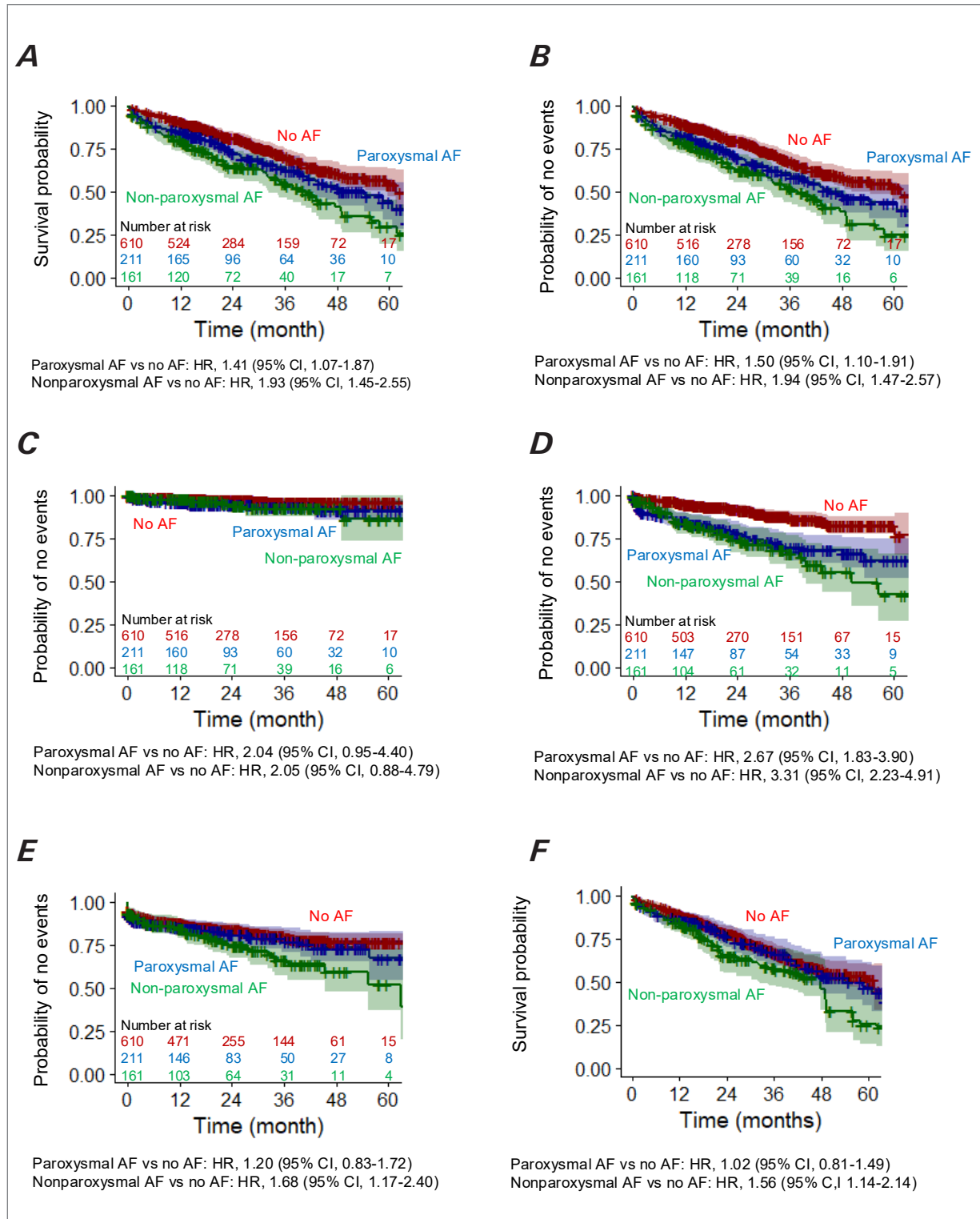
Fig. 1 Kaplan-Meier curves for late outcomes of interest show freedom from (**A**) all-cause mortality before IPW, (**B**) all-cause mortality or stroke before IPW, (**C**) all incidence of stroke before IPW, (**D**) rehospitalization for HF before IPW, (**E**) overt bleeding before IPW, and (**F**) all-cause mortality after IPW.

AF, atrial fibrillation; HF, heart failure; IPW, inverse probability weighting; HR, hazard ratio.

TABLE III. Risk Analysis for All-Cause Mortality, Composite of All-Cause Mortality and Stroke, and Stroke

Variables	Hazard ratio (95% CI)		
	All-cause mortality	Composite outcome[a]	Stroke
Crude			
Paroxysmal AF[b]	1.41 (1.07-1.87)[c]	1.50 (1.10-1.91)[c]	2.04 (0.95-4.40)
Nonparoxysmal AF[b]	1.93 (1.45-2.55)[c]	1.94 (1.47-2.57)[c]	2.05 (0.88-4.79)
After IPW			
Paroxysmal AF[b]	1.02 (0.81-1.49)	1.13 (0.84-1.52)	1.85 (0.82-4.17)
Nonparoxysmal AF[b]	1.56 (1.14-2.14)[c]	1.54 (1.14-2.09)[c]	1.50 (0.60-3.76)
Multivariate			NA
Paroxysmal AF[b]	1.00 (0.75-1.33)	1.05 (0.80-1.38)	
Nonparoxysmal AF[b]	1.43 (1.06-1.93)[c]	1.42 (1.06-1.89)[c]	
Age, y	1.04 (1.02-1.06)[c]	1.04 (1.02-1.06)[c]	
Female sex	Not selected	0.84 (0.66-1.05)	
New York Heart Association class III and IV	Not selected	Not selected	
STS score	Not selected	1.02 (0.99-1.05)	
Diabetes	1.31 (1.03-1.66)[c]	1.24 (0.98-1.57)	
Chronic obstructive pulmonary disease	1.58 (1.21-2.06)[c]	1.41 (1.08-1.84)[c]	
Creatinine ≥2 mg/dL	1.45 (1.02-2.06)[c]	Not selected	
Hemoglobin, g/dL	0.91 (0.85-0.98)[c]	0.91 (0.85-0.98)[c]	
Albumin, g/dL	0.55 (0.42-0.73)[c]	0.53 (0.41-0.69)[c]	
Left ventricular ejection fraction, %	0.99 (0.98-0.998)[c]	Not selected	
Transaortic mean pressure gradient, mm Hg	0.99 (0.98-1.002)	0.99 (0.98-1.002)	
Tricuspid valve regurgitation of at least moderate intensity	1.62 (1.19-2.22)[c]	1.60 (1.19-2.17)[c]	

AF, atrial fibrillation; IPW, inverse probability weighting; NA, not applicable; STS, Society of Thoracic Surgeons.

SI conversion factor: To convert from mg/dL to μmol/L, multiply by 88.4. To convert from g/dL to d/L, multiply by 10.

[a] All-cause mortality and stroke.

[b] No-AF as reference.

[c] $P < .05$.

not. Atrial fibrillation type was not significantly associated with stroke. Both paroxysmal and nonparoxysmal AF, however, were associated with a higher risk of rehospitalization for HF compared with not having AF both before and after IPW and in multivariate analysis. The incidence of overt bleeding was comparable between patients without AF and patients with paroxysmal AF. In contrast, the incidence of overt bleeding was significantly higher in patients with nonparoxysmal AF compared with patients without AF both before and after IPW. Multivariate analysis, however, showed no statistically significant difference in overt bleeding between the 2 groups (Supplemental Table IV).

Discussion

This study found that nonparoxysmal AF was significantly associated with higher rates of periprocedural mortality, all-cause mortality, a composite of all-cause mortality or stroke, and rehospitalization for HF during follow-up compared with not having AF. Paroxysmal AF was not associated with increased rates of all-cause mortality, stroke, or overt bleeding, but the rate of rehospitalization for HF was significantly higher in patients with paroxysmal AF than in patients without AF. The prevalence of a history of AF in patients undergoing TAVR (37%), patients with periprocedural mortality (2.0%), and with 1-year and 5-year mortality rates (12% and 50%) were consistent with prevalence rates found in previous studies.[6,13] The current study is unique in that it compares TAVR outcomes by AF type while adjusting for confounders using the IPW method.

Atrial fibrillation is a well-known risk factor for all-cause mortality after TAVR for severe AS,[7-9] but studies of the effect of the AF type have been limited. The higher rate of late mortality after TAVR in patients with nonparoxysmal AF compared with patients without AF has been reported by Shaul et al[10] and Jaakkola et al.[11] The results of the current study are consistent with the results of these studies, even after adjustment of confounders using both IPW and multivariate analysis. The discrepancy in the results between patients with paroxysmal and nonparoxysmal AF compared with patients without AF was reasonable; a previous meta-analysis showed that nonparoxysmal AF was associated with a significantly higher risk of mortality than paroxysmal AF in the general population.[14] The authors of the meta-analysis speculated that worsening HF caused by long-standing AF, more severe stroke events, or a higher burden of noncardiovascular disease were potential causes of the poorer outcomes. In patients with AS, AF presents a particular challenge because it leads to increased left ventricular end-diastolic pressure. This increase in pressure can compromise left ventricular filling, a situation further exacerbated by AF because of the lack of atrial contraction. The current study even showed a significantly higher periprocedural mortality despite a comparable incidence of other major complications, including acute stroke. The cardiac damage and degeneration caused by long-standing AF may contribute to these results. Further research with a larger cohort is needed to validate the results of the current study and elucidate the mechanism of the potential periprocedural risks of nonparoxysmal AF in TAVR.

Atrial fibrillation is an important risk factor for thromboembolism and stroke, but no association between any type of AF and the incidence of stroke was observed in this study. These findings are in line with a previous meta-analysis[15] that showed no difference between patients who did not have AF and patients who did have AF after TAVR. Although not fully evaluated in the current study, optimal anticoagulation therapy could have played an important role in the lack of association of any subtype of AF with early or late stroke. Indeed, the observed low incidence of stroke over the 5-year follow-up period is consistent with findings from previous studies[16] and suggests that the patients likely benefited from optimal medical management. The current study conversely suggests that the incidence of overt bleeding after TAVR may be higher in patients with nonparoxysmal AF than in patients without AF. In addition to individualized optimal management for antithrombotic medications, the potential benefits of left atrial appendage closure and discontinuation of oral anticoagulants in patients with AF at high risk of bleeding who undergo TAVR warrant further investigation. The observed association between nonparoxysmal AF and increased mortality after TAVR underscores the need for further research to explore whether early screening and prevention of progression to nonparoxysmal AF in patients with early-stage AS could improve the prognosis for patients with AS and patients with AF.

Risk stratification has traditionally been based on the presence or absence of AF, but the current study shows that patients with nonparoxysmal AF have a poorer prognosis, while patients with paroxysmal AF have an outcome comparable to that of patients without AF in terms of survival and risk of stroke or bleeding. These findings underscore the critical need for stratification by AF type when assessing risk and prognosis for TAVR. This approach could lead to more personalized care and better health outcomes for patients with different types of AF.

Study Limitations

This was a single-center retrospective study that included a modest number of patients and that covered a relatively short period of observation. As a result, the study has limited statistical power, especially when examining outcomes with fewer events, such as stroke. In particular, an association between stroke and the AF groups was not observed in this study, which may be a result of the small study population and the limited number of stroke events observed. Secondly, patient

characteristics were heterogeneous across the groups. To address this limitation, IPW and multivariable analysis methods were used. Inverse probability weighting is commonly used to balance treatment choices, but it is also useful to adjust for confounders in observational studies in which the primary aim is to assess the impact of specific factors on outcomes.[17,18] Despite best efforts to mitigate confounding factors through the use of IPW, mild imbalance (absolute standardized mean difference >0.2) remained in several variables. The possibility of unmeasured confounders, such as the duration of AF, left atrial volume, and pulmonary pressure, could have a further impact on the results of this study. The consistency observed between the results of IPW and multivariate analysis could nevertheless strengthen the validity of the study's findings by providing a more comprehensive approach to addressing confounding factors. In addition, the current study's database did not include detailed records of medication regimens, particularly anticoagulation therapy, during follow-up, which hindered a comprehensive analysis including these variables. The consistency of survival rates and stroke incidence in previous studies,[13] however, supports the external generalizability of the current study's results, despite the data limitations encountered.

Conclusion

In patients undergoing TAVR for AS, nonparoxysmal AF was associated with worse clinical outcomes in terms of higher risk of periprocedural mortality, all-cause mortality, and rehospitalization for HF compared with not having AF. The risk of overt bleeding may also be higher. Patients with paroxysmal AF had comparable rates of mortality, stroke, and overt bleeding compared with patients without AF, though the rate of rehospitalization for HF was higher.

Article Information

References

1. Gao P, Gao X, Xie B, Tse G, Liu T. Aging and atrial fibrillation: a vicious circle. *Int J Cardiol.* 2024;395:131445. doi:10.1016/j.ijcard.2023.131445

2. Lee KS, Park DI, Lee J, Oh O, Kim N, Nam G. Relationship between comorbidity and health outcomes in patients with heart failure: a systematic review and meta-analysis. *BMC Cardiovasc Disord.* 2023;23(1):498. doi:10.1186/s12872-023-03527-x

3. Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *EuroIntervention.* 2022;17(14):e1126-e1196. doi:10.4244/EIJ-E-21-00009

4. Smith CR, Leon MB, Mack MJ, et al; PARTNER Trial Investigators. Transcatheter versus surgical aortic-valve replacement in high-risk patients. *N Engl J Med.* 2011;364(23):2187-2198. doi:10.1056/NEJMoa1103510

5. Reardon MJ, Van Mieghem NM, Popma JJ, et al; SURTAVI Investigators. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med.* 2017;376(14):1321-1331. doi:10.1056/NEJMoa1700456

6. Arnold SV, Manandhar P, Vemulapalli S, et al. Mediators of improvement in TAVR outcomes over time: insights from the STS-ACC TVT Registry. *Circ Cardiovasc Interv.* 2023;16(7):e013080. doi:10.1161/CIRCINTERVENTIONS.123.013080

7. Lee SY, Choi KH, Park TK, et al. Impact of atrial fibrillation on patients undergoing transcatheter aortic valve implantation (TAVI): the K-TAVI Registry. *Yonsei Med J.* 2023;64(7):413-422. doi:10.3349/ymj.2022.0649

8. Nishida K, Saji M, Higuchi R, et al. Predictors for all-cause mortality in men after transcatheter aortic valve replacement: a report from the LAPLACE-TAVI registry. *Int J Cardiol Heart Vasc.* 2023;48:101257. doi:10.1016/j.ijcha.2023.101257

9. Mesnier J, Ternacle J, Cheema AN, et al. Cardiac death after transcatheter aortic valve replacement with contemporary devices. *JACC Cardiovasc Interv.* 2023;16(18):2277-2290. doi:10.1016/j.jcin.2023.07.015

10. Shaul AA, Kornowski R, Bental T, et al. Type of atrial fibrillation and clinical outcomes in patients undergoing transcatheter aortic valve replacement. *Ann Noninvasive Electrocardiol.* 2016;21(5):519-525. doi:10.1111/anec.12345

11. Jaakkola J, Jaakkola S, Airaksinen KEJ, et al. Subtype of atrial fibrillation and the outcome of transcatheter aortic valve replacement: the FinnValve study. *PLoS One.* 2020;15(9):e0238953. doi:10.1371/journal.pone.0238953

12. Généreux P, Piazza N, Alu MC, et al; VARC-3 WRITING COMMITTEE. Valve Academic Research Consortium 3: updated endpoint definitions for aortic valve clinical research. *J Am Coll Cardiol.* 2021;77(21):2717-2746. doi:10.1016/j.jacc.2021.02.038

13. Hahn RT, Webb J, Pibarot P, et al. 5-year follow-up from the PARTNER 2 aortic valve-in-valve registry for degenerated aortic surgical bioprostheses. *JACC Cardiovasc Interv.* 2022;15(7):698-708. doi:10.1016/j.jcin.2022.02.014

14. Mojoli M, Gersh BJ, Barioli A, et al. Impact of atrial fibrillation on outcomes of patients treated by transcatheter aortic valve implantation: a systematic review and meta-analysis. *Am Heart J.* 2017;192:64-75. doi:10.1016/j.ahj.2017.07.005

15. Sannino A, Gargiulo G, Schiattarella GG, et al. 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.* 2016;12(8):e1047-e1056. doi:10.4244/EIJY15M11_12

16. Mack MJ, Leon MB, Thourani VH, et al; PARTNER 3 Investigators. Transcatheter aortic-valve replacement in low-risk patients at five years. *N Engl J Med.* 2023;389(21):1949-1960. doi:10.1056/NEJMoa2307447

17. Yang E, Vaishnav J, Song E, et al. Atrial fibrillation is an independent risk factor for heart failure hospitalization in heart failure with preserved ejection fraction. *ESC Heart Fail.* 2022;9(5):2918-2927. doi:10.1002/ehf2.13836

18. Wang W, Dong Y, Zhang Q, Gao H. Atrial fibrillation is not an independent determinant of 28-day mortality among critically III sepsis patients. *BMC Anethesiol.* 2023;23(1):336. doi:10.1186/s12871-023-02281-z