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ORIGINAL RESEARCH ARTICLE

Conduction Disturbances and Outcome After Surgical Aortic Valve Replacement in Patients With Bicuspid and Tricuspid Aortic Stenosis

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BACKGROUND: This study aimed to compare the incidence and prognostic implications of new-onset conduction disturbances after surgical aortic valve replacement (SAVR) in patients with bicuspid aortic valve (BAV) aortic stenosis (AS) versus patients with tricuspid aortic valve (TAV) AS (ie, BAV-AS and TAV-AS, respectively). Additionally, the study included stratification of BAV patients according to subtype.

METHODS: In this cohort study, the incidence of postoperative third-degree atrioventricular (AV) block with subsequent permanent pacemaker requirement and new-onset left bundle-branch block (LBBB) was investigated in 1147 consecutive patients without preoperative conduction disorder who underwent isolated SAVR (with or without ascending aortic surgery) between January 1, 2005, and December 31, 2022. The groups were stratified by aortic valve morphology (BAV, n=589; TAV, n=558). The outcomes of interests were new-onset third-degree AV block or new-onset LBBB during the index hospitalization. The impact of new-onset postoperative conduction disturbances on survival was investigated in BAV-AS and TAV-AS patients during a median follow-up of 8.2 years. BAV morphology was further categorized according to the Sievers and Schmidtke classification system (possible in 307 BAV-AS patients) to explore association between BAV subtypes and new-onset conduction disturbances after SAVR.

RESULTS: The overall incidence of third-degree AV block and new-onset LBBB after SAVR was 4.5% and 7.8%, respectively. BAV-AS patients had a higher incidence of both new-onset third-degree AV block (6.5% versus 2.5%; P=0.001) and new-onset LBBB (9.7% versus 5.7%; P=0.013) compared with TAV-AS patients. New-onset LBBB was associated with an increased all-cause mortality during follow-up (adjusted hazard ratio, 1.60 [95% CI, 1.12–2.30]; P=0.011), whereas new-onset third-degree AV block was not associated with worse prognosis. Subgroup analysis of the BAV cohort revealed that BAV-AS patients with fusion of the right- and non-coronary cusps had the highest risk of new-onset third-degree AV block (adjusted odds ratio [aOR], 8.33 [95% CI, 3.31–20.97]; P<0.001, with TAV as reference group) and new-onset LBBB (aOR, 4.03 [95% CI, 1.84–8.82]; P<0.001, with TAV as reference group), whereas no significant association was observed for the other BAV subtypes.

CONCLUSIONS: New-onset LBBB after SAVR is associated with increased all-cause mortality during follow-up, and is more frequent complication in BAV AS patients compared with TAV-AS patients. BAV-AS patients with fusion of the right- and non-coronary cusps have an increased risk for conduction disturbances after SAVR. This should be taken into consideration when managing these patients.

Key Words: atrioventricular block ■ bicuspid aortic valve disease ■ bundle-branch block ■ cardiac conduction system disease ■ pacemaker, artificial ■ prognosis

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Clinical Perspective

What Is New?

- This is the first study to investigate the incidence and prognostic relevance of new-onset cardiac conduction disturbances after surgical aortic valve replacement separately in bicuspid and tricuspid aortic valve patients with aortic stenosis.
- Despite the younger age and lower prevalence of cardiovascular risk factors, bicuspid aortic valve aortic stenosis patients had a markedly elevated risk of permanent pacemaker implantation and new-onset left bundle-branch block compared with tricuspid aortic valve aortic stenosis patients, in particular bicuspid aortic valve aortic stenosis patients with fusion of the right- and non-coronary cusps.
- New-onset left bundle-branch block after surgical aortic valve replacement was associated with an increased all-cause mortality during follow-up.

What Are the Clinical Implications?

- The findings of this study underscore the potential benefit of a preoperative cardiac multidetector computed tomography for determination of aortic valve morphology to optimize risk assessment and patient management.
- Because of the prognostic relevance of new-onset left bundle-branch block after surgical aortic valve replacement, close monitoring of these patients might be necessary to prevent serious complications during follow-up.

Nonstandard Abbreviations and Acronyms

AS	aortic stenosis
AV	atrioventricular
BAV	bicuspid aortic valve
LBBB	left bundle-branch block
L/N-BAV	bicuspid aortic valve with raphe between the left- and non-coronary cusps
L/R-BAV	bicuspid aortic valve with raphe between the left- and right-coronary cusps
LVEF	left ventricular ejection fraction
R/N-BAV	bicuspid aortic valve with raphe between the right- and non-coronary cusps
SAVR	surgical aortic valve replacement
TAV	tricuspid aortic valve

New-onset third-degree atrioventricular (AV) block and left bundle-branch block (LBBB) are clinically relevant conduction disturbances that can occur after surgical aortic valve replacement (SAVR). Third-degree AV block with subsequent need for permanent pacemaker implantation has a reported incidence of 2.5% to 7% after SAVR[1–4] and is associated with an increased morbidity and mortality, mainly from cardiac implantable electronic device infections and pacing-induced cardiomyopathy.[1,5,6] New-onset LBBB occurs in 4% to 6.5% after conventional SAVR.[7–9] Although LBBB is generally considered to be associated with an increased risk of heart failure and arrhythmic events, and therefore worse prognoses,[10] contemporary data regarding prognostic implications of new-onset LBBB after SAVR are scarce.

The risk of developing severe postoperative conduction disturbances is associated with surgical insults to vital parts of the conduction system.[11] The 2 most common etiologies of aortic stenosis (AS) in the Western world are degenerative tricuspid aortic valve (TAV) disease or congenital bicuspid aortic valve (BAV) disease.[12] Although it is not known whether aortic valve morphology affects risk for new-onset LBBB after SAVR, BAV-AS patients have an overall increased risk for needing a postoperative permanent pacemaker compared with TAV-AS patients, although the mechanisms behind this remain unclear.[13] BAV morphology is further subcategorized according to the number of a raphes, as well as the spatial position of the cusps and raphes.[14] The burden of fibrosis and calcification is greater in BAV-AS patients compared with TAV-AS patients,[15] and the deposition is typically concentrated to the raphe and the adjacent aortic annular region.[16] It has never been investigated whether the risk of clinically relevant conduction disturbances after SAVR is influenced by the BAV morphology.

The primary aim was to investigate the incidence and prognostic implications of new-onset conduction disturbances after SAVR in patients with BAV and TAV-AS. The secondary aim was to investigate whether different BAV morphologies influence the risk of new-onset postoperative conduction disturbances differently.

METHODS

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Design and Study Population

In this observational study, all patients with severe AS who underwent primary SAVR at Uppsala University Hospital (Uppsala, Sweden) between January 1, 2005, and December 31, 2022, were eligible for inclusion. The patients were identified from the institutional database, which contains prospectively collected data. Patients with a history of coronary artery disease, previous open-heart surgery, previous percutaneous atrial fibrillation or atrial flutter ablation, coexisting moderate or severe aortic regurgitation, coexisting moderate or severe mitral stenosis or regurgitation, and concomitant surgical procedures other than ascending aorta surgery were not eligible for inclusion in the study. All patients with a preoperative conduction disorder (permanent pacemaker, LBBB or right bundle-branch block) were excluded, as were patients with a missing preoperative or postoperative ECG. Patients who died during the procedure were also excluded. The inclusion process is illustrated in Figure 1. The study was approved by the Regional Ethics Review Committee and compiled with the Declaration of Helsinki. The need for informed consent was waived. The reporting of this study conforms to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement.[17]

Definition of Aortic Valve Morphology

Patients were stratified according to aortic valve morphology (ie, BAV or TAV). The aortic valve morphology was determined from the surgeon's visual description, which was documented in the medical records. Further categorization of the BAV morphology according to the Sievers and Schmidtke classification system was possible in 307 BAV-AS patients.

Definition of New-Onset Conduction Disturbances

Baseline ECGs were obtained during the preoperative assessment, which occurred ≤2 weeks before SAVR. All patients had ≥1 postoperative ECG, obtained on the third postoperative day per institution routine. Additional ECGs could be obtained before or after the third postoperative day if deemed clinically indicated. New-onset conduction disturbances were defined as either a new-onset LBBB or a new-onset third-degree AV block during the index hospitalization associated with SAVR, we did not include new-onset conduction disturbances after discharge. New-onset LBBB was defined according to recommendations.[18,19] Third-degree AV block was defined as the absence of AV nodal conduction[19] that did not resolve during the postoperative period, ultimately resulting in a permanent pacemaker implantation during the index hospitalization. The decision of permanent pacemaker implantation was at the discretion of the responsible surgeon, after discussion with an electrophysiologist. Transient third-degree AV block events that did not develop into a permanent pacemaker need were not considered a new-onset conduction disorder.

End Points

The primary outcomes of interest were incidence of new-onset third-degree AV block or new-onset LBBB in BAV-AS and TAV-AS patients after SAVR during the index hospitalization. We also investigated whether new-onset conduction disturbances were associated with all-cause mortality during follow-up. The start of follow-up was set to the end of the index SAVR, as we considered all new-onset conduction disturbances to be

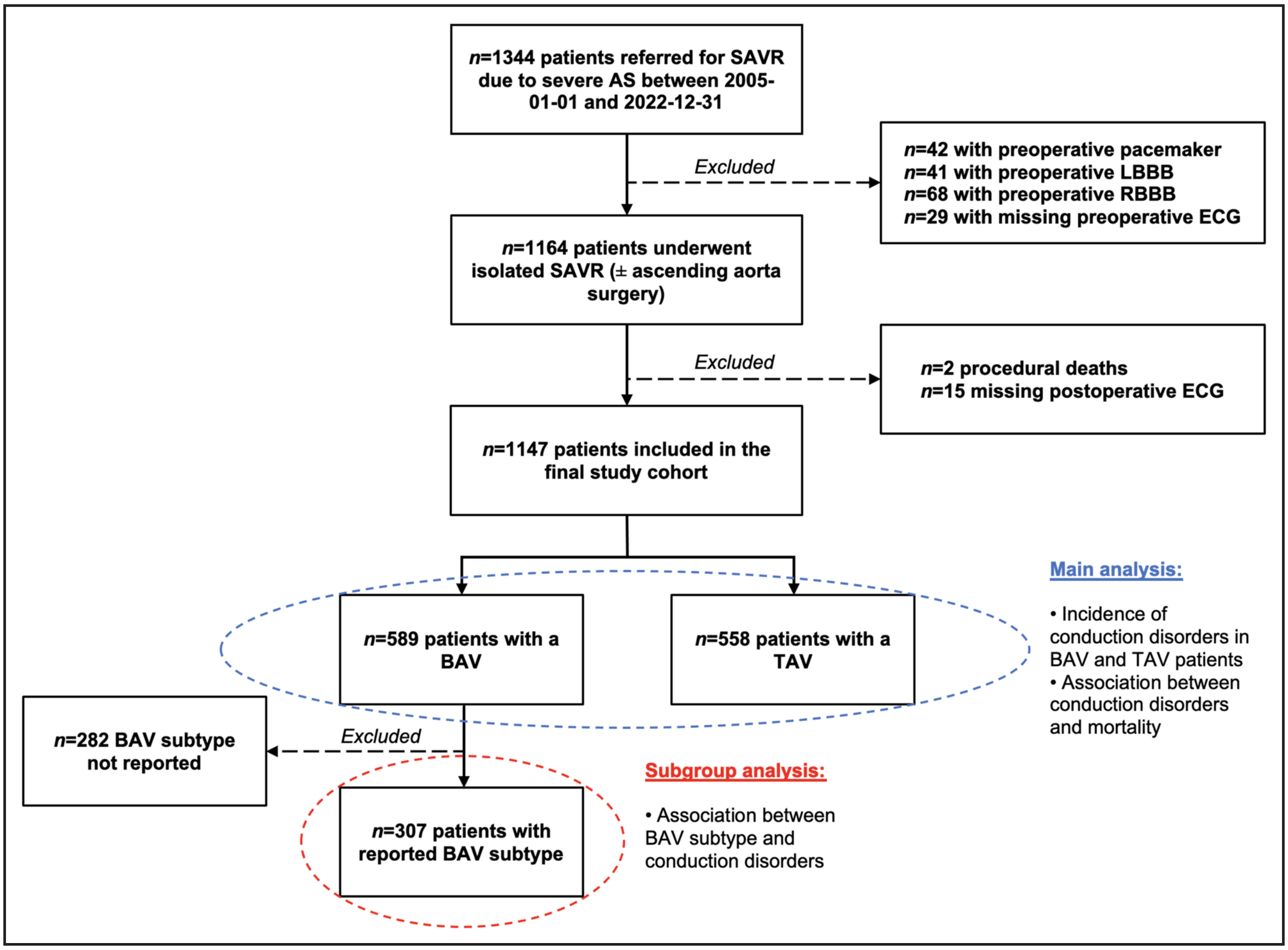

Figure 1. Study overview.
Flow chart illustrating the patient selection process for the main and subgroup analyses. AS indicates aortic stenosis; BAV, bicuspid aortic valve; LBBB, left bundle branch block; RBBB, right bundle branch block; SAVR, surgical aortic valve replacement; and TAV, tricuspid aortic valve.

associated with the surgical trauma. Information on mortality was obtained from the institutional database, which is linked to the Swedish Population Register. Follow-up was administratively censored on December 31, 2023. In a subgroup analysis, we specifically aimed to assess the incidence of new-onset conduction disturbances according to bicuspid aortic valve morphology stratified according to the Sievers and Schmidtke classification.[14]

Statistical Analysis

Statistical analyses were performed in R version 3.3.1. Two-tailed *P* values <0.05 were considered statistically significant. Continuous data are presented as mean±SD, whereas categorical data are reported in frequencies with percentages. For comparison of continuous baseline variables between BAV and TAV patients, the independent-samples *t* test was used. For comparison of categorical baselines variables between BAV and TAV patients, the χ^2 test or the Fisher exact test was used as appropriate. Comparison of continuous variables between >2 groups was performed with the use of 1-way ANOVA, followed by post hoc Bonferroni tests. The association between aortic valve morphology and postoperative conduction disorders was investigated with the use of univariable and multivariable logistic regression models. Results are presented as crude odds ratios (ORs) and adjusted OR (aOR) with 95% CI, respectively. Adjustments were made for age, sex, preoperative left ventricular ejection fraction (LVEF), and size of the prosthetic aortic valve, based on a directed acyclic graph (Figure S1).

Using a multivariable Cox proportional hazards regression analysis, it was investigated whether new-onset third-degree AV block and new-onset LBBB were associated with all-cause mortality after SAVR. Adjustments were made for age, sex, preoperative LVEF, and aortic valve morphology (BAV or TAV), based on a directed acyclic graph (Figure S2). Interaction was assessed through the introduction of a multiplicative interaction term. We also conducted a stratified Cox proportional hazards regression analysis by aortic valve morphology to account for the inherent heterogeneity between the BAV-AS and TAV-AS groups. The assumption of proportional hazards was tested with the use of a 2-sided Schoenfeld residuals test, and there were no signs of violation of the proportional hazards assumption. The results from the Cox proportional hazards regression analysis are reported as crude hazard ratios (HR) and adjusted hazard ratios (aHRs) with 95% CI. The survival probability in the respective groups during follow-up after SAVR is graphically illustrated in Kaplan–Meier survival curves.

In the subgroup analysis, univariable and multivariable logistic regression analyses were conducted to investigate the association between new-onset conduction disturbances and BAV subcategory. We only investigated subgroups with an event. The TAV cohort (n=558) served as a reference group. Adjustments were made for age, sex, preoperative LVEF, and size of the prosthetic aortic valve. Results are presented as crude OR and aOR with 95% CI.

RESULTS

Main Analysis

Baseline Characteristics

We included 1147 patients in the study, of which 589 (51.4%) had BAV and 558 (48.6%) had a TAV. The median follow-up time was 8.2 years (interquartile range, 5.6–11.8 years), which was similar for BAV AS and TAV AS patients (8.3 years versus 8.1 years; *P*=0.292). The baseline characteristics of the whole cohort are summarized in Table 1. BAV patients were younger (64 years versus 72 years of age; *P*<0.001) and more often male compared with TAV patients (63% versus 53%; *P*<0.001). The BAV patients had fewer cardiovascular comorbidities in terms of hypertension (53% versus 70%; *P*<0.001), diabetes (10% versus 22%; *P*<0.001), hypercholesterolemia (31% versus 42%; *P*<0.001), and preoperative atrial fibrillation (9% versus 15%; *P*<0.001), as well as chronic pulmonary disease (11% versus 13%; *P*=0.048). The perioperative characteristics are presented in the Table S1.

New-Onset Third-Degree AV Block

The overall incidence of persisting third-degree AV block, requiring permanent pacemaker implantation during the index hospitalization after SAVR, was 4.5%, with a significant difference between BAV and TAV patients (6.5% versus 2.5%, *P*=0.001; crude OR, 2.68 [95% CI, 1.44–5.00]; *P*=0.002). The association between BAV and postoperative permanent pacemaker implantation remained significant after adjusting for age, sex, preoperative LVEF, and size of the prosthetic aortic valve (aOR, 2.42 [95% CI, 1.22–4.79]; *P*=0.011). On average, permanent pacemaker implantation occurred 5±2 days after SAVR, with no difference between BAV and TAV patients.

New-Onset LBBB

The overall incidence new-onset LBBB after SAVR was 7.8%, with a significantly greater incidence in the BAV-AS group compared with the TAV-AS group (9.7% versus 5.7%, *P*=0.001; crude OR, 1.76 [95% CI, 1.12–2.76]). In the multivariable logistic regression analysis, BAV remained an independent risk factor for new-onset LBBB (aOR, 1.74 [95% CI, 1.06–2.86]; *P*=0.029).

Survival

A total of 379 patients (28.6%) died during follow-up. Neither new-onset third-degree AV block nor new-onset LBBB were associated with worse prognoses in the unadjusted Cox proportional hazards regression model (Figure 2A). In the adjusted Cox proportional hazards regression model, new-onset LBBB after SAVR was associated with an increased all-cause mortality during follow-up (aHR, 1.60 [95% CI, 1.12–2.30]; *P*=0.011; Figure 2B), whereas new-onset third-degree AV block with subsequent permanent pacemaker implantation was not associated with worse prognosis during follow-up (aHR, 0.87 [95% CI, 0.46–1.64]; *P*=0.662; Figure 2B). New-onset LBBB after SAVR remained independently associated with all-cause mortality even after further adjustments for additional potential confounders (Table S3). No significant interaction between new-onset LBBB and aortic valve morphology on all-cause mortality was observed (*P*=0.753).

Table 1. Characteristics of Patients with Severe Aortic Stenosis Undergoing Surgical Aortic Valve Replacement*

	Bicuspid aortic valve (n=589)	Tricuspid aortic valve (n=558)	*P* value
Age, y	63.8±11	72.2±8	<0.001
Male sex, n (%)	372 (63.2)	296 (53.0)	<0.001
Height, cm†	172.2±11	170.0±10	<0.001
Weight, kg†	81.1±16	80.1±16	0.516
Body mass index, g/m²†	27.3±5.4	27.6±5.1	0.356
Hypertension, n (%)	309 (52.5)	393 (70.4)	<0.001
Diabetes mellitus, n (%)	62 (10.5)	122 (21.9)	<0.001
Hypercholesterolemia, n (%)	183 (31.1)	232 (41.6)	<0.001
Chronic pulmonary disease, n (%)	59 (10.0)	77 (13.8)	0.048
Atrial fibrillation, n (%)	49 (8.3)	84 (15.1)	<0.001
Ascending aortic aneurysm, n (%)	105 (17.8)	20 (3.6)	<0.001
New York Heart Association classification, n (%)			0.014
I	43 (7.3)	33 (5.9)	
II	188 (31.9)	135 (24.2)	
III	339 (57.6)	369 (66.1)	
IV	19 (3.2)	21 (3.8)	
Left ventricular ejection fraction			0.697
≥50%	501 (85.1)	470 (84.2)	
<50%	88 (14.9)	88 (15.8)	
Preoperative ECG findings†			
Heart rate, bpm	70±13	71±14	0.127
PQ interval, ms‡	171.9±29.0	176.7±62.6	0.097
QRS interval, ms	100.0±17.9	99.9±22.4	0.890
QTc interval, ms	437.0±27.4	444.6±158.0	0.250

All data shown as n (%) unless otherwise indicated. bpm indicates beats per minute.
*N=1147.
†Data expressed as mean±SD.
‡n=1014.

When exploring the association between new-onset conduction disturbances and all-cause mortality in the stratified Cox proportional hazards regression analysis, the association between new-onset LBBB and all-cause mortality was borderline significant in the unadjusted model (HR, 1.65 [95% CI, 0.99–2.76]; *P*=0.056). In the adjusted model, new-onset LBBB (aHR, 1.69 [95% CI 1.01-2.86]; *P*=0.048; Figure 3), but not third-degree AV block with subsequent permanent pacemaker implantation (aHR, 0.86 [95% CI, 0.38–1.98]; *P*=0.728), was associated an increased mortality in the BAV-AS cohort (Figure S3 in the Supplemental Material). Survival for BAV-AS patients with new-onset LBBB was similar to that of TAV-AS patients without new-onset LBBB (Figure 3).

Subgroup Analysis

Baseline Characteristics

It was possible to subcategorize the aortic valve morphology in 307 BAV-AS patients. Our distribution of BAV type 0 (8.5%), BAV with raphe between the left- and right-coronary cusps ([L/R-BAV] 69.1%), BAV with raphe between the right- and non-coronary cusps ([R/N-BAV] 19.5%), and BAV with raphe between the left- and non-coronary cusps ([L/N-BAV] 2.9%) was similar to that previously reported.[14] Baseline characteristics in patients with different BAV morphologies categorized according to the Sievers and Schmidtke classification compared with TAV-AS patients are presented in Table S2.

New-Onset Third-Degree AV Block

The incidence of new-onset third-degree AV block stratified according to Sievers and Schmidtke aortic valve morphology in the subgroup of 307 BAV-AS patients is presented in Figure 4A. Implantation of a postoperative pacemaker was most common within the R/N-BAV group (18.3%), followed by type 0 (11.5%) and type 1 L/R-BAV (6.6%). None of the 9 patients with L/N-BAV developed new-onset third-degree AV block. In an unadjusted logistic regression analysis, all BAV subtypes were associated with an increased risk of new-onset third-degree AV block with subsequent permanent pacemaker

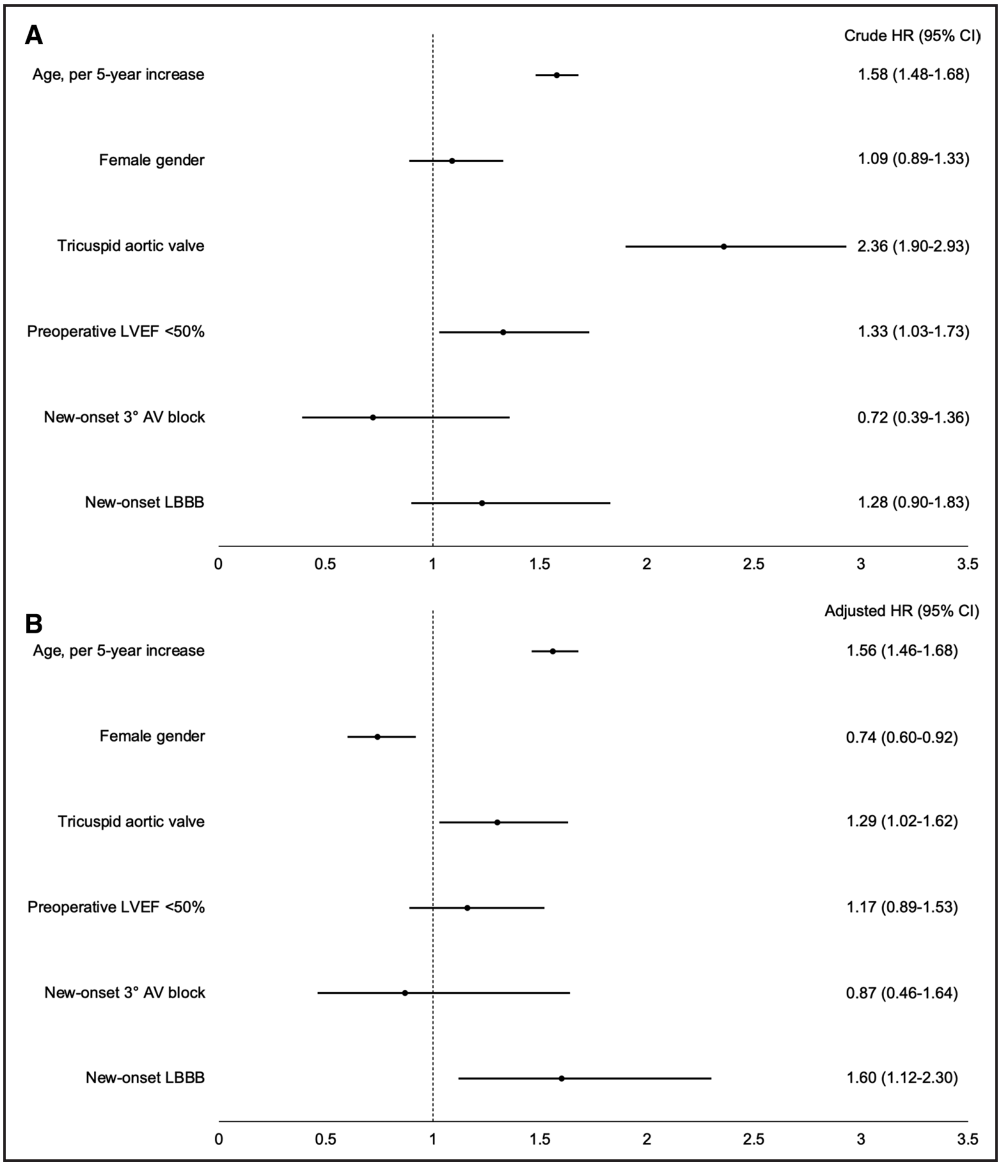

Figure 2. Predictors of all-cause mortality after SAVR.
Forest plot illustrating the results from the unadjusted (**A**) and adjusted (**B**) Cox proportional hazards models investigating the association to all-cause mortality after SAVR. New-onset left bundle branch block (LBBB) was independently associated with all-cause mortality after SAVR. AV indicates atrioventricular; LVEF, left ventricular ejection fraction; and SAVR, surgical aortic valve replacement.

implantation compared with TAV-AS patients (Table 2). After adjusting for age, sex, LVEF, and prosthetic valve size, this association remained significant for type 0 BAV-AS patients (aOR, 4.82 [95% CI, 1.17–19.95]; P=0.030) and for BAV-AS patients with R/N-BAV fusion (aOR, 8.33 [95% CI, 3.31–20.97]; P<0.001). After further adjustments for all potential confounders entered in the preconstructed directed acyclic graph (Figure S1), type 0 BAV and R/N-BAV remained independently associated with new-onset third-degree AV block (Table 2; Table S4).

New-Onset LBBB

A new-onset LBBB developed in 20.0% of R/N-BAV, 15.4% of type 0 BAV, 5.7% of L/R-BAV, and 0% of L/N-BAV (Figure 4B). In the logistic regression analysis, only R/N-BAV was associated with new-onset LBBB after adjusting for age, sex, LVEF, and prosthetic aortic valve size (aOR, 4.03, [95% CI, 1.84–8.82]; P<0.001; Table 2). Table 2 and Table S4 illustrates that R/N-BAV remained independently associated with new-onset LBBB after further adjusting for all potential confounders entered in the preconstructed directed acyclic graph (Figure S1).

DISCUSSION

This is the first study to investigate the frequency and clinical implications of new-onset conduction disturbances after SAVR in BAV-AS and TAV-AS patients

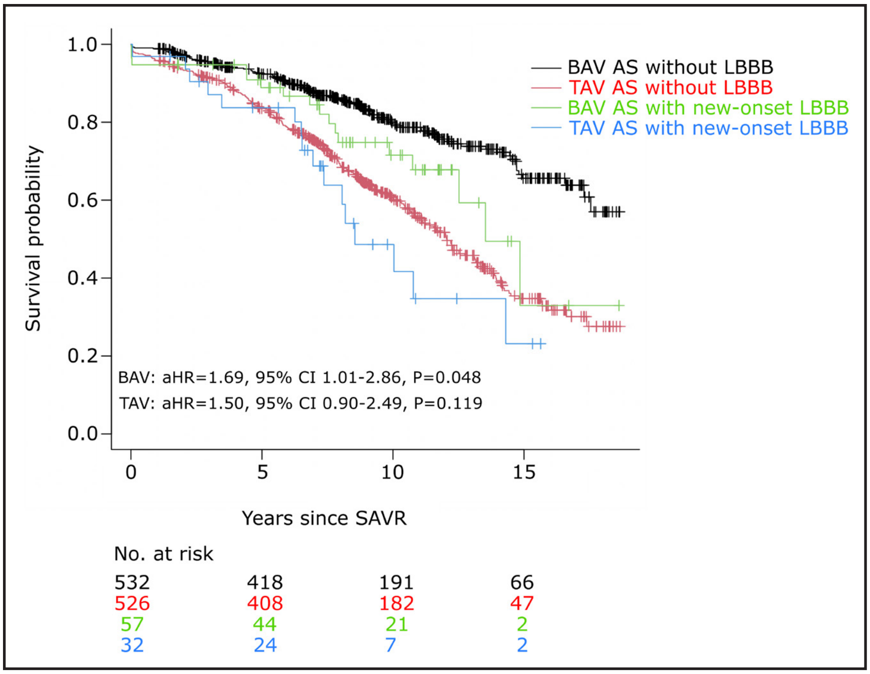

Figure 3. Survival in BAV-AS and TAV-AS patients with and without new-onset LBBB.
Kaplan Meier survival curves illustrating the survival probability after SAVR in BAV-AS and TAV-AS patients with and without new-onset LBBB. aHR indicates adjusted hazard ratio; BAV-AS, bicuspid aortic valve aortic stenosis; LBBB, left bundle branch block; SAVR, surgical aortic valve replacement; and TAV-AS, tricuspid aortic valve aortic stenosis.

separately. The major findings are: (1) permanent pacemaker implantation and new-onset LBBB after SAVR occurred more frequently in BAV-AS patients than in TAV-AS patients; (2) new-onset LBBB was associated with an increased all-cause mortality, most likely driven by the worse outcome observed in BAV-AS patients; and (3) BAV-AS patients with fusion of the right- and non-coronary cusps had the greatest risk for developing clinically relevant conduction disorders after SAVR.

We demonstrate that BAV-AS patients have a greater risk for developing new-onset LBBB after SAVR compared with TAV-AS patients. Although there was no interaction between new-onset LBBB and aortic valve morphology on all-cause mortality, we are concerned that new-onset LBBB is a highly relevant clinical issue in BAV-AS patients in particular. They developed new-onset LBBB to a greater extent than TAV-AS patients, and new-onset LBBB was independently associated with worse outcomes on follow-up. Our stratified analysis suggests that BAV-AS patients who develop a new-onset LBBB after SAVR have worse prognosis compared with BAV-AS patients who do not develop a new-onset LBBB. The prognostic relevance of new-onset LBBB after aortic valve replacement (either surgical or transcatheter) in terms of mortality has remained unclear, as studies report conflicting results, mainly because of short follow-up times which may obscure the long-term effects of a LBBB.[7,20–23] In addition, previous studies have not investigated the prognostic impact of new-onset LBBB exclusively in BAV-AS and TAV-AS patients. In contrast to previous studies, we had an adequate follow-up to evaluate the detrimental effects of a new-onset LBBB in the long-term. Interestingly, survival in the new-onset LBBB group began to decline about 6 years after SAVR. As we investigated a SAVR cohort, and because new-onset LBBB was more common in BAV-AS patients, the

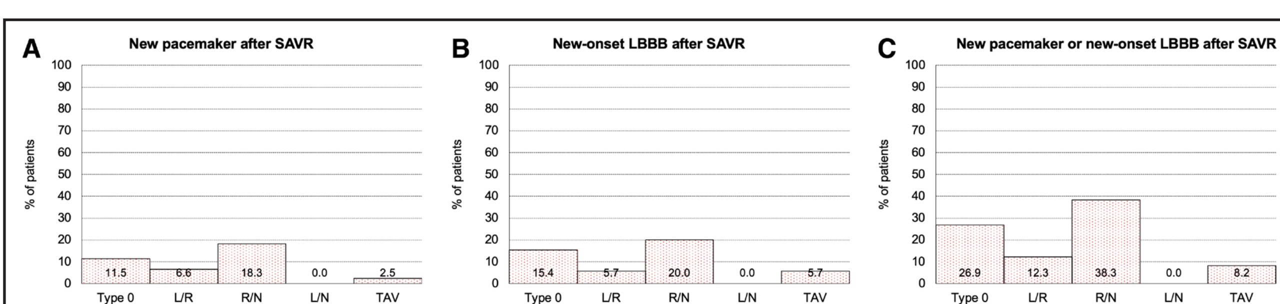

Figure 4. Incidence of new-onset conduction disorders stratified according to BAV subtype.
The incidence of new-onset third-degree atrioventricular (AV) block (**A**), new-onset LBBB (**B**), and the composite of new-onset third-degree AV block or new-onset LBBB (**C**) stratified according to BAV subtype in the subgroup analysis. BAV aortic stenosis patients with fusion of the right- and non-coronary cusps (R/N) had the highest incidence of new-onset conduction disorders. BAV indicates bicuspid aortic valve; LBBB, left bundle branch block; L/R, left- and right-coronary cusps; L/N, left- and non-coronary cusps; SAVR, surgical aortic valve replacement; and TAV, tricuspid aortic valve.

Table 2. Univariable and Multivariable Logistic Regression Analysis in a Subgroup of BAV-AS Patients*

				Adjusted			
		Unadjusted		Model 1‡		Model 2§	
	At-risk/events, n/N†	OR (95% CI)	*P* value	OR (95% CI)	*P* value	OR (95% CI)	*P* value
New-onset third-degree AV block with PPI							
TAV	558/14	1	Ref	1	Ref	1	Ref
Type 0 BAV	26/3	5.07 (1.36–18.88)	0.016	4.82 (1.17–19.95)	0.030	5.11 (1.18–22.09)	0.029
L/R-BAV	212/14	2.75 (1.29–5.87)	0.014	2.25 (0.98–5.19)	0.057	2.34 (0.97–5.65)	0.060
R/N-BAV	60/11	8.72 (2.97–17.60)	<0.001	8.33 (3.31–20.97)	<0.001	10.87 (4.06–29.08)	<0.001
New-onset LBBB							
TAV	558/32	1	Ref	1	Ref	1	Ref
Type 0 BAV	26/4	2.99 (0.97–9.19)	0.056	2.88 (0.87–9.52)	0.084	3.00 (0.89–10.13)	0.078
L/R-BAV	212/12	0.99 (0.50–1.95)	0.968	0.91 (0.44–1.91)	0.804	0.72 (0.31–1.65)	0.432
R/N-BAV	60/12	4.11 (1.99–8.50)	<0.001	4.03 (1.84–8.82)	<0.001	3.91 (1.73–8.79)	<0.001

Aims of analysis presented included investigating the association between BAV subtype and conduction disturbances after surgical aortic valve replacement. TAV-AS patients in Reference category, n=558. AV indicates atrioventricular; BAV, bicuspid aortic valve; L/R-BAV, bicuspid aortic valve with raphe between the left- and right-coronary cusps; LBBB, left bundle branch block; N, non-coronary cusp; OR, odds ratio; PPI, permanent pacemaker implantation; R/N-BAV, bicuspid aortic valve with raphe between the right- and non-coronary cusps; Ref, reference; and TAV, tricuspid aortic valve.

*n=307.

†n/N reflects the patients at risk to the number of events that occurred.

‡Adjustments were made for age, sex, preoperative left ventricular ejection fraction, and prosthesis size suggested by the preconstructed directed acyclic graph (Figure S1).

§Adjustments were made for all potential confounding variables in the preconstructed directed acyclic graph (Figure S1).

mean age in our patients was considerably lower compared with patients in other studies, such as that from Nazif et al (64 years compared with 81 years of age, respectively).[22] This is important considering the longer life-expectancy in patients undergoing SAVR in general, and BAV-AS patients in particular. Our observation that survival of BAV-AS patients with new-onset LBBB is similar to that of TAV-AS patients without new-onset LBBB is therefore intriguing.

LBBB is associated with insufficient reverse left ventricular remodeling and failure to improve postprocedural LVEF, as it causes a mechanical dyssynchrony with deteriorating diastolic and systolic left ventricular function, which can progress to congestive heart failure.[20,24] Both heart failure and LBBB itself are associated with progressive conduction disturbances, resulting in an increased risk for life-threatening bradyarrhythmias or ventricular tachyarrhythmias and sudden cardiac death.[22,25] Heart failure may also present with acute mechanical failure and resulting cardiogenic shock. This is important because BAV-AS patients already have worse left ventricular diastolic and systolic function before SAVR compared with TAV-AS patients.[26,27] Although we did not investigate specific causes of death in the present study, we believe that the increased mortality observed in this group is mainly because of complications related to the LBBB.

The incidence of new-onset third-degree AV block with subsequent permanent pacemaker implantation was also higher for BAV-AS patients as compared with TAV-AS patients. It is known that right ventricular pacing may cause pacing-induced cardiomyopathy, which is associated with worse prognoses, and that having a cardiac implantable electronic device is associated with an increased risk for infection complications.[1,5,28,29] In contrast with findings of other studies,[1,5,6] there was no association between postoperative permanent pacemaker implantation after SAVR and mortality during follow-up in our study. This was probably attributable to the relatively few postoperative pacemaker events in this cohort.

The risk for developing severe postoperative conduction disturbances is associated with surgical and direct mechanical insults to vital parts of the conduction system, where the AV node, bundle of His and left bundle branch are located in close proximity to the commissure between the right- and non-coronary aortic valve cusps.[11] Previous studies have established BAV as a risk factor for permanent pacemaker implantation after SAVR,[13,30] but it has never been investigated whether this depends on the morphology of the BAV. In our study, we found that BAV-AS patients with fusion of the right- and non-coronary cusps had a 4-fold increased risk of new-onset LBBB and an 8-fold increased risk of permanent pacemaker implantation after SAVR. Our findings suggest that the previously proposed risk increase for BAV patients in general is a result of the significantly increased risk in the R/N-BAV subtype in particular. This is most likely explained by the anatomic location of the raphe, as it is in close proximity to vital parts of the cardiac conduction system. The fibrotic and calcific burden is generally higher at the site of the raphe and the adjacent annular region.[31–34] Theoretically, the extensive decalcification of the aortic valve, the raphe and the aortic annulus during aortic valve replacement could inflict damages to the conduction system, resulting in severe postoperative conduction disturbances.[35] Although surgical damage to the conduction system most likely explains the increased frequency of conduction disturbances in these patients, an underlying pathology of the conduction system could also contribute to the risk of new-onset conduction disorders. A previous study has found that BAV patients without valvular disease have significantly longer His ventricular intervals, as well as an increased risk for permanent pacemaker during follow-up, compared with TAV patients,[36] suggesting that BAV patients may also be more prone to conduction disturbances before SAVR. In our study, we excluded patients with preoperative RBBB or LBBB and permanent pacemaker, but the prevalence of preoperative conduction disorders did not differ between BAV-AS and TAV-AS patients. Additionally, the PQ interval was similar in the different aortic valve morphologies. This argues towards a mechanical damage of the cardiac conduction system during surgery rather than an underlying primary pathology of the conduction system in BAV-AS patients.

Clinical Implications and Future Directions

The findings of the present study, which is the first to investigate the correlation between aortic valve morphology and clinically relevant conduction disorders after SAVR, have some important clinical implications. The risk of new-onset clinically relevant conduction disorders after SAVR is higher in BAV-AS patients compared with TAV-AS patients, despite their younger age and overall lower prevalence of cardiovascular risk factors. Furthermore, new-onset LBBB was associated with worse prognosis in BAV-AS patients, which stresses the importance of close monitoring to prevent serious complications during follow-up.

Notably, 38% of patients with the R/N-BAV morphology in our study developed either a need for a postoperative permanent pacemaker (18%) or a new-onset LBBB (20.0%). The knowledge obtained regarding the relation between BAV subtypes and risk for postoperative conduction disorder provide vital information that could influence the management of these patients with regards to surgical technique, prosthetic valve size and postoperative monitoring. Extra consideration during decalcification of the raphe and aortic annulus should be taken in R/N–BAV-AS patients. Our findings could influence the individual assessment of when to intervene in patients with severe AS. Earlier intervention in R/N–BAV-AS patients could result in less extensive calcification of the aortic valve and aortic annulus, potentially decreasing the risk of postoperative permanent pacemaker implantation and new-onset LBBB. This is supported by our observation that severe preoperative heart failure symptoms (New York Heart Association functional class III or IV) were associated with an increased risk of postoperative permanent pacemaker implantation. Finding the etiology behind aortic valve degeneration in BAV-AS and TAV-AS could help identifying therapies to halt or inhibit progressive aortic valve calcification and thereby limit AS related complications, including postoperative permanent pacemaker implantation and new-onset LBBB.[37]

We suggest that a preoperative cardiac multidetector computed tomography for determination of aortic valve morphology[38,39] may optimize the management of AS patients referred for SAVR, and provide useful knowledge in communicating potential risks of the surgical intervention with the patients. Future studies should focus on how to mitigate the risk of permanent pacemaker implantation and new-onset LBBB in R/N–BAV-AS patients. To further investigate the relationship of BAV morphology and postoperative permanent pacemaker need, future studies should also focus on which patients remain pacemaker-dependent and which patients develop a future need.

Limitations

This was an observational, single-center study, therefore the results might not be generalized to other populations. However, the distribution of the different BAV subtypes was representative to what has been previously reported.[14] Another limitation is the small sample size in some of the BAV-AS subgroups; including more patients would enable more confident conclusions. Our BAV-AS cohort is large and very well-characterized, containing consecutive patients without any patient selection. Despite this, the BAV subtype was only reported in 52% of the BAV patients. The clinical relevance of the findings of the present study stresses the importance of a standardized reporting of aortic valve morphology.

Conclusions

New-onset LBBB after SAVR was associated with worse prognosis during follow-up. Compared with TAV-AS patients, BAV-AS patients have a higher risk of developing severe conduction disorders after SAVR for severe AS, particularly those with fusion of the right- and non-coronary cusps. Preoperative assessment of the aortic valve morphology may be conducted routinely to optimize management of patients referred for SAVR.

ARTICLE INFORMATION

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Disclosures

Drs Grinnemo, Rodin, and Simonson are shareholders at AVulotion AB. The other authors report no conflicts.

Supplemental Material

Figures S1–S3

Tables S1–S4

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