

Procedural and clinical outcomes of transcatheter aortic valve replacement in bicuspid aortic valve patients: a systematic review and meta-analysis

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Background: Currently, bicuspid aortic valve (BAV) anatomy remains a relative contraindication for transcatheter aortic valve replacement (TAVR) due to concerns of suboptimal anatomy. However, recent advancements in the field have provided a wealth of promising data and more clinicians are opting for TAVR as an alternative to surgical repair. We aim to review and analyze the available data for TAVR in BAV patients, targeting procedural outcomes, clinical outcomes and mortality with up to two years of follow-up.

Methods: A literature search of five databases was performed and all primary studies published between 2002 and 2021 that reported procedural, clinical or mortality outcome data were identified. Following data extraction, a meta-analysis of means or proportions was performed using a random effects model. Heterogeneity was assessed using the I^2 statistic.

Results: A total of 22 studies with 1,945 BAV patients were identified. The mean age was 74.1 years and 58.8% of patients were male. Device success rates was 87.5%. Moderate to severe paravalvular leak (PVL) was seen in 3.7% of procedures. Clinical outcomes included new permanent pacemaker insertion (PPI) (11.8%), major bleeding (3.5%), major vascular complications (2.5%), stroke (2.3%), acute kidney injury (2.1%) and coronary obstruction (0.1%). Mortality in hospital, at 30-days, one and two years of follow-up were 1.9%, 2.1%, 9.6% and 12.9%, respectively.

Conclusions: This assessment of the available data on TAVR for BAV shows promising outcomes and low rates of complications. However, further research is warranted to reduce the heterogeneity of the available data and provide insight into outcomes beyond two years of follow-up.

Keywords: Transcatheter aortic valve replacement (TAVR); bicuspid aortic valve (BAV); systematic review; meta-analysis; mortality; outcomes



Submitted Mar 30, 2022. Accepted for publication Jun 27, 2022.

doi: 10.21037/acs-2022-bav-22

View this article at: <https://dx.doi.org/10.21037/acs-2022-bav-22>

Introduction

Bicuspid aortic valve (BAV) anatomy affects up to 2% of the population and is an important risk factor for the development of aortic stenosis (AS) (1). Development of moderate to severe AS occurs in 12–37% of patients with BAV and AS may manifest up to 20 years earlier in these patients compared to those with a tricuspid aortic valve

(TAV) (2,3). 20% of patients with AS over the age of 80 have BAV anatomy, and surgical aortic valve replacement (SAVR) is the current mainstay of treatment.

Traditionally, transcatheter aortic valve replacement (TAVR) has been reserved for patients ineligible or unsuitable for SAVR. Recent data has shown, however, that TAVR produces comparable or potentially favorable

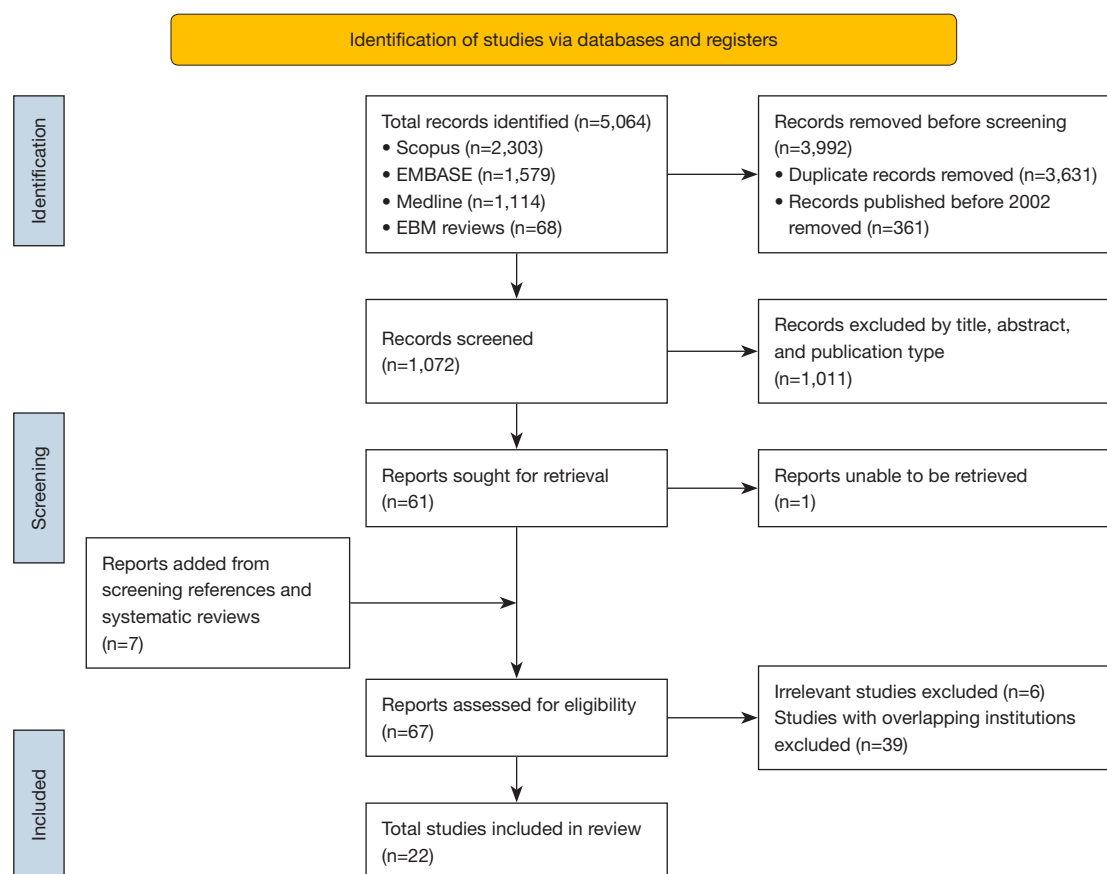


Figure 1 PRISMA search strategy. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-analyses; n, number of patients; EBM, evidence-based medicine.

outcomes compared to SAVR (4-7).

Currently, BAV remains a relative contraindication for TAVR due to concerns associated with suboptimal valve-in-valve anatomy (8,9). Such concerns include increased annular ellipticity and asymmetric calcification, potentially resulting in inadequate fixation of the prosthetic valve, leading to an increased risk of paravalvular leak (PVL) or prosthesis migration (8,9). In contrast, SAVR avoids these potential issues via resection of the diseased valve and fixation of the prosthesis (5,10). Clinical trials regarding TAVR have therefore excluded patients with BAV and as such, BAV remains outside TAVR guidelines (4,5,11-13).

However, recently increasing off-label use of TAVR for BAV stenosis and improved valve technology have shown promising outcomes, comparable both to TAVR in TAV stenosis and to SAVR in BAV stenosis (14-18). These results primarily stem from high-risk patients ineligible for SAVR, but there remains optimism that TAVR could be a viable

or preferred treatment for all patients with BAV stenosis. Currently, long-term data regarding efficacy and outcomes of TAVR in BAV patients is scarce. This study aims to investigate the rapidly growing body of literature on both short- and mid-term outcomes of TAVR in BAV patients.

Methods

Literature search strategy

The systematic review was conducted under the direction of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (*Figure 1*) (19). An electronic keyword and medical subject heading (MeSH) search was performed on Medline, Scopus, Embase, Cochrane and EBM Reviews Databases with the following search terms: (“transcatheter aortic valve replacement” OR “transcatheter valve replacement” OR “TAVR” OR “transcatheter aortic valve implantation” OR “TAVI” OR

“percutaneous aortic valve implantation” OR “PAVR”) AND (“bicuspid” OR “bicuspid aortic valve” OR “BAV”). Studies containing search terms in the title or abstract published between January 2002 and September 2021 were included for screening and duplications were removed. All references and published systematic reviews were manually screened for additional studies.

Eligibility criteria

Studies were screened for inclusion and exclusion criteria independently by two authors (CHJ Chen, H Jiang). Discrepancies were discussed until an agreement was reached. Studies fulfilling the following criteria were included in this study: (I) studies including BAV patients undergoing TAVR; (II) adult (>18 years of age) human studies with more than ten patients; (III) studies reporting survival outcomes at 30-days, one or two years; (IV) English studies. Studies were excluded if the inclusion criteria were not met or if it satisfied one of the following exclusion criteria: (I) case reports, editorials, reviews, commentaries and conference abstracts; (II) studies with patients undergoing TAVR as a redo procedure; (III) studies with patients with endocarditis. Where studies contained overlapping data, preference was given to the study with the longest follow-up period.

Data extraction and critical appraisal

Data was extracted from text, figures and tables by three authors independently (CHJ Chen, H Jiang, O Martin). Endpoints were derived from Valve Academic Research Consortium-2 (VARC-2) consensus document in conjunction with commonly reported outcomes in reviewed studies (20). Reported endpoints with a total number of patients less than 10% of the total study population were excluded from the analysis. The primary endpoint was mortality and secondary endpoints include post-procedural and clinical outcomes. Quality assessment was performed using a modified schema designed for assessing case series, developed by the Institute of Health Economics (Alberta, Canada) (Table S1) (21). Study quality was determined via assessment of study objective, design, population, intervention, outcome measures, statistical analysis, appropriateness of results and conclusions and competing interests. Studies were determined to be of low quality if they satisfied fewer than 10 criteria, of moderate quality if they satisfied 10–12 criteria and of high quality if they satisfied more than 12 criteria.

Statistical analysis

Meta-analyses of means and proportions were performed using the continuous and binary Dersimonian-Laird random effects models, respectively. Pooled means are presented as a mean value (95% confidence interval). Pooled proportions are presented as a percentage (95% confidence interval). Data reported as median and interquartile range was assumed to be skewed and converted into mean \pm standard deviation using the Box-Cox method as described by McGrath *et al.* (22). Heterogeneity assessment across the studies was performed using the I^2 statistic. I^2 values of 0–49%, 50–74% and 75–100% were deemed to represent low, moderate and high heterogeneity, respectively. Statistical analysis was performed on OpenMeta[Analyst] (Center for Evidence-based Medicine, Brown University, USA) (23). P values <0.05 were considered statistically significant.

Results

Study details

A total of 5,064 records were identified following a literature search, of which 22 studies were included in this study after exclusion (Figure 1). The majority of the data was sourced from the United States (five studies), Mainland China (four studies), Italy (three studies), Poland (three studies) and France (three studies) (Table 1). Other countries/region involved in the study included Korea, Taiwan, Denmark, Germany, Israel, The Netherlands, Switzerland, Japan and Canada. Seven studies were found to be of high quality, 13 studies of medium quality and two studies of low quality (Table 1).

Baseline characteristics

A total of 1,945 patients with BAV stenosis undergoing TAVR from 22 studies were included in the meta-analysis. Of these patients, 59.1% (95% CI: 56.2–62.0%; $I^2=12\%$) were male. The mean age in this cohort was 74.1 (95% CI: 72.4–75.9; $I^2=94\%$) years. The Society of Thoracic Surgeons-Predicted Risk of Mortality (STS-PROM) was 5.39 (95% CI: 4.45–6.34; $I^2=98\%$) and the proportion of heart failure patients with function within New York Heart Association (NYHA) class III or IV was 71.8% (95% CI: 63.4–80.2%; $I^2=93\%$). General echocardiographic findings of the patient population included a left ventricular ejection fraction (LVEF) of 52.2% (95% CI: 50.0–54.5%; $I^2=91\%$), a mean aortic gradient of 54 mmHg (95% CI: 51–58 mmHg;

Table 1 Details of studies included in meta-analysis

Study, publication year	Study type	Patient recruitment	Data source	Country/region	Comparison	N	Quality of evidence
Husso (15), 2021	Cohort	Retrospective	FinnValve Registry	Finland	SAVR	103	High
Sun (24), 2021	Cohort	Prospective	First Affiliated Hospital of Air Force Medical University	China	TAV	51	Medium
Gorla (25), 2021	Cohort	Retrospective	3 academic centres	Italy	Prosthetic type	56	Medium
Jung (26), 2021	Cohort	Prospective	Seoul National University Hospital	Korea	TAV	19	Medium
Kumar (27), 2021	Cohort	Retrospective	Knight Cardiovascular Institute	United States	BAV morphology	30	Low
Tsai (16), 2021	Cross-sectional	Retrospective	Cheng-Hsin General Hospital	Taiwan	SAVR	48	Low
Kochman (28), 2020	Case series	Retrospective	Polish Registry	Poland	n/a	24	High
Pineda (29), 2020	Cohort	Retrospective	Duke aortic valve disease database	United States	TAV	50	Medium
Yoon (30)*, 2020	Cohort	Prospective*	International Bicuspid Aortic Valve Stenosis Registry	International	BAV calcification	1,034	Medium
Fu (31), 2020	Cohort	Retrospective	Beijing Fuwai Hospital	China	BAV morphology	44	High
Waksman (32), 2020	Case series	Retrospective	LRT Trial	United States	TAV	61	Medium
Fan (33), 2020	Cohort	Prospective	Second Affiliated Hospital of Zhejiang University	China	n/a	83	Medium
Aalaei-Andabali (34), 2018	Cohort	Prospective	University of Florida Health Care Centre	United States	TAV	32	High
Liao (18), 2018	Cohort	Prospective	West China Hospital, Sichuan	China	TAV	87	Medium
De Biase (35), 2018	Cohort	Prospective	Groupe Cardiovasculaire Interventionel, Clinique Pasteur	France	TAV	83	Medium
Djordjevic (36), 2017	Case series	Retrospective	Deutsches Herzzentrum Berlin	Germany	TAV	33	Medium
Watanabe (37), 2015	Cohort	Prospective	Teikyo University Hospital	Japan	n/a	11	High
Costopoulos (38), 2014	Cohort	Retrospective	San Raffaele Scientific Institute Clinical Institute S. Ambrogio	Italy	TAV	21	Medium
Kochman (39), 2014	Cohort	Retrospective	5 academic centres	Poland	TAV	28	High
Hayashida (40), 2013	Cohort	Prospective	Institut Cardiovasculaire, Paris	France	TAV	21	High
Himbert (41), 2012	Case series	Retrospective	Bichat-Claude Bernard Hospital, Paris	France	TAV	15	Medium
Wijesinghe (42), 2010	Case series	Retrospective	St. Paul's Hospital Quebec Heart and Lung Institute Hamilton Health Sciences Centre	Canada	n/a	11	Medium

*, the study by Yoon *et al.* [2020] drew from the International Bicuspid Aortic Valve Stenosis Registry in which patients were recruited both retrospectively and prospectively. BAV, bicuspid aortic valve; TAV, tricuspid aortic valve; SAVR, surgical aortic valve replacement; N, number of patients with bicuspid valves included in each study; LRT, low-risk TAVR; TAVR, transcatheter aortic valve replacement; n/a, not available.

Table 2 Baseline characteristics

Characteristic	Patients [studies], n	Weighted pooled estimate [95% CI]	Heterogeneity I^2 (%)
Age (years)	1,945 [22]	74.1 [72.4–75.9]	94
Male sex (%)	1,844 [20]	59.1 [56.2–62.0]	12
STS-PROM score	1,861 [18]	5.39 [4.45–6.34]	98
NYHA class III/IV (%)	1,743 [16]	71.8 [63.4–80.2]	93
LVEF (%)	1,741 [19]	52.2 [50.0–54.5]	91
Mean aortic gradient (mmHg)	1,728 [18]	54 [51–58]	91
Aortic valve area (cm ²)	1,492 [14]	0.64 [0.60–0.69]	91
Aortic annulus area (mm ²)	298 [6]	530 [490–580]	91
Mean aortic annulus diameter (mm)	403 [12]	25.7 [24.5–26.9]	96
Ascending aortic size (mm)	1,510 [14]	74.1 [72.4–75.9]	91

CI, confidence interval; n, number of patients; STS-PROM, Society of Thoracic Surgeons-Predicted Risk of Mortality; NYHA, New York Heart Association; LVEF, left ventricular ejection fraction.

$I^2=91\%$), an aortic valve area of 0.64 cm² (95% CI: 0.60–0.69 cm²; $I^2=91\%$), an aortic annulus area of 530 mm² (95% CI: 490–580 mm²; $I^2=91\%$), a mean aortic annulus diameter of 25.7 mm (95% CI: 24.5–26.9 mm; $I^2=96\%$), and an ascending aortic size of 74.1 mm (95% CI: 72.4–75.9 mm; $I^2=91\%$) (Table 2, Figure S1). All P values were statistically significant.

Procedures

The route of access was reported in 18 studies, and 91.8% of procedures were transfemoral. The most common devices used were the CoreValve (Medtronic, Minneapolis, Minnesota, USA) and Evolut R (Medtronic) (15,18,25–27, 29,30,32–41), used in 17 studies, and the SAPIEN 3 (Edwards Lifesciences, Irvine, California, USA) and SAPIEN XT valves (Edwards Lifesciences), used in 13 studies (15,26,30,32–40,42). The Lotus EDGE (Boston Scientific, Marlborough, Massachusetts, USA) was used in six studies (15,25,26,28,33,35) and the VenusA-valve (Venus MedTech, Hangzhou, China) was used in four studies from Mainland China (18,24,31,33). Other less commonly used valves included the Arcuate *neo* valve (Boston Scientific), the VITAFLOW aortic valve system (Microport, Shanghai, China), the TaurusOne transcatheter aortic valve system (Peijia Medical, Suzhou, China) and the Portico system (Abbott Structural Heart, St. Paul, Minnesota, USA).

Post-procedural outcomes

The overall device success rate was 87.5% (95% CI: 82.4–92.7%; $I^2=72\%$). Moderate to severe PVL was seen in 3.7% (95% CI: 2.2–5.3%; $I^2=46\%$) of patients. Echocardiographic findings following TAVR included a mean aortic gradient of 11.2 mmHg (95% CI: 9.8–12.6 mmHg; $I^2=96\%$), an effective orifice area of 1.70 cm² (95% CI: 1.67–1.73 cm²; $I^2=91\%$) and a LVEF of 55.2% (95% CI: 53.0–57.5%; $I^2=81\%$). Device migration was reported in 2.5% (95% CI: 0.5–4.5%; $I^2=0\%$) of procedures (Table 3, Figure S2). All P values were statistically significant.

Clinical outcomes

The mean hospital stay was 7.68 days (95% CI: 6.17–9.19 days; $I^2=99\%$). New permanent pacemaker insertion (PPI) was required in 11.8% (95% CI: 7.9–15.8%; $I^2=87\%$) of procedures. The most common clinical complication was major bleeding (3.5%; 95% CI: 1.8–5.2%; $I^2=36\%$), followed by major vascular complications (2.5%; 95% CI: 1.2–3.9%; $I^2=41\%$), stroke (2.3%; 95% CI: 1.6–3.0%; $I^2=0\%$), acute kidney injury (2.1%; 95% CI: 1.0–3.1%; $I^2=48\%$) and coronary obstruction (0.1%; 95% CI: 0.1–0.2%; $I^2=0\%$). Conversion to open surgery was required in 1.0% of procedures (95% CI: 0.5–1.5%; $I^2=0\%$) (Table 4, Figure S3). The P value for coronary obstruction was 0.294. All other P values were statistically significant.

Table 3 Post-procedural outcomes

Outcome	Patients [studies], n	Weighted pooled estimate [95% CI]	Heterogeneity I^2 (%)
Device success (%)	483 [11]	87.5 [82.4–92.7]	72
Moderate/severe PVR (%)	1,806 [18]	3.7 [2.2–5.3]	46
Mean aortic gradient (mmHg)	1,661 [18]	11.2 [9.8–12.6]	96
Effective orifice area (cm ²)*	1,077 [3]	1.70 [1.67–1.73]	91
LVEF (%)	1,354 [10]	55.2 [53.0–57.5]	81
Device migration (n)	223 [7]	2.5 [0.5–4.5]	0

*, Djordjevic *et al.* was excluded following sensitivity analysis. CI, confidence interval; LVEF, left ventricular ejection fraction; PVR, pulmonary vascular resistance.

Table 4 Clinical outcomes

Outcome	Patients [studies], n	Weighted pooled estimate [95% CI]	Heterogeneity I^2 (%)
Length of hospital stay (days)	465 [10]	7.68 [6.17–9.19]	99
Coronary obstruction (%)	1,531 [14]	0.1 [0.1–0.2]	0
Conversion to surgery (%)	1,448 [13]	1.0 [0.5–1.5]	0
Major vascular complication (%)	1,542 [12]	2.5 [1.2–3.9]	41
Major bleeding (%)	1,471 [13]	3.5 [1.8–5.2]	36
Stroke (%)	1,872 [19]	2.3 [1.6–3.0]	0
Acute kidney injury* (%)	1,355 [9]	2.1 [1.0–3.1]	48
New PPI (%)	1,824 [18]	11.8 [7.9–15.8]	87

*, Pineda *et al.* was excluded following sensitivity analysis. CI, confidence interval; PPI, permanent pacemaker insertion.

Table 5 All-cause mortality

Length of time post-operation	Patients [studies], n	Weighted pooled estimate [95% CI]	Heterogeneity I^2 (%)
In-hospital (%)	588 [15]	1.9 [0.8–3.1]	7
30-day (%)	1,867 [19]	2.1 [1.2–2.9]	15
1-year (%)	1,143 [11]	9.6 [5.7–13.6]	62
2-year (%)	635 [4]	12.9 [10.4–15.4]	0

CI, confidence interval.

All-cause mortality

The mean in-hospital mortality of BAV patients following TAVR was 1.9% (95% CI: 0.8–3.1%; $I^2=7\%$). The mortality at 30 days and one-year post-procedure was 2.1% (95% CI: 1.2–2.9%; $I^2=15\%$) and 9.6% (95% CI: 5.7–13.6%;

$I^2=62\%$), respectively. Mean mortality at two years post-procedure was 12.9% (95% CI: 10.4–15.4%; $I^2=0\%$). Two papers reported mortality rates of 11.0% and 15.8% at their respective follow-ups of 2.1±1.6 and 2.86±1.47 years (Table 5, Figure 2), respectively (15,16). All P values were statistically significant.

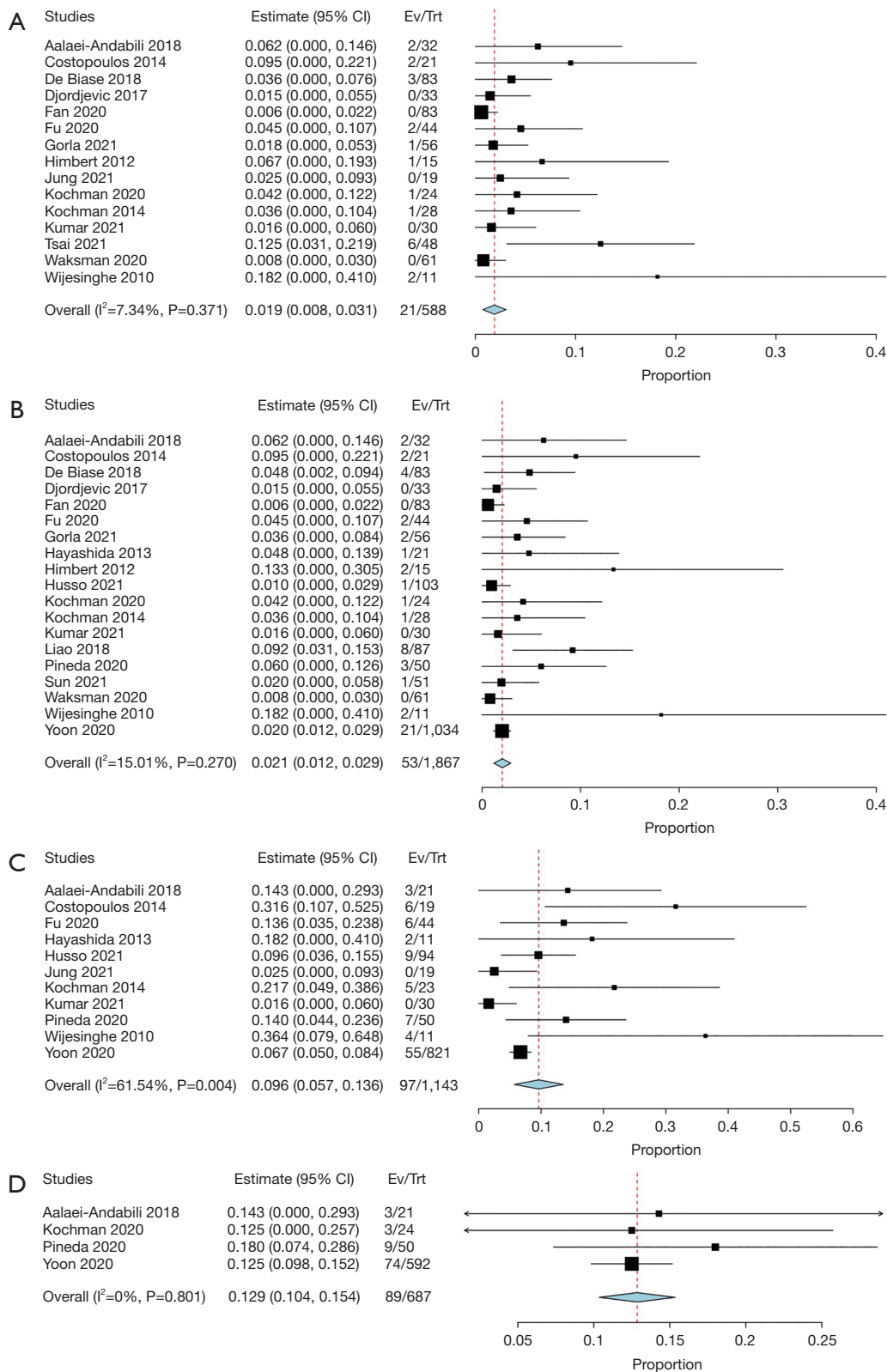


Figure 2 Forest plots of included studies comparing mortality. (A) In-hospital mortality; (B) 30-day mortality; (C) 1-year mortality; (D) 2-year mortality. CI, confidence interval; Ev/Trt, events/total patients in treatment group.

Discussion

BAV has traditionally been a contraindication to TAVR, due to complications arising from the abnormal anatomy of the aortic valve, which is not excised and remains *in situ* following TAVR (30). As a result, BAV patients have been excluded from landmark TAVR randomized controlled trials (RCTs) and its efficacy and safety profile in BAV patients remain uncertain (43,44). SAVR has been the mainstay of treatment for BAV stenosis; however, with the increasing use of TAVR in BAV patients, data comparing the outcomes of TAVR and SAVR in BAV patients is becoming more available (15,16,45). Husso *et al.* conducted a cohort study of 75 propensity score-matched patients and found that 30-day and two-year mortality of BAV patients undergoing SAVR were 5.3% and 18.7%, respectively, and the difference compared to TAVR was not statistically significant (15). Elbadawi *et al.* also found in a cross-sectional study of over 1,000 patients that there was no significant difference in in-hospital mortality between SAVR and TAVR for BAV patients (45). Interestingly, a recent cross-sectional study of 48 BAV patients found that although there was no difference in survival rates between BAV patients undergoing TAVR and SAVR, functional recovery (as defined by patient-reported maximum activity level) after six months was greater in SAVR patients compared to TAVR (16). These studies show promising short- and mid-term results for TAVR as an alternative to SAVR in BAV patients, and long-term follow-up studies investigating both morbidity and mortality are warranted to further assess the safety and efficacy of TAVR in BAV patients.

The current study found that BAV patients undergoing TAVR had a 30-day and one-year overall mortality of 2.1% and 9.6% respectively. Included studies that reported the highest 30-day mortality were from 2010 to 2014, while studies that reported the lowest 30-day mortality were from 2020 to 2021 (15,24,27,38,41,42). This trend was also seen in one-year mortality results, where the three studies that reported the highest one-year mortality were from 2010 to 2014, while the three studies with the lowest one-year mortality were from 2020 to 2021 (26,27,30,38,39,42). This may suggest an improved safety profile of TAVR in BAV patients, as centers are increasingly incorporating TAVR as an alternative or even preferred treatment for BAV stenosis. Two-year mortality was found to be 12.9% in the current patient cohort, and this is the only systematic review to our knowledge that reports aggregated two-year mortality in

BAV patients undergoing TAVR.

This systematic review found low rates of procedural and clinical outcomes. Device success rate (87.5%) reported in this study is comparable with previously published systematic reviews, which range from 85.8% to 95.2% (46-49). Post-procedural mean aortic gradient (11.2 mmHg) was also comparable with previously published gradients, which range from 6.0 to 16.0 mmHg (49,50). The rate of moderate to severe PVL (3.7%) was found to be lower in this cohort compared to previously published cohorts, which range from 8.8% to 12.2% (46-48,50). It is interesting to note that 82.4% of patients from this systematic review are from studies published after 2020, suggesting that increased experience with TAVR in BAV may play a role in mitigating post-procedural PVL.

The risk of requiring a new PPI (11.8%) was highest following TAVR in BAV patients, although there was significant heterogeneity within the reported studies. Major bleeding (3.5%), major vascular complications (2.5%) and acute kidney injury (2.1%) were the next most common complications in this patient cohort. This is consistent with previously published systematic reviews, which reported a new PPI rate of 12.2–18.5%, a major bleeding rate of 4.2–20.0%, an acute kidney injury risk of 2.04–6.50%, and a major vascular complication rate of 1.3–8.5% (46,48-56). Following sensitivity analysis, Pineda *et al.* was excluded from meta-analysis of AKI due to its significantly high rate, which was not representative of the current patient cohort. This may be attributable to the high rate of comorbidities in their patient cohort compared to other studies in the systematic review, including 84% of patients with hypertension and 46% of patients with diabetes mellitus (15,16,29,30,32). The rate of coronary obstruction (0.1%) reported in this systematic review was lower than previously published rates (0.5–1.6%) (49,52,53,56). Yoon *et al.* reported no coronary obstructions in 1,034 patients, and while this significantly impacted the data following sensitivity analysis, the study contributed more than half of the patients included in this systematic review and was included for meta-analysis (30). The same study also reported low rates of stroke and conversion to open surgery (30). Nevertheless, studies comparing these post-procedural outcomes to those of SAVR are warranted to further assess the complication risk of TAVR in BAV stenosis versus standard treatment.

Several large, multicenter studies have found no differences in clinical outcomes and survival between BAV

and TAV patients undergoing TAVR, with rates similar to those reported in the current study (14,57,58). Yoon *et al.* compared short- and mid-term mortality between 546 pairs of propensity score-matched TAV and BAV patients undergoing TAVR and found that there were no significant differences in 30-day, one-year or two-year mortality (14). Interestingly, the same study found that while BAV patients undergoing TAVR using new-generation devices (Sapien 3, Lotus, Evolut R) do not differ in PVL, device failure, second valve implantation or conversion to surgery compared to TAV patients, patients using old-generation devices (Sapien XT, CoreValve) experienced higher rates of these complications (14). Similar results were found in another 2017 prospective cohort study of 400 patients, which reported higher rates of procedural complications (device failure, second valve implantation, moderate/severe aortic regurgitation) 30-day mortality, aortic regurgitation and major vascular complications when using old-generation devices, regardless of valve anatomy (59). Despite this, recent unpublished data suggests that there are still areas of concern for the use of TAVR in BAV stenosis, as higher rates of PVL, annular rupture and cerebral ischemic events were reported compared to TAV (60). Results from the current study include both old- and new-generation devices and are comparable to morbidity and mortality results from TAVR studies in TAV patients (14,59). Taken together, this data shows increasing promise for the role of TAVR as a treatment option in BAV stenosis.

Limitations and future directions

There are several limitations to this study. BAV patients in this systematic review were studied as a single cohort, and subgroup analyses were not performed between different groups of BAV patients. There was significant heterogeneity within the baseline characteristics of the study population (Figure S1). However, following sensitivity analysis, no single study was found to significantly affect overall study outcomes. Previous studies have identified several procedural and patient specific variables that may impact the mortality and clinical outcomes in BAV patients undergoing TAVR. These include BAV morphology and degree of calcification, device type/generation, radiological features and surgical approach (14,30,59,61-63). Additionally, long-term follow-up data was not included in this study, due to the lack of available studies in the current literature. Currently, several RCTs (NCT03163329, NCT02541877)

and a long-term follow-up study (NCT0365424) are running, and results from these studies will add valuable information to the existing body of literature regarding the viability of TAVR as a treatment modality for BAV stenosis.

Conclusions

This evaluation of the progress of TAVR for BAV stenosis demonstrates that it is associated with promising short- and mid-term morbidity and mortality outcomes. Recent TAVR developments are in the right direction for it to become a viable alternative to SAVR. Long-term outcomes remain unclear for TAVR in BAV and randomized trials with long-term follow-up will provide greater insight into its safety and efficacy.

Acknowledgments

The authors would like to acknowledge the following contributors: (I) Dr. David Tian for his contribution to the direction of the study; (II) Librarian Linda Mulheron of Westmead Hospital Library for her contribution to the systematic review; (III) Consultant statistician Jim Matthews for his contribution to the meta-analysis.

Funding: None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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Cite this article as: Chen CHJ, Jiang H, Martin O, Wilson-Smith AR. Procedural and clinical outcomes of transcatheter aortic valve replacement in bicuspid aortic valve patients: a systematic review and meta-analysis. *Ann Cardiothorac Surg* 2022;11(4):351-362. doi: 10.21037/acs-2022-bav-22