Title

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Journal

Journal of the American Heart Association, 5(6)

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Publication Date

2016-06-13

DOI

10.1161/JAHA.115.003191

ORIGINAL RESEARCH

Transcatheter Aortic Valve Implantation With or Without Preimplantation Balloon Aortic Valvuloplasty: A Systematic Review and Meta-Analysis

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***Background*—**Preimplantation balloon aortic valvuloplasty (BAV) is considered a routine procedure during transcatheter aortic valve implantation (TAVI) to facilitate prosthesis implantation and expansion; however, it has been speculated that fewer embolic events and/or less hemodynamic instability may occur if TAVI is performed without preimplantation BAV. The aim of this study was to systematically review the clinical outcomes associated with TAVI undertaken without preimplantation BAV.

***Methods and Results*—**We conducted a search of Medline and Embase to identify studies that evaluated patients who underwent TAVI with or without preimplantation BAV for predilation. Pooled analysis and random-effects meta-analyses were used to estimate the rate and risk of adverse outcomes. Sixteen studies involving 1395 patients (674 with and 721 without preimplantation BAV) fulfilled the inclusion criteria. Crude device success was achieved in 94% (1311 of 1395), and 30-day all-cause mortality occurred in 6% (72 of 1282) of patients. Meta-analyses evaluating outcomes of strategies with and without preimplantation BAV showed no statistically significant differences in terms of mortality (relative risk [RR] 0.61, 95% CI 0.32–1.14, P=0.12), safety composite end point (RR 0.85, 95% CI 0.62–1.18, P=0.34), moderate to severe paravalvular leaks (RR 0.68, 95% CI 0.23–1.99, P=0.48), need for postdilation (RR 0.86, 95% CI 0.66–1.13, P=0.58), stroke and/or transient ischemic attack (RR 0.72, 95% CI 0.30–1.71, P=0.45), and permanent pacemaker implantation (RR 0.80, 95% CI 0.49–1.30, P=0.37).

***Conclusions*—**Our analysis suggests that TAVI procedures with or without preimplantation BAV were associated with similar outcomes for a number of clinically relevant end points. Further studies including a large number of patients are needed to ascertain the impact of TAVI without preimplantation BAV as a standard practice. **(*J Am Heart Assoc*. 2016;5:e003191 doi: 10.1161/JAHA.115.003191)**

Key Words: aortic stenosis • aortic valve replacement • balloon aortic valvuloplasty • transcutaneous aortic valve implantation • transfemoral aortic valve implantation

Transcatheter aortic valve implantation (TAVI) is the definitive alternative option for patients with severe symptomatic aortic stenosis that are considered either unsuitable or high risk for surgical aortic valve replacement.[1,2] Preimplantation balloon aortic valvuloplasty (BAV) is a standard procedure during TAVI. Predilation BAV creates fractures of calcified leaflets and increases leaflet flexibility, thereby facilitating delivery of the TAVI catheter across the aortic valve and enhancing prosthesis implantation and expansion within the calcified aortic valve annulus.

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Received January 5, 2016; accepted April 19, 2016.

Importantly, it has been speculated that fewer embolic events and/or less hemodynamic instability may occur if TAVI is performed without preimplantation BAV. Nonetheless, there is also a concern that omitting preimplantation BAV may result in the need for more postimplant BAV postdilation and possible associated complications. Notably, this approach has been proposed only in single-center studies with relatively small sample sizes; therefore, the benefits of TAVI without preimplantation BAV may be overestimated and subject to significant selection biases. We sought to undertake a systematic review and meta-analysis to study the clinical outcomes associated with TAVI procedures performed with and without preimplantation BAV to gain insight into optimal practice during TAVI procedures.

Methods

Eligibility Criteria

We included studies that evaluated patients who underwent TAVI with and without preimplantation (procedural) BAV for predilation. Studies included in the meta-analysis had to be parallel group in design, with one group having TAVI with preimplantation BAV and the other having TAVI without preimplantation BAV. We also included single-arm studies that evaluated the feasibility of performing TAVI without preimplantation BAV. In terms of outcomes, included studies must have evaluated procedural or device success and ≥1 of the following events: need for postimplantation balloon postdilation, valve embolization, need for a second valve, vascular complications, bleeding, neurological events (stroke or transient ischemic attack), acute kidney injury, permanent pacemaker implantation, significant residual aortic regurgitation or paravalvular leakages (PVLs), and mortality. Early safety end point, if available, was reported in accordance to Valve Academic Research Consortium (VARC-2) definitions[3]: all-cause mortality (at 30 days), all stroke (disabling and nondisabling), life-threatening bleeding, acute kidney injury stage 2 or 3 (including renal replacement therapy), coronary artery obstruction requiring intervention, major vascular complication, valve-related dysfunction requiring repeat procedure (BAV, TAVI, or surgical valve replacement). The reporting of outcomes had to include either crude events in each group or any risk or odds estimate (relative risk [RR], hazard ratio, odds ratio) with a 95% CI. There was no restriction based on the design of the study or the duration of follow-up. We excluded reports in which BAV may have been performed weeks or months before TAVI (so-called bridge-to-TAVI procedure) and isolated case reports, reviews, and editorials.

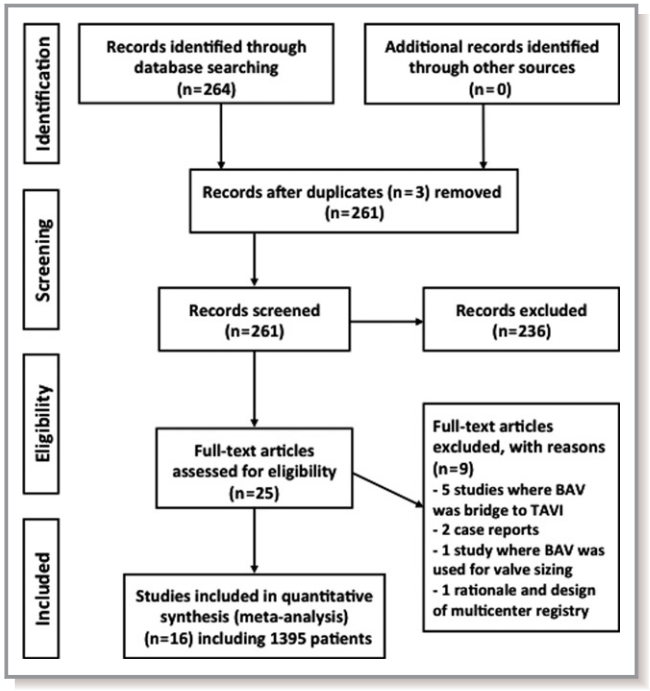

Figure 1. Flow diagram based on the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA). BAV indicates balloon aortic valvuloplasty; TAVI, transcatheter aortic valve implantation.

Search Strategy

We conducted a search of Medline and Embase from conception to September 20, 2015, using OvidSP (Ovid Technologies). The following exact search terms were used: ("transcatheter aortic valve implantation" OR "TAVI" OR "transcatheter aortic valve replacement" OR "TAVR") AND ("Balloon aortic valvuloplasty"). There was no restriction based on language of study, and abstracts and unpublished studies were included. The references of the included studies and relevant reviews were checked for additional studies. A flow diagram is provided following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) (Figure 1).

Institutional review board approval and patient consent were not required because of the nature of this study as a systematic review and meta-analysis.

Study Selection

Two reviewers (R.B. and C.S.K.) independently checked all titles and abstracts for studies that met the inclusion criteria. The full reports of potentially relevant studies were retrieved, and data were independently extracted on study design, participant characteristics, treatment groups, outcome events, follow-up, and results. Any discrepancies between reviewers were resolved by consensus after consulting a third reviewer (M.A.M.).

Table 1. Characteristics of the Study Population

Study and Year of Publication	Without BAV	Age Female	Mean Gradient AVA (cm^2) LVEF	EuroSCORE STS-PROM	With BAV	Age Female	Mean Gradient AVA (cm^2) LVEF	EuroSCORE STS-PROM	Differences Between Baseline Characteristics
Grube et al[5] 2011	60	80.1±6.4 53.3%	47.8±15.5 0.66±0.2 NA	23.3±15.2 NA	—	—	—	—	—
Wendler et al[6] 2012	6	82±3 33%	49±5 0.6±0.18 NA	30±12 NA	—	—	—	—	—
Mendiz et al[7] 2013	51	79±8 65%	80±22 (peak) 0.7±0.2 56±10%	20±15 NA	—	—	—	—	—
Rück et al[8] 2013	78	NA	NA	19 NA	—	—	—	—	—
Fiorina et al[9] 2014	55	83±7 51%	44±13 0.39±0.1* 49±13%	27±18 10±8*	45	83±8 44%	48±16 0.36±0.1* 49±13%	22±14 7±4*	1. Indexed AVA, *P*=0.09 2. STS score, *P*=0.03 3. Prior MI 20% no-BAV vs 6% in BAV, *P*=0.05
Davies et al[10] 2014	12	83±3 50%	56±19 (peak) 0.7±0.2 56±19%	23±12 6±3	—	—	—	—	—
Conradi et al[11] 2014	50	78±8 46%	28±14 0.9±0.4 NA	21±14 8±7	50	81±7 52%	31±17 0.8±0.2 NA	23±13 8±5	Similar
Aggarwal et al[12] 2014	52	NA	NA	NA	61	NA	NA	NA	NA
Giustino et al[13] 2014	73	NA	NA	NA	133	NA	NA	NA	Similar
Möllmann et al[14] 2014	26	81.6±6.5 42.3%	36.0±17.3* 0.7±0.2 55%*	24.6±8.7 6.2±2.7	30	82.2±5.4 43.3%	48.5±17.7* 0.6±0.2 60%*	21.4±12.1 6.2±3.1	1. LVEF 55% (IQR 35.0–60.0%) in non-BAV vs 60% (IQR 53.8–65.0%) in BAV group, *P*=0.01 2. Mean gradient, *P*=0.01
Kochman et al[15] 2014	8	78.1±8.4 50%	46.0±14.1 0.58±0.15 38.4%	20±6 NA	16	83.3±3.7 31.3%	55.9±12.0 0.59±0.17 46.8%	19±7 NA	Similar
Kempfert et al[16] 2015	40	79 30%	42 NA 52%	NA 7.62	40	80 30%	40 NA 51%	NA 7.22	Differences were observed between the no-BAV and BAV groups before adjustment for variables male sex (52% vs 70%, *P*=0.05) and stroke (23% vs 7%, *P*=0.01). The cohorts were similar after propensity score matching.
Islas et al[17] 2015	79[§]	82.4±5.5 65.7%	47.3±14.7 0.6±0.2 56.9±12.5%	18.6±9.8 NA	170[‡]	82.8±5.7 64.7%	50.1±17.7 0.7±0.2 58.7±13.4%	17.9±9.6 NA	Similar
Conradi et al[18] 2015	26	81.3±6.3 61.5%	38±14 0.8±0.2 19% ≤45%[†]	15±13 6±3	26	81.7±5.2 61.4%	42±17 0.7±0.2 15% ≤45%[†]	15±12 5±2	Similar

Continued

Table 1. Continued

Study and Year of Publication	Without BAV	Age Female	Mean Gradient AVA (cm^2) LVEF	EuroSCORE STS-PROM	With BAV	Age Female	Mean Gradient AVA (cm^2) LVEF	EuroSCORE STS-PROM	Differences Between Baseline Characteristics
Wong et al[19] 2015	50	84.3±6.6 58%	44±13 0.7±0.2 50±14%	NA 8.5±4.6	71	84.4±7.5 46%	51±14 0.7±0.2 49±15%	NA 9.4±5.3	In the transfemoral BAV group, smoking was 42% vs 68% in transapical no-BAV (P=0.005), peripheral vascular disease was 20% vs 38% in transapical no-BAV (P=0.03). AV calcification tended to be higher (P=0.07) in the transfemoral BAV vs the transapical no-BAV group. Conversely, the transapical no-BAV tended to have more (P=0.06) porcelain aorta than the transfemoral BAV group.
Bijuklic et al[20] 2015	55	82.9±6.8 47.3%	40.0±12.7 0.71±0.2 53.0±13.8%	21.4±15.1 NA	32	83.8±5.2 56.2%	40.5±13.4 0.71±0.2 57.2±11.9%	23.7±16.0 NA	Similar

Values are expressed as number of patients for no-BAV (without preimplantation BAV) and BAV (with preimplantation BAV). Values are expressed as mean±SD for age and mean gradient (mm Hg). AV indicates aortic valve; AVA, aortic valve area; BAV, balloon aortic valvuloplasty; IQR, interquartile range; Log-EuroSCORE, logistic European system for cardiac operative risk evaluation; LVEF, left ventricle ejection fraction; MI, myocardial infarction; NA, not available; STS-PROM, Society of Thoracic Surgeons Score for Prediction of Mortality.

*Difference was encountered.

†Edwards SAPIEN XT, n=51; Medtronic CoreValve, n=28.

‡Edwards SAPIEN XT, n=115; Medtronic CoreValve, n=55.

§Percentage of patients with LVEF ≤45%.

Quality Assessment

Risk of bias was assessed by considering ascertainment of treatment groups, ascertainment of outcomes, loss to follow-up, and consideration of potential confounders in the data analysis. Publication bias was assessed using funnel plots if there were >10 studies in a meta-analysis and no evidence of substantial statistical heterogeneity.[4]

Data Analysis

We used RevMan (version 5.1.7; Nordic Cochrane Centre) to perform random-effects meta-analysis using the Mantel–Haenszel method to determine pooled risk ratios for dichotomous data. The I^2 statistic was used to assess the consistency among studies, with I^2<25% considered low, I^2=50% considered moderate, and I^2>75% considered high heterogeneity. If data or studies for meta-analysis were insufficient, we pooled the studies using a weighted average or performed a narrative synthesis of studies that were too heterogeneous to pool. Sensitivity analyses were further performed according to the access site and type of valve for meta-analysis.

Results

Study Population

A total of 16 studies[5–20] including 1395 patients fulfilled the inclusion criteria (Figure 1). The sample size, age, sex, hemodynamic echocardiographic data, predicted operative mortality risk evaluation scores, and some of the baseline characteristics are described in Table 1. Among the studied populations, TAVI was performed without preimplantation BAV in 721 patients and with preimplantation BAV in 674 patients. The mean age was 81.3 years, and 49.6% of participants were female in 14 studies that reported both age and sex.[5–9,11,14–20] The balloon-expandable Edwards SAPIEN XT or SAPIEN 3 valve was implanted in 10 studies[6,10–12,14,16–20] including 793 patients, and the self-expandable Medtronic CoreValve was used in 7

Table 2. Design and Quality Assessment of Included Studies

Study and Year of Publication	Design; Dates; Country	Ascertainment of Treatment Group	Ascertainment of Outcomes	Loss to Follow-up	Adjustment for Confounders
Grube et al[5] 2011	Prospective cohort study; 2009–2010; international	Reliable	Follow-up by clinical visits and echocardiography	None	None, crude results
Wendler et al[6] 2012	Cohort study; unclear; United Kingdom	Reliable	Assessment at 30 days	None	None, crude results
Mendiz et al[7] 2013	Prospective cohort study; May 2010 to May 2012; Argentina	Reliable	Follow-up by clinical visits, echocardiography and telephone calls	None	None, crude results
Rück et al[8] 2013	Cohort study; started September 2012; Sweden	Reliable	Unclear	None	None, crude results
Fiorina et al[9] 2014	Prospective cohort study; June 2012 to June 2013; Italy	Reliable	Follow-up by clinical visits and echocardiography	None	None, crude results
Davies et al[10] 2014	Prospective cohort study; unclear; United Kingdom	Reliable	Unclear	None	None, crude results
Conradi et al[11] 2014	Retrospective cohort study; May 2011 to December 2012; Germany	Reliable	Clinical end points were adjudicated	None, retrospective	None, crude results
Aggarwal et al[12] 2014	Retrospective cohort; March 2012 to April 2014; United Kingdom	Reliable	Unclear	None, retrospective	None, crude results
Giustino et al[13] 2014	Cohort study; November 2007 to September 2013; Italy	Reliable	Assessment at 30 days and 12 months	None	None, crude results
Möllmann et al[14] 2014	Case–control study; unclear; Germany	Reliable	Assessment at 30 days	None	None, crude results
Kochman et al[15] 2014	Case-matched study; March 2010 to April 2013; Poland	Reliable	Follow-up by clinical visits at 30 days, 6 months and 12 months	None	Case-matched analysis
Kempfert et al[16] 2015	Propensity-matched analysis; March 2012 to July 2013; Germany	Reliable	Clinical follow-up at 30 days	None	Propensity-matched analysis
Islas et al[17] 2015	Cohort study; January 2009 to August 2014; Spain	Reliable	Clinical follow-up at 30 days	None	None, crude results
Conradi et al[18] 2015	Case-matched study; unclear; Germany	Reliable	Clinical end points were adjudicated	None, retrospective	Matched by logistic regression and nearest neighbors
Wong et al[19] 2015	Retrospective cohort; May 2012 to December 2013; United States	Reliable	Follow-up by clinical visits	None, retrospective	None, crude results
Bijuklic et al[20] 2015	Case–control study; unclear; Germany	Reliable	Follow-up at 30 days	None, retrospective	None, crude results

studies[5,7–9,13,15,17] including 602 patients. One study included both types of bioprostheses.[17] Access was transfemoral, exclusively, in 8 studies[5,7,8,12,14,17,18,20]; transfemoral, transsubclavian, or direct aortic in 4 studies[9,10,13,15]; transapical in 3 studies[6,11,16]; and transfemoral or transapical access in 1 study.[19] There were 4 prospective cohort studies,[5,7,9,10] 4 cohort studies,[6,8,13,17] 3 retrospective cohort studies,[11,12,19] 2 case-matched studies,[15,18] 2 case–control studies,[14,20] and 1 propensity-matched study.[16]

Study Designs and Quality Assessment

Study design, time frame, country of origin, and quality assessment for included studies are reported in Table 2. Ascertainment of outcomes varied from medical record reviews to prospective evaluation with adjudicated clinical end points. All studies contained reliable data, and there was no loss to follow-up. Follow-up of patients varied and included in-hospital outcomes, clinical visits, echocardiographic

Table 3. Procedure-Related and Clinical Outcomes

Study and Year of Publication	Type of Valve, Approach	Time Frame of Assessment	Assessment Definitions	Outcomes	No-BAV	BAV
Grube et al[5] 2011	CoreValve, transfemoral	30 days	VARC	Procedural success	58/60 (96.7)	NA
				Need for a second valve	1/60 (1.7)	
				Conversion to surgery	1/60 (1.7)	
				Postdilation	10/60 (16.7)	
				Moderate/severe AR	0/60 (0)	
				Myocardial infarction	0/60 (0)	
				Stroke/TIA	3/60 (50)	
				Pacemaker implantation	7/60 (11.7)	
				Major vascular complication	6/60 (10)	
				All-cause mortality	4/60 (6.7)	
Wendler et al[6] 2012	SAPIEN XT, transapical	30 days	VARC	Procedural success	6/6 (100)	NA
				Postdilation	0/6 (0)	
				Moderate/severe AR	0/6 (0)	
				Trivial or mild AR	3/6 (50)	
				Acute kidney injury	1/6 (16.7)	
				All-cause mortality	0/6 (0)	
Mendiz et al[7] 2013	CoreValve, transfemoral	12 months	VARC	Device success	48/51 (94.2)	NA
				Need for bailout BAV predilation[#]	1/51 (1.96)	
				Postdilation	16/51 (31.4)	
				Moderate AR	1/51 (1.96)	
				Pacemaker implantation	14/49 (28.6)	
				Major vascular complication	3/51 (5.9)	
				Cardiac tamponade	1/51 (1.96)	
				Conversion to surgery	1/51 (1.96)	
				Stroke	1/51 (1.96)	
				Combined safety end point	8/51 (15.7)	
				30-day mortality	2/51 (3.9)	
				7-month (median time) mortality	7/51 (13.7)	
Rück et al[8] 2013	CoreValve, transfemoral	In hospital or 30 days	Unclear	Procedural success	77/78 (98.7)	NA
				Need for bailout BAV predilation[#]	1/78 (1.3)	
				Postdilation	19/78 (24.4)	
				Need for a second valve	14/78 (17.9)	
				Moderate AR	11/78 (14.1)	
				Severe AR	0/78 (0)	
				Myocardial infarction	0/78 (0)	
				Stroke	0/78 (0)	
				Pacemaker implantation	20/78 (25.6)	
				30-day mortality	5/78 (6.4)	
Fiorina et al[9] 2014	CoreValve, transfemoral or direct aortic	30 days	VARC-2	Device success	47/55 (85.5)*	29/45 (64.4)
				Need for bailout BAV predilation[#]	1/55 (1.8)	—
				Need for a second valve	2/55 (3.6)	2/45 (4.4)
				Moderate or severe PVL	5/55 (9.1)	15/45 (33)**

Continued

Table 3. Continued

Study and Year of Publication	Type of Valve, Approach	Time Frame of Assessment	Assessment Definitions	Outcomes	No-BAV	BAV
				Postdilation	19/55 (34.5)	23/45 (51.1)¶
				Myocardial infarction	0/55 (0)	0/45 (0)
				Stroke	0/55 (0)	0/45 (0)
				Acute kidney injury	3/55 (5.5)	1/45 (2.2)
				Major vascular complication	2/55 (3.6)	1/45 (2.2)
				Minor vascular complication	0/55 (0)	4/45 (8.9)
				Major bleeding	3/55 (5.5)	1/45 (2.2)
				Pacemaker implantation	3/55 (5.5)	7/45 (15.6)¶
				Safety end point	8/55 (14.5)	4/45 (8.9)
				All-cause mortality	1/55 (1.8)	2/45 (4.4)
Davies et al[10] 2014	SAPIEN XT, transfemoral or direct aortic	Unclear	Unclear	Device success	12/12 (100)	NA
				Bleeding needing transfusion	0/12 (0)	
				Stroke	1/12 (8.3)	
				Pacemaker implantation	0/12 (0)	
				All-cause mortality	0/12 (0)	
Conradi et al[11] 2014	SAPIEN XT, transapical	30 days	VARC-2	Device success	47/50 (94)	43/50 (86)
				Postdilation	4/50 (8)	2/50 (4)
				Need for a second valve	1/50 (2)	1/50 (2)
				Conversion to surgery	1/50 (2)	0/50 (0)
				Stroke	1/50 (2)	3/50 (6)
				Myocardial infarction	0/50 (0)	0/50 (0)
				Major bleeding	1/50 (2)	1/50 (2)
				Major access site complications	1/50 (2)	1/50 (2)
				Acute kidney injury	1/50 (2)	2/50 (4)
				Pacemaker implantation	5/50 (10)	4/50 (8)
				Early safety end point	7/50 (14)	12/50 (24)
				All-cause mortality	2/50 (4)	5/50 (10)
Aggarwal et al[12] 2014	SAPIEN XT and SAPIEN 3 Transfemoral	NA	VARC-2	Device success	50/52 (96.1)	60/61 (98.3)
				Moderate or severe AR	3/52 (5.8)	3/61 (4.9)
				Postdilation	2/52 (4.0)	2/61 (3.4)
				Procedural safety	18/52 (34.6)	31/61 (50.8)
Giustino et al[13] 2014	CoreValve, transfemoral, direct aortic, or subclavian	30 days and 12 months	VARC-2	Device success	73/73 (100)	133/133 (100)
				Cardiac tamponade	6/73 (8.2)§	3/133 (2.3)
				Moderate AR needing postdilation	36/73 (49.3)§§	47/133 (35.6)
				Acute kidney injury	14/73 (19.4)	43/133 (32.3)‡
				30-day all-cause mortality	4/73 (5.5)	4/133 (3.0)
				30-day cardiovascular mortality	4/73 (5.5)	2/133 (1.5)
				Long-term† all-cause mortality	17/73 (23.3)	24/133 (17.8)
				Long-term† cardiovascular mortality	13/73 (17.6)	18/133 (13.3)
Möllmann et al[14] 2014	SAPIEN XT, transfemoral	In hospital and 30 days	VARC-2	Procedural success	26/26 (100)	30/30 (100)
				Postdilation	3/26 (11.5)	3/30 (10)
				Cardiac tamponade	1/26 (3.8)	0/30 (0)

Continued

Table 3. Continued

Study and Year of Publication	Type of Valve, Approach	Time Frame of Assessment	Assessment Definitions	Outcomes	No-BAV	BAV
				Moderate PVL	0/26 (0)	0/30 (0)
				Major vascular complication	2/26 (7.7)	0/30 (0)
				Pacemaker implantation	2/26 (7.7)	0/30 (0)
				Acute kidney injury	1/26 (3.8)	0/30 (0)
				30-day mortality	0/26 (0)	3/30 (10)
Kochman et al[15] 2014	CoreValve, transfemoral or subclavian	12 months	VARC-2	Device success	8/8 (100)	15/16 (93.8)
				Postdilation	3/8 (37.5)	2/16 (12.5)
				Life-threatening bleeding	1/8 (12.5)	0/16 (0)
				Major vascular complication	2/8 (25)	6/16 (37.5)
				Minor vascular complication	5/8 (62.5)	12/16 (75)
				Pacemaker implantation	2/8 (25)	4/16 (25)
				Myocardial infarction	0/8 (0)	1/16 (6)
				Stroke	0/8 (0)	0/16 (0)
				In-hospital mortality	0/8 (0)	1/16 (6)
				12-month mortality	1/8 (12.5)	2/16 (12.5)
Kempfert et al[16] 2015	SAPIEN XT, transapical	30 days	Unclear	Device success	40/40 (100)	40/40 (100)
				Need for a second valve	1/40 (2.5)	1/40 (2.5)
				Postdilation	4/40 (10)	6/40 (15)
				Mild or more residual PVL	4/40 (10)	3/40 (7.5)
				Stroke	0/40 (0)	0/40 (0)
				TIA	3/40 (7.5)	3/40 (7.5)
				Pacemaker implantation	1/40 (2.5)	2/40 (5)
				30-day mortality	1/40 (2.5)	3/40 (7.5)
Islas et al[17] 2015	SAPIEN XT (n=166) and CoreValve (n=83), transfemoral	30 days	VARC-2	Procedural success	73 (92.3)	153 (90.1)
				Need for a second valve	3 (3.8)	9 (5.3)
				Conversion to surgery	2 (2.3)	9 (5.3)
				Postdilation	14 (17.7)	32 (18.8)
				Mild or more residual PVL	3 (3.8)	6 (3.5)
				Stroke	1 (1.2)	3 (1.7)
				Pacemaker implantation	5 (6.3)	24 (14.1)∫
				30-day mortality	2 (2.5)	20 (11.8)∫∫
Conradi et al[18] 2015	SAPIEN XT and SAPIEN 3, transfemoral	30 days	VARC-2	Device success	25/26 (96.2)	24/26 (92.3)
				Need for a second valve	1/26 (3.8)	1/26 (3.8)
				Annular rupture	0/26 (0)	1/26 (3.8)
				Postdilation	0/26 (0)	3/26 (11.5)
				Myocardial infarction	0/26 (0)	0/26 (0)
				Stroke	1/26 (3.8)	2/26 (7.7)
				Major or life-threatening bleeding	2/26 (7.7)	2/26 (7.7)
				Major access site complications	2/26 (7.7)	3/26 (11.5)
				Acute kidney injury	3/26 (11.5)	0/26 (0)
				Pacemaker implantation	4/26 (15.4)	4/26 (15.4)
				30-day mortality	2/26 (7.7)	2/26 (7.7)

Continued

Table 3. Continued

Study and Year of Publication	Type of Valve, Approach	Time Frame of Assessment	Assessment Definitions	Outcomes	No-BAV	BAV
				Early safety	4/26 (15.4)	5/26 (19.2)
Wong et al[19] 2015	SAPIEN and SAPIEN XT, transfemoral or transapical	30 days	VARC-2	Device success	47/50 (94)	63/71 (88.7)
				Valve embolization	1/50 (2)	0/71 (0)
				Annular rupture	0/50 (0)	1/71 (1.4)
				Postdilation	15/50 (30)	24/71 (34)
				Myocardial infarction	0/50 (0)	0/71 (0)
				Stroke	0/50 (0)	2/71 (2.8)
				Bleeding complications	4/50 (8.0)	2/71 (2.8)
				Vascular complications	2/50 (4)	2/71 (2.8)
				Transfusions	28/50 (56)√	17/71 (23.9)
				Acute kidney injury	3/50 (6)	2/71 (2.8)
				Pacemaker implantation	5/50 (10)	4/71 (5.6)
				30-day all-cause mortality	4/50 (8)	3/71 (4.2)
				Cardiac mortality	3/50 (6)	3/71 (4.2)
				Composite safety	7/50 (14)	7/71 (9.9)
Bijuklic et al[20] 2015	SAPIEN XT and SAPIEN 3, transapical	30 days	VARC-2	Device success	54/55 (98.2)	30/32 (93.5)
				Postdilation	3/55 (5.5)	1/32 (3.1)
				Moderate PVL	1/55 (1.8)	2/32 (6.5)
				Myocardial infarction	0/55 (0)	0/32 (0)
				Stroke	3/58 (5.2)	1/33 (3.0)
				30-day all-cause mortality	0/55 (0)	2/32 (2.8)

Values are expressed as the occurrence of an event or sample size and (%). VARC-2 definitions: Device success indicates absence of procedural mortality, correct positioning of a single prosthetic heart valve into the proper anatomical position, intended performance of the prosthetic heart valve (no prosthesis–patient mismatch and mean aortic valve gradient <20 mm Hg or peak velocity <3 m/s and no moderate or severe prosthetic valve regurgitation). Early safety at 30 days indicates all-cause mortality (at 30 days), all stroke (disabling and nondisabling), life-threatening bleeding, acute kidney injury stage 2 or 3 (including renal replacement therapy), coronary artery obstruction requiring intervention, major vascular complication, valve-related dysfunction requiring repeat procedure (BAV, TAVI or surgical aortic replacement). AR indicates aortic regurgitation; BAV, balloon aortic valvuloplasty; NA, not available; PVL, paravalvular leakage; TIA, transient ischemic attack; VARC-2, Valve Academic Research Consortium.

#Bailout BAV predilation due to difficulties in crossing the aortic valve.

*P=0.014, **P=0.02, ¶P=0.09, §P=0.078, §§P=0.056, ‡P=0.049.

†Median time of 429 days.

√P<0.001, ∫P=0.03, ∫∫P=0.018.

assessment, and telephone calls up to 12 months from the date of implant.

Association of Preimplantation BAV Versus No BAV and Outcomes

Device type, access site, procedure-related outcomes, and follow-up assessment for all included studies reporting crude rate of events are summarized in Table 3. A pooled analysis reporting crude rates for outcomes of studies with and without preimplantation BAV according to valve type is shown in Table 4. Further separate analyses were performed including only studies of patients undergoing TAVI without preimplantation BAV (Table 5) and with preimplantation BAV (Table 6).

In-Hospital and 30-Day Outcomes

Crude device success rate was reported in all studies[5–20] and achieved in 94% (1311 of 1395) of patients without differences between valve types. Crude all-cause mortality at 30 days was reported in 15 studies[5–11,13–20] and occurred in 6% (72 of 1282) of patients. The safety composite end point was reported in 6 studies[7,9,11,12,18,19] and occurred in 21% (111 of 537) of patients. The crude incidence of residual moderate or severe aortic regurgitation or PVL was reported in 9 studies[5–9,12–14] and occurred in 16% (124 of 757) of patients. In this regard, 4 studies used the balloon-expandable valve[6,12,14,20] with a 3% rate (9 of 262 patients), and 5 studies used the self-expandable valve[5,7–9,13] with a 23% rate (115 of 495 patients). Of note, the need for postimplantation postdilation was reported in

Table 4. Pooled Analysis for Adverse Outcomes Without and With Preimplantation BVA According to Valve Type

Outcome	Studies	Cumulative	%	Studies	Edwards SAPIEN XT or SAPIEN 3	%	Studies	Medtronic CoreValve	%
Device success	16	1311/1395	94	10	823/876	94	6	488/519	94
Postdilation	14	210/1177	18	9	118/864	14	5	92/313	29
Need for second valve	7	37/719	5	4	18/481	4	3	19/238	8
Conversion to surgery	4	14/460	3	2	12/349	3	2	2/111	2
Moderate or severe AR/PVL	9	124/757	16	4	9/262	3	5	115/495	23
Mild AR/PVL	3	19/335	6	3	19/335	6	NA	NA	NA
Stroke/TIA	12	28/1014	3	7	24/701	3	5	4/313	1
Myocardial infarction	8	1/622	0.2	4	0/360	0	4	1/262	0.4
Major or life-threatening bleeding	6	17/409	4	4	12/285	4	2	5/124	4
Annulus rupture	2	2/173	1	2	2/173	1	NA	NA	NA
Cardiac tamponade	3	11/313	4	1	1/56	2	2	10/257	4
Acute kidney injury	7	74/641	12	5	13/335	4	2	61/306	20
Pacemaker implantation	12	117/983	12	7	60/670	9	5	57/313	18
Major vascular complications	6	26/412	6	2	6/177	3	4	20/235	9
Minor vascular complications	2	21/124	17	NA	NA	NA	2	21/124	17
Safety composite end point	6	111/537	21	4	91/386	24	2	20/151	13
Mortality	15	72/1282	6	9	49/763	6	6	23/519	4

AR indicates aortic regurgitation; BAV, balloon aortic valvuloplasty; NA, not available; PVL, paravalvular leakage; TIA, transient ischemic attack.

14[5–9,11–19] studies and occurred in 18% (210 of 1177) of patients; 9 studies used the balloon-expandable valve[6,11–14,16–19] with a 14% rate (118 of 864 patients), and 6 studies used the self-expandable valve[5,7–9,13,15] with a 29% rate (92 of 313 patients). The crude cerebrovascular events, including stroke or transient ischemic attack, were reported in 12 studies[5,7–11,15–20] and occurred in 3% (28/1014) of patients; 7 studies used the balloon-expandable valve[10,11,16–20] with a 3% rate (24 of 701 patients), and 5 studies used the self-expandable valve[5,7–9,15] with a 1% rate (4 of 313 patients). The need for permanent pacemaker implantation was reported in 12 studies[5,7–11,14–19] and occurred in 12% (117 of 983) of patients; 7 studies used the balloon-expandable valve[10,11,14,16–19] with a 9% rate (60 of 670 patients), and 5 studies used the self-expandable valve[5,7–9,15] with an 18% rate (57 of 313 patients).

Importantly, meta-analyses evaluating outcomes using strategies with and without preimplantation BAV showed no statistically significant differences. Notably, device success (RR 1.02, 95% CI 0.98–1.06, *P*=0.24), mortality (RR 0.61, 95% CI 0.32–1.14, *P*=0.12), safety composite end point (RR 0.85, 95% CI 0.62–1.18, *P*=0.34), moderate to severe PVL (RR 0.68, 95% CI 0.23–1.99, *P*=0.48), need for postimplantation postdilation (RR 0.86, 95% CI 0.66–1.13, *P*=0.28), stroke or transient ischemic attack (RR 0.72, 95% CI 0.30–1.71, *P*=0.45), permanent pacemaker implantation (RR 0.80, 95% CI 0.49–1.30, *P*=0.37), or acute kidney injury (RR 1.10, 95% CI 0.49–2.45, *P*=0.82). The remaining outcomes are shown in Tables 4 through 6.

Sensitivity Analysis

We conducted a sensitivity analysis for clinical outcomes with and without preimplantation BAV according to the different access sites, comparing the transfemoral with transapical and transfemoral or any other access including the direct aortic and trans-subclavian routes (Table 7, Figures 2 through 4). Those who underwent TAVI without preimplantation BAV and with the transfemoral or any other access were marginally associated with more cardiac tamponade (RR 3.61, 95% CI 1.04–12.56, *P*=0.04). Studies including the transfemoral access only were associated with higher mortality among patients who underwent TAVI with preimplantation BAV (RR 0.30, 95% CI 0.11–0.82, *P*=0.02); however, this difference disappeared when analyzed as a whole access-site sample (RR 0.61, 95% CI 0.32–1.14, *P*=0.12).

We also performed sensitivity analysis according to valve type (Table 8, Figures 5 through 7). The self-expandable valve tended to be associated with more cardiac tamponade (RR 3.64, 95% CI 0.94–14.14, *P*=0.06) when the procedure was

Table 5. Analysis for Adverse Outcomes Without Preimplantation BAV According to Valve Type

Outcome	Studies	Cumulative	%	Studies	Edwards SAPIEN XT or SAPIEN 3	%	Studies	Medtronic CoreValve	%
Device success	16	691/721	96	10	380/396	96	6	311/325	96
Postdilation	14	112/636	18	9	45/384	12	5	67/252	27
Need for second valve	7	23/388	6	4	6/195	3	3	17/193	9
Conversion to surgery	4	5/240	2	2	3/129	2	2	2/111	2
Moderate or severe AR/PVL	9	57/456	13	4	4/139	3	5	53/317	17
Mild AR/PVL	3	10/125	8	3	10/125	8	NA	NA	NA
Stroke/TIA	12	14/564	2	7	10/312	3	5	4/252	2
Myocardial infarction	8	0/382	0	4	0/181	0	4	0/201	0
Major or life-threatening bleeding	6	11/201	5	4	7/138	5	2	4/63	6
Annulus rupture	2	0/76	0	2	0/76	0	NA	NA	NA
Cardiac tamponade	3	8/150	5	1	1/26	4	2	7/124	2
Acute kidney injury	7	26/286	9	5	9/158	6	2	17/128	13
Pacemaker implantation	12	68/535	13	7	22/283	8	5	46/252	18
Major vascular complications	6	17/250	7	2	4/76	5	4	13/174	7
Minor vascular complications	2	5/63	8	NA	NA	NA	2	5/63	8
Safety composite end point	6	52/284	18	4	36/178	20	2	16/106	15
Mortality	15	27/669	4	9	11/344	3	6	16/325	5

AR indicates aortic regurgitation; BAV, balloon aortic valvuloplasty; NA, not available; PVL, paravalvular leakage; TIA, transient ischemic attack.

performed without preimplantation BAV and became significant when analyzed with the whole sample for type of valve (RR 3.61, 95% CI 1.04–12.56, P=0.04).

No significant differences were found between the different access sites and valve types among the remaining analyzed variables. Importantly, neither the access site nor

Table 6. Analysis for Adverse Outcomes With Preimplantation BAV According to Valve Type

Outcome	Studies	Cumulative	%	Studies	Edwards SAPIEN XT or SAPIEN 3	%	Studies	Medtronic CoreValve	%
Device success	11	620/674	92	8	443/480	92	3	177/194	91
Postdilation	10	98/541	18	8	73/480	15	2	25/61	41
Need for second valve	5	14/331	4	4	12/286	4	1	2/45	4
Conversion to surgery	2	9/220	4	2	9/220	4	NA	NA	NA
Moderate or severe AR/PVL	5	67/301	22	3	5/123	4	2	62/178	35
Mild AR/PVL	2	9/210	4	2	9/210	4	NA	NA	NA
Stroke/TIA	8	14/450	3	6	14/389	4	2	0/61	0
Myocardial infarction	6	1/240	0.4	4	0/179	0	2	1/61	2
Major or life-threatening bleeding	5	6/208	3	3	5/147	3	2	1/61	2
Annulus rupture	2	2/97	2	2	2/97	2	NA	NA	NA
Cardiac tamponade	2	3/163	2	1	0/30	0	1	3/133	2
Acute kidney injury	6	48/355	14	4	4/177	2	2	44/178	25
Pacemaker implantation	8	49/448	11	6	38/387	10	2	11/61	18
Major vascular complications	4	9/162	6	2	2/101	2	2	7/61	6
Minor vascular complications	2	16/61	26	NA	NA	NA	2	16/61	26
Safety composite end point	5	59/253	23	4	55/208	26	1	4/45	9
Mortality	10	45/613	7	7	38/419	9	3	7/194	4

AR indicates aortic regurgitation; BAV, balloon aortic valvuloplasty; NA, not available; PVL, paravalvular leakage; TIA, transient ischemic attack.

Table 7. Sensitivity Analysis With Risk of Outcomes Without or With Preimplantation BAV According to Access Site

Outcome or Subgroup	Studies	Patients	Relative Risk (95% CI)
Device success	11	1188	1.02 (0.98–1.06)
Transfemoral	5	557	1.01 (0.97–1.04)
Transapical	2	180	1.04 (0.90–1.19)
Transfemoral or any other access	4	451	1.09 (0.87–1.36)
Postdilation	10	982	0.86 (0.66–1.13)
Transfemoral	5	557	0.95 (0.58–1.56)
Transapical	2	180	0.99 (0.35–2.78)
Transfemoral or any other access	3	245	0.87 (0.53–1.43)
Need for a second valve	5	581	0.82 (0.34–1.98)
Transfemoral	2	301	0.76 (0.24–2.42)
Transapical	2	180	1.00 (0.14–6.94)
Transfemoral or any other access	1	100	0.82 (0.12–5.58)
Conversion to surgery	2	349	0.69 (0.16–2.89)
Transfemoral	1	249	0.48 (0.11–2.16)
Transapical	1	100	3.00 (0.13–71.92)
Moderate or severe AR/PVL	4	506	0.68 (0.23–1.99)
Transfemoral	2	200	0.77 (0.21–2.82)
Transfemoral or any other access	2	306	0.65 (0.13–3.39)
Mild AR/PVL	2	329	1.19 (0.44–3.19)
Transfemoral	1	249	1.08 (0.28–4.19)
Transapical	1	80	1.33 (0.32–5.58)
Stroke/TIA	6	689	0.72 (0.30–1.71)
Transfemoral	3	388	0.87 (0.24–3.23)
Transapical	2	180	0.70 (0.20–2.49)
Transfemoral or any other access	1	121	0.28 (0.01–5.76)
Myocardial infarction	1	24	0.63 (0.03–13.93)
Transfemoral or any other access	1	24	0.63 (0.03–13.93)
Major or life-threatening bleeding	5	397	1.98 (0.76–5.18)
Transfemoral	1	52	1.00 (0.15–6.57)
Transapical	1	100	1.00 (0.06–15.55)
Transfemoral or any other access	3	245	3.03 (0.89–10.28)
Annulus rupture	2	173	0.40 (0.04–3.72)
Transfemoral	1	52	0.33 (0.01–7.82)
Transfemoral or any other access	1	121	0.47 (0.02–11.32)
Cardiac tamponade	2	262	3.61 (1.04–12.56)
Transfemoral	1	56	3.44 (0.15–81.09)
Transfemoral or any other access	1	206	3.64 (0.94–14.14)
Acute kidney injury	6	635	1.10 (0.49–2.45)
Transfemoral	2	108	5.05 (0.59–43.03)
Transapical	1	100	0.50 (0.05–5.34)
Transfemoral or any other access	3	427	0.98 (0.37–2.58)
Pacemaker implantation	8	782	0.80 (0.49–1.30)
Transfemoral	3	357	0.79 (0.29–2.17)
Transapical	2	180	1.02 (0.34–3.09)
Transfemoral or any other access	3	245	0.85 (0.32–2.25)
Major vascular complications	4	301	1.15 (0.45–2.99)
Transfemoral	1	56	5.74 (0.29–114.41)
Transfemoral or any other access	3	245	0.96 (0.35–2.63)
Minor vascular complications	2	124	0.38 (0.03–4.92)
Transfemoral or any other access	2	124	0.38 (0.03–4.92)
Safety composite end point	4	434	0.85 (0.62–1.18)
Transfemoral	1	113	0.68 (0.44–1.07)
Transapical	1	100	0.58 (0.25–1.36)
Transfemoral or any other access	2	221	1.02 (0.66–1.58)
Mortality	10	1075	0.61 (0.32–1.14)
Transfemoral	4	357	0.30 (0.11–0.82)
Transapical	2	180	0.38 (0.10–1.37)
Transfemoral or any other access	4	451	1.38 (0.58–3.32)

Any other access, trans-subclavian or direct aortic. AR indicates aortic regurgitation; BAV, balloon aortic valvuloplasty; PVL, paravalvular leakage; TIA, transient ischemic attack.

the valve type affected device success rate, safety composite end point, or mortality (Tables 7 and 8).

Discussion

The results of this meta-analysis show no significant differences between patients undergoing TAVI either with or without preimplantation BAV with respect to mortality, neurological events, permanent pacemaker implantation, or improvement in device success (including repeat procedure,

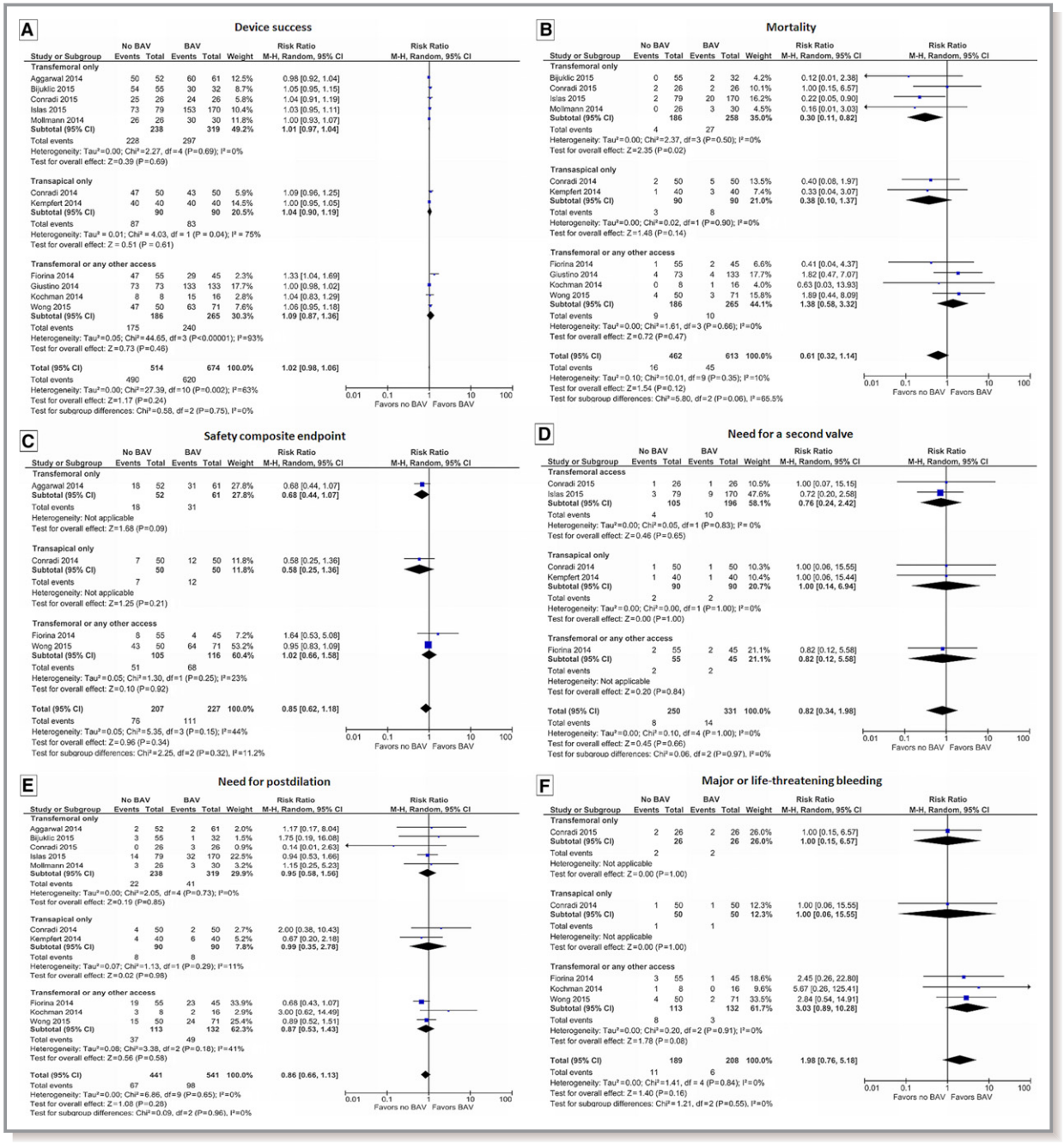

Figure 2. Meta-analyses evaluating (A) device success, (B) mortality, (C) safety composite end point, (D) need for a second valve, (E) postdilation, and (F) major or life-threatening bleeding for patients with and without preimplantation BAV, according to access site. BAV indicates balloon aortic valvuloplasty; M-H, Mantel–Haenszel.

significant residual PVL or aortic regurgitation, and the need for postimplantation postdilation).

Rationale and Adjunctive Utilities of Preimplantation BAV During TAVI

The pathophysiology of aortic stenosis and calcification make it reasonable to hypothesize that crossing the heavily calcified valve by the transapical antegrade approach would not require predilation.[6,11,16,19] In contrast, in transfemoral or other retrograde procedures, preimplantation BAV remains important to ensure smooth crossing of the TAVI delivery system.

Notably, our results show more cardiac tamponade without BAV, although one may be cautious in interpreting results based on only 2 studies.[13,14] Forceful pushing of the device and movement of the stiff wire inside the ventricle might cause this issue. Importantly, even if the valve is successfully crossed with the TAVI system, failure to fully expand the

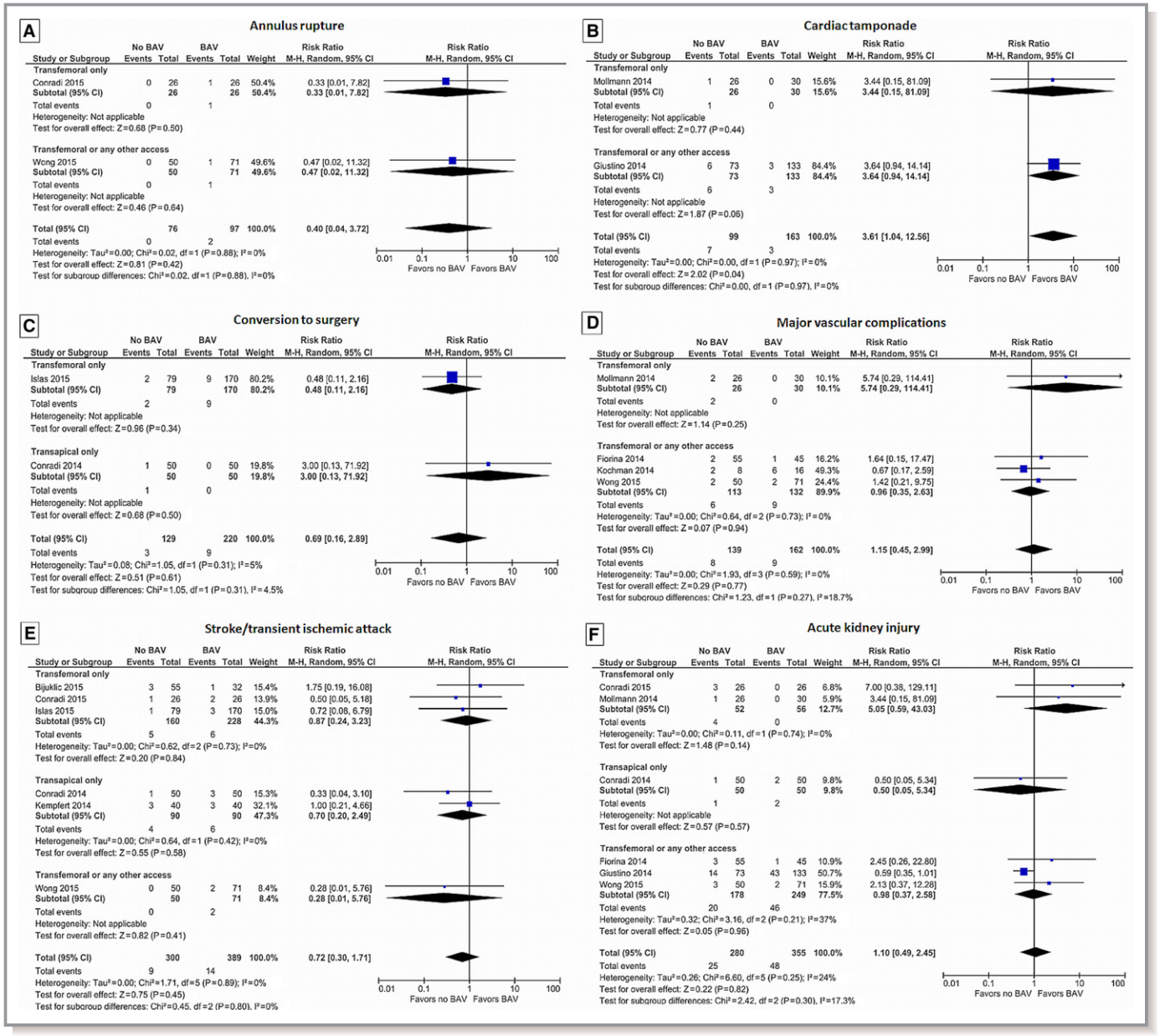

Figure 3. Meta-analyses evaluating the risk of (A) annulus rupture, (B) cardiac tamponade, (C) conversion to surgery, (D) major vascular complications, (E) stroke or transient ischemic attack, and (F) acute kidney injury for patients with and without preimplantation BAV, according to access site. BAV indicates balloon aortic valvuloplasty; M-H, Mantel–Haenszel.

transcatheter valve may translate into hemodynamic instability due to leaflet incompetence, significant PVL, valve migration, or further need for postdilation with inherent risk of valve migration.[5,9,21] In fact, some studies reported the need for bailout BAV predilation when TAVI was initially planned without preimplantation BAV.[7–9,21] Moreover, a partial balloon-tip inflation technique was reported to facilitate crossing of the aortic valve.[10,12]

Coronary ostia <10 to 11 mm from the aortic annulus represent a hazard for coronary obstruction,[22,23] especially in narrow, tubular, or porcelain aortic roots exhibiting longitudinal remodeling.[22,24] In these cases, simultaneous aortogram at the time of BAV is helpful to assess the behavior of the heavily calcified aortic leaflets, especially the left leaflet toward the left main coronary artery.[9,22] Finally, performing preimplantation BAV also allows confirmation of reliable pacing-wire capture. In the case of capture failure, albeit rare, it is preferable to deal with this issue during BAV rather than during balloon-expandable valve deployment.

Residual Aortic Regurgitation and PVL

It is well known that the incidence of PVL is associated with worse short- and long-term outcomes.[25–27] Our results show a

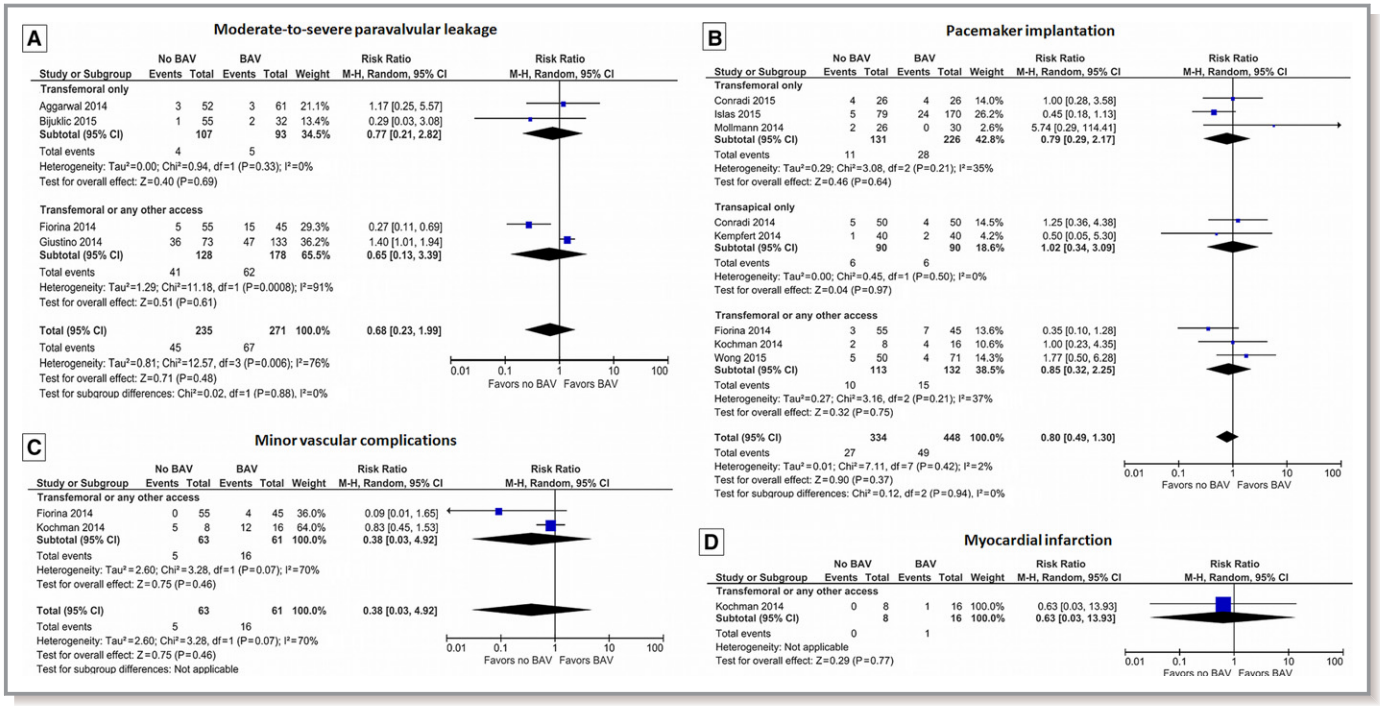

Figure 4. Meta-analyses evaluating the risk of (A) moderate to severe paravalvular leakage, (B) pacemaker implantation, (C) minor vascular compilations, and (D) myocardial infarction for patients with and without preimplantation BAV, according to access site. BAV indicates balloon aortic valvuloplasty; M-H, Mantel–Haenszel.

higher pooled incidence of PVL with the self-expanding valve compared with the balloon-expandable valve, and these percentages remained much higher even if analyzing groups with and without preimplantation BAV separately. Indeed, these results are in line with previously reported evidence.[27,28] Interestingly, Fiorina and colleagues[9] reported lower incidence of moderate to severe PVL without preimplantation BAV; however, hemodynamics were not statistically different between the 2 strategies, as assessed by aortic regurgitation index, likely due to low incidence of severe PVL. It is quite provocative to suggest that performing TAVI without preimplantation BAV may reduce PVL, mostly using the self-expandable valve because of its delivery mechanism, composed of a self-expanding nitinol frame. Regarding the balloon-expandable bioprosthesis, PVL reduction might have been related to better understanding of valve sizing (and slight oversizing) that progressed along the same learning curve and led to confidence in direct implantation. In addition, some studies included the SAPIEN 3 bioprosthesis, which includes a specific anti-PVL sealing design.

Need for Postimplantation Postdilation

According to our results, the self-expanding valve was associated with a crude 2-fold greater need for postdilation. Importantly, postimplantation postdilation can also cause device migration and thus increase PVL[9] as well as the risk for annular rupture with postdilation than with predilation. Although avoiding BAV minimizes manipulation of the severely calcified aortic annulus or native valve, it must be balanced with the potential need for more postdilation to correct a significant residual PVL. Furthermore, the impact of postdilation on the long-term valve outcome remains unknown.

Aortic Valve Calcification Assessment to Plan TAVI Without Preimplantation BAV

The degree and distribution of aortic valve calcification and annular morphology has been correlated with postprocedural PVL.[29–32] Moreover, the location and/or asymmetry of this calcification, more often located at the noncoronary cusp and/or device landing zone, is more important than the total calcium load.[20,29,31] Interestingly, Mollmann and colleagues[14] showed no differences in the extent of valve calcification, as assessed by Agatston score, among patients treated with the 2 strategies. In addition, they found no correlation between the aortic valve area and load of calcification with the duration of the procedure, fluoroscopy time, radiation dose, or contrast amount. Similarly, Fiorina et al[9] found no correlation between residual PVL and the degree of calcification in the device landing zone among those who received TAVI without preimplantation BAV. Of note, the authors also reported that among patients who received preimplantation BAV, bigger prosthesis size indicated higher incidence of significant PVL, although that relationship was not observed in patients in which TAVI was undertaken without preimplantation BAV.[9]

Table 8. Sensitivity Analysis With Risk of Outcomes Without or With Preimplantation BAV According to Valve Type

Outcome or Subgroup	Studies	Patients	Relative Risk (95% CI)
Device success	10	1101	1.02 (0.98–1.07)
SAPIEN	7	609	1.01 (0.98–1.04)
CoreValve	3	330	1.11 (0.69–1.78)
Postdilation	9	733	0.84 (0.62–1.14)
SAPIEN	7	609	0.92 (0.60–1.40)
CoreValve	2	124	1.17 (0.28–4.82)
Need for a second valve	4	332	0.92 (0.27–3.12)
SAPIEN	3	232	1.00 (0.21–4.84)
CoreValve	1	100	0.82 (0.12–5.58)
Conversion to surgery	1	100	3.00 (0.13–71.92)
SAPIEN	1	100	3.00 (0.13–71.92)
Moderate or severe AR/PVL	4	506	0.68 (0.23–1.99)
SAPIEN	2	200	0.77 (0.21–2.82)
CoreValve	2	306	0.65 (0.13–3.39)
Mild AR/PVL	1	80	1.33 (0.32–5.58)
SAPIEN	1	80	1.33 (0.32–5.58)
Stroke/TIA	5	440	0.72 (0.28–1.84)
SAPIEN	5	440	0.72 (0.28–1.84)
Myocardial infarction	1	24	0.63 (0.03–13.93)
CoreValve	1	24	0.63 (0.03–13.93)
Major or life-threatening bleeding	5	397	1.98 (0.76–5.18)
SAPIEN	3	273	1.63 (0.52–5.06)
CoreValve	2	124	3.27 (0.53–19.93)
Annulus rupture	2	173	0.40 (0.04–3.72)
SAPIEN	2	173	0.40 (0.04–3.72)
Cardiac tamponade	2	262	3.61 (1.04–12.56)
SAPIEN	1	56	3.44 (0.15–81.09)
CoreValve	1	206	3.64 (0.94–14.14)
Acute kidney injury	6	635	1.10 (0.49–2.45)
SAPIEN	4	329	1.93 (0.60–6.27)
CoreValve	2	306	0.79 (0.26–2.41)
Pacemaker implantation	7	533	0.98 (0.56–1.72)
SAPIEN	5	409	1.30 (0.66–2.57)
CoreValve	2	124	0.56 (0.20–1.56)
Major vascular complications	4	301	1.15 (0.45–2.99)
SAPIEN	2	177	2.14 (0.42–10.80)
CoreValve	2	124	0.83 (0.26–2.70)
	2	124	0.38 (0.03–4.92)
Minor vascular complications			
CoreValve	2	124	0.38 (0.03–4.92)
Safety composite end point	4	434	0.85 (0.62–1.18)
SAPIEN	3	334	0.79 (0.52–1.20)
CoreValve	1	100	1.64 (0.53–5.08)
Mortality	9	826	0.78 (0.41–1.48)
SAPIEN	6	496	0.52 (0.28–1.40)
CoreValve	3	330	1.15 (0.38–3.47)

SAPIEN includes SAPIEN XT and SAPIEN 3 valves. AR indicates aortic regurgitation; BAV, balloon aortic valvuloplasty; PVL, paravalvular leakage; TIA, transient ischemic attack.

Islas and colleagues[17] reported favorable and unfavorable features relevant to the decision to perform TAVI without preimplantation BAV using 3-dimentional transesophageal echocardiography. Notably, unfavorable features included heavy or severe aortic valve calcification, defined as leaflet thickness >5 mm with large nodules and diffuse calcification of the aortic annulus; an asymmetric and bulky calcification distribution; valve area <0.4 cm^2 with an eccentric and/or irregular orifice; moderately or severely restricted mobility; presence of calcification nodules at the left ventricle outflow tract or close to coronary ostia; and moderate aortic regurgitation. In this regard, Bijuklic et al[20] also reported that in cases of severe asymmetric aortic valve calcification or a tight aortic effective orifice area (planimetry ≤0.5 cm^2), as assessed by intraprocedural transesophageal echocardiography, preimplantation BAV was performed even if the newest generation lower profile Edwards SAPIEN 3 valve was available.

Neurological Events

It has been hypothesized that TAVI without preimplantation BAV may be associated with fewer embolic events, especially fewer cerebrovascular accidents. Strikingly, relatively low stroke rates have been reported with the 2 strategies and the 2 TAVI devices. The different technique by which the balloon-expandable valve is deployed, more often oversized, compared with the self-expandable valve (less aggressive expansion technique) may explain the higher potential for calcific embolization. In this regard, the new-generation balloon-expandable Edwards SAPIEN 3 valve requires less overexpansion compared with the SAPIEN XT; however, most of the analyzed studies failed to support avoiding a preimplantation BAV strategy with reduced neurological complications. Moreover, Aggarwal and colleagues[12] reported no differences between groups in terms of embolic load based on

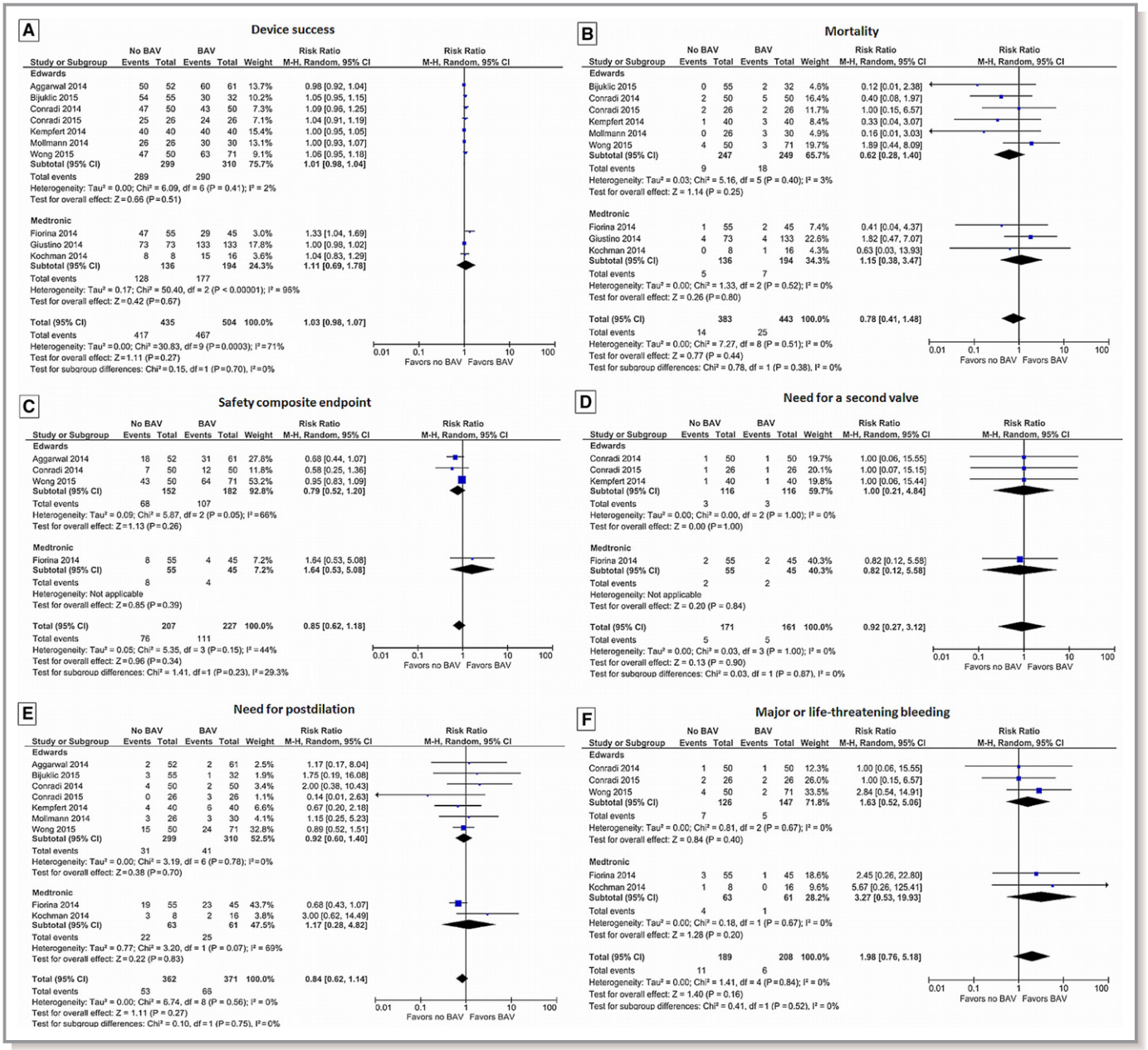

Figure 5. Meta-analyses evaluating (A) device success, (B) mortality, (C) safety composite end point, (D) need for a second valve, (E) postdilation, and (F) major or life-threatening bleeding for patients with and without preimplantation BAV, according to valve type. BAV indicates balloon aortic valvuloplasty; M-H, Mantel–Haenszel.

transcranial Doppler, including number in solid, gaseous, or total emboli (P>0.05 for all). In addition, Bijuklic et al[20] showed no difference in terms of silent embolic events assessed by diffusion-weighted cerebral magnetic resonance. Interestingly, a large volume was observed among those undergoing TAVI without preimplantation BAV. Importantly, the authors reported that 4 patients experienced stroke, 3 of them without preimplantation BAV and 1 patient with preimplantation BAV. Nonetheless, because of the exclusion criteria stated in the methodology, these patients were excluded from analysis because of a clinically apparent stroke within 3 days after TAVI.[20]

Potential Benefits of TAVI Without Preimplantation BAV

Preimplantation BAV might be poorly tolerated by certain patients. The time between BAV predilation and TAVI is a particularly crucial period, especially in patients with preexisting severe left ventricular systolic dysfunction and/or

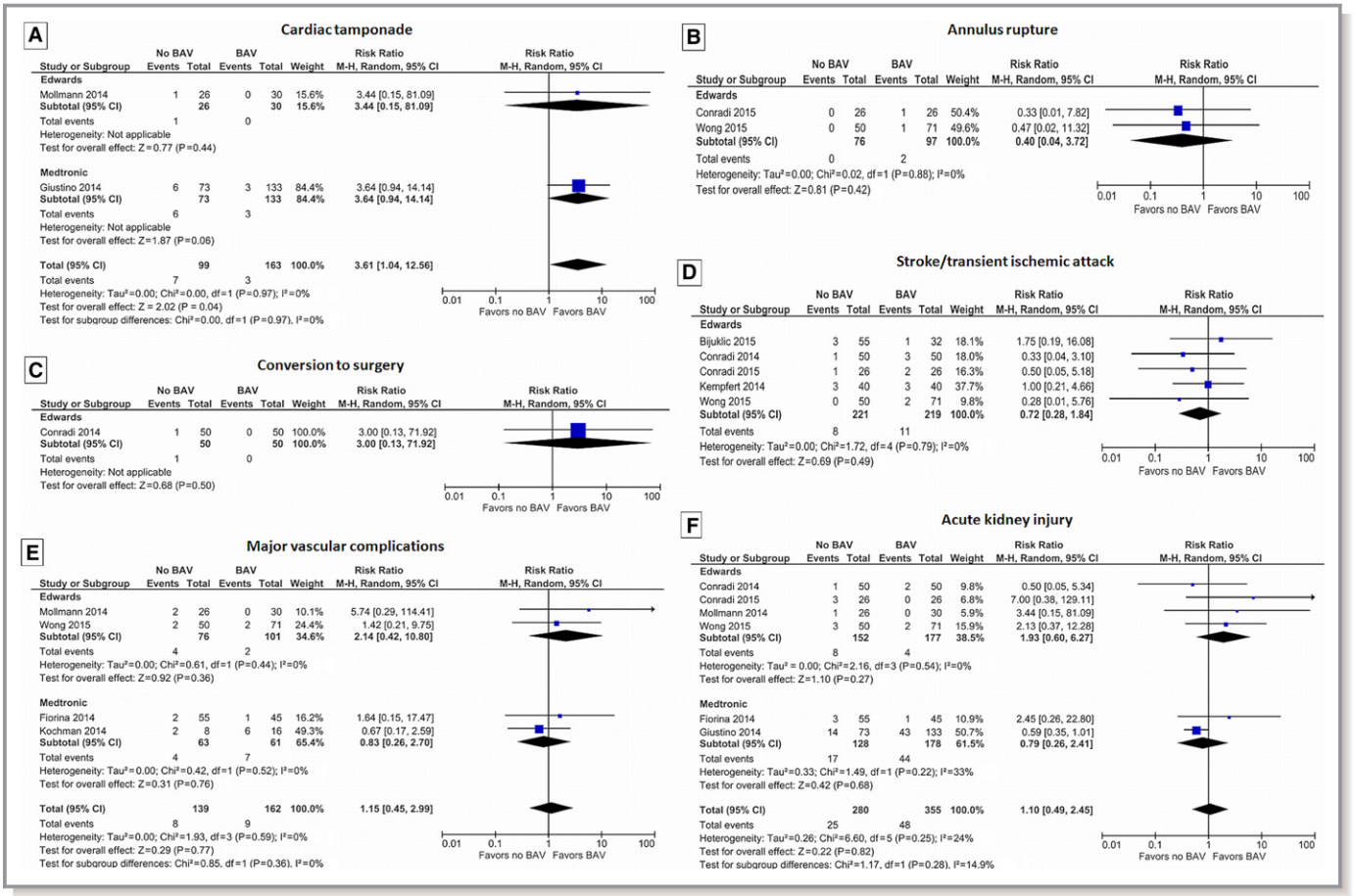

Figure 6. Meta-analyses evaluating the risk of (A) cardiac tamponade, (B) annulus rupture, (C) conversion to surgery, (D) stroke or transient ischemic attack, (E) major vascular complications, and (F) acute kidney injury for patients with and without preimplantation BAV, according to valve type. BAV indicates balloon aortic valvuloplasty; M-H, Mantel–Haenszel.

pulmonary hypertension. Moreover, the temporary interruption in ventricular output during rapid ventricular pacing and BAV outflow occlusion itself can result in hemodynamic compromise. Furthermore, significant aortic regurgitation following BAV can precipitate clinically important instability, even in patients with normal left ventricular function; this hemodynamic deterioration can be sudden, profound, and not entirely predictable. The special subset of patients presenting with and/or prone to hemodynamic instability can experience multiorgan hypoperfusion, mainly cerebral and renal; therefore, avoiding a rapid pacing run for BAV may prevent an unnecessary period of hypotension in certain cases.

Alternatively, it is logical that performing TAVI without preimplantation BAV is associated with a reduction in contrast volume,[6,11,14,18,20] fluoroscopy time,[12,16,18] radiation dose,[14] or total procedural time.[6,17,20] The clinical impact of these differences is uncertain.

Limitations

The present study has several limitations. The main limitation lies with the small number of patients within each study and the nonrandomized nature of the included studies that may introduce selection bias. Importantly, the decision of whether or not to predilate was made at the discretion of the TAVI team operator and may relate to the complexity of the valve anatomy and the operator's perception of successful valve delivery; therefore, it is possible that BAV was undertaken in more complex and challenging cases, subjecting comparison of outcomes to selection bias. In addition, patient-level data were not available for this analysis, precluding more robust adjustment for any differences in clinical or anatomical variables. Nevertheless, in studies that reported clinical demographics and anatomical features of the patients, these variables were relatively well matched in both BAV/non-BAV studied cohorts. Notably, many of the studies included in this analysis lacked data on whether patients had hemodynamic compromise and/or poor left ventricle function necessitating BAV prior to the index TAVI procedure (bridge to TAVI). Finally, patients exhibiting major comorbidities and clinically uncertain benefit from TAVI may have been offered BAV as a potential bridge or palliation due to an adverse profile, with subsequent definitive treatment (TAVI) offered after substantial improvement.

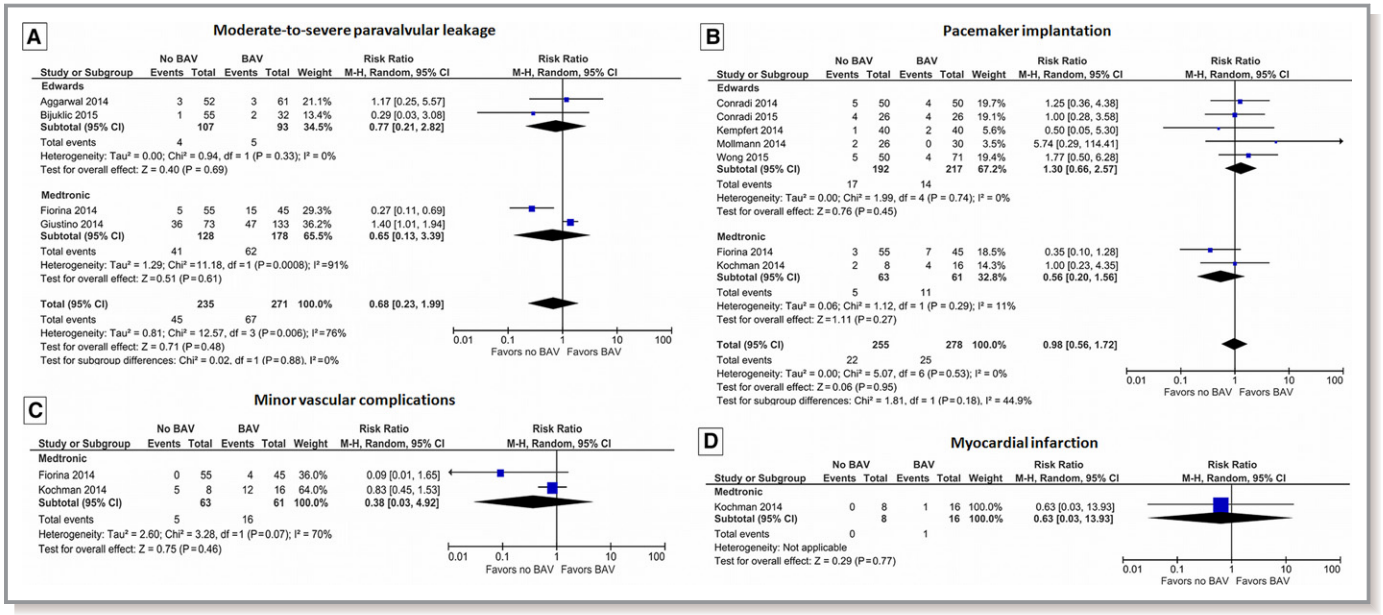

Figure 7. Meta-analyses evaluating the risk of (A) moderate to severe paravalvular leakage, (B) pacemaker implantation, (C) minor vascular compilations, and (D) myocardial infarction for patients with and without preimplantation BAV, according to valve type. BAV indicates balloon aortic valvuloplasty; M-H, Mantel–Haenszel.

Conclusion

Our analysis suggests that TAVI procedures with or without preimplantation BAV were associated with similar outcomes for a number of clinically relevant end points. Further studies including large number of patients are needed to ascertain the impact of TAVI without preimplantation BAV as a standard practice. Meanwhile, our findings provide real-world data that may contribute to the current practice of TAVI operators and influence future perspectives. Notably, a simplified procedure can be safely performed and achieve comparable results.

Sources of Funding

Supported in part by a Program of Experimental Medicine (POEM) Research Award, Department of Medicine, Western University.

Disclosures

None.

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