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.
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: 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.

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 (cm²) LVEF | EuroSCORE | With BAV | Age Female | Mean Gradient AVA (cm²) LVEF | EuroSCORE | Differences Between Baseline Characteristics |
|--------------------------------|-------------|------------|-----------------------------|------------|---------|------------|-----------------------------|------------|------------------------------------------|
| Grube et al<sup>6</sup> 2011   | 60          | 80.1±6.4  | 53.3%                       | 47.8±15.5 | 0.66±0.2 | 23.3±15.2 | NA                          | —         | —                                         |
| Wendler et al<sup>6</sup> 2012 | 6           | 82±3      | 33%                         | 49±5      | 0.6±0.18 | 30±12      | NA                          | —         | —                                         |
| Mendiz et al<sup>7</sup> 2013  | 51          | 79±8      | 65%                         | 80±22     | 0.7±0.2  | 20±15      | NA                          | —         | —                                         |
| Ruck et al<sup>8</sup> 2013    | 78          | NA        | NA                          | 19        | NA      | —         | —                          | —         | —                                         |
| Fiorina et al<sup>9</sup> 2014 | 55          | 83±7      | 51%                         | 44±13     | 0.39±0.1*| 27±18      | 10±8*                      | 45        | 83±8                                    |
| Davies et al<sup>10</sup> 2014 | 12          | 83±3      | 50%                         | 56±19     | (peak)   | 23±12      | 6±3                        | —         | —                                         |
| Conradi et al<sup>11</sup> 2014| 50          | 78±8      | 46%                         | 28±14     | 0.9±0.4  | 21±14      | 8±7                        | 50        | 81±7                                    |
| Aggarwal et al<sup>12</sup> 2014| 52          | NA        | NA                          | NA        | 61      | NA         | NA                          | NA        | NA                                       |
| Giustino et al<sup>13</sup> 2014| 73          | NA        | NA                          | NA        | 133     | NA         | NA                          | NA        | NA                                       |
| Möllmann et al<sup>14</sup> 2014| 26          | 81.6±6.5  | 42.3%                       | 36.0±17.3 | 0.7±0.2  | 24.6±8.7   | 6.2±2.7                    | 30        | 82.2±5.4                                |
| Kochman et al<sup>15</sup> 2014| 8           | 78.1±8.4  | 50%                         | 46.0±14.1 | 0.58±0.15| 20±6       | NA                          | 16        | 83.3±3.7                                |
| Kempfert et al<sup>16</sup> 2015| 40          | 79        | 30%                         | 42        | NA      | 7.62        | 40                          | 80        | 40                                      |
| Islas et al<sup>17</sup> 2015  | 79          | 82.4±5.5  | 65.7%                       | 47.3±14.7 | 0.6±0.2  | 18.6±9.8   | NA                          | 170<sup>1</sup> | 82.8±5.7                              |
| Conradi et al<sup>18</sup> 2015| 26          | 81.3±6.3  | 61.5%                       | 38±14     | 0.8±0.2  | 15±13      | 6±3                        | 26        | 81.7±5.2                                |

Continued
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 I² statistic was used to assess the consistency among studies, with I²<25% considered low, I²=50% considered moderate, and I²>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 studies5–20 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 studies5,10–12,14,16–20 including 793 patients, and the self-expandable Medtronic CoreValve was used in 7
studies5,7–9,13,15,17 including 602 patients. One study included both types of bioprostheses17. Access was transfemoral, exclusively, in 8 studies5,7,8,12,14,17,18,20; transfemoral, trans-subclavian, or direct aortic in 4 studies9,10,13,15; transapical in 3 studies6,11,16; and transfemoral or transapical access in 1 study.19 There were 4 prospective cohort studies5,7,9,10 4 cohort studies,6,8,13,17 3 retrospective cohort studies11,12,19 2 case-matched studies,15,18 2 case–control studies,14,20 and 1 propensity-matched study.16

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 al5 2011            | Prospective cohort study; 2009–2010; international | Reliable | Follow-up by clinical visits and echocardiography | None | None, crude results |
| Wendler et al6 2012          | Cohort study; unclear; United Kingdom | Reliable | Assessment at 30 days | None | None, crude results |
| Mendiz et al7 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 al8 2013             | Cohort study; started September 2012; Sweden | Reliable | Unclear | None | None, crude results |
| Fiorina et al9 2014          | Prospective cohort study; June 2012 to June 2013; Italy | Reliable | Follow-up by clinical visits and echocardiography | None | None, crude results |
| Davies et al10 2014          | Prospective cohort study; unclear; United Kingdom | Reliable | Unclear | None | None, crude results |
| Conradi et al11 2014         | Retrospective cohort study; May 2011 to December 2012; Germany | Reliable | Clinical end points were adjudicated | None, retrospective | None, crude results |
| Aggarwal et al12 2014        | Retrospective cohort; March 2012 to April 2013; United Kingdom | Reliable | Unclear | None, retrospective | None, crude results |
| Giustino et al13 2014        | Cohort study; November 2007 to September 2013; Italy | Reliable | Assessment at 30 days and 12 months | None | None, crude results |
| Möllmann et al14 2014        | Case-control study; unclear; Germany | Reliable | Assessment at 30 days | None | None, crude results |
| Kochman et al15 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 al16 2015        | Propensity-matched analysis; March 2012 to July 2013; Germany | Reliable | Clinical follow-up at 30 days | None | Propensity-matched analysis |
| Islas et al17 2015           | Cohort study; January 2009 to August 2014; Spain | Reliable | Clinical follow-up at 30 days | None | None, crude results |
| Conradi et al18 2015         | Case-matched study; unclear; Germany | Reliable | Clinical end points were adjudicated | None, retrospective | Matched by logistic regression and nearest neighbors |
| Wong et al19 2015            | Retrospective cohort; May 2012 to December 2013; United States | Reliable | Follow-up by clinical visits | None, retrospective | None, crude results |
| Bijuklic et al20 2015        | Case-control study; unclear; Germany | Reliable | Follow-up at 30 days | None, retrospective | None, crude results |

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...
| Study and Year of Publication | Type of Valve, Approach | Time Frame of Assessment | Assessment Definitions | Outcomes | No-BAV | BAV |
|-------------------------------|-------------------------|--------------------------|-----------------------|----------|-------|-----|
| Grube et al5 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 al6 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 al7 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 al8 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 al9 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) |
| | | | | Moderate or severe PVL | 5/55 (9.1) |

Continued
Table 3. Continued

| Study and Year of Publication | Type of Valve, Approach | Time Frame of Assessment | Assessment Definitions | Outcomes | No-BAV | BAV |
|-------------------------------|-------------------------|--------------------------|-----------------------|----------|--------|-----|
| Davies et al10 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 al11 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) | 1/50 (2) | |
|                               |                         |                         | 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 al12 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 al13 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-term1 all-cause mortality | 17/73 (23.3) | 24/133 (17.8) | |
|                               |                         |                         | Long-term1 cardiovascular mortality | 13/73 (17.6) | 18/133 (13.3) | |
| Möllmann et al14 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) | |

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### Table 3. Continued

| Study and Year of Publication | Type of Valve, Approach | Time Frame of Assessment | Assessment Definitions | Outcomes | No-BAV | BAV |
|------------------------------|-------------------------|--------------------------|------------------------|----------|--------|-----|
| Kochman et al15 2014         | CoreValve, transfemoral or subclavian | 12 months | VARC-2 | 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) |
|                              |                         |                          |                        | 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 al16 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 al17 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 al18 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) |
Table 3. Continued

| Study and Year of Publication | Type of Valve, Approach | Time Frame of Assessment | Assessment Definitions | Outcomes | No-BAV | BAV |
|------------------------------|-------------------------|--------------------------|-----------------------|----------|--------|-----|
| Wong et al19 2015            | SAPIEN and SAPIEN XT, transfemoral or transapical | 30 days | VARC-2 | Early safety | 4/26 (15.4) | 5/26 (19.2) |
|                             |                         |                          |                       | 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 al20 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, 5P = 0.056, 6P = 0.049.
6Median time of 429 days.
7P = 0.001, 8P = 0.03, 9P = 0.018.

In-Hospital and 30-Day Outcomes

Crude device success rate was reported in all studies5–20 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 studies5–11,13–20 and occurred in 6% (72 of 1282) of patients. The safety composite end point was reported in 6 studies7,9,11,12,18,19 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 studies5–9,12–14 and occurred in 16% (124 of 757) of patients. In this regard, 4 studies used the balloon-expandable valve5,12,14,20 with a 3% rate (9 of 262 patients), and 5 studies used the self-expandable valve5,7–9,13 with a 23% rate (115 of 495 patients). Of note, the need for postimplantation postdilation was reported in

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).
14–9,11–19 studies and occurred in 18% (210 of 1177) of patients; 9 studies used the balloon-expandable valve6,11–14,16–19 with a 14% rate (118 of 864 patients), and 6 studies used the self-expandable valve5,7–9,13,15 with a 29% rate (92 of 313 patients). The crude cerebrovascular events, including stroke or transient ischemic attack, were reported in 12 studies5,7–11,15–20 and occurred in 3% (28/1014) of patients; 7 studies used the balloon-expandable valve10,11,16–20 with a 3% rate (24 of 701 patients), and 5 studies used the self-expandable valve5,7–9,15 with a 1% rate (4 of 313 patients). The need for permanent pacemaker implantation was reported in 12 studies5,7–11,14–19 and occurred in 12% (117 of 983) of patients; 7 studies used the balloon-expandable valve10,11,14–19 with a 9% rate (60 of 670 patients), and 5 studies used the self-expandable valve5,7–9,15 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 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 % Studies** |
| **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 | 0 | NA |
| **Stroke/TIA** | 12 | 28/1014 3 | 7 | 24/701 3 | 5 | 4/313 1 |
| **Myocardial infarction** | 8 | 1/822 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 | 0 | 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 | 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.
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 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 | % Studies |
|--------------------------------|---------|------------|-----------|-------------------------------|-----------|---------------------|-----------|
| Device success                 | 16      | 691/721    | 96        | 10                            | 380/396   | 96                  | 311/325   | 96       |
| Postdilation                   | 14      | 112/636    | 18        | 9                             | 45/384    | 12                  | 67/252    | 27       |
| Need for second valve          | 7       | 23/388     | 6         | 4                             | 6/195     | 3                   | 17/193    | 9        |
| Conversion to surgery          | 4       | 5/240      | 2         | 2                             | 3/129     | 2                   | 2/111     | 2        |
| Moderate or severe AR/PVL      | 9       | 57/456     | 13        | 4                             | 4/139     | 3                   | 53/317    | 17       |
| Mild AR/PVL                    | 3       | 10/125     | 8         | 3                             | 10/125    | 8                   | NA        | NA       |
| Stroke/TIA                     | 12      | 14/564     | 2         | 7                             | 10/312    | 3                   | 4/252     | 2        |
| Myocardial infarction          | 8       | 0/382      | 0         | 4                             | 0/181     | 0                   | 0/201     | 0        |
| Major or life-threatening bleeding | 6   | 11/201     | 5         | 4                             | 7/138     | 5                   | 4/63      | 6        |
| Annu1ls rupture                | 2       | 0/76       | 0         | 2                             | 0/76      | 0                   | NA        | NA       |
| Cardiac tamponade              | 3       | 8/150      | 5         | 1                             | 1/26      | 4                   | 7/124     | 2        |
| Acute kidney injury            | 7       | 26/286     | 9         | 5                             | 9/158     | 6                   | 17/128    | 13       |
| Pacemaker implantation         | 12      | 68/535     | 13        | 7                             | 22/283    | 8                   | 46/252    | 18       |
| Major vascular complications   | 6       | 17/250     | 7         | 2                             | 4/76      | 5                   | 13/174    | 7        |
| Minor vascular complications   | 2       | 5/63       | 8         | NA                            | NA        | NA                  | 5/63      | 8        |
| Safety composite end point     | 6       | 52/284     | 18        | 4                             | 36/178    | 20                  | 16/106    | 15       |
| Mortality                      | 15      | 27/669     | 4         | 9                             | 11/344    | 3                   | 16/325    | 5        |

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

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### 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 | % Studies |
|--------------------------------|---------|------------|-----------|-------------------------------|-----------|---------------------|-----------|
| Device success                 | 11      | 620/674    | 92        | 8                             | 443/480   | 92                  | 177/194   | 91       |
| Postdilation                   | 10      | 98/541     | 18        | 8                             | 73/480    | 15                  | 25/61     | 41       |
| Need for second valve          | 5       | 14/331     | 4         | 4                             | 12/286    | 4                   | 2/45      | 4        |
| Conversion to surgery          | 2       | 9/220      | 4         | 2                             | 9/220     | 4                   | NA        | NA       |
| Moderate or severe AR/PVL      | 5       | 67/301     | 22        | 3                             | 5/123     | 4                   | 62/178    | 35       |
| Mild AR/PVL                    | 2       | 9/210      | 4         | 2                             | 9/210     | 4                   | NA        | NA       |
| Stroke/TIA                     | 8       | 14/450     | 3         | 6                             | 14/389    | 4                   | 0/61      | 0        |
| Myocardial infarction          | 6       | 1/240      | 0.4       | 4                             | 0/179     | 0                   | 1/61      | 2        |
| Major or life-threatening bleeding | 5   | 6/208      | 3         | 3                             | 5/147     | 3                   | 1/61      | 2        |
| Annu1ls rupture                | 2       | 2/97       | 2         | 2                             | 2/97      | 2                   | NA        | NA       |
| Cardiac tamponade              | 2       | 3/163      | 2         | 1                             | 0/30      | 0                   | 3/133     | 2        |
| Acute kidney injury            | 6       | 48/355     | 14        | 4                             | 4/177     | 2                   | 44/178    | 25       |
| Pacemaker implantation         | 8       | 49/448     | 11        | 6                             | 38/387    | 10                  | 11/61     | 18       |
| Major vascular complications   | 4       | 9/162      | 6         | 2                             | 2/101     | 2                   | 7/61      | 6        |
| Minor vascular complications   | 2       | 16/61      | 26        | NA                            | NA        | NA                  | 16/61     | 26       |
| Safety composite end point     | 5       | 59/253     | 23        | 4                             | 55/208    | 26                  | 4/45      | 9        |
| Mortality                      | 10      | 45/613     | 7         | 7                             | 38/419    | 9                   | 7/194     | 4        |

AR indicates aortic regurgitation; BAV, balloon aortic valvuloplasty; NA, not available; 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,
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 hypothesis that crossing the heavily calcified valve by the transapical antegrade approach would not require predilation. 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. 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 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.](image-url)
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.\textsuperscript{5,9,21} In fact, some studies reported the need for bailout BAV predilation when TAVI was initially planned without preimplantation BAV.\textsuperscript{7–9,21} Moreover, a partial balloon-tip inflation technique was reported to facilitate crossing of the aortic valve.\textsuperscript{10,12}

Coronary ostia <10 to 11 mm from the aortic annulus represent a hazard for coronary obstruction,\textsuperscript{22,23} especially in narrow, tubular, or porcelain aortic roots exhibiting longitudinal remodeling.\textsuperscript{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.\textsuperscript{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.\textsuperscript{25–27} Our results show a
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 colleagues9 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 PVL⁹ 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 colleagues¹⁴ 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 al⁹ 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 (0.28–4.92)       |
| 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)       |

Table 8. Continued

| Outcome or Subgroup                  | Studies | Patients | Relative Risk (95% CI) |
|--------------------------------------|---------|----------|------------------------|
| 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 colleagues17 reported favorable and unfavorable features relevant to the decision to perform TAVI without preimplantation BAV using 3-dimensional 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 cm² 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 al20 also reported that in cases of severe asymmetric aortic valve calcification or a tight aortic effective orifice area (planimetry ≤0.5 cm²), 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 calcification 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 colleagues12 reported no differences between groups in terms of embolic load based on...
transcranial Doppler, including number in solid, gaseous, or total emboli (P>0.05 for all). In addition, Bijuklic et al20 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...
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 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.
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.

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Disclosures

None.

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