SYSTEMATIC REVIEW AND META-ANALYSIS

Transcatheter Aortic Valve Implantation With and Without Resheathing and Repositioning: A Systematic Review and Meta-analysis

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BACKGROUND: There is a concern that resheathing/repositioning of transcatheter heart valves during transcatheter aortic valve implantation (TAVI) may lead to an increased risk of periprocedural complications. We aimed to evaluate the short- and long-term impact on clinical outcomes of resheathing for repositioning of transcatheter heart valves during TAVI procedures.

METHODS AND RESULTS: We conducted a systematic search of Embase, MEDLINE, and Cochrane Central Register of Controlled Trials databases to identify studies comparing outcomes between patients requiring resheathing/repositioning during TAVI and those who did not. Random-effects meta-analyses were used to estimate the association of resheathing compared with no resheathing with clinical outcomes after TAVI. Seven studies including 4501 participants (pooled mean age, 80.9±7.4 years; 54% women; and 1374 [30.5%] patients requiring resheathing/repositioning) were included in this study. No significant differences between the 2 groups were identified with regards to safety: 30-day mortality (n=3125; odds ratio [OR], 0.74 [95% confidence interval [CI], 0.41–1.33]; P²=0%), coronary obstruction (n=3000; OR, 2.35 [95% CI, 0.17–33.47]; P²=75%), major vascular complications (n=3125; OR, 0.92 [95% CI, 0.66–1.33]; P²=0%), major bleeding (n=3125; OR, 1.13 [95% CI, 0.94–2.01]; P²=39%), acute kidney injury (n=3495; OR, 1.30 [95% CI, 0.64–2.62]; P²=44%), and efficacy outcomes: device success (n=1196; OR, 0.77 [95% CI, 0.51–1.14]; P²=0%), need for a second valve (n=3170; OR, 2.86 [95% CI, 0.96–8.48]; P²=62%), significant (moderate or higher) paravalvular leak (n=1151; OR, 1.53 [95% CI, 0.83–2.80]; P²=0%), and permanent pacemaker implantation (n=1908; OR, 1.04 [95% CI, 0.68–1.57]; P²=58%). One-year mortality was similar between groups (n=1972; OR, 1.00 [95% CI, 0.68–1.47]; P²=0%).

CONCLUSIONS: Resheathing of transcatheter heart valves during TAVI is associated with similar periprocedural risk compared with no resheathing in several patient-important outcomes. These data support the safety of current self-expanding transcatheter heart valves with resheathing features.

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Key Words: aortic stenosis ■ repositioning ■ resheathing ■ self-expanding ■ TAVI ■ TAVR ■ transcatheter

The new generation of self-expanding and mechanically expandable transcatheter heart valves (THVs) has been designed with resheathing features to recapture and reposition the THV to achieve predictable and accurate device deployment during transcatheter aortic valve implantation (TAVI).\(^1-3\) Enhancements

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in THV technology, alongside improvements in patient selection, procedural planning, and implantation techniques, have resulted in improved device success, procedural mortality, lower rates of permanent pacemaker implantation (PPI), and decreased incidence of significant paravalvular regurgitation.\(^1,3-5\) Although higher success rates and improved outcomes are associated with the use of newer THVs, there have been concerns that resheathing/recapture for THV repositioning could be associated with higher rates of periprocedural complications caused by extended manipulations at the level of the aortic valvar complex.\(^6,7\) Therefore, the aim of this study was to perform a systematic review and meta-analysis to evaluate outcomes following TAVI procedures with resheathing/recapture for THV repositioning versus those that did not require resheathing/recapture.

**METHODS**

The authors declare that all supporting data are available within the article and its online supplementary files. Institutional review board approval and patient consent were not required because of the systematic review and meta-analysis nature of this study.

**Search Strategy**

We conducted a search of Embase, MEDLINE, and Cochrane Central Register of Controlled Trials, from inception to September 2021. The keywords for the systematic search included “transcatheter aortic valve implantation,” “transcatheter aortic valve replacement,” “resheath,” and “repositioning.” The specific queries for each literature database are reported in Table S1.

**Study Selection**

The titles and abstracts yielded by the search were independently screened and extracted by 2 investigators (F.M. and R.B.). Bibliography of included studies and relevant reviews were retrieved to check for additional studies. Full reports of potentially relevant studies were retrieved, and data were independently extracted on study design, individual characteristics, periprocedural events, and follow-up. Any discrepancies were resolved by consensus.

**Eligibility Criteria**

All studies comparing TAVI outcomes between cases requiring resheathing/recapture and those not needing it were included in the analysis. The primary safety outcomes were 30-day mortality, stroke, coronary obstruction, major vascular complications, major bleeding events, and acute kidney injury (AKI). The primary efficacy outcomes were device success, need for >1 valve, moderate or higher paravalvular leak, and PPI. The secondary end point was 1-year mortality. End points were reported in accordance with the Valve Academic Research Consortium-2 (VARC-2) definition\(^8\) or individual author’s definitions. Outcomes reporting had to include either crude events in each group or any risk estimate (odds ratio [OR] with 95% confidence interval [CI]). There were no restrictions based on the

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**Nonstandard Abbreviations and Acronyms**

| Abbreviation | Description |
|--------------|-------------|
| AKI          | acute kidney injury |
| PPI          | permanent pacemaker implantation |
| ROBINS-I     | Risk of Bias in Non-randomised Studies of Interventions |
| SOLVE-TAVI   | Comparison of Second-Generation Self-Expandable Versus Balloon-Expandable Valves and General Versus Local Anesthesia in Transcatheter Aortic Valve Implantation |
| STS          | Society of Thoracic Surgeons |
| TAVI         | transcatheter aortic valve implantation |
| THV          | transcatheter heart valve |
| VARC-2       | Valve Academic Research Consortium-2 |
study design or reporting in follow-up data. Case reports/case series (≤3 patients), reviews, and editorial comments on the subject were excluded. When more than one report on the same study cohort was identified, only the one with the most complete data and detailed methodology description was included or updated from its initial search. This study reports data following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement9 (Figure 1 and Table S2). The protocol for this systematic review and meta-analysis protocol was registered on the international prospective register of

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram. Flow diagram based on 2020 PRISMA version.
systematic reviews (PROSPERO: registration number CRD42021273715, registered September 16, 2021).

Quality and Risk-of-Bias Assessment

The risk of bias of the selected studies was assessed using the Risk of Bias in Non-randomised Studies of Interventions (ROBINS-I) tool10 and the strength of evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) tool.11

Data Analysis

RevMan (Review Manager version 5.5, The Cochrane Collaboration) was used to perform random-effects meta-analyses using the Mantel-Haenszel method to determine pooled ORs for dichotomous data with regards to outcomes of patients with TAVI requiring resheathing/repositioning versus those in whom the latter was not required. The random-effects model was selected to take into consideration the heterogeneity in study designs (subanalysis of randomized controlled trial as well as prospective or retrospective observational studies). In addition, sample sizes varied substantially as well as the devices between most of the studies. Therefore, the use of a random-effects model would allow estimation of the mean of a distribution of effects. Consistency among studies was assessed with the Cochran Q statistic (I²) and a result of I² <25% indicates low, I² 25% to 50% moderate, I² 50% to 75%, and I² >75% indicate high, moderate, substantial, and high degree of statistical heterogeneity, respectively.12

To investigate the potential source of clinical heterogeneity,13 a prespecified sensitivity analysis was performed to determine whether the type of valve influenced the incidence of adverse events. Therefore, we excluded studies using the mechanically-expandable Lotus Valve (Boston Scientific), which was withdrawn from the market, as well as the balloon-expandable SAPIEN THV (Edwards Lifesciences), which does not have a resheathing feature. Furthermore, post hoc exploratory analyses were conducted to investigate the impact of single versus multiple (≥2) resheathing/repositioning attempts on safety outcomes. Hence, frequentist-approach network meta-analyses were performed using the netmeta package of R version 4.0.2 (R Foundation for Statistical Computing). We used a random-effects model to allow for apparent heterogeneity between studies in treatment comparison effects. Where there were insufficient data or studies for meta-analysis, we pooled the studies using weighted average or reported narrative results among individual studies.

RESULTS

Study Population and Procedural Data

A total of 7 studies6,7,14–18 met the inclusion criteria for the meta-analysis (Figure 1), and included 4501 participants, of which 1374 (30.5%) required the use of the resheathing/repositioning feature during TAVI. Reporting of resheathing/repositioning ranged from 12% to 61% (Table 1). Only 2 studies16,18 reported outcomes between single and multiple resheathing; therefore, for the purpose of the primary analyses, those who required multiple resheathing were pooled in the “resheathing” group.

The pooled mean age was 80.9±7.4 years and 54% of patients were women. The pooled mean Society of Thoracic Surgeons (STS) predicted risk of mortality score was 4.9±0.8. Transfemoral access was the most common access route. Further details on participants baseline characteristics are presented in Table 1.

In most of the studies, the Evolut self-expanding THV (Evolut R/PRO, Medtronic Inc.) was used, followed by the mechanically expandable Lotus Valve system and the Portico (Abbott) THV. The type of anesthesia was reported in 4 studies,7,14,15,18 with conscious sedation/local anesthesia administered in 48% (95% CI, 41%–55%) of resheathing patients and in 54% (95% CI, 42%–66%) of their no-resheathing counterparts. Contrast volume was reported in 3 studies,6,15,16 with a pooled mean volume of 198±25 mL in the resheathing group versus 160±48 mL in the no-resheathing group. Table 2 describes procedural data and crude event rates for the main reported outcomes of each study.

Quality Assessment

Ascertainment of outcomes was prospective in most of the studies,6,14–17 and one study used retrospective review of medical records and procedural reports and images.18 One study14 did not report on baseline differences between the analyzed groups. Overall baseline characteristics appear balanced between the no-resheathing and resheathing groups, except for 2 studies7,17 where patients showed differences in baseline characteristics.

No study reported on the number of patients lost at follow-up. Risk-of-bias assessment according to ROBINS-I indicated that the risk of bias was low or moderate among all studies and outcomes (Table S3). Publication bias could not be assessed using funnel plots with credible output because there were <10 studies in this meta-analysis, therefore, lacking power to distinguish chance from real asymmetry.19,20 The strength of evidence as appraised by the GRADE tool is shown in Table 3.
| Author, year | No. | Valve type | Arm | Age, y | Women | STS score | Transfemoral | Previous pacemaker | LVEF | Diabetes | COPD | PAD |
|--------------|-----|------------|-----|--------|-------|-----------|--------------|-------------------|------|----------|------|-----|
| Rashid, 2017 | 125 | Lotus      | NR (49) | 80.3±5.8 | 32 (65) | 5.6±2.5 | 49 (100) | 5 (10) | 7 (14) | 59±12.4 | 56.5±13.7 | 11 (22) | 13 (27) | 3 (6.1) | 6 (7.9) |
| Grube, 2017   | 1038| Evolut R   | NR (763) | 81.8±6.2 | 674 (65) | 5.5±4.5 | 748 (96) | 124 (12) | 13 (27) | 60.6±12.0 | 310 (30) | 267 (26) | 236 (23) |
| Seeger, 2019  | 200 | Evolut R/PRO-Lotus-SAPIEN 3 | NR (177) Resheathing (265 [26%]) | 80.5±6.2 | 96 (54) | 5.9±4.6 | 177 (100) | NA | NA | 56 (32) | 94 (53) | NA |
| Attizzani, 2017 | 946 | Evolut R/PRO | NR (628) | 75.8±6.4 | 280 (45) | 2.6±1.4 | 615 (98) | 27 (4.3) | 9 (2.8) | 64.9±7.8 | 64.4±7.9 | 200 (32) | 144 (24) | 79 (13) | 35 (11) |
| Kefer, 2020   | 170 | Evolut R-Portico | NR (131) Resheathing (39 [23%]) | 83.0±6.0 | 73 (56) | 5.6±3.6 | 131 (100) | NA | NA | 59±12 | 66.0±10 | 23 (17) | 16 (12) | 19 (14) | 4 (10) |
| Seeger, 2020  | 996 | Lotus      | NR (683) Resheathing (313 [31%]) | 80.9±6.3 | 355 (52) | 5.6±3.6 | 683 (100) | 91 (13) | 41 (13) | 56±13 | 56.2±12 | 151 (23) | 68 (22) | NA | NA |
| Bernardi, 2021 | 1026 | Evolut R/PRO-Portico | NR (596) SR (245 [24%]) MR (65 [9%]) | 80.8±7.5 | 382 (56) | 4.9±2.9 | 606 (89) | 98 (15) | 29 (12) | 56±13 | 56.2±12 | 146 (20) | 34 (16) | 221 (32) | 43 (18) | 161 (24) | 51 (21) | 118 (17) | 12 (13) |

Values are expressed as mean±SD or number (percentage) unless otherwise noted. COPD indicates chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; MR, multiple resheathing; NA, not available; NR, no resheathing; PAD, peripheral artery disease; SR, single resheathing; and STS, Society of Thoracic Surgeons.

### Efficacy Outcomes

Two studies reported on 1-year mortality, and there was no significant difference between the resheathing and the no-resheathing groups (OR, 1.53 [95% CI, 0.88–2.80]; p=0.26).

Two studies 7,18 reported on the incidence of device success, and no statistically significant difference was found between the resheathing and the no-resheathing groups (OR, 0.71 [95% CI, 0.51–1.0]; p=0.06).

Four studies 7,14 reported on the incidence of bleeding events. No differences in effect estimates were observed between the resheathing group and the no-resheathing group (OR, 0.92 [95% CI, 0.66–1.3]; p=0.79). A second valve was reported in 3 studies, with a rate of 2.86% (95% CI, 0.96–6.49). Yet, these studies were not statistically significant.

Two studies 7,14 reported on the need for re-access, with a rate of 3.02% (95% CI, 0.96–9.60). Yet, these studies were not statistically significant.

### Secondary Outcome

Two studies 7,18 reported on 1-year mortality, and no significant difference was detected between the resheathing group and the no-resheathing group (OR, 0.92 [95% CI, 0.66–1.3]; p=0.06). Two studies 7,18 reported on the incidence of device success, and no statistically significant difference was found between the resheathing and the no-resheathing groups (OR, 0.71 [95% CI, 0.51–1.0]; p=0.06).

### Safety Outcomes

**Resheathing and Repositioning During TAVI**

The incidence of 30-day mortality was reported in 4 studies, which included 3125 patients. There was no statistically significant difference in effect estimates for patients who required valve resheathing (OR, 1.30 [95% CI, 0.64–2.62]; p=0.44) and those who did not (15 of 999 [1.5%] versus 43 of 2126 [2.0%], respectively, OR, 0.74 [95% CI, 0.41–1.33]; p=0.06).

### Efficacy Outcomes

Two studies 7,14 reported on 1-year mortality, and no significant difference was detected between the resheathing group and the no-resheathing group (OR, 0.71 [95% CI, 0.51–1.0]; p=0.06).

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Two studies 7,18 reported on the incidence of device success, and no statistically significant difference was found between the resheathing and the no-resheathing groups (OR, 0.71 [95% CI, 0.51–1.0]; p=0.06).

### Safety Outcomes

Resheathing and Repositioning During TAVI
Table 2. Procedural Characteristics and Outcomes

| Author, year | Procedural characteristics, n/N (%) | Time frame of assessment | Outcome          | No resheathing, n/N (%) | Resheathing, n/N (%) |
|--------------|-------------------------------------|-------------------------|-------------------|-------------------------|----------------------|
| Rashid, 2017 | No resheathing                       |                         |                  |                         |                      |
|              | General anesthesia 31/49 (63)       |                         |                  |                         |                      |
|              | TEE 31/49 (63)                      |                         |                  |                         |                      |
|              | Contrast volume 184±70 mL           |                         |                  |                         |                      |
|              | Resheathing                         |                         |                  |                         |                      |
|              | General anesthesia 48/76 (63)       |                         |                  |                         |                      |
|              | TEE 48/76 (63)                      |                         |                  |                         |                      |
|              | Contrast volume 209±83 mL           |                         |                  |                         |                      |
|              | 30 d                                 |                         |                  | 7/49 (14.0)             | 9/76 (12.0)          |
|              | Time frame of assessment             |                         |                  |                         |                      |
|              | Outcome                              |                         |                  |                         |                      |
|              | No resheathing, n/N (%)              |                         |                  | 5/763 (0.6)             | 5/265 (1.8)          |
|              | Tamponade                            |                         |                  | 8/763 (1.0)             | 2/265 (0.7)          |
|              | Myocardial infarction                |                         |                  | 0/763 (0.0)             | 0/265 (0.0)          |
|              | 30-d mortality                       |                         |                  | 147/763 (1.8)           | 5/265 (1.8)          |
|              | 30-d stroke                          |                         |                  | 22/763 (2.8)            | 7/265 (2.6)          |
|              | 30-d major vascular complication     |                         |                  | 48/763 (6.0)            | 17/265 (6.4)         |
|              | 30-d major bleeding                  |                         |                  | 26/763 (3.4)            | 4/265 (1.5)          |
|              | 30-d moderate or higher paravalvular leakage |         |                  | 1/45 (2.0)              | 2/76 (2.6)           |
| Grube, 2017  | No resheathing                       |                         |                  |                         |                      |
|              | Local anesthesia 520/763 (68)        |                         |                  |                         |                      |
|              | Resheathing                          |                         |                  |                         |                      |
|              | Local anesthesia 152/265 (57)        |                         |                  |                         |                      |
|              | 30 d                                 |                         |                  | 5/763 (0.6)             | 5/265 (1.8)          |
|              | Need for >1 valve                    |                         |                  | 8/763 (1.0)             | 2/265 (0.7)          |
|              | AKI                                  |                         |                  | 0/763 (0.0)             | 0/265 (0.0)          |
|              | Coronary obstruction                 |                         |                  | 147/763 (1.8)           | 5/265 (1.8)          |
|              | 30-d mortality                       |                         |                  | 22/763 (2.8)            | 7/265 (2.6)          |
|              | 30-d major vascular complication     |                         |                  | 48/763 (6.0)            | 17/265 (6.4)         |
|              | 30-d major bleeding                  |                         |                  | 26/763 (3.4)            | 4/265 (1.5)          |
| Seeger, 2019 | No resheathing                       |                         |                  |                         |                      |
|              | Fluoroscopy time 1137±368 s          |                         |                  |                         |                      |
|              | Contrast media 86±35 mL              |                         |                  |                         |                      |
|              | Resheathing                          |                         |                  |                         |                      |
|              | Fluoroscopy time 1195±368 s          |                         |                  |                         |                      |
|              | Contrast media 139±181 mL            |                         |                  |                         |                      |
|              | 30 d                                 |                         |                  | 5/763 (0.6)             | 5/265 (1.8)          |
|              | Need for >1 valve                    |                         |                  |                        |                      |
|              | AKI                                  |                         |                  | 3/777 (1.7)             | 2/23 (8.6)           |
|              | Coronary obstruction                 |                         |                  | 0/763 (0.0)             | 0/23 (0.0)           |
|              | 30-d mortality                       |                         |                  | 147/763 (1.8)           | 5/265 (1.8)          |
|              | 30-d stroke                          |                         |                  | 22/763 (2.8)            | 7/265 (2.6)          |
|              | 30-d major vascular complication     |                         |                  | 48/763 (6.0)            | 17/265 (6.4)         |
|              | 30-d major bleeding                  |                         |                  | 26/763 (3.4)            | 4/265 (1.5)          |
|              | 30-d moderate or higher paravalvular leakage |         |                  | 1/45 (2.0)              | 2/76 (2.6)           |
| Attizzani,   | No resheathing                       |                         |                  |                         |                      |
| 2020        | General anesthesia 345/628 (55)      |                         |                  |                         |                      |
|              | Procedural time 147±52 min           |                         |                  |                         |                      |
|              | Resheathing                          |                         |                  |                         |                      |
|              | General anesthesia 177/318 (56)      |                         |                  |                         |                      |
|              | Procedural time 151±56 min           |                         |                  |                         |                      |
|              | 30 d                                 |                         |                  | 8/628 (1.3)             | 5/318 (1.5)          |
|              | Need for >1 valve                    |                         |                  |                        |                      |
|              | AKI                                  |                         |                  | 3/628 (0.4)             | 7/318 (2.2)          |
|              | Coronary obstruction                 |                         |                  | 1/628 (0.1)             | 5/318 (1.5)          |
|              | 30-d mortality                       |                         |                  | 2/628 (0.2)             | 1/318 (0.3)          |
|              | 30-d stroke                          |                         |                  | 15/628 (2.4)            | 13/318 (4.1)         |
|              | 30-d major vascular complications    |                         |                  | 25/628 (3.9)            | 9/318 (2.8)          |
|              | 30-d major bleeding                  |                         |                  | 9/628 (1.4)             | 8/318 (2.5)          |
|              | 30-d permanent pacemaker implantation|                         |                  | 98/601 (16.0)           | 5/309 (19.0)         |
|              | 1-y mortality                        |                         |                  | 15/628 (2.4)            | 5/318 (1.5)          |
|              | 1-y stroke                           |                         |                  | 20/628 (3.2)            | 18/318 (5.6)         |
|              | 1-y major vascular complications     |                         |                  | 25/628 (3.9)            | 9/318 (2.8)          |
|              | 1-y major bleeding                   |                         |                  | 9/628 (1.4)             | 8/318 (2.5)          |
|              | 1-y permanent pacemaker implantation |                         |                  | 109/601 (18.0)          | 65/309 (21.0)        |
|              | 1-y moderate or higher paravalvular leakage |         |                  | 17/628 (2.7)           | 9/318 (2.8)          |
| Kefer, 2020  | No resheathing                       |                         |                  |                         |                      |
|              | Fluoroscopy time 18±7 min            |                         |                  |                         |                      |
|              | Contrast volume 217±93 mL            |                         |                  |                         |                      |
|              | Resheathing                          |                         |                  |                         |                      |
|              | Fluoroscopy time 20±7 min            |                         |                  |                         |                      |
|              | Contrast volume 243±93 mL            |                         |                  |                         |                      |
|              | In-hospital                          |                         |                  | 128/131 (98.0)          | 39/39 (100.0)        |
|              | Device success                       |                         |                  | 2/131 (1.5)             | 1/39 (2.5)           |
|              | Need for >1 valve                    |                         |                  | 4/131 (3.0)             | 0/39 (0.0)           |
|              | AKI                                  |                         |                  | 0/131 (0.0)             | 0/39 (0.0)           |
|              | Myocardial infarction                |                         |                  | 1/131 (0.7)             | 1/39 (2.5)           |
|              | Stroke                               |                         |                  | 2/131 (1.4)             | 0/39 (0.0)           |
|              | Major vascular complications         |                         |                  | 3/131 (2.2)             | 2/39 (5.1)           |
|              | Major bleeding                       |                         |                  | 21/131 (16.0)           | 10/39 (26.0)         |

(Continued)
Sensitivity Analysis

We performed sensitivity analysis excluding studies using the Lotus valve, which is no longer available on the market, and the Edwards SAPIEN THV, which does not include a dedicated resheatable system. The results suggest no changes in the magnitude or the direction of the effect estimates for 30-day mortality, 30-day stroke, major vascular complications, bleeding, AKI, and need for PPI (Figure 4).

Single Versus Multiple Resheathing: An Exploratory Network Meta-Analysis

Two studies\textsuperscript{16,18} reported separated event rates for single and multiple resheathing/repositioning attempts for ≥1 of the outcomes of interest of the present meta-analysis. We therefore performed a post hoc network meta-analysis to determine whether multiple resheathing/repositioning attempts were associated with differences in the occurrence of adverse events compared with single and no resheathing. Network meta-analyses showed that multiple resheathing attempts appeared to be associated with significantly lower device success rates (OR, 0.45 [95% CI, 0.24–0.87]) and significantly higher need for a second valve (OR, 10.47 [95% CI, 3.99–27.48]) when compared with single resheathing and no resheathing. Moreover, multiple resheathing attempts appeared to be associated to an increased risk of 1-year mortality (OR, 1.98 [95% CI, 1.12–3.48]) compared with single resheathing and no resheathing. It should be highlighted that these results were mainly influenced by one study reporting on multiple resheathing, with these outcomes hampering the credibility around the point estimates and CIs. Importantly, no significant differences between the 3 groups were detected in terms of 30-day mortality, stroke, major vascular complications, major bleeding, AKI, and need for PPI (Table 4). The interpretation of these results warrant caution because of the exploratory nature of the analysis and based on the quality of the available data.

**DISCUSSION**

Our meta-analysis of 7 observational studies including 4501 participants (1374 [30.5%] requiring resheathing) suggests that the use of the resheathing feature for THV repositioning was associated with similar event rates around several periprocedural patient-important outcomes. Notably, these results were consistent after sensitivity analysis limited to currently available self-expanding THVs. Nonetheless, the overall evidence basis consists of low-quality studies highly confounded by selection bias. On the other hand, since resheathing technology is a dedicated feature of commercially available self-expanding valves, it is unlikely that the issue of resheathing/multiple resheathing will be further...
Table 3. GRADE Assessment of Overall Quality of Evidence

| Certainty assessment | Patient n/N (%) | Effect |
|----------------------|-----------------|--------|
|                      | Relative OR     | Absolute with 95% CI | Certainty |
|                      | (95% CI)        | 95% CI | |
| 30-d mortality       |                 |        |
| Attizzani, 2020      | 43/2126         | 0.74   | +OOO |
| Bernardi, 2021       | 15/999          | 0.41–1.33 | Very low |
| Grube, 2017          |                 |        |
| Rashid, 2017         |                 |        |
| No Resheathing       |                 | 5 fewer per 1000 |
| Resheathing          |                 | from 14 fewer to 5 more |
| 30-d stroke          |                 |        |
| Attizzani, 2020      | 79/2809         | 1.09   | +OOO |
| Bernardi, 2021       | 41/1312         | 0.74–1.62 | Very low |
| Grube, 2017          |                 |        |
| Rashid, 2017         |                 |        |
| Seeger, 2020         |                 |        |
| Coronary obstruction |                 |        |
| Attizzani, 2020      | 7/2077 (0.3)    | 2.35   | +OOO |
| Bernardi, 2021       | 7/923 (0.7)     | 0.17–33.47 | Very low |
| Grube, 2017          |                 |        |
| Rashid, 2017         |                 |        |
| Coronary obstruction |                 |        |
| Attizzani, 2020      | 115/2126        | 0.92   | +OOO |
| Bernardi, 2021       | 52/999          | 0.66–1.30 | Very low |
| Grube, 2017          |                 |        |
| Rashid, 2017         |                 |        |
| 30-d major vascular complications | 66/2126 | 1.13 | +OOO |
| Attizzani, 2020      | 41/999          | 0.64–2.01 | Very low |
| Bernardi, 2021       |                 |        |
| Grube, 2017          |                 |        |
| Rashid, 2017         |                 |        |
| AKI                  |                 |        |
| Attizzani, 2020      | 67/2434         | 1.30   | +OOO |
| Bernardi, 2021       | 39/1061         | 0.64–2.62 | Very low |
| Grube, 2017          |                 |        |
| Kofre, 2009          |                 |        |
| Rashid, 2017         |                 |        |
| Seeger, 2019         |                 |        |
| (Continued)
Table 3. Continued

| Certainty assessment | Patient n/N (%) | Effect | Other Considerations | Relative OR (95% CI) | Absolute with 95% CI | Certainty |
|----------------------|----------------|--------|----------------------|----------------------|----------------------|-----------|
| **Device success**   |                |        |                      |                      |                      |           |
| Kefer 2020<sup>16</sup> Bernardi 2021<sup>18</sup> | 1 observational prospective, 1 retrospective | Serious* | Not serious | Serious<sup>1</sup> Not serious | Residual confounding may have a significant influence on the observed direction of effect | 745/817 (91.2) | 335/379 (88.4) | 0.77 (0.51–1.14) | 28 fewer per 1000 (from 65 fewer to 9 more) | +OOO Very low |
| **Need for more than 1 valve** |                |        |                      |                      |                      |           |
| Attizzani 2020<sup>7</sup> Bernardi 2021<sup>18</sup> Grube 2017<sup>14</sup> Kefer 2020<sup>16</sup> | 1 trial sub-analysis, 2 observational prospective, 1 retrospective | Very serious<sup>*</sup> | Serious<sup>1</sup> | Serious<sup>1</sup> Serious<sup>3</sup> | 20/2208 (0.9) | 30/962 (3.1) | 2.86 (0.96–8.48) | 22 more per 1000 (from 10 more to 33 more) | +OOO Very low |
| **30-d moderate or more paravalvular leak** |                |        |                      |                      |                      |           |
| Bernardi 2021<sup>18</sup> Rashid 2017<sup>15</sup> | 1 observational prospective, 1 retrospective | Very serious<sup>*</sup> | Serious<sup>1</sup> | Serious<sup>1</sup> Not serious | Residual confounding may have a significant influence on the observed direction of effect | 25/735 | 20/416 | 1.53 (0.89–2.80) | 14 more per 1000 (from 10 fewer to 38 more) | +OOO Very low |
| **30-d permanent pacemaker implantation** |                |        |                      |                      |                      |           |
| Attizzani 2020<sup>7</sup> Bernardi 2021<sup>18</sup> Rashid 2017<sup>15</sup> | 1 trial sub-analysis, 1 observational prospective, 1 retrospective | Very serious<sup>1</sup> | Serious<sup>1</sup> | Not serious | 209/1233 | 130/675 | 1.04 (0.68–1.57) | 23 more per 1000 (from 13 fewer to 59 more) | +OOO Very low |
| **1-y mortality** |                |        |                      |                      |                      |           |
| Attizzani 2020<sup>7</sup> Bernardi 2021<sup>18</sup> | 1 trial sub-analysis, 1 retrospective | Very serious<sup>*</sup> | Serious<sup>1</sup> | Not serious | 67/1314 | 43/658 | 1.00 (0.68–1.47) | 14 more (from 7 fewer to 36 more) | +OOO Very low |

AKI indicates acute kidney injury; and OR, odds ratio.
*Serious or very serious because of confounding bias.
<sup>1</sup>Large variation of point estimates and significant heterogeneity.
<sup>2</sup>Multiple valve types, imbalance of valve type between cases and controls.
<sup>3</sup>Concern for heterogeneity in outcome definition.
<sup>4</sup>Small number of events, large CI, which crosses neutrality.
<sup>5</sup>Rare events.
Figure 2. Forest plots of pooled treatment effect estimates for safety outcomes in patients undergoing transcatheter aortic valve implantation requiring resheathing/repositioning versus not requiring it.

M-H indicates Mantel-Haenszel.
Figure 3. Forest plots of pooled treatment effect estimates for efficacy and secondary outcomes in patients undergoing transcatheter aortic valve implantation requiring resheathing/repositioning versus not requiring it. M-H indicates Mantel-Haenszel.
Figure 4. Sensitivity analysis evaluating the cumulative risk of outcomes by excluding mechanically and balloon-expandable transcatheter heart valves. M-H indicates Mantel-Haenszel.
Resheathing, Repositioning, and the Potential for Periprocedural Adverse Events

Resheathing/recapture of self-expanding THVs has been reported in 25% to 35% of patients with the Evolut R/PRO device\cite{14,21} and 33% to 44% of patients with the Portico device\cite{2,5,22}. Resheathing/recapture and repositioning maneuvers aim to achieve optimal THV positioning but also prove useful to overcome unforeseen scenarios such as pop-out or coronary obstruction during TAVI. These may lead to prolonged catheter manipulation in the ascending aorta and the aortic valve complex with potential for debris embolization but also requirement for more contrast injections and interaction with the conduction system. Indeed, Attizzani et al\cite{7} showed that the time spent with the delivery system in the body was significantly longer for

| Study                                                                 | No Resheathing | Single Resheathing | Multiple Resheathing |
|----------------------------------------------------------------------|----------------|--------------------|----------------------|
| 30-d mortality                                                       |                |                    |                      |
| OR (95% CI)                                                          | …              | 1.33 (0.69–2.55)   | 1.53 (0.62–3.78)     |
| No. of studies                                                       | 4              | 4                  | 2                    |
| No. of patients                                                      | 2126           | 885                | 114                  |
| 30-d stroke                                                          |                |                    |                      |
| OR (95% CI)                                                          | …              | 0.94 (0.59–1.49)   | 1.05 (0.49–2.28)     |
| No. of studies                                                       | 5              | 5                  | 2                    |
| No. of patients                                                      | 2809           | 1198               | 114                  |
| 30-d major vascular complications                                    |                |                    |                      |
| OR (95% CI)                                                          | …              | 1.04 (0.72–1.51)   | 0.95 (0.37–2.45)     |
| No. of studies                                                       | 3              | 3                  | 1                    |
| No. of patients                                                      | 2077           | 828                | 95                   |
| 30-d major bleeding                                                  |                |                    |                      |
| OR (95% CI)                                                          | …              | 0.84 (0.52–1.36)   | 1.07 (0.37–3.11)     |
| No. of studies                                                       | 3              | 3                  | 1                    |
| No. of patients                                                      | 2077           | 828                | 95                   |
| AKI                                                                 |                |                    |                      |
| OR (95% CI)                                                          | …              | 0.89 (0.54–1.47)   | 1.32 (0.58–3.01)     |
| No. of studies                                                       | 5              | 5                  | 1                    |
| No. of patients                                                      | 2385           | 790                | 95                   |
| Device success                                                       |                |                    |                      |
| OR (95% CI)                                                          | …              | 1.01 (0.63–1.65)   | 0.45 (0.24–0.87)     |
| No. of studies                                                       | 2              | 2                  | 1                    |
| No. of patients                                                      | 745            | 284                | 95                   |
| Need for >1 valve                                                   |                |                    |                      |
| OR (95% CI)                                                          | …              | 0.39 (0.21–0.76)   | 10.47 (3.99–27.48)   |
| No. of studies                                                       | 4              | 4                  | 1                    |
| No. of patients                                                      | 2208           | 867                | 95                   |
| 30-d permanent pacemaker implantation                               |                |                    |                      |
| OR (95% CI)                                                          | …              | 0.81 (0.62–1.06)   | 1.26 (0.70–2.25)     |
| No. of studies                                                       | 2              | 2                  | 1                    |
| No. of patients                                                      | 1189           | 525                | 81                   |
| 1-y mortality                                                       |                |                    |                      |
| OR (95% CI)                                                          | …              | 1.36 (0.86–2.16)   | 1.98 (1.12–3.48)     |
| No. of studies                                                       | 2              | 2                  | 1                    |
| No. of patients                                                      | 1314           | 563                | 95                   |

AKI indicates acute kidney injury. Odd ratios (ORs) are comparing no resheathing as the group of reference.
procedures requiring resheathing/recapture (18.5±19.0 minutes versus 15.6±17.4 minutes, P=0.02), while in other studies the fluoroscopy time was numerically higher but did not reach statistical significance.\textsuperscript{6,16}

Seeger et al\textsuperscript{6} showed a morphologic and morphometric characterization of debris retrieved from cerebral embolic protection devices. Notably the proportion of patients in whom embolic debris was retrieved did not differ between the repositioning and no-repositioning groups. However, patients who had at least one resheathing/repositioning attempt were found to have a larger overall cumulative debris area and more commonly calcific or myocardial fragments retrieved from the filters, which may be consistent with a prolonged (traumatic) interaction between the delivery system and the aortic valve complex. Nonetheless, the increase in particle number and size did not appear to translate in a significant increase in clinical strokes in that study\textsuperscript{6} or in any of the individual studies analyzed in the present work.\textsuperscript{7,14,15,17,18}

One reason for resheathing is that the THV was initially positioned deep into the left ventricular outflow tract, therefore requiring reposition of the THV before deployment. Studies have shown an increased risk in new-onset conduction disturbances following TAVI,\textsuperscript{7,14,16} and this is consistent with the lower final implantation depth of the THV,\textsuperscript{7,14} resulting in direct interaction of the THV with the conduction system.\textsuperscript{23} Of note, even though the main results of the present meta-analysis show similar odds of PPI among patients requiring resheathing/repositioning, this was subject to substantial heterogeneity (I\textsuperscript{2}=58\%). Therefore, we performed sensitivity analysis limited to 2 studies\textsuperscript{7,15} using self-expanding THVs (excluding the Lotus valve) and the results did not show statistical significance.

Seeger\textsuperscript{6} and Kefer\textsuperscript{16} and colleagues found that patients undergoing resheathing/repositioning required a higher volume of contrast during TAVI. In this regard, Seeger\textsuperscript{6} and Attizzani\textsuperscript{7} report a higher incidence of AKI among individuals requiring resheathing/repositioning; however, it did not appear to be the case in the other studies included in the present meta-analysis, which led to a pooled effect estimate crossing neutrality.

Could Resheathing and Repositioning Be a Surrogate of a More Complex Patient Case?

While resheathing for THV repositioning represents a bail-out strategy to improve the results of TAVI, the need for resheathing, or multiple attempts, may represent a surrogate for more complex patient cases and procedures such as those with less favorable anatomies (ie, significant concomitant aortic insufficiency, large aortic annuli, horizontal aorta, only mild aortic calcification, or low coronary height). Seeger et al\textsuperscript{17} reported a higher preprocedural risk as assessed by the STS score among patients requiring resheathing. Moreover, Kefer and colleagues\textsuperscript{16} reported a higher proportion of patients with porcelain aorta, which has been, per se, associated with worse outcomes after TAVI,\textsuperscript{24} yet this variable is not included in the STS score. In this regard, while Kefer and colleagues\textsuperscript{16} did not find the need for resheathing as a variable associated with adverse events, Bernardi et al\textsuperscript{18} showed that participants requiring multiple resheathing did; yet, the STS score was not significantly different in that study. Nonetheless, participants in the multiple resheathing group showed a higher prevalence of preprocedural atrial fibrillation and cerebrovascular disease, both of which have been associated with significant cardiovascular morbidity and mortality.\textsuperscript{25–27}

Bernardi et al\textsuperscript{16} observed a higher risk of mortality at 1 year among patients requiring multiple resheathing; however, this effect may be partially explained by a higher comorbidity burden,\textsuperscript{28} baseline patient complexity, suboptimal result of the intervention, or periprocedural complications that ultimately impact mortality.\textsuperscript{29}

Our post hoc network meta-analysis showed that, in comparison with no resheathing or single resheathing, the need for multiple resheathing appeared to be associated with lower device success rates, higher rates of need for a second valve, and 1-year mortality. Again, these results should be interpreted with caution because of the exploratory nature of the analysis and the data driven by a single study.\textsuperscript{16} Despite the latter, it is worth to be highlighted the estimate for treatment effect was similar for those with single resheathing than no resheathing in terms of device success, and favorable with regards to the need for a second valve.

Multiple resheathing could, in fact, be a signal of a more complex procedure and/or anatomical features, but also the translation of low annual TAVI-center caseload or time-dependent effect on learning curve and outcomes,\textsuperscript{29} which likely supports a reverse causality issue. Moreover, allocating and thus analyzing resheathing/repositioning as a dichotomous variable (instead of categorical), a sizable number of TAVI procedures in which multiple resheathing/repositioning are required would be pooled as “resheathing.”

Limitations

The main limitations of the study are the small number of studies, participants, and events while reporting on outcomes of interest, which could have affected the power of the meta-analysis. Furthermore, the nonrandomized nature of the included studies is a source of selection bias. Individual-patient level data were not available, precluding more robust adjustment for any differences in clinical, anatomical, and procedural variables among the groups. Also, in the absence of
a dedicated/prospective case report form, multiple resheathing/repositioning would also be classified as single resheathing simply because of underreporting or misreporting. Notably, the decision to perform resheathing for THV reposition versus no resheathing was at the discretion of the TAVI operators and, based on the nature of this maneuver, without consistent applicability. Therefore, procedural variables and anatomical features might have been heterogeneous among the studies in addition to differences in Heart Team experience (ie, annual caseload with a given device) and also the threshold and preference to recapture and reposion the THV. The above-mentioned limitations lead to low certainty of evidence in this field, however, although randomized controlled trials may help determine the ideal scenario for resheathing and repositioning, they are unlikely to be performed. Finally, whether the resheathing and repositioning feature of new-generation self-expanding or mechanically expanding prostheses could provide an edge over other THVs that do not have such a feature because of intrinsic design, ie balloon-expandable valves, will remain unknown. Only limited randomized controlled data exist comparing new-generation self-expanding with balloon-expanding THV. The recent SOLVE-TAVI (Comparison of Second-Generation Self-Expandable Versus Balloon-Expandable Valves and General Versus Local Anesthesia in Transcatheter Aortic Valve Implantation) study has shown clinical equivalence between the 2 classes of THVs.30 The trial, however, was not powered to detect superiority of self-expanding THVs. In addition, the relative importance of the resheathing feature in determining any potential difference in outcomes remains difficult to appreciate.

CONCLUSIONS

This analysis suggests that resheathing for THV repositioning during TAVI is associated with similar periprocedural risk of adverse outcomes in several patient-important outcomes. These data support the safety of current self-expanding THVs with resheathing/recapturability features.

ARTICLE INFORMATION

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None.

Supplemental Material

Tables S1–S3

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SUPPLEMENTAL MATERIAL
Table S1. Searching strategies for the main literature databases employed in the systematic search.

| Database        | Query                                                                 |
|-----------------|----------------------------------------------------------------------|
| Embase          | ((resheath or resheathing or repositioning or recapturable or recapture) and (transcatheter aortic valve replacement or tavr or transcatheter aortic valve implant or tavi)).af. |
| Cochrane central| ((resheath):ti,ab,kw OR (resheathing):ti,ab,kw OR "repositioning"):ti,ab,kw OR (recapturable):ti,ab,kw OR "recapture":ti,ab,kw) AND ((transcatheter aortic valve replacement):ti,ab,kw OR (tavr):ti,ab,kw OR (transcatheter aortic valve implant):ti,ab,kw OR (transcatheter aortic valve implantation):ti,ab,kw OR (TAVI):ti,ab,kw) |
| MEDLINE         | (resheath OR resheathing OR repositioning OR recapturable OR recapture) AND (transcatheter aortic valve replacement OR tavr OR transcatheter aortic valve implant OR tavi) |
| Section and Topic | Item # | Checklist item                                                                                                                                                                                                 | Location where item is reported |
|-------------------|--------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| **TITLE**         | 1      | Identify the report as a systematic review.                                                                                                                                                                    | Page 1                          |
| **ABSTRACT**      | 2      | See the PRISMA 2020 for Abstracts checklist.                                                                                                                                                                   | Page 2                          |
| **INTRODUCTION**  | 3      | Describe the rationale for the review in the context of existing knowledge.                                                                                                                                     | Page 7                          |
|                   | 4      | Provide an explicit statement of the objective(s) or question(s) the review addresses.                                                                                                                           | Page 7                          |
| **METHODS**       | 5      | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.                                                                                                    | Page 8                          |
|                   | 6      | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | Page 7                          |
|                   | 7      | Present the full search strategies for all databases, registers and websites, including any filters and limits used.                                                                                           | Page 7; Supplementary Table 1   |
|                   | 8      | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | Pages 7-8                       |
|                   | 9      | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | Page 8                          |
|                   | 10a    | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | Page 8                          |
|                   | 10b    | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | Page 8                          |
|                   | 11     | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | Page 8                          |
|                   | 12     | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.                                                                            | Page 9                          |
| **Synthesis methods** | 13a  | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | Page 9                          |
|                   | 13b    | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.                                                       | Page 9                          |
|                   | 13c    | Describe any methods used to tabulate or visually display results of individual studies and syntheses.                                                                                                        | Page 9                          |
|                   | 13d    | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the details of the methods.                                                   | Page 9                          |
| Section and Topic | Item # | Checklist item                                                                                                                                                                                                 | Location where Item is reported |
|-------------------|--------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------|
|                   | 13e    | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).                                                                             | Page 9                          |
|                   | 13f    | Describe any sensitivity analyses conducted to assess robustness of the synthesized results.                                                                                                                    | Page 9                          |
|                   | 14     | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).                                                                                           | Page 9                          |
|                   | 15     | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.                                                                                                            | Page 9                          |
| RESULTS           | 16a    | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.                     | Page 9; Figure 1                 |
|                   | 16b    | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.                                                                                      | Page 9; Table 1 and 2           |
|                   | 17     | Cite each included study and present its characteristics.                                                                                                                                                    | Pages 10-11; Supplemental Table 2|
|                   | 18     | Present assessments of risk of bias for each included study.                                                                                                                                                 | Table 2                         |
|                   | 19     | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | Table 2                         |
|                   | 20a    | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.                                                                                                       | Table 3                         |
|                   | 20b    | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | Pages 11-13; Figures 2-4; Table 4|
|                   | 20c    | Present results of all investigations of possible causes of heterogeneity among study results.                                                                                                                | -                               |
|                   | 20d    | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.                                                                                                  | Page 13; Figure 4               |
|                   | 21     | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.                                                                                         | -                               |
|                   | 22     | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.                                                                                                          | Table 3                         |
| DISCUSSION        | 23a    | Provide a general interpretation of the results in the context of other evidence.                                                                                                                           | Pages 13-16                     |
|                   | 23b    | Discuss any limitations of the evidence included in the review.                                                                                                                                            | Page 16                         |
|                   | 23c    | Discuss any limitations of the review processes used.                                                                                                                                                      | Page 16                         |
|                   | 23d    | Discuss implications of the results for practice, policy, and future research.                                                                                                                             | Page 13-16; Page 5              |
| Section and Topic      | Item # | Checklist item                                                                                                                                                                                                 | Location where item is reported |
|------------------------|--------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------|
| OTHER INFORMATION      | 24a    | Provide registration information for the review, including register name and registration number, or state that the review was not registered.                                                                                                       | Submitted to Prospero on August 16, 2021 (registration pending) |
|                        | 24b    | Indicate where the review protocol can be accessed, or state that a protocol was not prepared.                                                                                                                                                               | -                                |
|                        | 24c    | Describe and explain any amendments to information provided at registration or in the protocol.                                                                                                                                                            | -                                |
| Support                | 25     | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.                                                                                                                                 | Page 1                            |
| Competing interests    | 26     | Declare any competing interests of review authors.                                                                                                                                                                                                              | Page 1                            |
| Availability of data, code, and other materials | 27    | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | Page 9                            |

*From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

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Table S3. ROBINS-I risk of bias evaluation for individual outcomes assessed in the meta-analysis.

| Outcome Author, Year | Bias due to confounding | Bias in selection of participants into the study | Bias in classification of interventions | Bias due to deviations from intended interventions | Bias due to missing data | Bias in measurement of the outcome | Bias in selection of the reported result | Overall risk of bias |
|----------------------|-------------------------|-----------------------------------------------|----------------------------------------|--------------------------------------------------|-------------------------|-----------------------------------|------------------------------------------|-------------------|
| **Device success**   |                         |                                               |                                        |                                                  |                         |                                   |                                          |                   |
| Kefer, 2020          | Moderate                | Low                                           | Low                                    | Low                                              | Low                     | Low                               | Low                        | Low               |
| Bernardi, 2021       | Moderate                | Low                                           | Moderate                               | Low                                              | Low                     | Low                               | Low                        | Low               |
| **Need for >1 valve**|                         |                                               |                                        |                                                  |                         |                                   |                                          |                   |
| Grube, 2017          | High                    | Low                                           | Low                                    | Low                                              | Low                     | Low                               | Low                        | Moderate          |
| Attizzani, 2020      | High                    | Low                                           | Low                                    | Low                                              | Low                     | Severe                           | Low                        | Moderate          |
| Kefer, 2020          | Moderate                | Low                                           | Low                                    | Low                                              | Low                     | Low                               | Low                        | Low               |
| Bernardi, 2021       | Moderate                | Low                                           | Moderate                               | Low                                              | Low                     | Low                               | Low                        | Low               |
| **Coronary obstruction**|                         |                                               |                                        |                                                  |                         |                                   |                                          |                   |
| Grube, 2017          | High                    | Low                                           | Low                                    | Low                                              | Low                     | Low                               | Low                        | Moderate          |
| Attizzani, 2020      | High                    | Low                                           | Low                                    | Low                                              | Low                     | Severe                           | Low                        | Moderate          |
| Bernardi, 2021       | Moderate                | Low                                           | Moderate                               | Low                                              | Low                     | Low                               | Low                        | Moderate          |
| **Acute kidney injury**|                         |                                               |                                        |                                                  |                         |                                   |                                          |                   |
| Rashid, 2017         | Moderate                | Low                                           | Low                                    | Low                                              | Low                     | Low                               | Low                        | Low               |
| Grube, 2017          | High                    | Low                                           | Low                                    | Low                                              | Low                     | Severe                           | Low                        | Moderate          |
| Seeger, 2019         | Moderate                | Low                                           | Low                                    | Low                                              | Severe                 | Low                               | Moderate                   |                   |
| Attizzani, 2020      | High                    | Low                                           | Low                                    | Low                                              | Low                     | Low                               | Moderate                   |                   |
| Kefer, 2020          | Moderate                | Low                                           | Low                                    | Low                                              | Low                     | Low                               | Moderate                   |                   |
| Bernardi, 2021       | Moderate                | Low                                           | Moderate                               | Low                                              | Low                     | Low                               | Moderate                   |                   |
| **30-day mortality** |                         |                                               |                                        |                                                  |                         |                                   |                                          |                   |
| Rashid, 2017         | Moderate                | Low                                           | Low                                    | Low                                              | Low                     | Low                               | Low                        | Low               |
| Grube, 2017          | High                    | Low                                           | Low                                    | Low                                              | Low                     | Low                               | Moderate                   |                   |
| Attizzani, 2020      | High                    | Low                                           | Low                                    | Low                                              | Low                     | Low                               | Moderate                   |                   |
| Bernardi, 2021       | Moderate                | Low                                           | Low                                    | Low                                              | Low                     | Low                               | Moderate                   |                   |
| **30-day stroke**    |                         |                                               |                                        |                                                  |                         |                                   |                                          |                   |
| Rashid, 2017         | Moderate                | Low                                           | Low                                    | Low                                              | Low                     | Low                               | Low                        | Low               |
| Grube, 2017          | High                    | Low                                           | Low                                    | Low                                              | Low                     | Low                               | Moderate                   |                   |
| Attizzani, 2020      | High                    | Low                                           | Low                                    | Low                                              | Low                     | Low                               | Moderate                   |                   |
| Study            | Event Description                                      | High | Low | Low | Low | Low | Low | Moderate |
|------------------|--------------------------------------------------------|------|-----|-----|-----|-----|-----|----------|
| Seeger, 2020     | 30-day major vascular complications                     |      |     |     |     |     |     |          |
| Bernardi, 2021   | 30-day major bleeding                                    |      |     |     |     |     |     |          |
| Rashid, 2017     | 30-day permanent pacemaker implantation                 |      |     |     |     |     |     |          |
| Attizzani, 2020  | 30-day moderate or more paravalvular leak                |      |     |     |     |     |     |          |
| Grube, 2017      | 1-year mortality                                        |      |     |     |     |     |     |          |
| Attizzani, 2020  | 1-year mortality                                        |      |     |     |     |     |     |          |
| Bernardi, 2021   | 1-year mortality                                        |      |     |     |     |     |     |          |