Journal of the American Heart Association

SYSTEMATIC REVIEW AND META-ANALYSIS

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

Francesco Moroni, MD; Lorenzo Azzalini, MD, PhD, MSc; Lars Sondergaard, MD; Guilherme F. Attizzani, MD; Santiago García, MD; Hani Jneid, MD; Mamas A. Mamas, BMBCh, DPhil; Rodrigo Bagur, MD, PhD, FAHA, FSCAI

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]; I^2=0%), stroke (n=4121; OR, 1.09 [95% confidence interval [CI], 0.74–1.62]; I^2=0%), coronary obstruction (n=3000; OR, 2.35 [95% CI, 0.17–33.47]; I^2=75%), major vascular complications (n=3125; OR, 0.92 [95% CI, 0.66–1.33]; I^2=0%), major bleeding (n=3125; OR, 1.13 [95% CI, 0.94–2.01]; I^2=39%), acute kidney injury (n=3495; OR, 1.30 [95% CI, 0.64–2.62]; I^2=44%), and efficacy outcomes: device success (n=1196; OR, 0.77 [95% CI, 0.51–1.14]; I^2=0%), need for a second valve (n=3170; OR, 2.86 [95% CI, 0.96–8.48]; I^2=62%), significant (moderate or higher) paravalvular leak (n=1151; OR, 1.53 [95% CI, 0.83–2.80]; I^2=0%), and permanent pacemaker implantation (n=1908; OR, 1.04 [95% CI, 0.68–1.57]; I^2=58%). One-year mortality was similar between groups (n=1972; OR, 1.00 [95% CI, 0.68–1.47]; I^2=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.

REGISTRATION: URL: https://www.crd.york.ac.uk/prospero/; Unique identifier: CRD42021273715.

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

Correspondence to: Rodrigo Bagur, MD, PhD, University Hospital, London Health Sciences Centre, Western University, 339 Windermere Road, N6A 5A5, London, Ontario, Canada. Email: rodrigobagur@yahoo.com

This article was sent to John S. Ikonomidis, MD, PhD, Guest Editor, for review by expert referees, editorial decision, and final disposition.

Supplemental Material for this article is available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.121.024707

For Sources of Funding and Disclosures, see page 15.

JAHA is available at: www.ahajournals.org/journal/jaha

CLINICAL PERSPECTIVE

What Is New?

- Among the features of new-generation of transcatheter aortic valves, there is the possibility of resheathing and repositioning of the bioprosthesis to improve its positioning and final deployment.
- The resheathing and repositioning maneuvers may increase the risk of adverse events caused by prolonged catheter manipulation in the ascending aorta and aortic valve complex.
- The present systematic review and meta-analysis suggest that the use of the resheathing feature during transcatheter aortic valve implantation is not associated with an increased risk of periprocedural adverse events.

What Are the Clinical Implications?

- While the present systematic provide reassurance, further studies are needed to assess the role of multiple resheathing, and alternative technical strategies are to be explored when resheathing appears to be ineffective in obtaining an optimal result.

Nonstandard Abbreviations and Acronyms

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

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

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 statement[9] (Figure 1 and Table S2). The protocol for this systematic review and meta-analysis protocol was registered on the international prospective register of

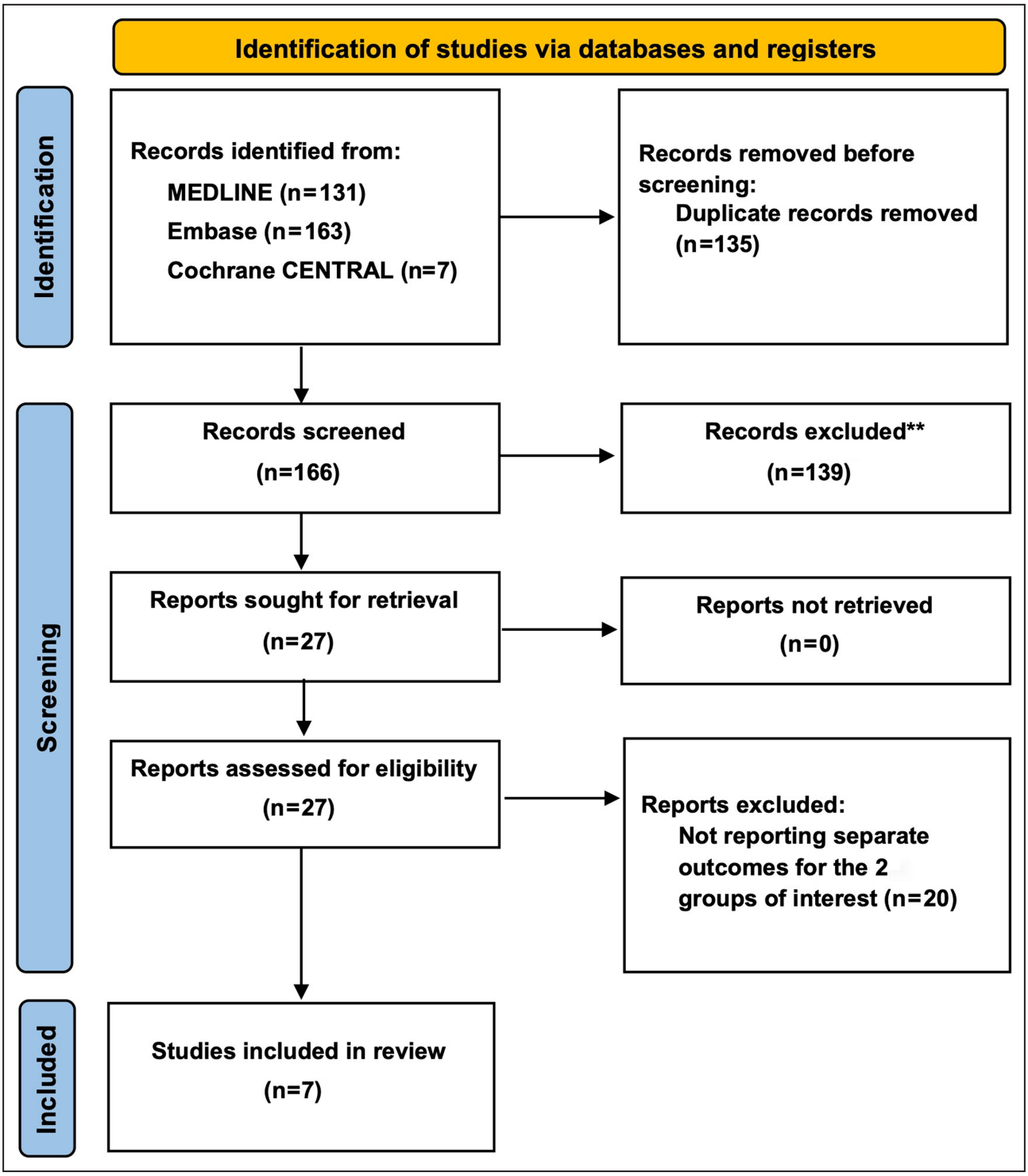

Figure 1. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram.
Flow diagram based on 2020 PRISMA version.

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) tool[10] 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 (I^2) and a result of I^2 <25%, I^2 25% to 50%, I^2 50% to 75%, and I^2 >75% indicate low, 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 studies[6,7,14–18] 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 studies[16,18] 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 study[14] 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 studies[7,17] 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.

Table 1. Baseline Characteristics of the Studies

Author, year	No.	Valve type	Arm	Age, y	Women	STS score	Transfemoral	Previous pacemaker	LVEF	Diabetes	COPD	PAD
Rashid, 2017[15]	125	Lotus	NR (49) Resheathing (76 [61%])	83.0±5.8 84.2±6.1	32 (65) 37 (49)	5.6±2.5 4.8±2.7	49 (100) 76 (100)	5 (10) 7 (9.2)	59.2±12.4 56.5±13.7	11 (22) 15 (20)	13 (27) 16 (21)	3 (6.1) 6 (7.9)
Grube, 2017[14]	1038	Evolut R	NR (763) Resheathing (265 [26%])	81.8±6.2	674 (65)	5.5±4.5	748 (98) 259 (98)	124 (12)	60.6±12.0	310 (30)	267 (26)	236 (23)
Seeger, 2019[6]	200	Evolut R/PRO-Lotus-SAPIEN 3	NR (177) Resheathing (23 [12%])	80.5±6.2 81.3±6.3	96 (54) 12 (52)	5.9±4.6 5.4±2.8	177 (100) 23 (100)	NA	NA	56 (32) 6 (26)	94 (53) 12 (52)	NA
Attizzani, 2020[7]	946	Evolut R/PRO	NR (628) Resheathing (318 [34%])	75.8±6.4 74.6±6.0	280 (45) 122 (38)	2.6±1.4 2.3±1.3	615 (98) 312 (98)	27 (4.3) 9 (2.8)	64.9±7.8 64.45±7.9	200 (32) 107 (34)	144 (24) 64 (21)	79 (13) 35 (11)
Kefer, 2020[16]	170	Evolut R-Portico	NR (131) Resheathing (39 [23%])	83.0±8.0 84.0±6.0	73 (56) 23 (59)	6.2±6.4 5.3±2.6	131 (100) 39 (100)	NA	59.0±12 66.0±10	23 (17) 7 (18)	16 (12) 7 (18)	19 (14) 4 (10)
Seeger, 2020[17]	996	Lotus	NR (683) Resheathing (313 [31%])	80.9±6.3 80.5±7.0	355 (52) 151 (48)	5.6±6.0 6.8±8.3	683 (100) 313 (100)	91 (13) 41 (13)	NA	155 (23) 68 (22)	NA	NA
Bernardi, 2021[18]	1026	Evolut R/PRO-Portico	NR (686) SR (245 [24%]) MR (95 [9%])	80.8±7.5 81.6±6.5 81.6±7.1	382 (56) 146 (60) 46 (48)	4.9±2.9 4.8±2.9 4.9±2.8	608 (89) 223 (91) 87 (92)	98 (15) 29 (12) 14 (15)	56.0±13 56.2±12 55.8±12	221 (32) 91 (37) 34 (36)	161 (24) 43 (18) 12 (13)	118 (17) 51 (21) 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.

Study Outcomes

Safety Outcomes

The incidence of 30-day mortality was reported in 4 studies,[7,14,15,18] which included 3125 patients. There was no statistically significant difference in effect estimates for patients who required resheathing/repositioning during TAVI 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]; I^2=0%). The incidence of 30-day stroke was reported in 5 studies,[7,14,15,17,18] which included 4121 patients. At 30 days, stroke occurred in 41 of 1312 (3.1%) patients who required valve resheathing/repositioning and in 79 of 2809 (2.8%) patients who did not (OR, 1.09 [95% CI, 0.74–1.62]; I^2=0%). Coronary obstruction was reported in 3 studies,[7,14,18] with one study[14] reporting no events. No significant difference was detected between the resheathing and the no-resheathing groups (OR, 2.35[95% CI, 0.17–33.47]), although these studies pulled their point estimates in different directions, leading to a marked imprecision around the CIs and, thus, a high degree (I^2=75%) of heterogeneity. Four studies[7,14,15,18] reported on the rate of both major vascular complications and bleeding events. No differences in effect estimates were observed between the resheathing group and the no-resheathing group (OR, 0.92 [95% CI, 0.66–1.33]; I^2=0%; OR, 1.13 [95% CI, 0.94–2.01]; I^2=39%, respectively). AKI was reported in 6 studies,[6,7,14–16,18] including a total of 3495 patients, and no significant difference in effect estimates was found between the 2 groups (OR, 1.30 [95% CI, 0.64–2.62]; I^2=44%) (Figure 2).

Efficacy Outcomes

Two studies[16,18] including 1196 patients reported on device success, and no statistically significant difference was found between the resheathing and the non-resheathing groups (OR, 0.77 [95% CI, 0.51–1.14]; I^2=0%). Four studies[7,14,16,18] reported on the need for >1 valve during the procedure. Importantly, although not statistically significant, procedures in which resheathing/repositioning was required were associated with almost a 3-fold increased risk of needing a second valve (OR, 2.86 [95% CI, 0.96–8.48]), yet with a substantial degree (I^2=62%) of heterogeneity. Three studies[7,15,18] reported on new PPI at 30 days, and no significant difference was detected between the 2 groups (OR, 1.04 [95% CI, 0.68–1.57]; I^2=58%). Two studies[15,18] reported on the incidence of moderate/severe paravalvular leak, and no significant difference was found between the groups (OR, 1.53 [95% CI, 0.83–2.80]; I^2=0%).

Secondary Outcome

Two studies[7,18] reported on 1-year mortality, and there was no significant difference between the

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[15]	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	AKI	7/49 (14.0)	9/76 (12.0)
			Tamponade	3/49 (6.1)	2/76 (2.6)
			Myocardial infarction	1/49 (2.0)	1/76 (1.3)
			30-d mortality	2/49 (4.0)	1/76 (1.3)
			30-d stroke	3/49 (6.1)	4/76 (5.2)
			30-d major vascular complication	7/49 (14.0)	7/76 (9.2)
			30-d major bleeding	7/49 (14.0)	11/76 (14.0)
			30-d permanent pacemaker implantation	15/44 (34.0)	13/69 (19.0)
			30-d moderate or higher paravalvular leakage	1/45 (2.0)	2/76 (2.6)
Grube, 2017[14]	No resheathing Local anesthesia 520/763 (68) Resheathing Local anesthesia 152/265 (57)	30 d	Need for >1 valve	5/763 (0.6)	5/265 (1.8)
			AKI	8/763 (1.0)	2/265 (0.7)
			Coronary obstruction	0/763 (0.0)	0/265 (0.0)
			30-d mortality	14/763 (1.8)	5/265 (1.8)
			30-d stroke	22/763 (2.8)	7/265 (2.6)
			30-d major vascular complication	46/763 (6.0)	17/265 (6.4)
			30-d major bleeding	26/763 (3.4)	4/265 (1.5)
Seeger, 2019[6]	No resheathing Fluoroscopy time 1137±368 s Contrast media 85±35 mL Resheathing Fluoroscopy time 1195±368 s Contrast media 139±181 mL	In-hospital	AKI	3/177 (1.7)	2/23 (8.6)
			Stroke	5/177 (2.8)	0/23 (0.0)
Attizzani, 2020[7]	No resheathing General anesthesia 345/628 (55) Procedural time 147±52 min Resheathing General anesthesia 177/318 (56) Procedural time 151±56 min	30 d and 1 y	Need for >1 valve	8/628 (1.3)	5/318 (1.5)
			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)	59/309 (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[16]	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	Device success	128/131 (98.0)	39/39 (100.0)
			Need for >1 valve	2/131 (1.5)	1/39 (2.5)
			AKI	4/131 (3.0)	0/39 (0.0)
			Myocardial infarction	0/131 (0.0)	0/39 (0.0)
			Stroke	1/131 (0.7)	1/39 (2.5)
			Major vascular complications	2/131 (1.4)	0/39 (0.0)
			Major bleeding	3/131 (2.2)	2/39 (5.1)
			Permanent pacemaker implantation	21/131 (16.0)	10/39 (26.0)

(*Continued*)

Table 2. Continued

Author, year	Procedural characteristics, n/N (%)	Time frame of assessment	Outcome	No resheathing, n/N (%)	Resheathing, n/N (%)
Seeger, 2020[17]	NA	In-hospital and 30 d	In-hospital stroke	21/683 (7.9)	10/313 (3.2)
			30-d stroke	21/683 (7.9)	11/313 (3.3)
Bernardi, 2021[18]	No resheathing Conscious sedation 417/686 (61) Valve-in-valve 59/686 (8.6) Resheathing Conscious sedation 167/340 (49) Valve-in-valve 40/340 (12)	Procedural, 30 d and 1 y	Device success	617/686 (90.0)	296/340 (87.0)
			Procedural mortality	21/686 (3.0)	8/340 (2.3)
			Need for >1 valve	4/686 (0.5)	19/340 (5.6)
			AKI	42/686 (6.1)	19/340 (5.6)
			Coronary obstruction	6/686 (0.8)	2/340 (0.5)
			30-d mortality	25/686 (3.6)	11/340 (3.2)
			30-d stroke	18/686 (2.6)	6/340 (1.7)
			30-d vascular complication	37/686 (5.4)	19/340 (5.6)
			30-d bleeding	24/686 (3.5)	18/340 (5.3)
			30-d new-onset conduction abnormality	111/686 (16.0)	81/340 (24.0)
			30-d permanent pacemaker implantation	96/588 (16.0)	58/297 (19.0)
			30-d moderate or higher paravalvular leakage	24/686 (3.5)	18/340 (5.2)
			1-y mortality	65/587 (11.0)	27/250 (11.0)

AKI indicates acute kidney injury; NA, not available; and TEE, transesophageal echocardiography.

no-resheathing and the resheathing groups (OR, 1.00 [95% CI, 0.68–1.47]; I^2=0%). Figure 3 shows the forest plots for the efficacy and secondary analyses.

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[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		
Studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other Considerations	No Resheathing	Resheathing	Relative OR (95% CI)	Absolute with 95% CI	Certainty
30-d mortality											
Attizzani, 2020[7] Bernardi, 2021[18] Grube, 2017[14] Rashid, 2017[15]	One trial subanalysis, 2 observational prospective, 1 retrospective	Very serious*	Serious*	Serious†	Not serious	Residual confounding may have a significant influence on the observed direction of effect	43/2126	15/999	0.74 (0.41–1.33)	5 fewer per 1000 (from 14 fewer to 5 more)	+OOO Very low
30-d stroke											
Attizzani 2020[7] Bernardi 2021[18] Grube 2017[14] Rashid 2017[15] Seeger 2020[17]	One trial subanalysis, 3 observational prospective, one retrospective	Very serious*	Serious*	Serious†	Not serious		79/2809	41/1312	1.09 (0.74–1.62)	3 more per 1000 (from 14 fewer to 8 more)	+OOO Very low
Coronary obstruction											
Attizzani 2020[7] Bernardi 2021[18] Grube 2017[14]	One trial subanalysis, 1 observational prospective, 1 retrospective	Very serious*	Serious*	Serious†	Very serious‖	Extremely rare event––one study reporting no events at all	7/2077 (0.3)	7/923 (0.7)	2.35 (0.17–33.47)	4 more per 1000 (from 2 less to 10 more)	+OOO Very low
30-d major vascular complications											
Attizzani 2020[7] Bernardi 2021[18] Grube 2017[14] Rashid 2017[15]	One trial subanalysis, 2 observational prospective, 1 retrospective	Very serious*	Serious*	Serious†	Not serious		115/2126	52/999	0.92 (0.66–1.30)	2 fewer per 1000 (from 18 fewer to 14 more)	+OOO Very low
30-d major bleeding											
Attizzani 2020[7] Bernardi 2021[18] Grube 2017[14] Rashid 2017[15]	One trial subanalysis, 2 observational prospective, 1 retrospective	Very serious*	Serious*	Serious†	Not serious		66/2126	41/999	1.13 (0.64–2.01)	9 more per 1000 (from 5 fewer to 24 more)	+OOO Very low
AKI											
Attizzani 2020[7] Bernardi 2021[18] Grube 2017[14] Kefer 2020[16] Rashid 2017[15] Seeger 2019[6]	1 trial subanalysis, 4 observational prospective, 1 retrospective	Very serious*	Serious*	Very serious‡	Not serious	Concerns for non-uniform definition of the outcome	67/2434	39/1061	1.30 (0.64–2.62)	9 more per 1000 (from 4 fewer to 22 more)	+OOO Very low

(*Continued*)

Table 3. Continued

Certainty assessment							Patient n/N (%)		Effect		
Studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other Considerations	No Resheathing	Resheathing	Relative OR (95% CI)	Absolute with 95% CI	Certainty
Device success											
Kefer 2020[16] Bernardi 2021[18]	1 observational prospective, 1 retrospectiv	Serious*	Not serious	Serious†	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[7] Bernardi 2021[18] Grube 2017[14] Kefer 2020[16]	1 trial sub-analysis, 2 observational prospective, 1 retrospective	Very serious*	Serious*	Serious†	Serious§		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[18] Rashid 2017[15]	1 observational prospective, 1 retrospective	Very serious*	Serious*	Serious†	Not serious	Residual confounding may have a significant influence on the observed direction of effect	25/735	20/416	1.53 (0.83–2.80)	14 more per 1000 (from 10 fewer to 38 more)	+OOO Very low
30-d permanent pacemaker implantation											
Attizzani 2020[7] Bernardi 2021[18] Rashid 2017[15]	1 trial sub-analysis, 1 observational prospective, 1 retrospective	Very serious-	Serious*	Serious†	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[7] Bernardi 2021[18]	1 trial sub-analysis, 1 retrospective	Very serious*	Serious*	Serious†	Not serious	Residual confounding may have a significant influence on the observed direction of effect	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.
†Large variation of point estimates and significant heterogeneity.
‡Multiple valve types, imbalance of valve type between cases and controls.
§Concern for heterogeneity in outcome definition.
‖Small number of events, large CI, which crosses neutrality.
¶Rare events.

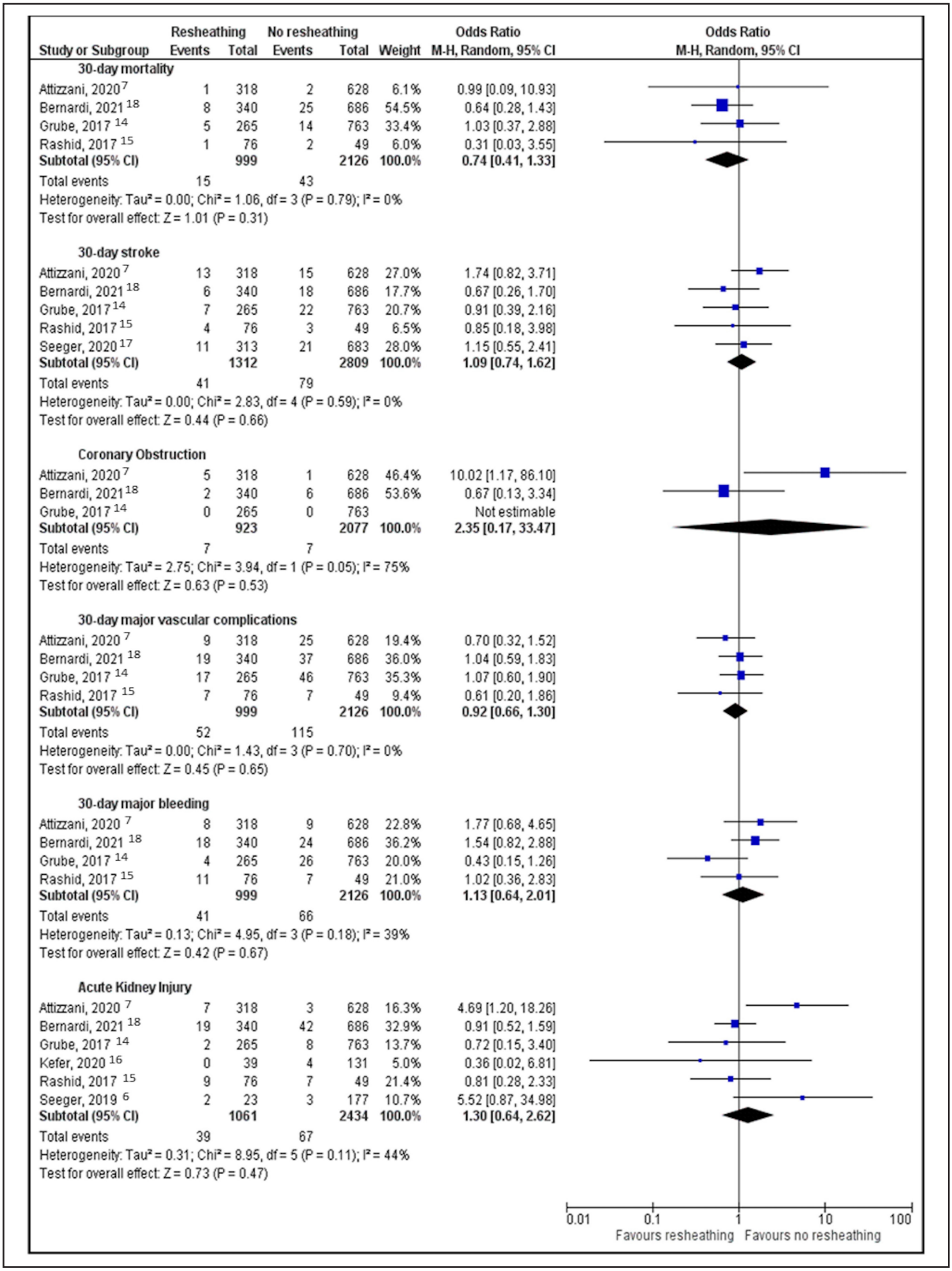

Figure 2. Forest plots of pooled treatment effect estimates for safety outcomes in patients undergoing transcatheter aortic valve implantation requiring resheathing/repositioning versus not requiring it.
M-H indicates Mantel-Haenszel.

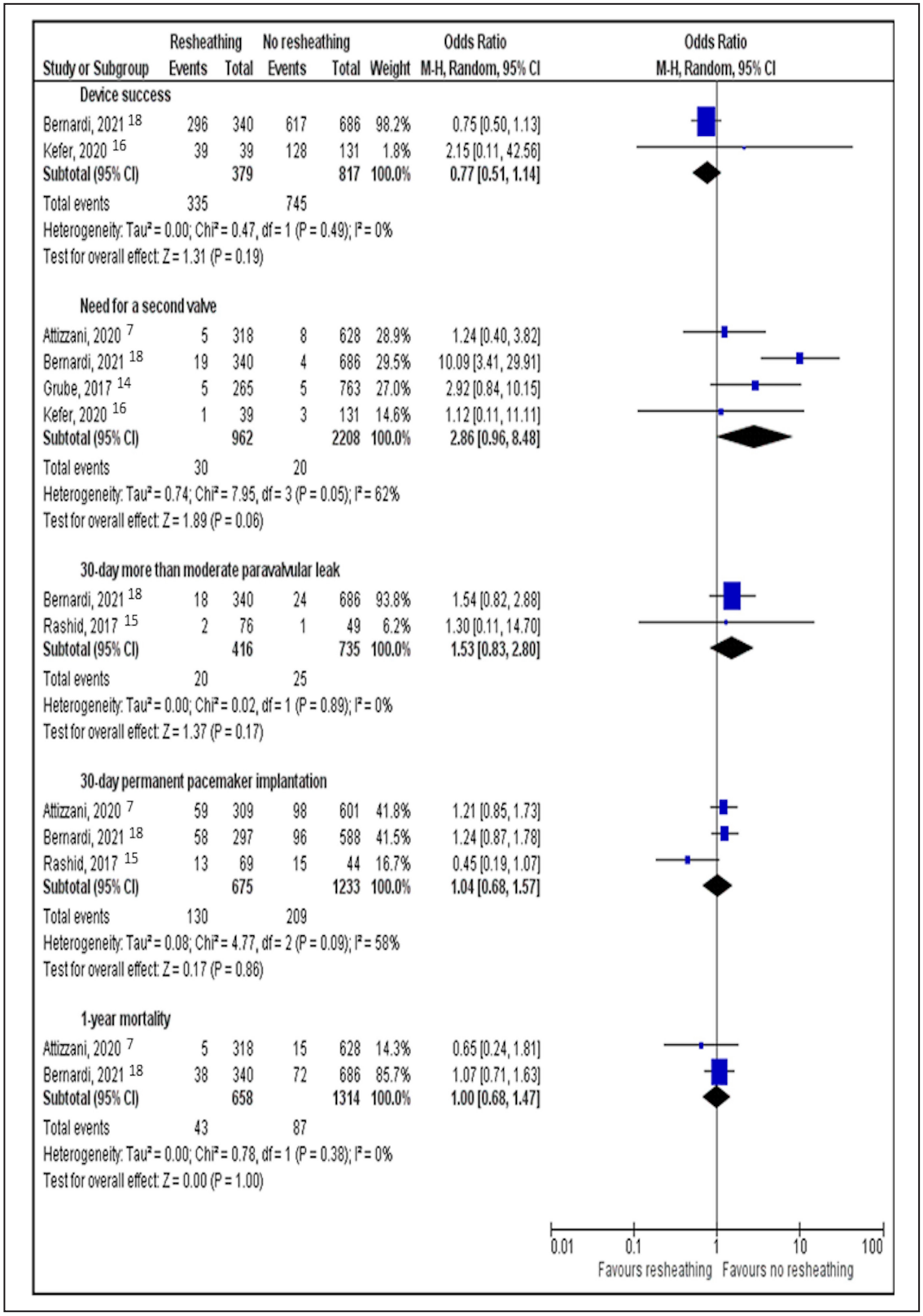

Figure 3. Forest plots of pooled treatment effect estimates for efficacy and secondary outcomes in patients undergoing transcatheter aortic valve implantation requiring resheathing/repositioning versus not requiring it.
M-H indicates Mantel-Haenszel.

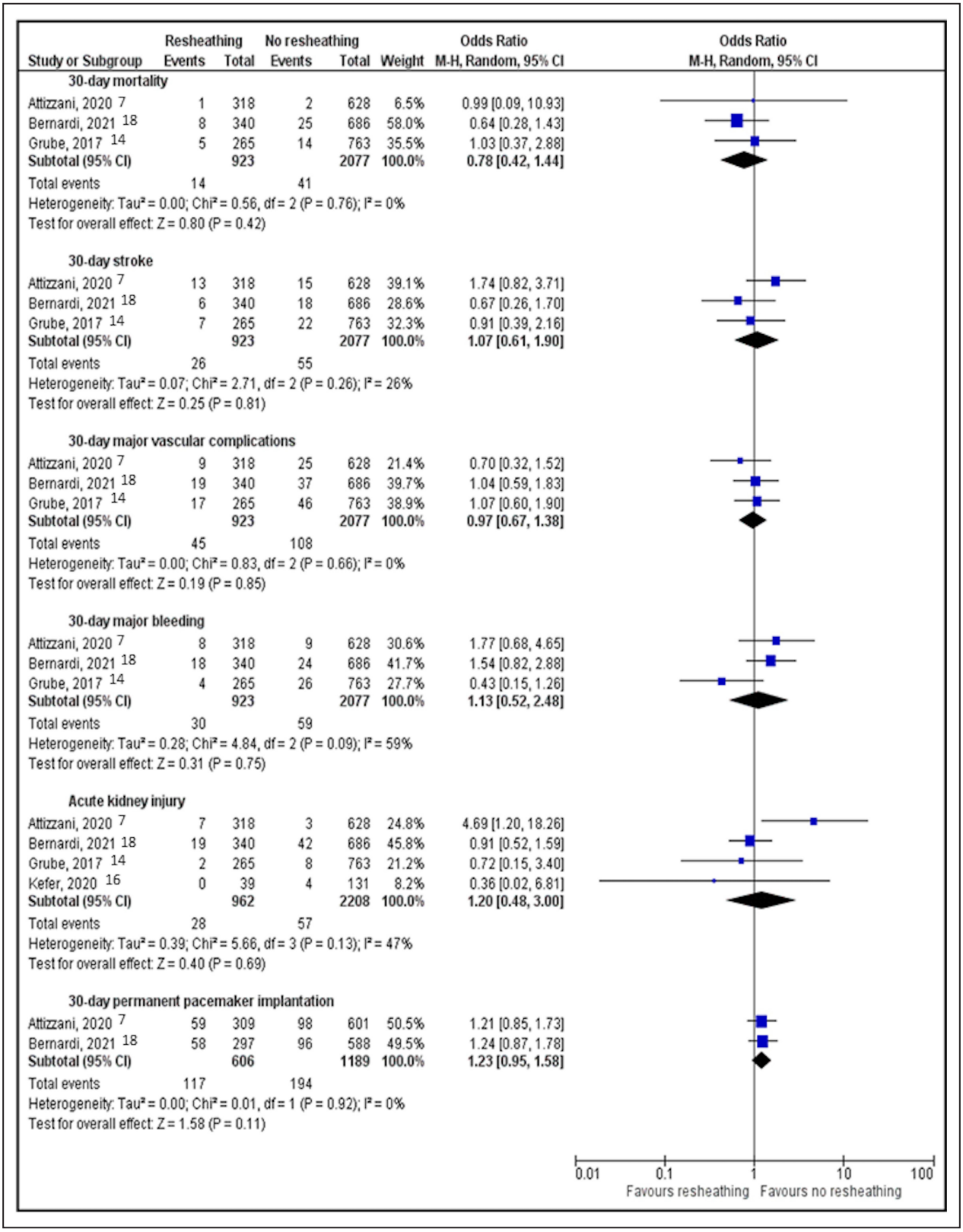

Figure 4. Sensitivity analysis evaluating the cumulative risk of outcomes by excluding mechanically and balloon-expandable transcatheter heart valves.
M-H indicates Mantel-Haenszel.

Table 4. Sensitivity Analysis for Clinical Outcomes Comparing No Resheathing Versus Single and Multiple Resheathing Using Network Meta-Analysis

Outcome	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.

studied in randomized controlled trials; therefore, our study represents a critical appraisal of the available evidence.

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[7,14,21] and 33% to 44% of patients with the Portico device.[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[7] showed that the time spent with the delivery system in the body was significantly longer for

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.[6,16]

Seeger et al[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[6] or in any of the individual studies analyzed in the present work.[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,[7,14,18] and this is consistent with the lower final implantation depth of the THV,[7,14] resulting in direct interaction of the THV with the conduction system.[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^2=58%). Therefore, we performed sensitivity analysis limited to 2 studies[7,15] using self-expanding THVs (excluding the Lotus valve) and the results did not show statistical significance.

Seeger[6] and Kefer[16] and colleagues found that patients undergoing resheathing/repositioning required a higher volume of contrast during TAVI. In this regard, Seeger[6] and Attizzani[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 repositiong 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 us 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[17] reported a higher preprocedural risk as assessed by the STS score among patients requiring resheathing. Moreover, Kefer and colleagues[16] reported a higher proportion of patients with porcelain aorta, which has been, per se, associated with worse outcomes after TAVI,[24] yet this variable is not included in the STS score. In this regard, while Kefer and colleagues[16] did not find the need for resheathing as a variable associated with adverse events, Bernardi et al[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.[25–27]

Bernardi et al[18] 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,[28] baseline patient complexity, suboptimal result of the intervention, or periprocedural complications that ultimately impact mortality.[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.[18] 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,[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."[29]

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 reposition 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

Received November 14, 2021; accepted April 13, 2022.

Affiliations

Division of Cardiology, Pauley Heart Center, Virginia Commonwealth University, Richmond, VA (F.M.); Division of Cardiology, Department of Medicine, University of Washington, Seattle, WA (L.A.); The Heart Centre, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark (L.S.); Harrington Heart and Vascular Institute, University Hospitals Cleveland Medical Center, Cleveland, OH (G.F.A.); The Carl and Edyth Lindner Center for Research and Education, The Christ Hospital, Cincinnati, OH (S.G.); Division of Cardiology, Baylor School of Medicine and the Michael E. DeBakey VAMC, Houston, TX (H.J.); Keele Cardiovascular Research Group, Centre for Prognosis Research, Institute of Primary Care and Health Sciences, Keele University, Stoke-on-Trent, United Kingdom (M.A.M., R.B.); and Department of Epidemiology and Biostatistics, Schulich School of Medicine & Dentistry, Western University, London, Ontario, Canada (R.B.).

Sources of Funding

None.

Disclosures

None.

Supplemental Material

Tables S1–S3

REFERENCES

1. Solomonica A, Choudhury T, Bagur R. The mechanically expandable lotus valve and lotus edge transcatheter aortic valve systems. *Expert Rev Med Devices*. 2018;15:763–769. doi: 10.1080/17434440.2018.1536543
2. Søndergaard L, Rodés-Cabau J, Hans-Peter Linke A, Fichtlscherer S, Schäfer U, Kuck KH, Kempfert J, Arzamendi D, Bedogni F, Asch FM, et al. Transcatheter aortic valve replacement with a repositionable self-expanding prosthesis: the PORTICO-I trial 1-year outcomes. *J Am Coll Cardiol*. 2018;72:2859–2867. doi: 10.1016/j.jacc.2018.09.014
3. Choudhury T, Solomonica A, Bagur R. The Evolut R and Evolut PRO transcatheter aortic valve systems. *Expert Rev Med Devices*. 2019;16:3–9. doi: 10.1080/17434440.2019.1557045
4. Forrest JK, Kaple RK, Tang GH, Yakubov SJ, Nazif TM, Williams MR, Zhang A, Popma JJ, Reardon MJ. Three generations of self-expanding transcatheter aortic valves: a report from the STS/ACC TVT registry. *JACC Cardiovasc Interv*. 2020;13:170–179. doi: 10.1016/j.jcin.2019.08.035
5. Fontana GP, Bedogni F, Groh M, Smith D, Chehab BM, Garrett HE Jr, Yong G, Worthley S, Manoharan G, Walton A, et al. Safety profile of an intra-annular self-expanding transcatheter aortic valve and next-generation low-profile delivery system. *JACC Cardiovasc Interv*. 2020;13:2467–2478. doi: 10.1016/j.jcin.2020.06.041
6. Seeger J, Romero M, Schuh C, Virmani R, Wöhrle J. Impact of repositioning during transcatheter aortic valve replacement on embolized debris. *J Invasive Cardiol*. 2019;31:282–288.
7. Attizzani GF, Dallan LA, Markowitz A, Yakubov SJ, Deeb GM, Reardon MJ, Forrest JK, Mangi AA, Huang J, Popma JJ. Impact of repositioning on outcomes following transcatheter aortic valve replacement with a self-expandable valve. *JACC Cardiovasc Interv*. 2020;13:1816–1824. doi: 10.1016/j.jcin.2020.04.028
8. Kappetein AP, Head SJ, Genereux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document (VARC-2). *Eur J Cardiothorac Surg*. 2012;42:S45–S60. doi: 10.1093/ejcts/ezs533
9. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71. doi: 10.1136/bmj.n71
10. Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*. 2016;355:i4919. doi: 10.1136/bmj.i4919
11. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ. Grade: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*. 2008;336:924–926. doi: 10.1136/bmj.39489.470347.AD
12. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003;327:557–560. doi: 10.1136/bmj.327.7414.557
13. Gagnier JJ, Morgenstern H, Altman DG, Berlin J, Chang S, McCulloch P, Sun X, Moher D. Ann Arbor Clinical Heterogeneity Consensus G. Consensus-based recommendations for investigating clinical heterogeneity in systematic reviews. *BMC Med Res Methodol*. 2013;13:106. doi: 10.1186/1471-2288-13-106
14. Grube E, Van Mieghem NM, Bleiziffer S, Modine T, Bosmans J, Manoharan G, Linke A, Scholtz W, Tchetche D, et al. Clinical outcomes

with a repositionable self-expanding transcatheter aortic valve prosthesis: the international forward study. *J Am Coll Cardiol*. 2017;70:845–853. doi: 10.1016/j.jacc.2017.06.045
15. Rashid HN, Gooley R, McCormick L, Zaman S, Ramkumar S, Jackson D, Amiruddin A, Nasis A, Cameron J, Meredith IT. Safety and efficacy of valve repositioning during transcatheter aortic valve replacement with the lotus valve system. *J Cardiol*. 2017;70:55–61. doi: 10.1016/j.jjcc.2016.11.002
16. Kefer J, Maes F, Renkin J, Kautbally S, De Meester C, Delacour M, Pouleur AC. Resheathing of self-expanding bioprosthesis: impact on procedural results, clinical outcome and prosthetic valve durability after transcatheter aortic valve implantation. *Int J Cardiol Heart Vasc*. 2020;26:100462. doi: 10.1016/j.ijcha.2019.100462
17. Seeger J, Falk V, Hildick-Smith D, Bleiziffer S, Blackman DJ, Abdel-Wahab M, Allocco DJ, Meredith IT, Wöhrle J, Van Mieghem NM. Insights on embolic protection, repositioning, and stroke: a subanalysis of the respond study. *J Interv Cardiol*. 2020;2020:3070427. doi: 10.1155/2020/3070427
18. Bernardi FL, Rodés-Cabau J, Tirado-Conte G, Amat Santos IJ, Plachtzik C, Cura F, Sztejfman M, Mangione FM, Tumeleiro R, Esteves VB, et al. Incidence, predictor and clinical outcomes of multiple resheathing with self-expanding valves during transcatheter aortic valve replacement. *J Am Heart Assoc*. 2021;10:e020682. doi: 10.1161/JAHA.120.020682
19. Sirker A, Kwok CS, Kotronias R, Bagur R, Bertrand O, Butler R, Berry C, Nolan J, Oldroyd K, Mamas MA. Influence of access site choice for cardiac catheterization on risk of adverse neurological events: a systematic review and meta-analysis. *Am Heart J*. 2016;181:107–119. doi: 10.1016/j.ahj.2016.06.027
20. Page M, Higgins J, Sterne J. Chapter 13: Assessing risk of bias due to missing results in a synthesis. In: Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, eds. *Cochrane Handbook for Systematic Reviews of Interventions version 6.2 (updated February 2021)*. Cochrane, 2021: Available from www.training.cochrane.org/handbook. Accessed August 15, 2021
21. Forrest JK, Mangi AA, Popma JJ, Khabbaz K, Reardon MJ, Kleiman NS, Yakubov SJ, Watson D, Kodali S, George I, et al. Early outcomes with the Evolut PRO repositionable self-expanding transcatheter aortic valve with pericardial wrap. *JACC Cardiovasc Interv*. 2018;11:160–168. doi: 10.1016/j.jcin.2017.10.014
22. Mollmann H, Linke A, Holzhey DM, Walther T, Manoharan G, Schafer U, Heinz-Kuck K, Van Boven AJ, Redwood SR, Kovac J, et al. Implantation and 30-day follow-up on all 4 valve sizes within the portico transcatheter aortic bioprosthetic family. *JACC Cardiovasc Interv*. 2017;10:1538–1547. doi: 10.1016/j.jcin.2017.05.021
23. Bagur R, Rodés-Cabau J, Gurvitch R, Dumont É, Velianou JL, Manazzoni J, Toggweiler S, Cheung A, Ye J, Natarajan MK, et al. Need for permanent pacemaker as a complication of transcatheter aortic valve implantation and surgical aortic valve replacement in elderly patients with severe aortic stenosis and similar baseline electrocardiographic findings. *JACC: Cardiovasc Interv*. 2012;5:540–551. doi: 10.1016/j.jcin.2012.03.004
24. Zahn R, Schiele R, Gerckens U, Linke A, Sievert H, Kahlert P, Hambrecht R, Sack S, Abdel-Wahab M, Hoffmann E, et al. Transcatheter aortic valve implantation in patients with "porcelain" aorta (from a multicenter real world registry). *Am J Cardiol*. 2013;111:602–608. doi: 10.1016/j.amjcard.2012.11.004
25. Chen LY, Chung MK, Allen LA, Ezekowitz M, Furie KL, McCabe P, Noseworthy PA, Perez MV, Turakhia MP. American Heart Association Council on Clinical C, Council on C, Stroke N, Council on Quality of C, Outcomes R, Stroke C. Atrial fibrillation burden: moving beyond atrial fibrillation as a binary entity: a scientific statement from the American Heart Association. *Circulation*. 2018;137:e623–e644. doi: 10.1161/CIR.0000000000000568
26. Overtchouk P, Guedeney P, Rouanet S, Verhoye JP, Lefevre T, Van Belle E, Eltchaninoff H, Gilard M, Leprince P, Iung B, et al. Long-term mortality and early valve dysfunction according to anticoagulation use: the France TAVI registry. *J Am Coll Cardiol*. 2019;73:13–21. doi: t10.1016/j.jacc.2018.08.1045
27. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, Kamel H, Kernan WN, Kittner SJ, Leira EC, et al. 2021 guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/American Stroke Association. *Stroke*. 2021;52:e364–e467. doi: 10.1161/STR.0000000000000375
28. Bagur R, Martin GP, Nombela-Franco L, Doshi SN, George S, Toggweiler S, Sponga S, Cotton JM, Khogali SS, Ratib K, et al. Association of comorbid burden with clinical outcomes after transcatheter aortic valve implantation. *Heart*. 2018;104:2058–2066. doi: 10.1136/heartjnl-2018-313356
29. Bagur R. Resheathing and repositioning during transcatheter aortic valve implantation. *J Am Heart Assoc*. 2021;10:e022933. doi: 10.1161/JAHA.121.022933
30. Thiele H, Kurz T, Feistritzer HJ, Stachel G, Hartung P, Eitel I, Marquetand C, Nef H, Doerr O, Lauten A, et al. Comparison of newer generation self-expandable vs. Balloon-expandable valves in transcatheter aortic valve implantation: the randomized SOLVE-TAVI trial. *Eur Heart J*. 2020;41:1890–1899. doi: 10.1093/eurheartj/ehaa036

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)

Table S2. PRISMA 2020 Checklist.

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 7
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 7
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 8
Information sources	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
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 7; Supplementary Table 1
Selection process	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
Data collection process	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
Data items	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
Study risk of bias assessment	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
Effect measures	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.	-
	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	Page 9

Section and Topic	Item #	Checklist item	Location where item is reported
		model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	
	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
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 9
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 9
RESULTS			
Study selection	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.	-
Study characteristics	17	Cite each included study and present its characteristics.	Page 9; Table 1 and 2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Pages 10-11; Supplemental Table 2
Results of individual studies	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
Results of syntheses	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
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	-
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Table 3
DISCUSSION			
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			
Registration and protocol	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

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	Low	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	Low	Low	Moderate
Bernardi, 2021	Moderate	Low	Moderate	Low	Low	Low	Low	Low
Acute kidney injury								
Rashid, 2017	Moderate	Low	Low	Low	Low	Low	Low	Low
Grube, 2017	High	Low	Low	Low	Low	Low	Low	Moderate
Seeger, 2019	Moderate	Low	Low	Low	Low	Severe	Low	Moderate
Attizzani, 2020	High	Low	Low	Low	Low	Low	Low	Moderate
Kefer, 2020	Moderate	Low	Low	Low	Low	Low	Low	Low
Bernardi, 2021	Moderate	Low	Moderate	Low	Low	Low	Low	Low
30-day mortality								
Rashid, 2017	Moderate	Low	Low	Low	Low	Low	Low	Low
Grube, 2017	High	Low	Low	Low	Low	Low	Low	Moderate
Attizzani, 2020	High	Low	Low	Low	Low	Low	Low	Moderate
Bernardi, 2021	Moderate	Low	Low	Low	Low	Low	Low	Low
30-day stroke								
Rashid, 2017	Moderate	Low	Low	Low	Low	Low	Low	Low
Grube, 2017	High	Low	Low	Low	Low	Low	Low	Moderate
Attizzani, 2020	High	Low	Low	Low	Low	Low	Low	Moderate

Seeger, 2020	High	Low	Low	Low	Low	Low	Low	Moderate
Bernardi, 2021	Moderate	Low	Low	Low	Low	Low	Low	Low
30-day major vascular complications								
Rashid, 2017	Moderate	Low	Low	Low	Low	Low	Low	Low
Grube, 2017	High	Low	Low	Low	Low	Low	Low	Moderate
Attizzani, 2020	High	Low	Low	Low	Low	Low	Low	Moderate
Bernardi, 2021	Moderate	Low	Low	Low	Low	Low	Low	Low
30-day major bleeding								
Rashid, 2017	Moderate	Low	Low	Low	Low	Low	Low	Low
Grube, 2017	High	Low	Low	Low	Low	Low	Low	Moderate
Attizzani, 2020	High	Low	Low	Low	Low	Low	Low	Moderate
Bernardi, 2021	Moderate	Low	Low	Low	Low	Low	Low	Low
30-day permanent pacemaker implantation								
Rashid, 2017	Moderate	Low	Low	Low	Low	Low	Low	Low
Attizzani, 2020	High	Low	Low	Low	Low	Low	Low	Moderate
Bernardi, 2021	Moderate	Low	Low	Low	Low	Low	Low	Low
30-day moderate or more paravalvular leak								
Rashid, 2017	Moderate	Low	Low	Low	Low	Low	Low	Low
Bernardi, 2021	Moderate	Low	Low	Low	Low	Low	Low	Low
1-year mortality								
Attizzani, 2020	High	Low	Low	Low	Low	Low	Low	Moderate
Bernardi, 2021	Moderate	Low	Low	Low	Low	Low	Low	Low