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Meta-analysis

Outcomes of Transcatheter Aortic Valve Replacement Using Third-Generation Balloon-Expandable Versus Self-Expanding Valves: A Meta-analysis

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ABSTRACT

Background: The choice of transcatheter aortic valve replacement (TAVR) prosthesis is crucial in optimizing short- and long-term outcomes. The objective of this study was to conduct a meta-analysis comparing outcomes of third-generation balloon-expandable valves (BEV) vs self-expanding valves (SEV).

Methods: Electronic databases were searched from inception to June 2023 for studies comparing third-generation BEV vs SEV. Primary outcome was all-cause mortality. Secondary outcomes included clinical and hemodynamic end points. Random-effects models were used to calculate pooled odds ratios (ORs) or weighted mean differences (WMDs).

Results: The meta-analysis included 16 studies and 10,174 patients (BEV, 5753 and SEV, 4421). There were no significant differences in 1-year all-cause mortality (OR, 1.15; 95% CI, 0.89-1.48) between third-generation BEV vs SEV. TAVR with third generation BEV was associated with a significantly lower risk of TIA/stroke (OR, 0.62; 95% CI, 0.44-0.87), permanent pacemaker implantation (OR, 0.55; 95% CI, 0.44-0.70), and ≥moderate paravalvular leak (PVL, OR, 0.43; 95% CI, 0.25-0.75), and higher risk of ≥moderate patient-prosthesis mismatch (OR, 3.76; 95% CI, 2.33-6.05), higher mean gradient (WMD, 4.35; 95% CI, 3.63-5.08), and smaller effective orifice area (WMD, −0.30; 95% CI, −0.37 to −0.23), compared with SEV.

Conclusion: In this meta-analysis, TAVR with third-generation BEV vs SEV was associated with similar all-cause mortality, lower risk of TIA/stroke, permanent pacemaker implantation, and ≥moderate PVL, but higher risk of ≥moderate patient-prosthesis mismatch, higher mean gradient, and smaller effective orifice area. Large, adequately powered randomized trials are needed to evaluate long-term outcomes of TAVR with latest generations of BEV vs SEV.

Introduction

Transcatheter aortic valve replacement (TAVR) has revolutionized the treatment for patients with severe aortic stenosis (AS), especially those at prohibitive, high, or intermediate risk for surgery. TAVR is now increasingly being utilized as an alternative to surgery in low-risk and younger patients as well.[1–3] The evolution of TAVR devices has paralleled its clinical adoption, with continuous refinements in delivery systems and valve design aimed at improving clinical outcomes.[4–6] Among these, the balloon-expandable (BEV) and self-expanding (SEV) valves have been at the forefront of technological innovation, with each design positing distinct hemodynamic profiles and clinical implications. Despite the proven efficacy of TAVR, the differential impact of the latest generation BEV vs SEV on clinical end points remains underexplored. Previous randomized controlled trials (RCTs) have mainly concentrated on older generations of these devices, and there is a paucity of comparative effectiveness data on the most recent valve generations.[7–9] To address this knowledge gap, we conducted a systematic

Abbreviations: AS, aortic stenosis; BEV, balloon-expandable valves; EOA, effective orifice area; PPI, permanent pacemaker implantation; PPM, patient-prosthesis mismatch; SEV, self-expanding valves; STS PROM, Society of Thoracic Surgeons Predicted Risk of Mortality; SVD, structural valve deterioration; TAVR, transcatheter aortic valve replacement.

Keywords: balloon-expandable valve; outcomes; self-expanding valve; transcatheter aortic valve replacement.

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review and meta-analysis of studies comparing the clinical and echocardiographic outcomes of TAVR with third generation BEV vs SEV. A meticulous comparison of these devices will inform clinical decision-making and enhance patient-centered care. Further, if there is clinical equipoise, this would further support the need for an adequately powered RCT comparing the latest generation BEV vs SEV.

Methods

Search strategy

The study protocol was registered on PROSPERO (CRD42023434879) and adheres to the PRISMA-P guidelines to ensure a systematic and transparent approach to evidence synthesis.[10,11] A comprehensive literature search was conducted to identify studies on TAVR using the third generation BEV (SAPIEN 3, SAPIEN 3 Ultra, SAPIEN 3 Ultra RESILIA [Edwards Lifesciences]) vs SEV (Evolut PRO, Evolut PRO+, or Evolut FX [Medtronic]) valves. The search strategy was developed in consultation with a medical librarian to ensure a thorough and unbiased retrieval of relevant studies. Four electronic databases were systematically searched: PubMed, Embase, Web of Science, and Cumulative Index of Nursing and Allied Health Literature (CINAHL). The search terms included combinations of keywords and MeSH terms (Supplemental Table S1). The search was limited to articles published from the inception of each database up to June 12, 2023. This study was deemed exempt from institutional review board approval and informed consent as it exclusively used data from previously published sources.

Study selection

Studies were considered for inclusion if they met the following predefined criteria: (1) human study, (2) study published in English language, (3) RCT or observational study, (iv) study or study arms comparing TAVR with latest generation BEV vs SEV, and (v) study reported the outcome(s) of interest. Studies with a mix of older and latest generations of valves were eligible for inclusion if the proportion of older generation BEV/SEV was <50%. Exclusion criteria were in vitro/animal studies, single-arm studies, review articles, meta-analyses and systematic reviews, case reports/series, comparison of older generations of BEV and SEV, outcomes of interest not reported, comparison group not BEV vs SEV, studies comparing TAVR vs surgical aortic valve replacement (SAVR), and substudies or overlapping populations.

Data extraction

Two independent reviewers (S.A.S. and D.K.) conducted the screening process using Covidence, and any discrepancies between the reviewers were resolved through mutual consensus. Following the title and abstract screening, full-text articles were retrieved for those studies deemed potentially relevant. A detailed assessment was then conducted to identify studies to be included in the meta-analysis. Data extraction was performed independently by 2 reviewers (S.A.S. and S.K.) using a standardized data collection form. Extracted data included study characteristics (publication year, location, study design, sample size, valve type, and follow-up duration) and patient characteristics (age, sex, comorbidities, New York Heart Association [NYHA] functional class, left ventricular ejection fraction [LVEF], Society of Thoracic Surgeons Predicted Risk of Mortality [STS PROM] score, surgical risk category, bicuspid aortic valve, and small aortic annuli).

Quality assessment

The quality of included studies was assessed using the Newcastle-Ottawa Scale for observational studies and version 2 of the Risk-of-Bias tool (RoB 2) for RCT.[12,13] This assessment covered domains such as selection bias, study design, comparability of groups, outcome assessment, and follow-up adequacy.

Outcomes

The primary outcome of interest was all-cause mortality. Secondary outcomes included heart failure hospitalization, myocardial infarction, transient ischemic attack (TIA)/stroke, permanent pacemaker implantation (PPI), moderate or severe paravalvular leak (PVL), moderate or severe patient-prosthesis mismatch (PPM), mean gradient (mm Hg), effective orifice area (EOA; cm^2), hypoattenuated leaflet thickening/leaflet thrombosis, infective endocarditis, structural valve deterioration (SVD), and aortic valve reintervention.

Statistical analysis

The meta-analysis employed a random-effects model using the DerSimonian and Laird method to calculate pooled odds ratios (OR) for dichotomous outcomes and weighted mean differences (WMD) for continuous outcomes, with corresponding 95% CI. Heterogeneity among studies was quantified using the Higgins I^2 statistic, with values >50% indicating substantial heterogeneity. Publication bias was assessed visually by asymmetry in funnel plots and quantitatively using Egger's regression test.

We performed metaregression analyses to determine if baseline patient characteristics modified the effect of BEV vs SEV on the primary outcome of all-cause mortality. Covariates included in the metaregression were age, sex, prior coronary artery disease, NYHA functional class, LVEF, STS PROM score, bicuspid aortic valve, and small aortic annulus. Several sensitivity meta-analyses were performed: (1) including only propensity-matched studies and RCT, (2) excluding studies that also included a proportion of patients who underwent TAVR with the older generation of SEV, and (3) excluding 1 RCT that enrolled patients undergoing valve-in-valve TAVR. Lastly, we performed subgroup analyses stratified by study type (observational or RCT) to determine the relative contribution of each to the overall effects.

All statistical analyses were conducted using Stata version 17.0 BE (StataCorp LLC) with a significance threshold set at a 2-sided *P* value of <.05.

Results

The database search yielded 1179 articles. After excluding duplicates, 587 articles were screened, and 173 were excluded for various reasons (Supplemental Figure S1). Title and abstract screening was performed for 414 articles of which 390 were excluded due to reasons such as comparison between older generations of BEV and SEV, outcomes of interest not reported, comparison groups not BEV vs SEV, and single-arm studies. Twenty-four full-text articles were assessed for eligibility of which 16 were included in the final meta-analysis.

Study characteristics and quality

The characteristics of the included studies are shown in Table 1.[14–29] Of the 16 studies included in the meta-analysis, 14 were observational (5 propensity-matched) and 2 were RCT. The devices compared in the studies were predominantly third-generation BEV (SAPIEN 3 or SAPIEN

Table 1. Characteristics of studies included in the meta-analysis.

Study, year	Country/Region	Study design	N, BEV	N, SEV	Third-generation BEV	Third-generation SEV	Follow-up	Specific population
OBSERVANT II,[14] 2022	Italy	Observational	768	337	SAPIEN 3	Evolut PRO	1 y	
Medranda et al,[15] 2022	USA	Observational	222	167	SAPIEN 3	Evolut PRO/PRO+	1 y	Women, SAA
Kalogeras et al,[16] 2023	Greece, UK	Observational	756	917	SAPIEN 3/SAPIEN 3 Ultra	Evolut PRO/PRO+[a]	3 y	
TAVI-SMALL 2,[17] 2023	Europe	Observational	286	750	SAPIEN 3	Evolut PRO[a]	~1 y	SAA
Mosleh et al,[18] 2023	USA	Observational	337	236	SAPIEN 3 Ultra	Evolut PRO/PRO+[a]	5 y	SAA
Bern TAVI,[19] 2023	Switzerland	Observational (propensity matched)	171	171	SAPIEN 3/SAPIEN 3 Ultra[a]	Evolut PRO/PRO+[a]	5 y	SAA
Modolo et al,[20] 2020	Netherlands	Observational	397	95	SAPIEN 3	Evolut PRO	In-hospital	
OPERA-TAVI,[21] 2022	Europe, North America	Observational (propensity matched)	683	683	SAPIEN 3 Ultra	Evolut PRO/PRO+	30 d	
Ferrara et al,[22] 2022	France	Observational	76	26	SAPIEN 3	Evolut PRO	30 d	SAA
Fukui et al,[23] 2022	USA	Observational (prospective)	352	213	SAPIEN 3	Evolut PRO[a]	30 d	
Potratz et al,[24] 2022	Germany	Observational (propensity matched)	170	170	SAPIEN 3	Evolut PRO	30 d	
Rheude et al,[25] 2022	Germany	Observational (propensity matched)	205	205	SAPIEN 3 Ultra	Evolut PRO	30 d	
LYTEN,[26] 2022	Europe, North America	RCT	45	52	SAPIEN 3/SAPIEN 3 Ultra	Evolut PRO/PRO+[a]	30 d	ViV TAVR
Schmidt et al,[27] 2022	Germany	Observational	1146	268	SAPIEN 3	Evolut PRO	In-hospital	
TRITON,[28] 2023	Europe, India	Observational (propensity matched)	80	80	SAPIEN 3	Evolut PRO+	30 d	Bicuspid aortic valve
Elnaggar et al,[29] 2023	Germany	RCT	59	51	SAPIEN 3	Evolut PRO	In-hospital	

BEV, balloon-expandable valves; LYTEN, Comparison of the Balloon-Expandable Edwards Valve and Self-Expandable CoreValve Evolut R or Evolut PRO System for the Treatment of Small, Severely Dysfunctional Surgical Aortic Bioprotheses; OBSERVANT, Observational Study of Effectiveness of TAVI With New Generation Devices for Severe Aortic Stenosis Treatment; OPERA-TAVI, Comparative Analysis of Evolut PRO vs Sapien 3 Ultra Valves for Transfemoral Transcatheter Aortic Valve Implantation; RCT, randomized controlled trial; SAA, small aortic annulus; SEV, self-expanding valves; TAVI-SMALL, International Multicenter Registry to Evaluate the Performance of Self-Expandable Valves in Small Aortic Annuli; TAVR, transcather aortic valve replacement; ViV, valve-in-valve.

[a] Also included the older generation of valves (Kalogeras et al[16]: 27.2% Evolut R 34 mm; Mosleh et al[18]: 24.2% Evolut R; Bern TAVI[19]: 6.4% SAPIEN XT, 6.4% CoreValve; LYTEN.[26]: 38.5% Evolut R; TAVI-SMALL 2,[17] and Fukui et al[23] included Evolut R/PRO).

3 Ultra) vs third-generation SEV (Evolut PRO or Evolut PRO+). Follow-up duration was between 1 and 5 years in 6 studies and in-hospital or 30 days in 10 studies.

The studies included a total of 10,174 patients (5753 in the BEV group and 4421 in the SEV group). Baseline patient characteristics in the BEV vs SEV groups are summarized in Supplemental Table S2. The mean age of patients across the studies was 81 years, and 61.1% were women. The mean LVEF was 57.3% and the mean STS PROM score was 5.1%. Four studies included patients with small aortic annuli (n = 2442), and 1 study included patients who underwent valve-in-valve TAVR for small (<23 mm) failed surgical aortic valves (n = 97).

The quality of observational studies was assessed using the Newcastle-Ottawa Scale. Studies scored between 6/9 and 9/9, indicating a low risk of bias and strong methodological quality across key parameters such as cohort selection and outcome measurement (Supplemental Table S3). Using the RoB-2 tool, the 2 RCTs showed a low risk of bias in all assessed domains (Supplemental Figure S2).

Outcomes

There were no significant differences in 1-year all-cause mortality (OR, 1.15; 95% CI, 0.89-1.48; $P = .29$; $I^2 = 16.4\%$) or 1-year HF hospitalization (OR, 0.90; 95% CI, 0.65-1.24; $P = .50$; $I^2 = 11.5\%$) between third-generation BEV vs SEV (Figure 1).

Similarly, there were no significant differences in in-hospital or 30-day all-cause mortality (OR, 0.74; 95% CI, 0.42-1.33; $P = .32$; $I^2 = 54.6\%$) or myocardial infarction (OR, 0.93; 95% CI, 0.33-2.61; $P = .90$; $I^2 = 0\%$) between third-generation BEV vs. SEV (Figure 2). TAVR with third-generation BEV was associated with a significantly lower risk of in-hospital or 30-day TIA/stroke (OR, 0.62; 95% CI, 0.44-0.87; $P = .01$; $I^2 = 0\%$), PPI (OR, 0.55; 95% CI, 0.44-0.70; $P < .01$; $I^2 = 50\%$), and moderate or severe PVL (OR, 0.43; 95% CI, 0.25-0.75; $P < .001$; $I^2 = 54.1\%$), compared with SEV (Figures 3 and 4A).

The use of third generation BEV was associated with significantly higher risk of moderate or severe PPM (OR, 3.76; 95% CI, 2.33-6.05; $P < .001$; $I^2 = 83.8\%$), higher mean aortic valve gradient (WMD, 4.35; 95% CI, 3.63-5.08; $P < .001$; $I^2 = 91.8\%$), and smaller EOA (WMD, −0.30; 95% CI, –0.37 to –0.23; $P < .001$; $I^2 = 71.8\%$), compared with SEV (Figures 4B and 5).

For certain outcomes such as hypoattenuated leaflet thickening/leaflet thrombosis, infective endocarditis, SVD, and aortic valve reintervention, a meta-analysis was not feasible due to the small number of studies reporting these outcomes. Data from individual studies reporting these outcomes are summarized in Supplemental Table S4.

Publication bias

Visual assessment of funnel plots showed no obvious asymmetry, and formal assessment using Egger's test demonstrated no evidence of publication bias for the outcomes studied ($P > .05$ for all) (Supplemental Figure S3 and Supplemental Table S5).

Heterogeneity, metaregression, and sensitivity analyses

Substantial heterogeneity (Higgin's $I^2 > 50\%$) was noted for in-hospital or 30-day all-cause mortality, moderate or severe PVL, moderate or severe PPM, mean aortic valve gradient, and EOA. Heterogeneity in echocardiographic/hemodynamic outcomes likely reflects the inherent variability in the assessment/measurement of these variables.

Metaregression analyses showed no evidence of effect modification by age, sex, prior coronary artery disease, NYHA functional class, LVEF, STS PROM score, bicuspid aortic valve, or small aortic annulus on the

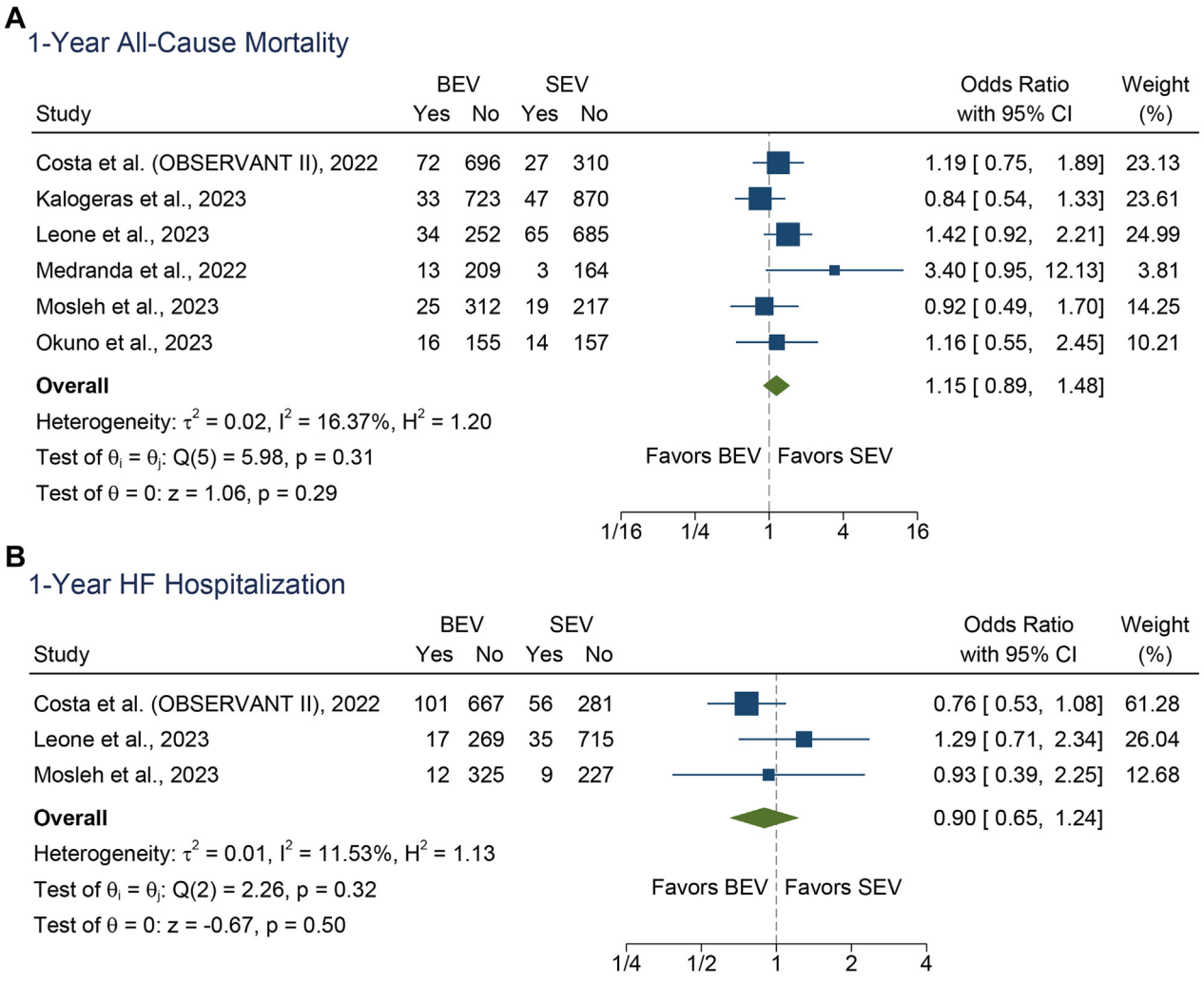


Figure 1.
One-year all-cause mortality (A) and heart failure hospitalization (B) after TAVR with third-generation balloon-expandable valves (BEV) vs self-expanding valves (SEV).

association of BEV vs SEV with the primary end point of all-cause mortality (Supplemental Figures S4 and S5).

Sensitivity analyses after including only propensity-matched studies and RCTs, after excluding studies that also included a proportion of patients with older generation of SEV, and after excluding 1 study on valve-in-valve TAVR showed results consistent with the primary analyses (Supplemental Tables S6-S8).

Subgroup analyses by study type

Subgroup analyses stratified by study type (observational vs RCT) showed no statistically significant between-group differences ($P > .05$), except for WMD for mean aortic valve gradient which was significantly larger in 1 RCT vs the pooled estimate from the observational studies ($P = .02$) (Supplemental Figure S6A-H).

Discussion

In this meta-analysis of 16 studies comparing clinical and hemodynamic outcomes of third-generation BEV vs SEV, we report the following salient findings (Central Illustration): (1) there were no significant differences in in-hospital/30-day or 1-year all-cause mortality and 1-year heart failure hospitalizations between patients undergoing TAVR with a third generation BEV vs SEV; (2) BEV use was associated with a significantly lower risk of TIA/stroke, moderate or severe PVL, and PPI, compared with SEV; (3) BEV demonstrated higher risk of moderate or severe PPM, higher mean gradients, and smaller EOA, compared with SEV; and (4) metaregression analyses demonstrated no evidence of effect modification by baseline characteristics on the association between valve type and all-cause mortality.

With tremendous growth in the adoption of TAVR in low-risk and younger patients including those <65 years of age, the choice of TAVR prosthesis is crucial in optimizing short- and long-term clinical outcomes.[1–3] The 2 main TAVR platforms currently utilized in the US are the third-generation iterations of the SAPIEN BEV and Evolut SEV. In recent years, both device platforms have undergone several improvements. In the SAPIEN platform, design iterations have included an enhanced polyethylene terephthalate skirt extending 40% higher above valve inflow to further minimize PVL in SAPIEN 3 Ultra, and enhanced anti-calcification technology with the RESILIA tissue in SAPIEN 3 Ultra RESILIA.[4,5,30] In the Evolut platform, a tall pericardial skirt with an enhanced outer pericardial wrap was added to the Evolut PRO+ to minimize PVL. The Evolut FX incorporates further design enhancements that include a redesigned nosecone for atraumatic vascular entry, a single spine to improve trackability, radioopaque "dot" markers to facilitate commissural alignment and depth assessment, and a stability layer for more predictable deployment.[4,6,31] To date, there are no adequately powered RCTs comparing outcomes with these latest iterations of BEV and SEV. Therefore, the results of our meta-analysis

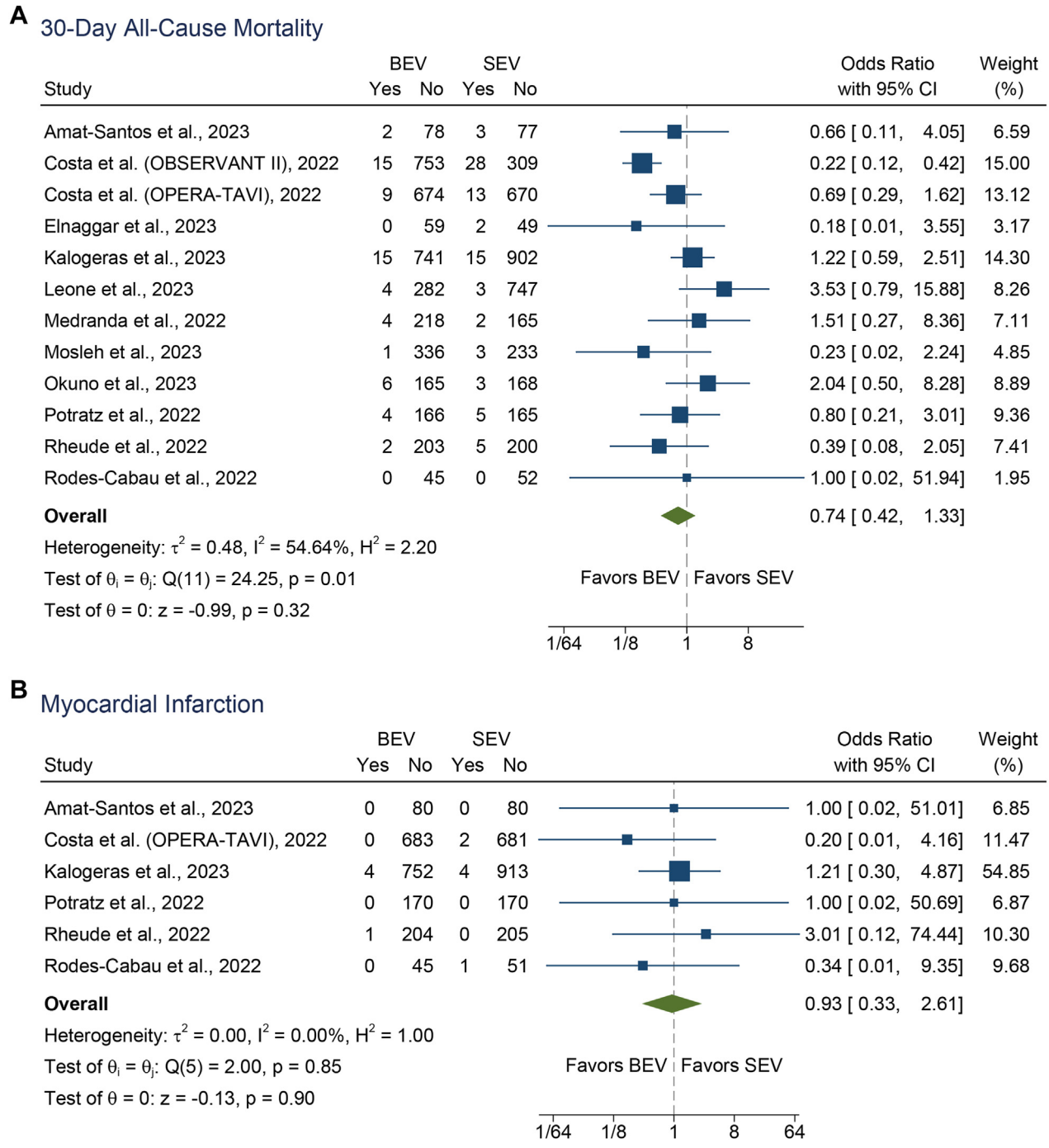


Figure 2.
In-hospital or 30-day all-cause mortality (A) and myocardial infarction (B) after TAVR with third-generation balloon-expandable valves (BEV) vs self-expanding valves (SEV).

comparing short- and mid-term clinical and echocardiographic/hemodynamic outcomes of third-generation SAPIEN vs Evolut platforms are important to inform clinical practice.

Our meta-analysis showed no significant differences in in-hospital/30-day and 1-year all-cause mortality between third-generation BEV vs SEV. Our results are consistent with prior RCT comparing older generations of BEV vs SEV. The CHOICE (A Comparison of Transcatheter Heart Valves in High-Risk Patients With Severe Aortic Stenosis) trial randomized 241 high-risk AS patients to second-generation BEV (SAPIEN XT) vs the first-generation SEV (CoreValve) and found no differences in the cumulative incidence of all-cause death at 1 year and at 5 years.[7,8] The SOLVE-TAVI (SecOnd-generation seLf-expandable Versus Balloon-expandable Valves and gEneral Versus Local Anesthesia in TAVI) trial randomized 447 intermediate- to high-risk AS patients to third-generation BEV (SAPIEN 3) vs second-generation SEV (Evolut R) and showed no difference in 30-day all-cause mortality.[9] Longer-term follow-up, potentially up to 10 years or beyond, might be needed to conclusively demonstrate presence, or lack thereof, of mortality differences between BEV and SEV.

We found significantly higher risk of TIA/stroke and moderate or severe PVL with third-generation SEV vs BEV. Because our meta-analysis included 14 observational studies and 2 small RCTs, unmeasured confounding due to preferential use of SEV in higher-risk anatomies (eg,

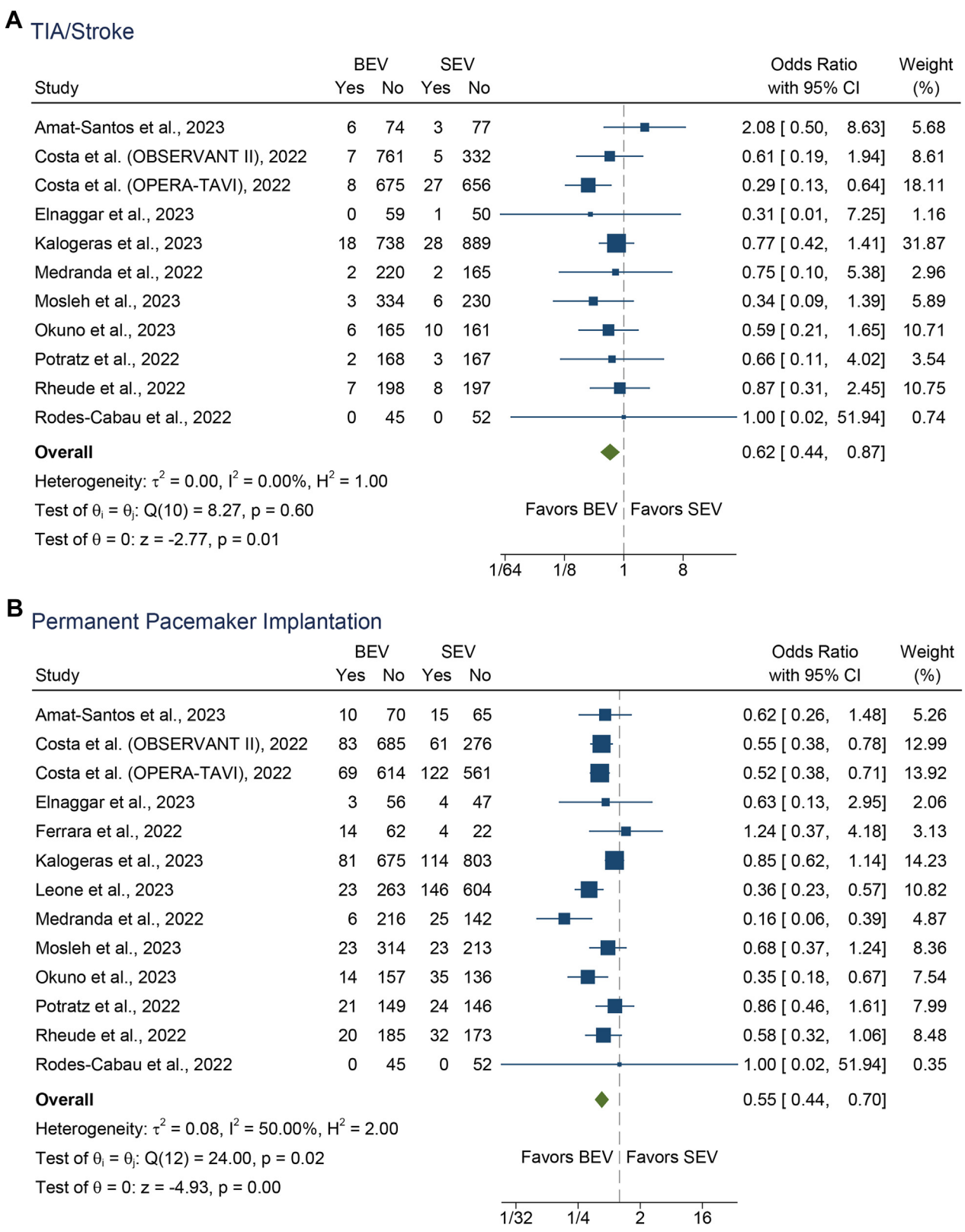


Figure 3.
In-hospital or 30-day transient ischemic attack (TIA)/stroke (A) and permanent pacemaker implantation (B) after TAVR with third-generation balloon-expandable valves (BEV) vs self-expanding valves (SEV).

severe calcification, bicuspid aortic valve) may potentially explain these findings. However, these results were consistent across multiple sensitivity analyses. Also, it is known that SEV deployment is technically more challenging, requires more frequent postdilation to achieve symmetric expansion or to mitigate PVL, and recaptures to optimize valve depth, which could mechanistically contribute to higher risk of stroke.[32]

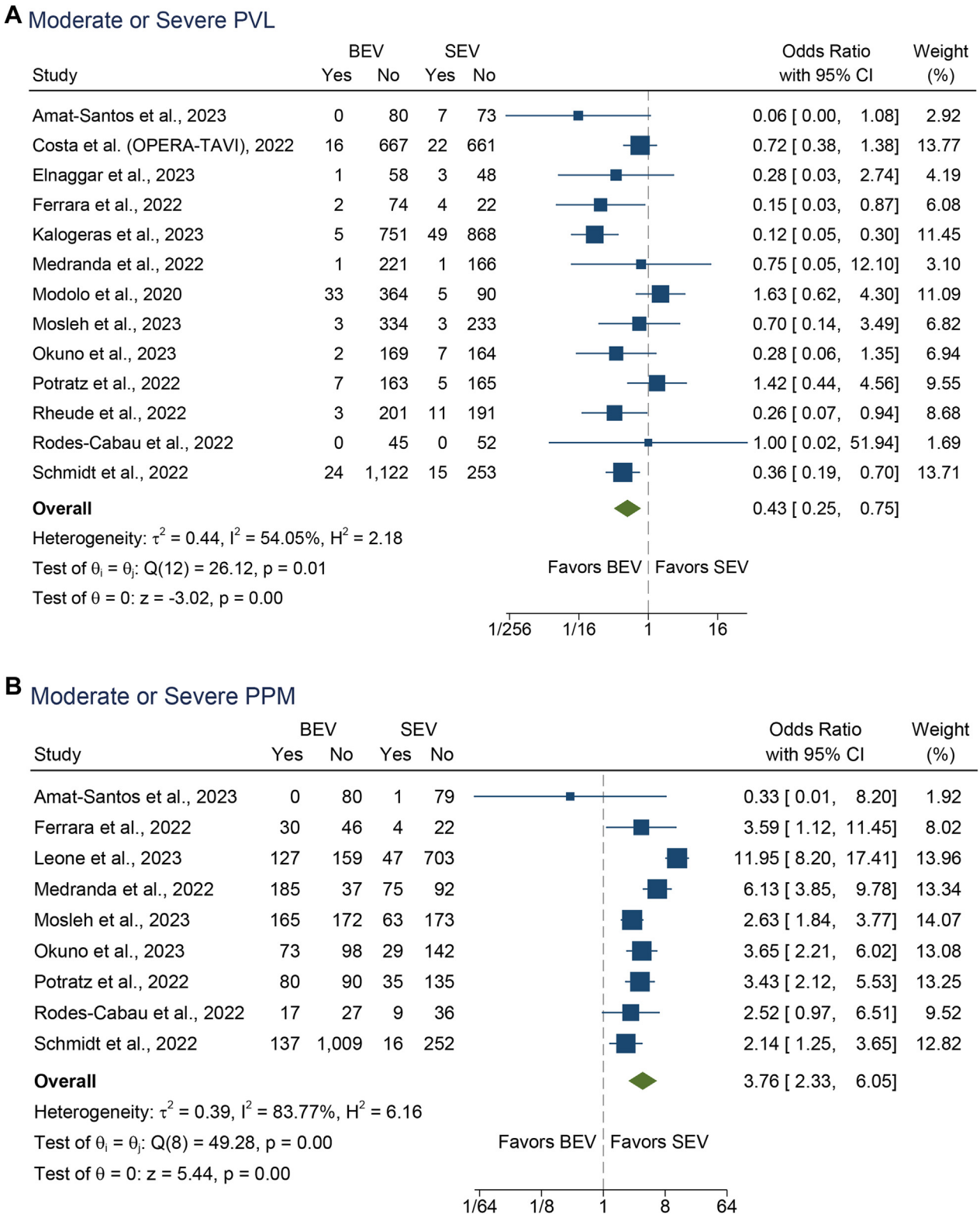


Figure 4.
In-hospital or 30-day moderate/severe paravalvular leak (PVL) (A) and moderate/severe patient-prosthesis mismatch (PPM) (B) after TAVR with third-generation balloon-expandable valves (BEV) vs self-expanding valves (SEV).

Further, the SOLVE-TAVI trial also demonstrated higher rates of 30-day stroke (4.7% vs 0.5%) and moderate or severe PVL (3.4% vs 1.5%) with second-generation SEV vs third-generation BEV.[9] These results are particularly important because it has been demonstrated that early stroke as well as ≥moderate PVL are associated with worse long-term outcomes.[33] Nonetheless, these findings from our meta-analysis are hypothesis-generating and need to be confirmed in adequately powered RCTs.

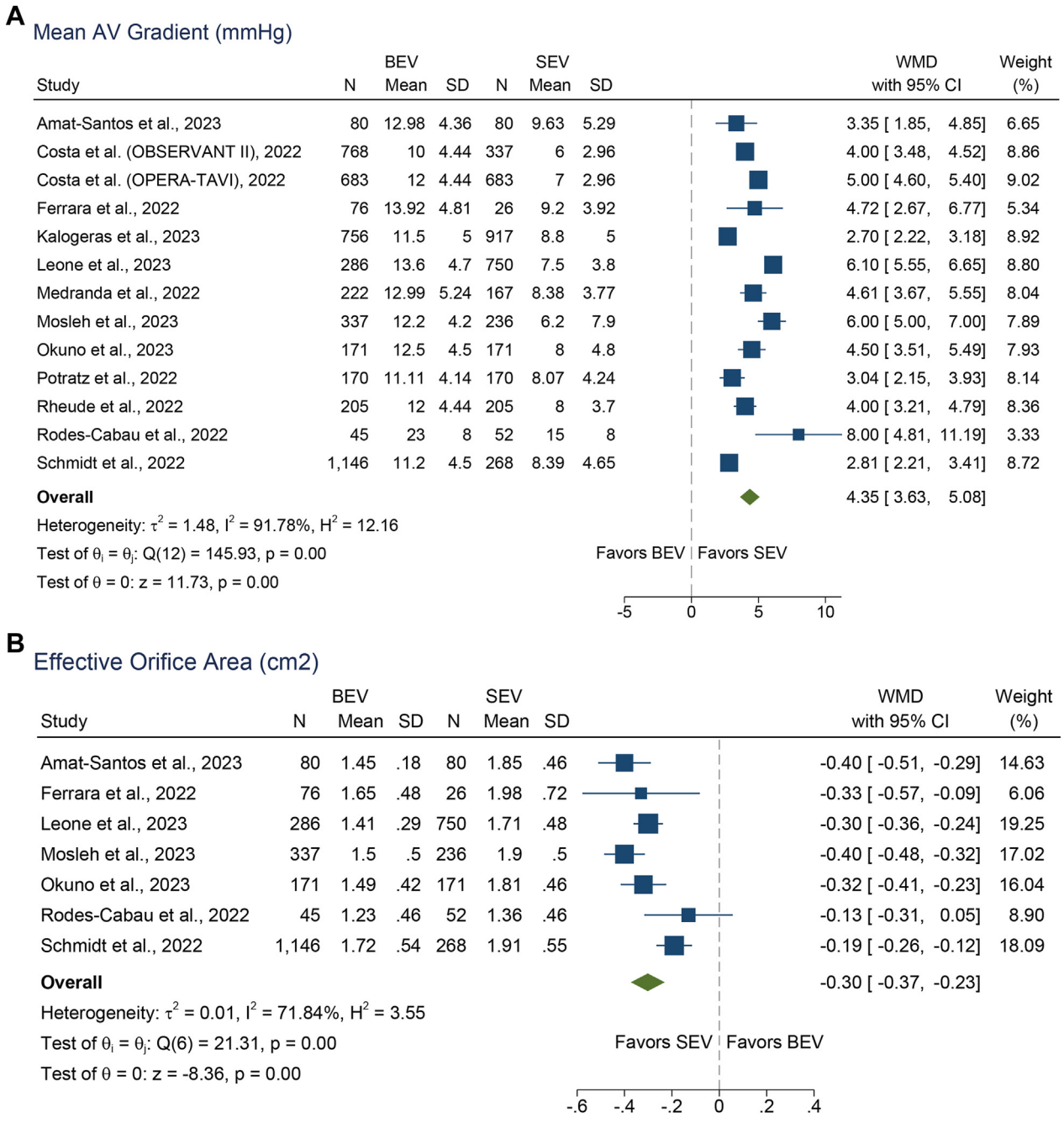
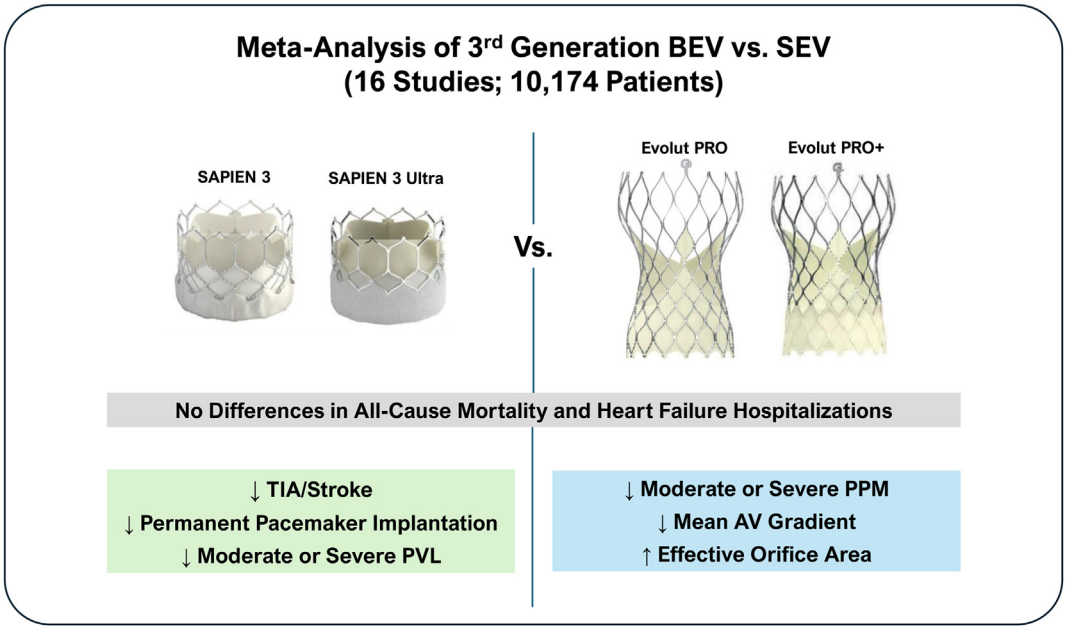


Figure 5.
In-hospital or 30-day mean aortic valve (AV) gradient (A) and effective orifice area (B) after TAVR with third-generation balloon-expandable valves (BEV) vs self-expanding valves (SEV).

The risk of PPI was approximately 45% lower with BEV vs SEV in our meta-analysis. Prior studies have also consistently demonstrated lower risk of PPI with earlier generations and third generation of SAPIEN vs Evolut platforms.[14,34,35] However, specifically for the Evolut platform, there has been an evolution in deployment practices such as use of the cusp-overlap technique facilitating higher implant and therefore, lower risk of PPI. In the single-arm Optimize PRO study with deployment of Evolut PRO/PRO+ valves using the cusp-overlap technique and an optimized TAVR care pathway, the incidence of new PPI was 9.8% in the overall cohort, and 5.8% in patients who underwent deployment in full compliance with the 4-step cusp-overlap technique.[36] The cusp-overlap technique was not routinely utilized in clinical practice during the time of most included studies in our meta-analysis; therefore, the findings of higher PPI rates with third generation SEV vs BEV may not apply to current clinical practice.

Lastly, our meta-analysis demonstrated that BEV use is associated with worse hemodynamics including a significantly higher risk of moderate or severe PPM, higher mean gradient, and lower EOA, compared with SEV. This may be explained by the supraannular leaflets of the Evolut platform potentially allowing for better hemodynamics, compared with the intraannular leaflets of the SAPIEN platform. However, prior studies have also demonstrated discordance between echocardiography-derived versus invasively measured mean gradients post-TAVR, particularly in BEV.[37] Nonetheless, whether the superior hemodynamic profile of SEV vs BEV leads to lower risk of SVD, aortic



Central Illustration.
Meta-analysis of studies comparing outcomes of third-generation balloon-expandable valves (BEV) vs self-expanding valves (SEV). AV, aortic valve; PPM, patient-prosthesis mismatch; PVL, paravalvular leak; TIA, transient ischemic attack.

valve reintervention, and/or mortality in the long term remains an unanswered question. In an analysis of pooled data from CoreValve US extreme, high, and intermediate risk trials and continued access registries, Evolut SEV was associated with 50% lower risk of SVD compared with SAVR, and SVD was associated with increased 5-year all-cause mortality, cardiovascular mortality, and valve disease or worsening heart failure hospitalizations.[38] In contrast, 5-year results from the PARTNER 3 (The Placement of Aortic Transcatheter Valves) trial showed similar rates of irreversible structural or hemodynamic valve deterioration and higher incidence of clinical valve thrombosis in TAVR vs SAVR.[1]

Two ongoing RCTs will be pivotal in understanding the differences in clinical and hemodynamic outcomes of the latest generations of BEV vs SEV in varied anatomies. The SMART trial of approximately 700 patients with small aortic annuli randomized to Evolut PRO/PRO+ vs SAPIEN 3/SAPIEN 3 Ultra will examine the coprimary clinical composite end point of all-cause mortality, disabling stroke, or heart failure hospitalization and valve function composite end point of bioprosthetic valve dysfunction at 1 year.[39] Patients will be followed annually for up to 5 years. The BEST trial (Balloon-Expandable vs Self-Expanding Transcatheter Heart Valve; NCT05454150) will randomize 1800 patients to third generation Evolut vs SAPIEN platforms across all annular sizes and includes a nested 400-patient computed tomography substudy.[40] The primary outcome will be all-cause mortality at 90 days and 1 year using a superiority design.

Study limitations

Our study is not without limitations. First, in the absence of data from large RCTs, this meta-analysis included predominantly observational studies and is subject to limitations of observational data including selection bias and unmeasured confounding. The different timelines for the approval of third generation BEV vs SEV may also influence the patient profile in the 2 groups in individual studies. Nonetheless, our findings are consistent with results of prior RCTs comparing older generations of BEV vs SEV.[7,9] Second, this meta-analysis used study-level data as we did not have access to individual patient-level data. Third, data on long-term outcomes were not available in the included studies; however, long-term follow-up from ongoing RCTs will not be available for the next 5 to 10 years. Last, the evolving nature of TAVR technology means that our results are a snapshot in a rapidly advancing field, and periodic updates to the evidence are necessary.

Conclusions

In this meta-analysis of 16 studies that included >10,000 patients who underwent TAVR with third-generation BEV or SEV, there were no significant differences in all-cause mortality or heart failure hospitalizations between BEV and SEV. The use of BEV was associated with a lower risk of TIA/stroke, moderate or severe PVL, and PPI, but a higher risk of moderate or severe PPM, higher mean gradient, and smaller EOA, compared with SEV. Ongoing RCTs such as SMART and BEST will provide definitive evidence on the clinical and hemodynamic performance of these 2 valve platforms and the role of tailored approach to valve selection in specific clinical situations and anatomies.

Declaration of competing interest

Ignacio Inglessis has received institutional research support from Medtronic, St. Jude Medical, and W.L. Gore and Associates; and is a proctor for Medtronic and Edwards Lifesciences. Jonathan J. Passeri reports grants and personal fees from Edwards Lifesciences and personal fees from Medtronic. Harold L. Dauerman has received research grants from Boston Scientific and Medtronic; and is a consultant for Medtronic, Boston Scientific, Edwards Lifesciences, American College of Cardiology, Recor Medical, Baim Institute for Clinical Research, and Cardiovascular Research Foundation. Sammy Elmariah has received research funding from Edwards Lifesciences, Medtronic, and Abbott; and is a consultant for Edwards Lifesciences and Medtronic. Dhaval Kolte has received research funding from the National Heart, Lung, and Blood Institute outside of the submitted work. All other authors have no relevant conflicts of interest to disclose.

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Ethics statement and patient consent

This study was deemed exempt from institutional review board approval and informed consent as it exclusively used data from previously published sources.

Supplementary material

To access the supplementary material accompanying this article, visit the online version of the *Journal of the Society for Cardiovascular Angiography & Interventions* at 10.1016/j.jscai.2024.102146.

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