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Effectiveness and Safety of Myval Versus Other Transcatheter Valves in Patients Undergoing TAVI: A Meta-Analysis

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ABSTRACT

Transcatheter aortic valve implantation (TAVI) has changed the treatment of aortic stenosis. The Myval transcatheter heart valve (THV), a novel balloon-expandable THV, has shown promising outcomes. Our aim is to compare the comparative safety and effectiveness of Myval THV against established THVs, such as Sapien and Evolut. A systematic review and meta-analysis was conducted, comparing the Myval THV with other contemporary THVs. Primary endpoints were periprocedural, 30-day and 1-year all-cause mortality. Seven studies involving 3106 patients (1027 Myval; 2079 other THVs) were included. No significant differences were observed in the primary endpoints. Myval demonstrated higher procedural success (RR: 1.04, 95% CI: 1.01–1.07, $I^2 = 29%$) and lower rates of permanent pacemaker implantation (PPI) during the index hospitalization (RR: 0.57, 95% CI: 0.36–0.92, $I^2 = 23%$) and 30-days (RR: 0.60, 95% CI: 0.40–0.89, $I^2 = 43%$), compared to other THV. At 30-day, Myval was associated with lower rates of moderate or severe transvalvular aortic regurgitation (RR: 0.33, 95% CI: 0.11–0.98, $I^2 = 57%$) and minor vascular complications (RR: 0.45, 95% CI: 0.23–0.90, $I^2 = 0%$). When compared to self-expandable THV, Myval was associated with higher procedural and device success, higher early safety, lower risk for PPI, minor vascular complications and at least moderate transvalvular AR. When compared to Sapien, procedural success and risk for in-hospital PPI was borderline higher and lower in favor of Myval, respectively. The Myval THV demonstrates comparable safety and effectiveness to contemporary THVs, with advantages in procedural success, PPI, and vascular complications.

Abbreviations: AKI, acute kidney injury; AR, aortic regurgitation; AS, aortic stenosis; AVR, aortic valve replacement; BEV, balloon-expandable valve; MOOSE, Meta-analyses of Observational Studies in Epidemiology; PPI, permanent pacemaker implantation; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PVL, paravalvular leakage; RCT, randomized-controlled trial; RoB, Cochrane Risk of Bias Tool 2; SAVR, surgical aortic valve replacement; SEV, self-expandable valve; TAVI, transcatheter aortic valve implantation; THV, transcatheter heart valve. Anastasios Apostolos and Nikolaos Ktenopoulos are equal contribution as first authors.

Patrick Serruys and Konstantinos Toutouzas are equal contribution as last authors.

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1 | Introduction

Aortic stenosis (AS) is one of the most prevalent and severe valvular heart diseases globally [1]. Noteworthy, AS is associated with increased morbidity and mortality, particularly when left untreated; 5-year survival rate of symptomatic patients without any intervention is about 20%. Therefore, the effective and timely therapeutic management is critical [2].

Over the last two decades, transcatheter aortic valve implantation (TAVI) has revolutionized the management of AS and has been considered as a viable therapeutic option for a wide variety of patients, including those considered as intermediate or even low risk [3]. Nowadays, TAVI accounts for more than the half of aortic valve replacements (AVR) in many healthcare systems [4, 5].

Advances in TAVI technology have led to the development of newer generation transcatheter heart valves (THV) that aim to improve procedural outcomes, eliminate complications, like paravalvular leak (PVL), conduction disturbances, and THV malposition and increase long-term durability. Among these, the Myval THV system (Meril Life Sciences, Vapi, India) represents a novel balloon-expandable device designed to enhance annular sealing, decrease PVL, and eliminate conduction abnormalities. In addition, Myval offers intermediate (46% in LANDMARK) and extra-large sizing options, allowing for more precise annular matching [6]. Early studies [6] and the first published randomized controlled trial (RCT) (LANDMARK) [7], have demonstrated encouraging outcomes with Myval, including lower rates of permanent pacemaker implantation (PPI) and reduced residual gradients, providing comparable safety and effectiveness with the other contemporary valves. Despite the first promising results, the comparative effectiveness and safety of Myval against established devices such as the SAPIEN THV and the Evolut Pro THV remain an area of active debate, due to the limited existing literature and the lack of randomized trials, except LANDMARK [7].

Aim of our systematic review and meta-analysis is to compare the short-, mid- and long-term safety and effectiveness and safety of Myval versus the other contemporary THVs in patients undergoing TAVI.

2 | Methods

Our systematic review and meta-analysis was performed in accordance with the updated Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement and MOOSE (Meta-analyses of Observational Studies in Epidemiology) Checklist [8, 9]. The rationale and design of our project was prospectively registered in the PROSPERO database (CRD42024612616). Institutional Review Board approval and patients' consent was not required as this was a study-level meta-analysis of previously published data.

2.1 | Eligibility Criteria

Studies were included in this systematic review and meta-analysis based on the following criteria: (1) RCTs, prospective cohort studies, retrospective studies, or registry-based analyses

comparing the Myval THV with other THVs in patients undergoing TAVI; (2) studies reporting on clinical outcomes irrespective the time-frame of evaluation; and (3) studies published in English in peer-reviewed journals.

2.2 | Outcomes of Interest

The primary endpoint of our systematic review and meta-analysis was the periprocedural, 30-day and 1-year all-cause mortality. Secondary endpoints included procedural success, technical success, device success, early safety, in-hospital and 30-day PPI, 30-day and 1-year stroke, in-hospital and 30-day acute kidney injury (AKI), in-hospital and 30-day major bleedings, in-hospital and 30-day major and minor vascular complications, annular rupture, cardiac tamponade, coronary obstruction/occlusion, device embolization, need for > 1 THV and at least moderate PVL and transvalvular aortic regurgitation (AR). Each endpoint was used as defined in each study, as they are presented in Supporting Information S1: Table 1.

2.3 | Information Sources

We conducted an electronic bibliographic screening in three major databases of the literature—Cochrane Central Register of Controlled Trials, Medline, and Scopus, to identify relevant studies published up to December 19, 2024. Moreover, we manually searched the reference lists of the eligible studies to detect any other eligible reports.

2.4 | Search Strategy

The electronic search included the following terms: “transcatheter aortic valve implantation,” “TAVI,” “transcatheter aortic valve replacement,” “TAVR,” “Myval,” and “Myval valve.” The comprehensive search strategy was presented in Supporting Information S1: Table 2. No language restrictions were applied.

2.5 | Selection Process

Initially, all identified citations of the systematic search of the electronic databases were imported into the reference management software Rayyan to remove duplicates. Titles, abstracts, and keywords of the remaining studies were screened by two independent reviewers (A.A. and N.K.) and non-relevant articles were removed, according to the prespecified inclusion criteria. Full-text reports were then evaluated by two reviewers (A.A. and N.K.) and any disagreements were resolved through discussion and consultation with a third investigator (K.T.).

2.6 | Data Collection Process

Data were extracted independently by two reviewers (A.A. and N.K.) using a standardized data extraction form designed specifically for this study. The form was piloted on a subset of studies to ensure clarity and consistency. After finalizing the

form, two of the authors (A.A. and N.K.) independently extracted the data from each study. A third study member (K.T.) validated the extracted data and resolved any disagreements.

2.7 | Data Items

We extracted the following data from the included studies: (i) the report: authors, year and source of publication; (ii) the study: sample size, inclusion and exclusion criteria; (iii) the participants: demographic details and comorbidities; (iv) the procedure: periprocedural characteristics, valve type, size, vascular access; and (v) outcomes during the follow-up period.

2.8 | Risk of Bias Assessment

The risk of bias for included studies was assessed independently by two reviewers (A.A. and N.K.) using appropriate tools for each study design. For RCTs, the Cochrane Risk of Bias Tool 2 (RoB 2) was preferred. Additionally, we used Newcastle-Ottawa Scale, which is indicated for observational studies [10]. The quality assessment was performed blindly and independently by two authors (A.A. and N.K.) and any discrepancy occurred during evaluation was resolved through the consultation of a third author (K.T.).

2.9 | Statistical Analysis

All analyses were performed at study level, using risk ratio (RR) with 95% confidence intervals (CIs) to estimate the effect of Myval THV and contemporary THV. Studies not providing results for a specific outcome were excluded from the specific analysis. The pooled RR was estimated by using a random-effect model (Mantel-Haenszel). Between-study heterogeneity was evaluated using the statistical inconsistency test ($I^2 = 100\% \times (Q-df)/Q$, where “Q” represents Chi-square (Cochran’s heterogeneity statistic) and df represents degrees of freedom). Low, moderate, and high heterogeneity were defined as $I^2 \leq 25\%$, $I^2 \leq 50\%$, and $I^2 > 50\%$, respectively [11]. $p < 0.05$ were considered significant. Sensitivity analysis using a *leave-one-out* approach was performed by systematically removing one study at a time and repeating the statistical analysis to assess whether a single study was driving the results. A prespecified subgroup analysis comparing Myval THV with SEV and Sapien was performed. The analysis was performed using the Review Manager software version 5.4 (Cochrane Collaboration).

3 | Results

3.1 | Search Results

Our systematic search identified a total of 262 records. After removal of duplicates, 143 records remained for title and abstract review, of which 20 underwent full-text screening. Overall, seven studies fulfilled our eligibility criteria and were included in our systematic review and meta-analysis [7, 11–16]. The systematic search of the literature is depicted in the PRISMA flowchart shown in Supporting Information S1: Figure 1.

3.2 | Studies’ Characteristics

Table 1 presents the characteristics of the included studies, and the inclusion and exclusion criteria for each study are provided in Supporting Information S1: Table 3 and 4. All studies, except one, were non-randomized; five of them retrospective and one prospective [11–16]. All the studies were published after 2022. Three studies used VARC-3 criteria and another three the VARC-2 [14]. Three studies [13, 14, 16] included only with tricuspid aortic valve, and TRITON study included only patients with bicuspid aortic valve [15]. In two studies, Myval was compared versus Sapien, in two versus Evolut, in two with both Evolut and Sapien and in the study by Santos-Martinez et al. with Sapien, Evolut, Acurate, Portico and Allegra. A total of 3106 patients were included in our analysis; 1027 patients underwent TAVI with Myval THV while the remaining 2079 underwent with a “contemporary” THV.

3.3 | Patients’ Characteristics

Supporting Information S1: Table 5 outlines the baseline characteristics of the study population, with a mean age of 79.6 ± 6.8 years in the Myval group compared to 80.7 ± 6.3 years in the comparator group. Supporting Information S1: Table 6 provides detailed preprocedural and echocardiographic findings, while information on femoral access, pre- and post-dilatation, and THV types is presented in Supporting Information S1: Table 7.

3.4 | Primary Analysis

RR, CIs and I^2 are synopsised in Table 2. Primary endpoint, namely periprocedural (RR: 0.62, 95% CI: 0.13–2.95, $I^2 = 0\%$) (Figure 1A), 30-day (RR: 0.78, 95% CI: 0.40–1.49, $I^2 = 0\%$) (Figure 1B) and 1-year mortality (RR: 0.75, 95% CI: 0.29–1.95, $I^2 = 35\%$) (Figure 1C) did not differ significantly between the two groups. In terms of in-hospital outcomes, procedural success was significantly higher in the Myval group compared to contemporary THVs (RR: 1.04, 95% CI: 1.01–1.07, $I^2 = 29\%$) (Supporting Information S1: Figure 2). However, there was no significant difference in technical success (RR: 1.00, 95% CI: 0.96–1.04, $I^2 = 76\%$) (Supporting Information S1: Figure 3). Myval demonstrated a lower risk of PPI during index hospitalization by 43% (RR: 0.57, 95% CI: 0.36–0.92, $I^2 = 23\%$) (Figure 2A). No significant differences between the groups were observed in outcomes such as minor vascular complications (Supporting Information S1: Figure 4), annular rupture (Supporting Information S1: Figure 5), in-hospital AKI (Supporting Information S1: Figure 6), major bleeding (Supporting Information S1: Figure 7), major vascular complications (Supporting Information S1: Figure 8), need for > 1 THV (Supporting Information S1: Figure 9), device embolization (Supporting Information S1: Figure 10), coronary obstruction/occlusion (Supporting Information S1: Figure 11), and cardiac tamponade (Supporting Information S1: Figure 12). By performing sensitivity analysis using a *leave-one-out* approach, we identified that procedural success becomes non-significant when we exclude the study by Santos-Martinez study (Central illustration 1).

At 30-day, device success slightly favored Myval (RR: 1.09, 95% CI: 1.00–1.19, $I^2 = 79\%$) (Supporting Information S1: Figure 12).

TABLE 1 | Studies' characteristics.

Study/first author	Year of publication	Countries/region	Study design	Study arms and devices	VARC	Max follow-up, months	N of participants
LANDMARK [7]	2024	Multicenter	RCT	Myval (Myval/Myval Inception/Myval Pro) versus Sapien (S3/S3 Ultra) and Evolut (Evolut R/Evolut PRO)	3	1	768
EVAL [12]	2023	Italy	Retrospective cohort	Myval vs Evolut (Evolut R)	3	12	166
TRITON [15]	2023	Multicenter	Retrospective registry	SAPIEN (S3 Ultra) versus Myval versus Evolut (Evolut PRO+)	3	1	360
Halim et al. [14]	2023	Netherlands	Retrospective single-center	Evolut (Evolut R/Pro) versus Myval	2	12	223
MYLAND [11]	2024	Multicenter	Retrospective, observational	Myval versus Sapien (S3 or S3 Ultra)	N/A	0	402
Santos-Martinez et al. [17]	2022	Multicenter	Retrospective registry	Myval versus Sapien (S3) versus Evolut (Evolut R/Pro) versus Acurate (Acurate Neo) versus Portico versus Allegra	2	0	1131
Delgado-Arana et al. [16]	2022	Multicenter	Prospective cohort	Myval versus Sapien (S3)	2	1	416

Abbreviations: N/A, not available; RCT, randomized controlled trial; VARC-2 or 3, valve academic research consortium 2 or 3 Criteria.

There was no significant difference in early safety outcomes (RR: 1.10, 95% CI: 0.95–1.27, $I^2 = 70\%$) (Supporting Information S1: Figure 14). Myval was also associated with a 40% reduced risk for PPI (RR: 0.60, 95% CI: 0.40–0.89, $I^2 = 43\%$) (Figure 2B), 55% for minor vascular complications (RR: 0.45, 95% CI: 0.23–0.90, $I^2 = 0\%$) (Supporting Information S1: Figure 15), and 77% for at least moderate AR (RR: 0.33, 95% CI: 0.11–0.98, $I^2 = 57\%$) (Supporting Information S1: Figure 16). However, there were no significant differences in stroke (Supporting Information S1: Figure 17), AKI (Supporting Information S1: Figure 18), any bleeding (Supporting Information S1: Figure 19) and major bleedings (Supporting Information S1: Figure 20), major vascular complications (Supporting Information S1: Figure 21) or at least mild PVL (Supporting Information S1: Figure 22). By performing sensitivity analysis using a *leave-one-out* approach, device success becomes non-significant when we exclude EVAL or TRITON and significant when we remove LANDMARK, early safety borderline significant when we exclude Delgado-Arena et al. 30-day minor vascular complications its significance when we remove either Delgado-Arena et al., EVAL or TRITON, and 30-day at least moderate AR its significance when we remove all the pooled studies, except LANDMARK.

At 1-year, no significant differences were observed between Myval and contemporary THVs in terms of stroke (RR: 0.56, 95% CI: 0.18–1.76, $I^2 = 0\%$) (Supporting Information S1: Figure 23).

3.5 | Myval Versus SEV

When compared to SEV, Myval was associated with 5% higher procedural success (RR: 1.05, 95% CI: 1.03–1.08, $I^2 = 0\%$) (Supporting Information S1: Figure 24), 8% higher device success (RR: 1.08, 95% CI: 1.03–1.13, $I^2 = 79\%$) (Supporting Information S1: Figure 25), 16% higher early safety (RR: 1.16, 95% CI: 1.04–1.28, $I^2 = 0\%$) (Supporting Information S1: Figure 26), 40% lower risk for PPI (RR: 0.60, 95% CI: 0.38–0.95, $I^2 = 44\%$) (Supporting Information S1: Figure 27), 58% lower risk for minor vascular complications (RR: 0.42, 95% CI: 0.18–0.98, $I^2 = 0\%$) (Supporting Information S1: Figure 28) and 81% lower risk for at least moderate transvalvular AR (RR: 0.19, 95% CI: 0.05–0.81, $I^2 = 76\%$) (Supporting Information S1: Figure 29). No significant differences between the two groups were identified in the remaining analyses. (Supporting Information S1: Figures 30–41).

3.6 | Myval Versus Sapien

When compared to Sapien, procedural success was borderline higher in favor of Myval (RR: 1.03, 95% CI: 1.00–1.05, $I^2 = 0\%$) (Supporting Information S1: Figure 42), but this result reached significance only after excluding the Delgado et. al's trial. Respectively, technical success was in favor of Sapien THV only when the TRITON trial was excluded (RR: 0.99, 95% CI: 0.94–1.04, $I^2 = 81\%$) (Supporting Information S1: Figure 43). In accordance with the previous analyses, Myval was associated with a 36% lower risk of PPI during index hospitalization (RR: 0.64, 95% CI: 0.42–0.98, $I^2 = 0\%$) (Supporting Information S1:

TABLE 2 | Summary of risk ratios, confidence intervals and I^2 .

Outcome	Figure	Risk ratio (RR)	95% Confidence Intervals (CI)	I^2 (%)
Primary analysis				
Periprocedural mortality	1A	0.62	0.13–2.95	0
30-day all-cause mortality	1B	0.78	0.40–1.49	0
1-year all-cause mortality	1C	0.75	0.29–1.95	35
In-hospital PPI	2A	0.57	0.36–0.92	23
30-day PPI	2B	0.60	0.40–0.89	43
Procedural success	S2	1.04	1.01–1.07	29
Technical success	S3	1.00	0.96–1.04	76
In-hospital minor vascular complications	S4	0.87	0.17–4.41	83
Annular rupture	S5	0.42	0.07–2.40	0
In-hospital AKI	S6	0.57	0.24–1.33	0
In-hospital major bleedings	S7	1.02	0.48–2.17	0
In-hospital major vascular complications	S8	0.60	0.06–5.69	0
Need for > 1 THV	S9	0.62	0.20–1.93	0
Device embolization	S10	0.52	0.18–1.57	0
Coronary arteries obstruction/occlusion	S11	0.48	0.15–1.57	0
Cardiac tamponade	S12	0.27	0.03–2.13	0
30-day device success	S13	1.09	1.00–1.19	79
30-day early safety	S14	1.10	0.95–1.27	70
30-day minor vascular complications	S15	0.45	0.23–0.90	0
30-day moderate or severe transvalvular AR	S16	0.33	0.11–0.98	57
30-day stroke	S17	0.87	0.43–1.73	5
30-day AKI	S18	0.85	0.27–2.71	55
30-day any bleeding	S19	0.58	0.12–2.88	83
30-day major bleeding	S20	1.38	0.68–2.81	0
30-day major vascular complications	S21	0.83	0.35–1.95	20
30-day greater than mild paravalvular AR	S22	0.52	0.19–1.44	0
1-year stroke	S23	0.56	0.18–1.76	0
MYVAL vs SEV				
Procedural success	S24	1.05	1.03–1.08	0
Device success	S25	1.08	1.03–1.13	79
30-day early safety	S26	1.16	1.04–1.28	0
30-day PPI	S27	0.60	0.38–0.95	44
30-day minor vascular complications	S28	0.42	0.18–0.98	0
30-day moderate or severe transvalvular AR	S29	0.19	0.05–0.81	76
Technical success	S30	1.01	0.98–1.05	0
Periprocedural mortality	S31	0.97	0.16–6.07	0
Need for > 1 THV	S32	0.36	0.10–1.31	0
Device embolization	S33	0.33	0.09–1.22	0
Cardiac tamponade	S34	0.27	0.03–2.13	0
30-day all-cause mortality	S35	0.80	0.38–1.69	0
30-day stroke	S36	0.99	0.46–2.11	0
30-day AKI	S37	0.71	0.33–1.53	0

(Continues)

TABLE 2 | (Continued)

Outcome	Figure	Risk ratio (RR)	95% Confidence Intervals (CI)	I ² (%)
30-day major vascular complications	S38	1.42	0.20–10.22	60
30-day greater than mild paravalvular AR	S39	0.43	0.15–1.25	0
Coronary arteries obstruction/occlusion	S40	0.56	0.15–2.03	0
30-day major bleeding	S41	1.03	0.44–2.41	60
MYVAL versus SAPIEN				
Procedural success	S42	1.03	1.00–1.05	0
Technical success	S43	0.99	0.94–1.04	81
In-hospital PPI	S44	0.64	0.42–0.98	0
In hospital minor vascular complications	S45	0.91	0.20–4.17	79
Periprocedural mortality	S46	0.22	0.03–1.78	0
Annular rupture	S47	0.31	0.25–1.55	0
In hospital AKI	S48	0.63	0.25–1.55	0
In hospital major bleeding	S49	1.17	0.02–36.13	85
In hospital major vascular complications	S50	0.74	0.02–36.13	85
Need for > 1 THV	S51	0.72	0.11–4.88	0
Device embolization	S52	0.96	0.22–4.20	0
Coronary arteries obstruction/occlusion	S53	0.30	0.05–1.70	0
Cardiac Tamponade	S54	0.20	0.02–1.59	0
30-day device success	S55	1.08	0.88–1.33	93
30-day all-cause mortality	S56	0.63	0.20–1.95	31
30-day early safety	S57	0.75	0.22–2.54	84
30-day stroke	S58	0.54	0.10–2.87	56
30-day PPI	S59	0.75	0.48–1.17	34
30-day AKI	S60	0.96	0.05–19.38	80
30-day major bleeding	S61	0.96	0.05–19.38	80
30-day major vascular complications	S62	0.71	0.22–2.28	32
30-day minor vascular complications	S63	0.35	0.09–1.41	34
30-day moderate or severe transvalvular AR	S64	1.94	0.69–5.44	0

Note: Low heterogeneity is marked with green, moderate with light blue and high with red. Statistically significant differences are marked with bold and gray. Abbreviations: AKI, acute kidney injury, AR, aortic regurgitation; PPI, permanent pacemaker implantation, THV, transcatheter heart valve.

Figure 44); however, minor vascular complications did not differ significantly (RR: 0.91, 95% CI: 0.20–4.17, I² = 79%) (Supporting Information S1: Figure 45). No significant difference was observed between the two groups in the rest analyses (Supporting Information S1: Figures 46–64).

3.7 | Risk of Bias Assessment

The quality of the non-randomized studies included in our analysis was assessed using the NOS, with scores ranging from 5 to 9. Among the six studies evaluated, five demonstrated high quality, with TRITON, Halim, MYLAND, and Delgado-Arana attaining the maximum score of 9, and EVAL achieving a score of 7. Santos-Martinez, with a score of 6, was categorized as moderate quality. These results reflect robust study designs and reliable outcomes across most of the included studies.

(Supporting Information S1: Table 8) The RoB 2 assessment for the LANDMARK trial evaluated five domains of potential bias, showing that the randomization process, the management of missing outcome data, the measurement of outcomes and the selection of reported results had a low risk of bias. However, our assessment identified some concerns regarding deviations from intended interventions, due to the open-label design of the study.

4 | Discussion

To the best of our knowledge, our systematic review and meta-analysis is the first to compare Myval with the other contemporary THVs available in the market. In accordance with the recently published LANDMARK RCT, this meta-analysis highlighted that Myval performance is comparable with the

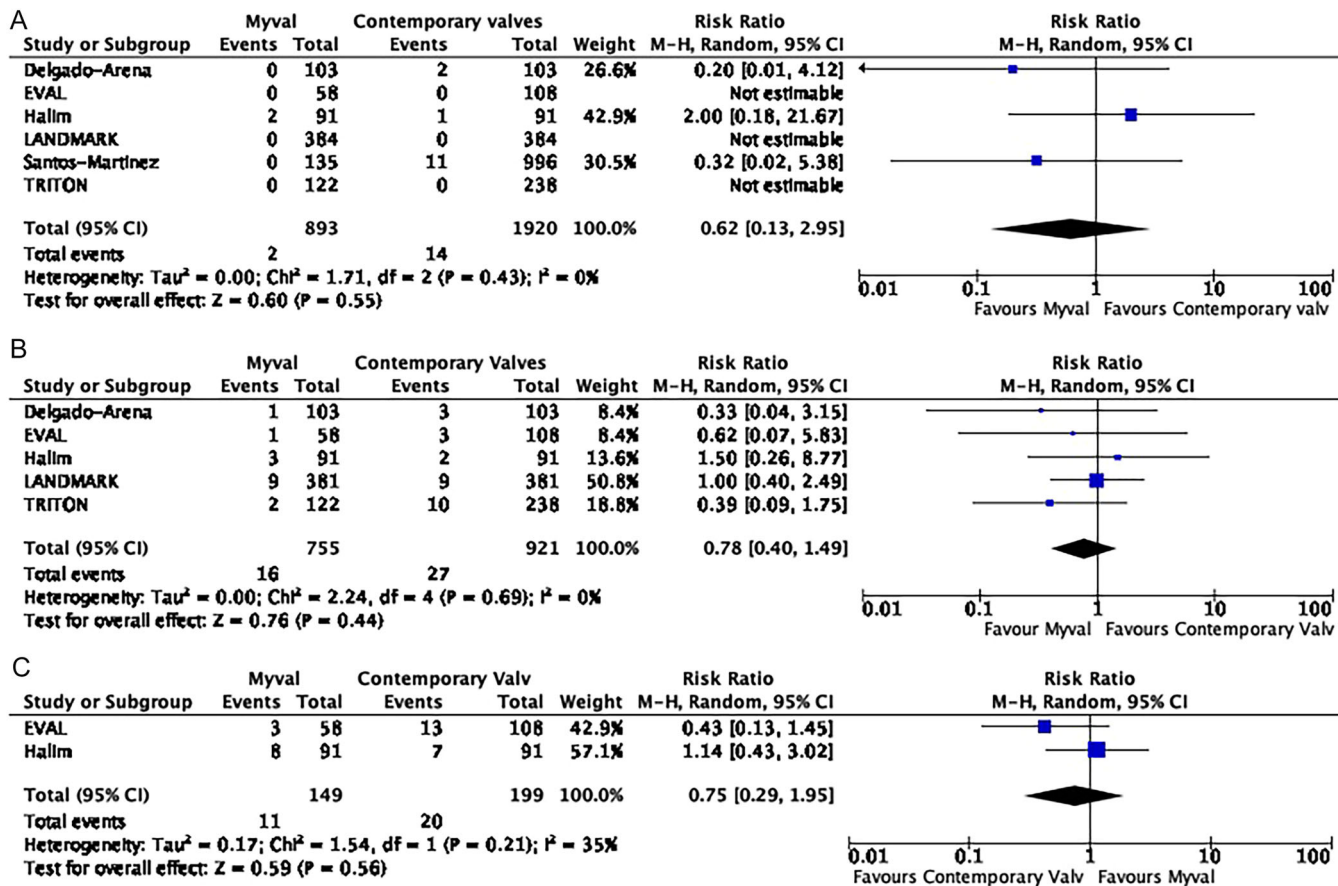


FIGURE 1 | Forest plot showing (A) periprocedural mortality, (B) 30-day, all-cause mortality and (C) 1-year, all-cause mortality between Myval and other contemporary valves, with risk ratio and 95% CIs. CI, confidence interval, M-H, Mantel-Haenszel. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com)]

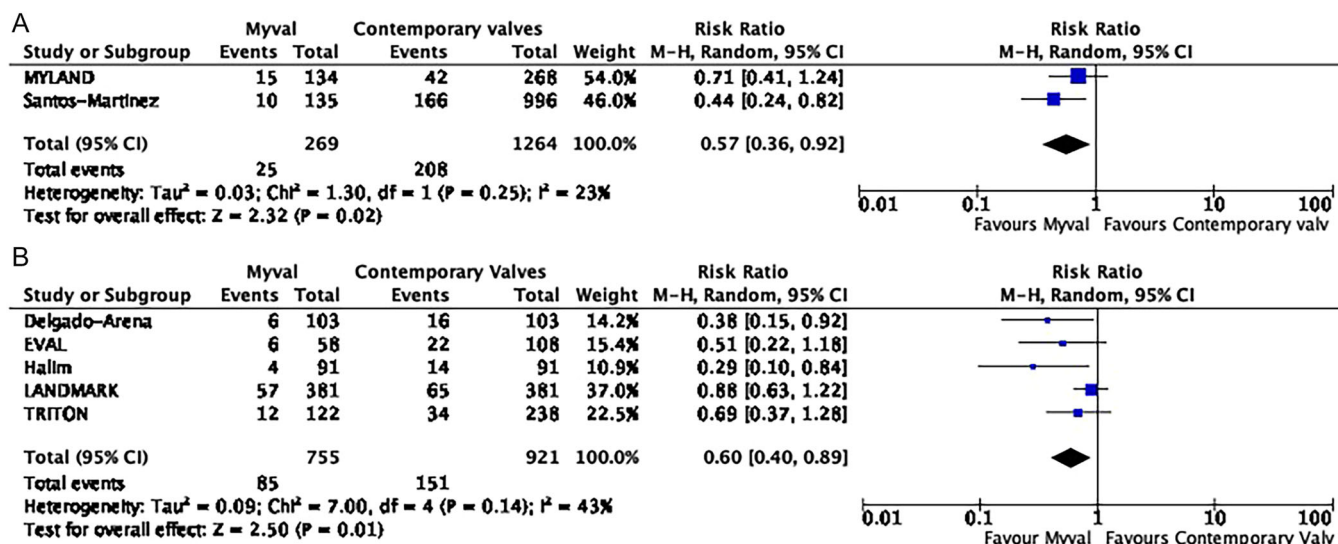
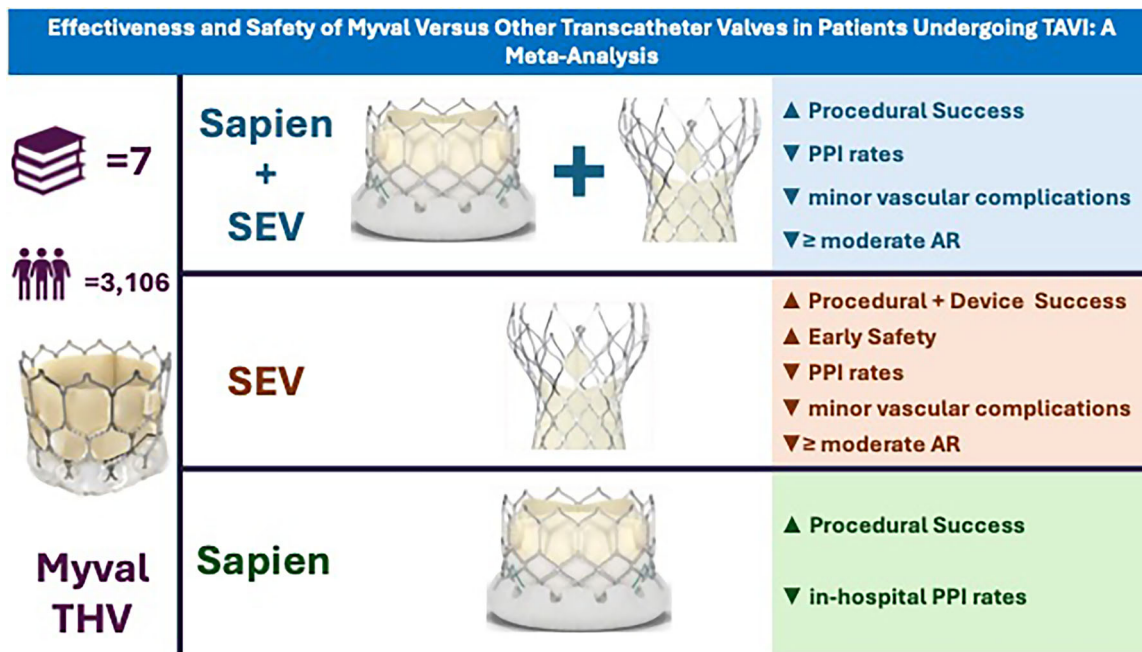


FIGURE 2 | Forest plot showing (A) in-hospital and (B) 30-day permanent pacemaker implantation incidence between Myval and other contemporary valves, with risk ratio and 95% CIs. CI, confidence interval; M-H, Mantel-Haenszel. [Color figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com)]



CENTRAL ILLUSTRATION 1 | This figure illustrates key clinical outcomes comparing transcatheter aortic valve implantation (TAVI) using Myval THV with other THVs. AR, aortic regurgitation; PPI, permanent pacemaker implantation; SEV, self-expandable valve. [Color figure can be viewed at wileyonlinelibrary.com]

available THV, in terms of safety and effectiveness. Noteworthy, Myval might be better in specific endpoints, such as procedural success, device success, PPI, minor vascular complications and at least moderate transvalvular AR rates.

With radical growth in the adoption of TAVI in even low-risk and patients younger than <65 years, the choice of TAVI prosthesis is vital for achieving short-, mid- and long-term optimal results. Globally, the two main THVs used for TAVI are the BEV SAPIEN and the SEV Evolut prostheses. Although the pros and cons of each platform are well-known, it remains unknown which THV should be preferred, considering that there are no adequately powered RCTs. In the SMART trial, a total of 716 patients (mean age, 80 years; 87% women) with symptomatic severe AS and an aortic-valve annulus area of $\leq 430 \text{ mm}^2$ (small annulus) were randomized to undergo TAVI with either a SEV or a BEV [18]. It showed that a SEV was non-inferior to a BEV with respect to clinical outcomes and superior with respect to bioprosthetic-valve dysfunction during the 12-month follow-up [18]. A recent meta-analysis including 16 studies and 10,174 patients showed that BEV was associated with similar all-cause mortality, lower risk of stroke, PPI, and at least moderate PVL, but with higher risk of at least moderate patient-prosthesis mismatch [19].

The LANDMARK trial was a prospective, multinational, randomized, non-inferiority study, evaluated the safety and effectiveness of the Myval THV compared to the contemporary SEV (Evolut) and BEV (Sapien) THVs in patients undergoing TAVI [7]. Conducted across 31 centers in 16 countries, the trial enrolled 768 participants aged 80 years on average. The primary endpoint, a composite measure including all-cause mortality, stroke, bleeding, AKI, vascular complications, valve regurgitation, and pacemaker implantation, was achieved in 25% of

Myval patients compared to 27% in the comparator group, confirming the non-inferiority of Myval with a risk difference of -2.3% ($p < 0.0001$ for non-inferiority). Recently, a sub-analysis of LANDMARK comparing separately the Myval THV to Sapien BEV and Evolut SEV was published, confirming the non-inferiority of this novel THV versus each of the two well-known THVs [20].

Furthermore, the need for PPI after TAVI remains an unsolved issue for this novel therapeutic approach of AS. It is estimated that the crude incidence of PPI after TAVI during 1-year follow-up is about 17% [21]. Although the advances in implantation techniques, such as cusp-overlap view, high-deployment and MIDAS technique and the recognition of high-risk patterns in baseline electrocardiogram, such as right bundle branch block (RBBB), SEV has been associated with a twofold increased risk, compared to BEV [21]. In our meta-analysis, the crude PPI rates observed during index hospitalization were 9.3% for Myval, 16.5% for all THV and 14.5% for Sapien. At the 30-day follow-up, the corresponding rates were 11.3%–12.4% for Myval, 16.4% for all THV, 17.6% for SEV, and 14.9% for Sapien. As we expected, Myval, as a BEV, was associated with lower PPI rates compared to SEV; additionally, our meta-analysis is the first to show that Myval was associated with 36% lower risk of PPI compared to Sapien during index hospitalization. This could be attributed to the hybrid honeycomb frame, which facilitates optimal radial force distribution, thereby reducing compression on the atrioventricular conduction system. Additionally, features such as precise implantation depth and the incorporation of a soft polyethylene terephthalate (PET) sealing cuff enhance the device's capacity to achieve a tailored fit, minimizing the risk of conduction disturbances [22]. Moreover, this advantage of Myval THV might be associated with the innovative 1.5 mm incremental sizing, which is facilitated with a more precise

valve-aortic annulus matching [13]. LANDMARK trial showed a numerical trend in favor of Myval, without reaching significance, as it was not properly powered for this comparison [20]. However, the COMPARE TAVI RCT, comparing the Myval THV with the Sapien THV, presented at PCR London Valves 2024, reported a higher incidence of PPI in the Myval group compared to the Sapien group [23]. It is important to note that these findings are based on the 1-year follow-up data, and the forthcoming publication of the study may provide further insights into in-hospital and 30-day PPI rates.

Successful implantation of THV remains the cornerstone for achieving the optimal results of TAVI. Although there are many different definitions describing successful placement, like procedural, device, technical success and early safety, they share numerous mutual features. Our analysis showed a trend in favor of Myval regarding successful implantation and this could be attributed to the unique design characteristics of the Myval THV, including its low-profile, extremely flexible and steerable delivery system, enhanced radial strength, improved deployment mechanism, and ability to adapt to different anatomies. These characteristics might contribute to improved device positioning, optimal sealing, and reduced PVL, ultimately enhancing procedural outcomes and overall implantation success [24].

Moreover, Myval was associated with lower rates of 30-day minor vascular complications in both primary analysis (RR: 0.45, 95% CI: 0.23–0.90, $P^2 = 0\%$) and analysis versus SEV (RR: 0.42, 95% CI: 0.18–0.98, $P^2 = 0\%$). Noteworthy, the difference was non-significant at the evaluation during index hospitalization and versus BEV. Considering that morbidity and mortality after TAVI is closely associated with vascular complications, our findings might reveal that Myval might present a more friendly platform regarding vascular access and complications [25, 26].

Finally, AR, either paravalvular or transvalvular, remains a frequent complication after TAVI and has a significant prognostic role. Our meta-analysis showed that there is no significant difference between Myval and contemporary THVs, either SEV or Sapien; nevertheless, Myval was associated with significantly less \geq moderate transvalvular AR compared with all the THV and SEV, but not with Sapien. This is partially explained by the sub-analysis of LANDMARK, where prosthetic valve regurgitation is 3.4% in Myval group and 7.4% in SEV and a borderline p-value of 0.06. These findings are in accordance with the SCOPE I and the SOLVE-TAVI trials, where BEV had lower rates than SEV [27, 28]. This could be explained by the need for post-dilation, which is mainly performed after SEV implantation, to minimize risk of paravalvular regurgitation (PVR) after TAVI [7]. However, it has been associated with damage of the prosthetic leaflets, which has been linked early risk of THV deterioration [29]. Further studies, such as the 1-year results of LANDMARK, might answer this dilemma.

4.1 | Limitations

Our systematic review and meta-analysis present several limitations, that should be acknowledged. First, it is a study-level meta-analysis, and the lack of patient-level data did not allow us to estimate their possible interaction on the outcomes. In

addition, only one study was RCT, which is the best sources for meta-analyses. Moreover, the *leave-one-out* approach revealed that exclusion of specific studies shifted the statistical significance in several analyses, highlighting that the overall findings are less robust and should be interpreted with caution. Additionally, only a limited proportion of the seven studies report each pre-specified endpoint (including the three primary endpoints), therefore the number of studies included in the analysis for most endpoints is low, limiting external generalizability and statistical power. Finally, heterogeneity was significant in numerous analyses. Therefore, we performed subgroup analyses based on the type of THV (SEV or Sapien).

5 | Conclusions

Our systematic review and meta-analysis, the first to comparing the Myval THV with established platforms, demonstrates its comparable safety and effectiveness to SAPIEN and Evolut THVs. Notably, Myval shows potential advantages in procedural success, reduced PPI, minor vascular complications, and lower rates of AR. Future RCTs with long-term follow-up are mandatory to confirm these findings and evaluate the durability and hemodynamic performance of this novel valve.

Acknowledgments

The authors have nothing to report.

Consent

The authors have nothing to report.

Conflicts of Interest

Andreas Baumbach: Consultation and speaker fees from: AstraZeneca, Sinomed, MicroPort, Medtronic, Faraday, Pi-Cardia, Biosensors, Jena-Valve and Meril Life Sciences. Patrick Serruys: Consultancy fees from SMT, Novartis, Meril Life Sciences, and Philips. Konstantinos Toutouzas: Proctorship with Abbott, Meril Life Sciences and Medtronic; consultancy fees from Gore Medical; Board member of the Hellenic Society of Cardiology. The other authors declare no conflicts of interest.

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Supporting Information

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