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Myval versus Contemporary Valves in Patients Undergoing Transcatheter Aortic Valve Implantation: A Systematic Review and Meta-Analysis

ABSTRACT

Background: Myval is a balloon-expandable valve (BEV) used in transcatheter aortic valve implantation (TAVI) with distinguished features. Data comparing Myval with contemporary transcatheter heart valves (THVs) is limited. The authors performed a meta-analysis of studies comparing Myval with contemporary THVs (Sapien series and Evolut series).

Methods: The authors searched PubMed, EMBASE, and Cochrane databases. The primary composite endpoint of early safety (freedom from death and major complications) and other outcomes were extracted as defined by the Valve Academic Research Consortium 3 (VARC 3). The authors computed risk ratios (RRs) with 95% CIs using a Mantel–Haenszel method with a random-effects model with Review Manager (Cochrane Collaboration).

Results: Six studies with 2084 patients were included. Myval had better early safety at 30 days as per VARC 3 (RR 1.12; 95% CI: 1.02-1.22; *P* = .01) and lower need for permanent pacemaker implantation (PPI) (RR 0.62; 95% CI: 0.45-0.86; *P* = .004). Other outcomes were comparable in both groups. Vis-à-vis Evolut, Myval had better 30-day device success and lower rates of moderate or severe paravalvular leak (PVL) in addition to better early safety and lower need for PPI. Subgroup analyses of Myval with Sapien showed non-inferiority of Myval.

Conclusion: Myval showed better safety and lower need for PPI and may become a promising alternative for concurrent THVs.

Keywords: Aortic valve replacement, interventional cardiology, Myval, transcatheter aortic valve implantation, valve disease

META-ANALYSIS

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INTRODUCTION

Transcatheter aortic valve implantation (TAVI) is a minimally invasive procedure for symptomatic and asymptomatic patients with severe aortic valve stenosis.[1] Previously considered a preferred treatment in patients with high risk for surgical aortic valve replacement,[2-6] it has become a treatment of choice in intermediate- and low-risk patients as well.[7-10] There are mainly 2 types of transcatheter heart valves (THVs) used in TAVI: balloon-expandable THV (BEV) and self-expandable THV. The former include Sapien family (Edwards Lifesciences, USA) and Myval family (Meril, India). Self-expandable THVs include Evolut R/Pro (Medtronic, USA), Navitor (Abbott Cardiovascular, USA), Acurate Neo, Acurate Neo 2 (Boston Scientific, USA), Allegra (Biosensors, Singapore), and Hydra THV (Sahajanand Medical Technologies, India). Self-expandable THVs with supra-annular leaflet position provide larger effective orifice area with lower gradients but a relatively increased chance of PVL as well as a need for permanent pacemaker implantation (PPI).[11,12]

Myval (Meril, India) is a novel BEV that has 1.5 mm incremental sizing capacity providing more accurate and precise annular matching. It does have extra-large sizes as well (30.5 mm and 32 mm).[13,14] It also has a lower unit cost compared to traditionally used THVs like Sapien or Evolut series. Myval has a 40-50% cost benefit when compared to Sapien or Evolut series THVs. However, Myval is CE

(Conformity to European standards) approved whereas Sapien and Evolut series THVs are CE as well as USFDA (United States Food and Drug Administration) approved for use in TAVI. Hence, Sapien and Evolut series THVs have much more acceptance globally. Myval Octacor is the newly designed version of Myval THV. It has the same frame height as the previous Myval version (17.35-21.14 mm) but only 2 rows of identical octagonal cells which reduce the foreshortening during expansion and facilitate accurate deployment (Figure 1). Moreover, it has a better-designed crimping process in which it is directly mounted on its balloon delivery system, which reduces the need for in situ maneuvering. This minimizes the procedural steps and ensures procedural success with less effort. A low-profile 14Fr Python introducer sheath is suitable for all Myval THV diameters (from 20 mm to 32 mm) with full retrievability in case the annulus cannot be crossed. The external skirt in Myval Octacor THV is up to 50% of the frame height which minimizes the propensity for paravalvular leak (PVL). A landing zone marker toward the ventricular end of the Navigator Inception THV delivery system facilitates precise positioning of Myval Octacor THV at the annulus.[15]

The safety and efficacy of Myval have been suggested in multiple studies, including in high, intermediate, and low-risk symptomatic severe aortic stenosis, as well as in patients with bicuspid aortic valve morphology.[16-25] Myval has been studied for long-term outcomes in patients undergoing TAVI and found to be safe and effective.[26] Further research has also shown that the need for PPI after TAVI with Myval can be predicted beforehand by using aortic knob calcification, which is a useful tool for planning the procedure.[27]

Myval has not been extensively studied in comparison to the contemporary THVs. There have been a few observational studies in the past comparing Myval with other THVs.[20,22-24,28] Vast majority of the data with Myval has been generated using Myval Gen 1 and Myval Octacor has been studied in a small number of patients. Recently, 1 RCT compared Myval THV with contemporary THVs, including Sapien THV series and Evolut THV series, and found that Myval THV is non-inferior to contemporary THVs for the primary endpoint, which was a composite of VARC-3[29] defined endpoints at 30 days.[30] How this data fares collectively is unknown. Considering its cost-effectiveness and ease of use, Myval may gain global acceptance provided further regulatory approvals. Large data is required for any change in the regulatory status of Myval as well as widespread acceptance in the global healthcare sector. The authors conducted a systematic review and meta-analysis to assess the aggregate data of studies comparing Myval THV with contemporary THVs.

HIGHLIGHTS

- Myval is a novel, low-cost and broadly available BEV.
- Myval appears to be safe and effective compared to Sapien series and fares better than Evolut in 30-day outcomes.
- Further larger and longer duration randomized controlled trials are needed to compare Myval with contemporary THVs.

METHODS

Eligibility Criteria

This systematic review and meta-analysis was performed and reported in accordance with the Cochrane Collaboration Handbook for Systematic Review of Interventions and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) Statement guidelines.[31,32]

The authors included studies that met all the following eligibility criteria: (1) observational studies or randomized controlled trials (RCTs); (2) comparing Myval THV to contemporary THVs (Sapien or Evolut or both); and (3) enrolling patients who underwent TAVI for severe aortic stenosis. In addition, studies were only included if they reported any of the outcomes of interest.

Search Strategy

The authors systematically searched PubMed, Embase, and Cochrane Central Register of Controlled Trials from inception to June 2024 with the following search terms: "Myval," "Evolut," "Sapien," "Transcatheter Aortic Valve Replacement," "balloon-expandable valves," and "self-expandable valves."

The references from all included studies, previous systematic reviews, and meta-analyses were also searched manually for any additional studies. Two authors (H.A. and L.C.) independently extracted the data following predefined search criteria and quality assessment. The prospective meta-analysis protocol was registered on PROSPERO under protocol ID CRD42024562100.

End Points

Primary endpoint was a composite of clinical endpoints defined as "Early Safety" as per VARC 3 criteria, which translates to freedom from all-cause mortality; stroke; VARC type 2-4 bleeding; major vascular, access related or cardiac structural complication; stage 3 or 4 AKI; moderate or severe aortic regurgitation; new PPI; surgery or intervention related to device. Secondary endpoints included outcomes like technical success, procedural death, valve embolization or malpositioning, coronary artery occlusion, annulus rupture, major vascular complication, major bleeding, moderate or severe PVL, need for PPI, 30-day device success, all-cause mortality, cardiovascular (CV) mortality, acute kidney injury (AKI), stroke, and myocardial infarction (MI).

VARC 3

Thirty-day device success was defined by VARC 3, which translates to technical success; intended performance of the THV; freedom from mortality or surgery or intervention related to the device; and freedom from major vascular, access related or cardiac structural complications.[29] Major bleeding was defined as VARC type 2-4 bleeding events, which are defined as follows.

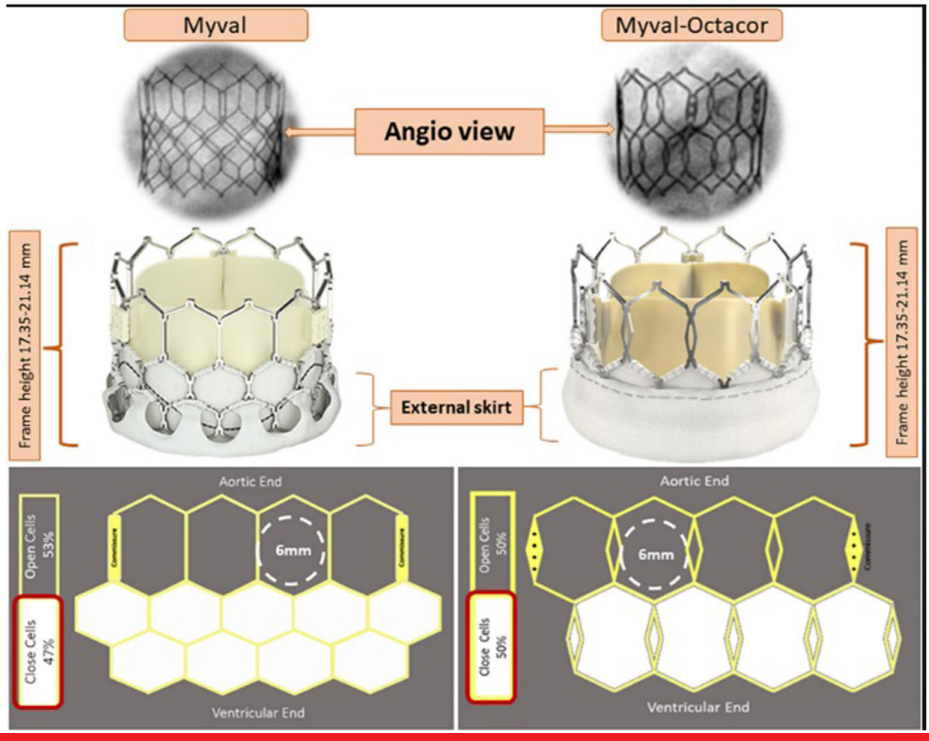

Figure 1. Features and differences between Myval and Myval Octacore devices.

Type 2

- Overt bleeding that requires a transfusion of 2-4 units of whole blood/red blood cells.
- Overt bleeding associated with a hemoglobin drop of >3 g/dL (>1.86 mmol/L) but <5 g/day (<3.1 mmol/L).

Type 3

- Overt bleeding in a critical organ, such as intracranial, intraspinal, intraocular, pericardial associated with hemodynamic compromise/tamponade and necessitating intervention), or intramuscular with compartment syndrome.
- Overt bleeding causing hypovolemic shock or severe hypotension (systolic blood pressure <90 mm Hg lasting >30 minutes and not responding to volume resuscitation) or requiring vasopressors or surgery.
- Overt bleeding requiring reoperation, surgical exploration, or re-intervention for the purpose of controlling bleeding.
- Post-thoracotomy chest tube output ≥ 2 L within a 24-hour period.
- Overt bleeding requiring a transfusion of ≥ 5 units of whole blood/red blood cells.
- Overt bleeding associated with a hemoglobin drop ≥ 5 g/dL (≥3.1 mmol/L).

Type 4

- Overt bleeding leading to death. Should be classified as:
- Probable: Clinical suspicion.
- Definite: Confirmed by autopsy or imaging.

Major vascular complications as per VARC 3 include any one of the following: aortic dissection or aortic rupture; vascular injury or compartment syndrome resulting in death, VARC type ≥ 2 bleeding, limb or visceral ischaemia, or irreversible neurologic impairment; distal embolization from a vascular source resulting in death, amputation, limb or visceral ischemia, or irreversible end-organ damage; unplanned endovascular or surgical intervention resulting in death, VARC type ≥ 2 bleeding, limb or visceral ischaemia, or irreversible neurologic impairment; and closure device failure resulting in death, VARC type ≥ 2 bleeding, limb or visceral ischemia, or irreversible neurologic impairment.[29]

The authors performed subgroup analyses comparing Myval with self-expandable THV Evolut series and Myval with BEV Sapien series.

Statistical Analysis and Software

The authors used DerSimonian and Laird random effects models, as recommended by the Cochrane Collaboration, in anticipation of high heterogeneity. Risk ratios (RRs) with 95% CIs were used to compare treatment effects for categorical endpoints. Cochran Q test and I^2 statistics were used to assess for heterogeneity; *P* values inferior to 0.10 and I^2 > 25% were considered significant for heterogeneity. Review Manager Web (manufactured in 2022 by The Cochrane Collaboration, Copenhagen, Denmark) was used for statistical analysis.[33]

Quality Assessment

Nonrandomized studies were appraised with the Risk of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool.[34] Quality assessment of RCT was performed using the Cochrane Collaboration's tool for assessing risk of bias in randomized trials (ROB-2), in which studies are scored as high, low, or unclear risk of bias in 5 domains: selection, performance, detection, attrition, and reporting biases.[35]

Publication bias was investigated by funnel-plot analysis of point estimates according to study weights. The authors performed sensitivity analyses of early safety and need for PPI outcomes with leave-one-out method.

Subgroups and Sensitivity Analyses

Myval was compared with Evolut and Sapien series THVs in subgroup analyses. The authors also performed a sensitivity analysis with the leave-one-out method. The authors performed odds ratio (OR) as well as risk difference for selected outcomes in sensitivity analyses.

RESULTS

Study Selection and Baseline Characteristics

As detailed in Figure 2, the initial search yielded 218 results. After removal of duplicate records and ineligible studies, 9 remained and were fully reviewed based on inclusion criteria. Of these, a total of 6 studies were included, comprising 2084 patients from 1 RCT[30] and 5 observational studies.[20,22-24,28]

A total of 892 (42.8%) patients received Myval and 1192 (57.2%) received contemporary THVs. Study characteristics are reported in Table 1. Mean age ranged from 73 years to 83 years. Male patients constituted 59.4% of the total population. Significant between-study variability existed as to follow-up periods (Table 1). Mean society of thoracic surgeons (STS) scores ranged between 2.6% and 4.7% across studies.

Pooled Analysis of All Included Studies

Myval had higher early safety at 30 days (RR 1.12; 95% CI 1.02-1.22; P = .01; I^2 = 58%; Figure 3A demonstrates better early safety with Myval) and lower need for PPI (RR 0.62; 95% CI 0.45-0.86; P = .004; I^2 = 34%; Figure 3B depicting lower need for PPI with Myval) as compared to contemporary THVs.

Technical success (RR 1; 95% CI 0.96-1.03; P = .76; I^2 = 64%); procedural death (RR 0.77; 95% CI 0.08-7.23; P = .82; I^2 = 28%); valve embolization or malpositioning (RR 0.72; 95% CI 0.25-2.08; P = .54; I^2 = 0%); coronary artery occlusion (RR 0.57; 95% CI 0.15-2.09; P = .39; I^2 = 0%); annulus rupture (RR 0.70; 95% CI 0.11-4.28; P = .70; I^2 = 0%); major vascular complication

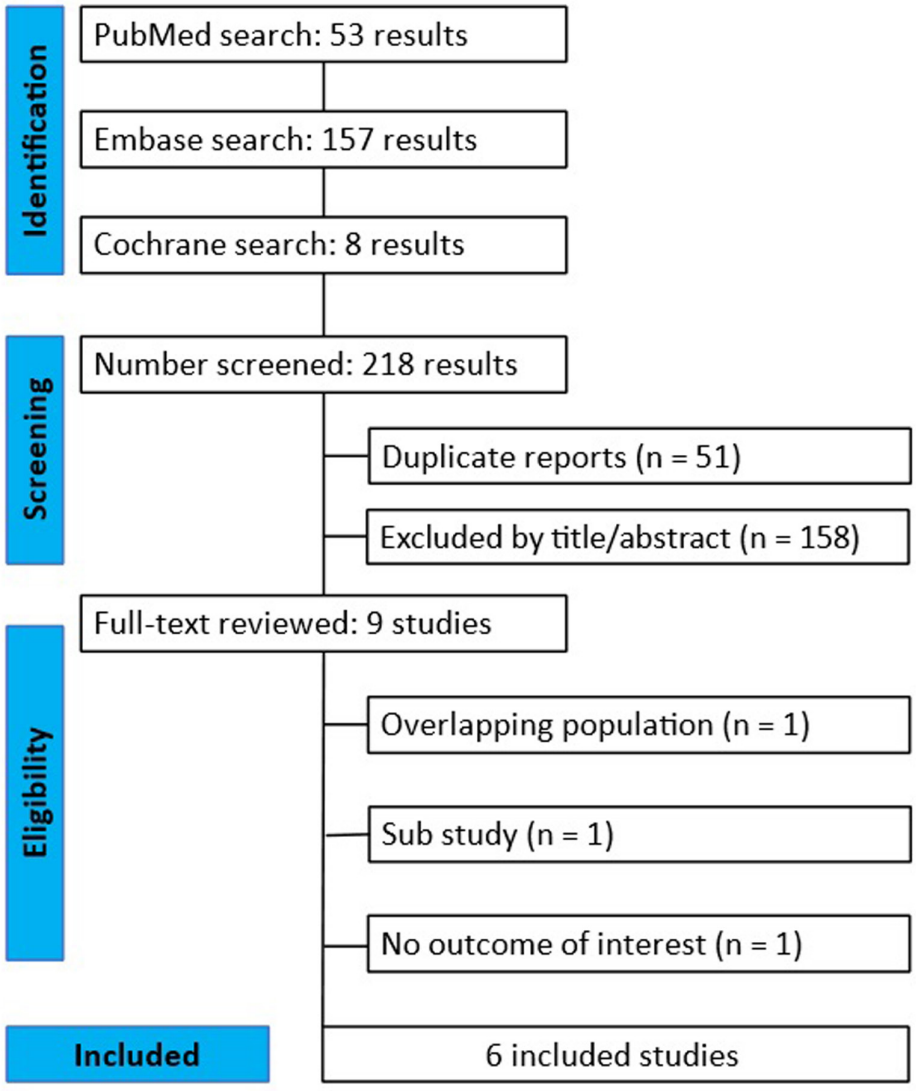

Figure 2. Preferred Reporting Items for Systematic Reviews and Meta-Analysis flow diagram of study screening and selection.

Table 1. Baseline Characteristics of the Included Studies

	Barki 2022	Delgado-Arana 2022	Amat-Santos 2023	Halim 2023	Baumbach 2024	Ubben 2024
Type of study	Observational	Observational	Observational	Observational	RCT	Observational
Intervention/control	Myval/Evolut R	Myval/Sapien 3	Myval/EvolutPro+ / Sapien3 Ultra	Myval/Evolut	Myval/(Evolut or Sapien)	Myval/Sapien
No. of patients	58/108	103/103	122/109/129	91/91	384/384	134/268
Age (years) (mean)	82/83	81/80.6	73/79/78	80/80.5	80/80.4	81/79.7
Male (%)	50/61	56.3/63.1	77.9/62.4/74.4	51/51	50/54	66/68
BMI (kg/m^2) (mean)	NA	26.6/28.2	25.5/25.6/27.1	28.3/28.2	28.2/28	26.9/27.3
NYHA class III-IV (%)	50/45	47.6/44.7	64/35/61	31/46	54/51	NA
STS score (mean/median)	3.3/3.9	3.3/3.5	4/4/2.7	NA	2.6/2.6	4.7/3.9
Prior stroke (%)	5/10	13.6/21.4	4.9/4.6/8.5	21/21	3/2	8.2/8.6
Prior PCI (%)	43/35	NA	NA	NA	8/7	44/43
Prior CABG (%)	5/10	6.8/3.9	7.4/3.7/1.6	14/11	3/5	14/11
Prior PPI (%)	5/16	6.8/8.7	9/14.7/14.7	7/5	3/5	13/13
Hypertension (%)	90/81	NA	NA	71/65	67/66	92/93
DM (%)	21/31	31.1/36.9	NA	37/35	29/30	25/31
CKD (%)	48/49	33/32	14.8/21.1/16.1	34/33	47/49	23/24
Atrial fibrillation (%)	31/38	18.4/19.4	8.2/9.2/10.9	29/27	24/26	NA
CAD (%)	60/48	41.7/36.9	34.4/36.7/43.4	45/41	14/15	NA
PAD (%)	31/14	9.7/19.4	9.8/12.1/6.3	13/13	NA	NA
Bicuspid aortic valve (%)	NA	NA	100/100/100	NA	6/8	9.8/11
Follow-up	180 days	30 days	30 days	365 days	30 days	1 day

BMI, body mass index; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CKD, chronic kidney disease; DM, diabetes mellitus; MI, myocardial infarction; NA, not available; NYHA, New York heart association; PAD, peripheral arterial disease; PCI, percutaneous coronary intervention; PPI, permanent pacemaker implantation; RCT, randomized controlled trial; STS, society of thoracic surgeons.

Figure 3A) Myval showed higher Early safety at 30 days compared to contemporary THVs (p=0.01)

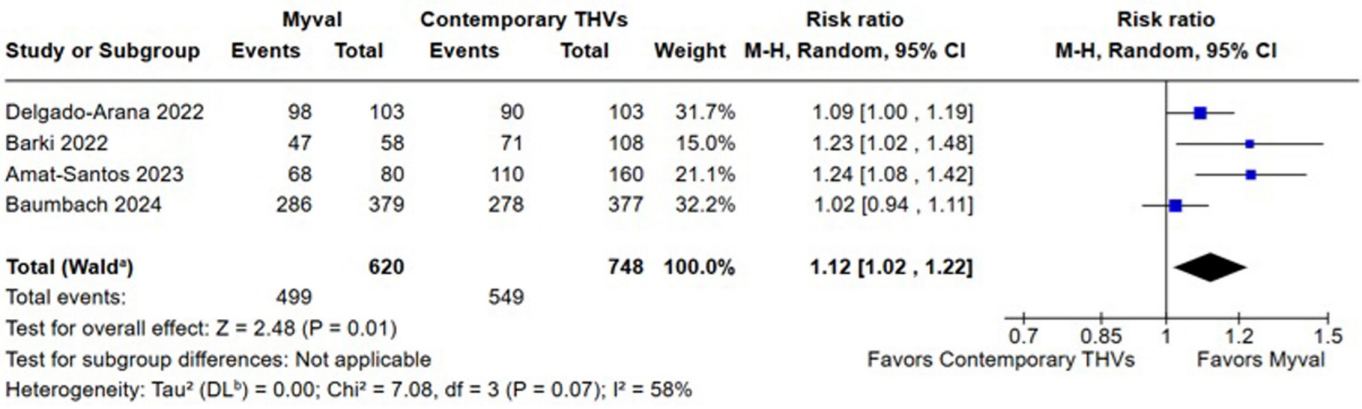

Figure 3B) Forest plot for Need for PPI outcome showing lower rates of need for PPI in Myval group as compared to Contemporary THVs (p=0.004)

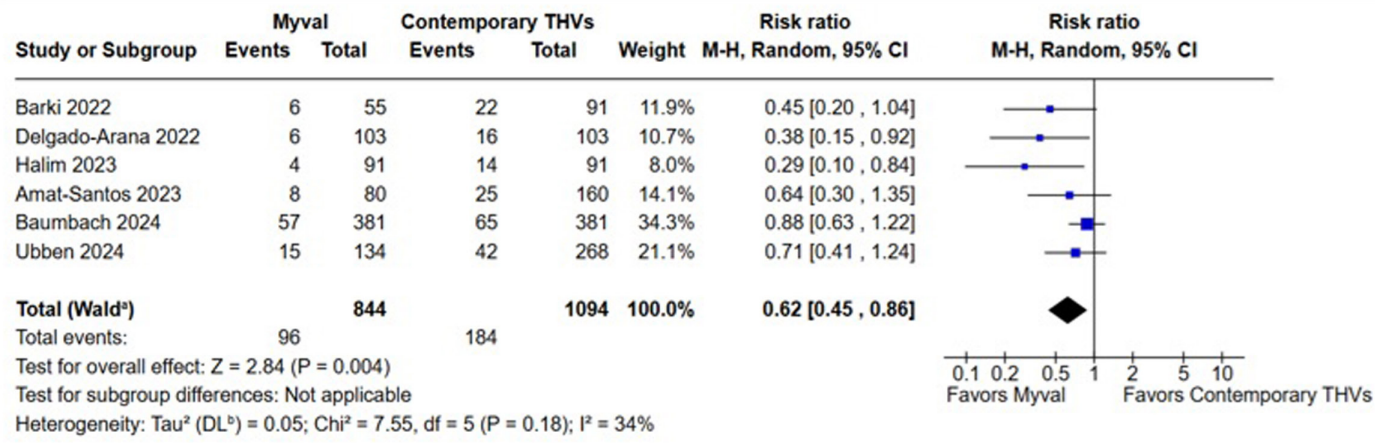

Figure 3. Forest plots for main analysis Myval vs. Contemporary thoracic heart valves. (A) Myval showed higher early safety at 30 days compared to contemporary thoracic heart valves (*P* = .01). (B) Forest plot for need for permanent pacemaker implantation outcome showing lower rates of need for permanent pacemaker implantation in Myval group as compared to contemporary thoracic heart valves (*P* = .004).

(RR 1.18; 95% CI 0.42-3.33; $P = .76$; $I^2 = 54\%$); major bleeding (RR 1.12; 95% CI 0.53-2.34; $P = .77$; $I^2 = 32\%$); and moderate or severe PVL (RR 0.58; 95% CI 0.33-1.02; $P = .06$; $I^2 = 0\%$) were comparable in both groups. There was no statistical difference between the groups regarding 30-day device success (RR 1.10; 95% CI 0.99-1.23; $P = .07$; $I^2 = 86\%$); all-cause mortality (RR 0.79; 95% CI 0.43-1.46; $P = .45$; $I^2 = 0\%$); CV mortality (RR 0.81; 95% CI 0.39-1.68; $P = .58$; $I^2 = 0\%$); AKI (RR 0.82; 95% CI 0.33-2.04; $P = .67$; $I^2 = 43\%$); stroke (RR 0.85; 95% CI 0.48-1.52; $P = .59$; $I^2 = 0\%$); and MI (RR 0.54; 95% CI 0.11-2.77; $P = .46$; $I^2 = 0\%$).

In subgroup analyses, Myval had higher early safety at 30 days (RR 1.16; 95% CI 1.04-1.29; $P = .006$; $I^2 = 33\%$; Figure 4A showing improved early safety with Myval); lower need for PPI (RR 0.57; 95% CI 0.35-0.95; $P = .03$; $I^2 = 46\%$; Figure 4B showing lesser PPI need with Myval); lower moderate or severe PVL (RR 0.36; 95% CI 0.20-0.65; $P = .0007$; $I^2 = 0\%$; Figure 5A demonstrates low PVL with Myval); and better 30-day device success (RR 1.13; 95% CI 1.03-1.24; $P = .01$; $I^2 = 69\%$; Figure 5B depicts better device success with Myval) as compared to Evolut series THVs.

When compared to Sapien series THVs, Myval had no significant difference with regards to early safety (RR 1.08; 95% CI 0.98-1.19; $P = .14$; $I^2 = 57\%$; Figure 6A showing non-inferiority of Myval) and need for PPI (RR 0.75; 95% CI 0.56-1; $P = .05$; $I^2 = 0\%$; Figure 6B depicting similar rates for Myval and Sapien). All the procedural and early clinical outcomes were also comparable in both subgroups, suggesting non-inferiority of Myval

Figure 4A) Forest plot for early safety showing better outcome with Myval than Evolut (p=0.006)

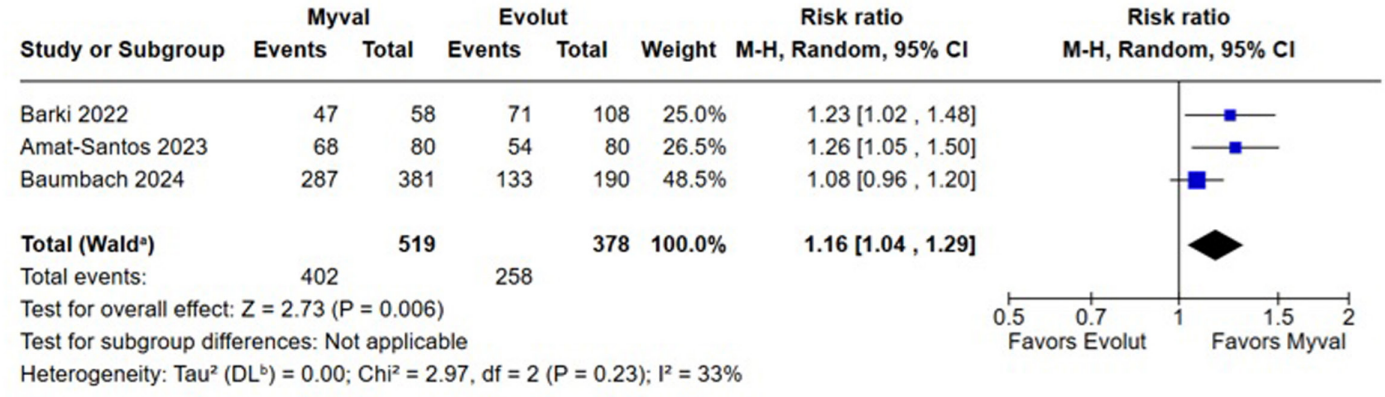

Figure 4B) Need for PPI was lower with Myval as compared to Evolut (p=0.03)

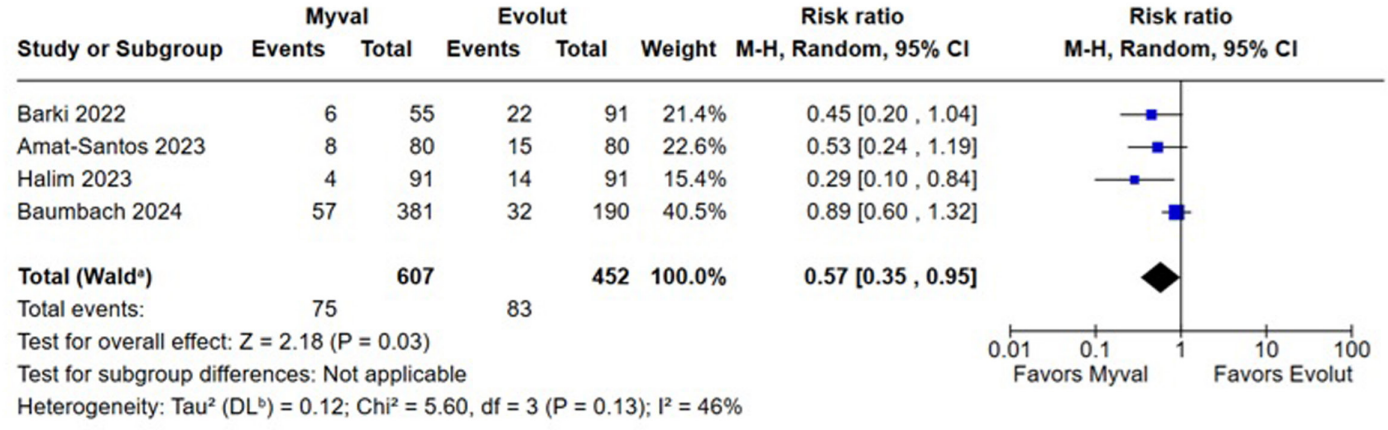

Figure 4. Forest plots for subgroup analysis Myval vs. Evolut. (A) Forest plot for early safety showing better outcome with Myval than Evolut (*P* = .006). (B) Need for permanent pacemaker implantation was lower with Myval as compared to Evolut (*P* = .03).

compared to Sapien series. (Supplementary Appendix: Supplementary Tables 1 and 2).

Sensitivity analysis with leave-one-out method showed no effect of a single study altering the results in 1 direction. The authors also performed OR, risk difference, and RR with fixed and random effects model and found similar results (Supplementary Appendix: Supplementary Figures 2 and 3).

Quality Assessment

Randomized controlled trial (RCT) appraisal is reported in the Supplementary Figure 1A (Supplementary Appendix). Three non-randomized studies matched intervention and control patients according to baseline characteristics.[22-24] In 2 studies, groups were not matched and therefore had few dissimilar baseline characteristics. Individual appraisal of non-randomized studies is reported in Supplementary Figure 1B (Supplementary Appendix). None of the included studies were considered at serious or critical risk of bias as assessed by 2 independent authors (Z.M. and T.T.). As shown in Figure 7, there was no evidence suggestive of publication bias; the funnel plot showed a symmetrical distribution of similar-weight studies with convergence toward the pooled treatment effect size as weights increased. As shown in Supplementary Table 3 (Supplementary Appendix), most of the studies reported outcomes in compliance with VARC 3 criteria, and Halim et al reported outcomes based on VARC 2, but they were included in analyses as they could be retrofitted to VARC 3 criteria as per definitions. There was significant heterogeneity in outcomes like 30-day device success and procedure success where I^2 was upward of 60%. In these cases, it would be prudent to acknowledge the heterogeneity involving patient characteristics (low risk vs. high risk; young vs. old; male vs. female), valve morphology (bicuspid

Figure 5A) Moderate or severe PVL was less with Myval compared to Evolut (p=0.0007)

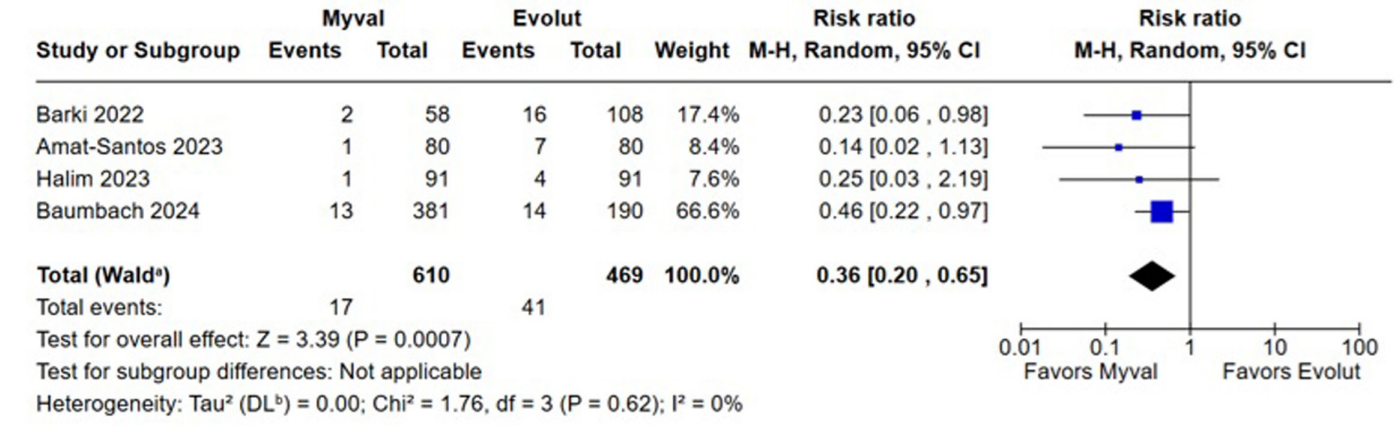

Figure 5B) 30-day device success was seen more with Myval compared to Evolut (p=0.01)

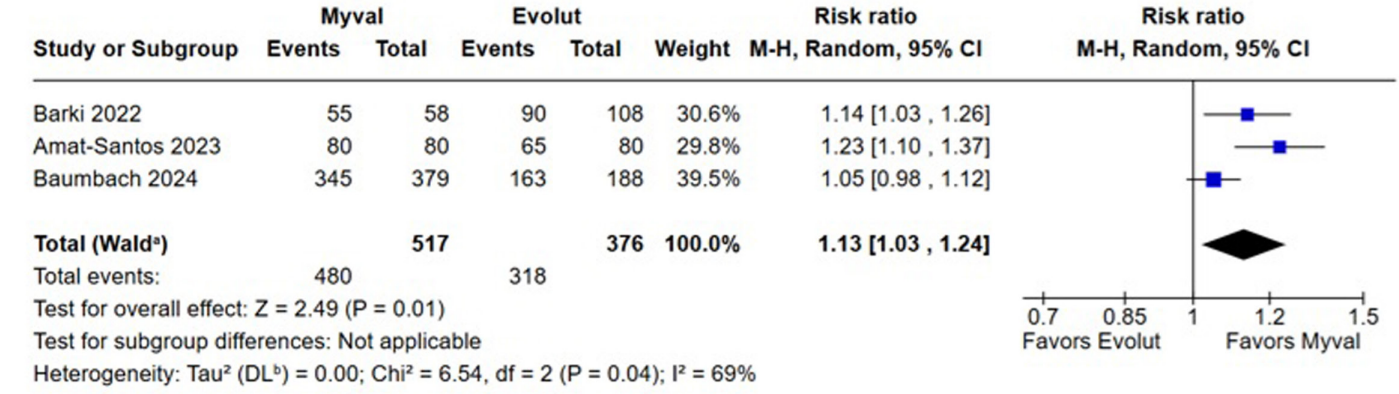

Figure 5. Forest plots for subgroup analysis Myval vs. Evolut. (A) Moderate or severe PVL was less with Myval compared to Evolut (*P* = .0007). (B) 30-day device success was seen more with Myval compared to Evolut (*P* = .01).

vs. tricuspid), and generation of THV (Sapien vs. Sapien3; Myval Gen 1 vs. Myval Octacor). The authors could not perform meta-regression due to lack of comprehensive data with respect to the covariates at hand, but it would have strengthened the association of the outcomes and made the authors' data more robust.

DISCUSSION

In this systematic review and meta-analysis of 6 studies involving 2084 patients, the authors compared the performance of Myval with contemporary THVs. Myval appeared to be associated with improved early safety, as defined by the VARC-3 criteria, and a reduced need for PPI. Although causality cannot be established due to the observational nature of most included studies, subgroup analyses based on the type of contemporary THVs showed no significant difference between Myval and Sapien, suggestive of non-inferiority of Myval. Furthermore, Myval appeared to have better 30-day device success and lower rates of moderate or severe PVL compared to the Evolut THV.

The authors' findings align with the outcomes observed in previous studies involving Myval, supporting the safety of this THV. In an open-label single-arm study involving intermediate-to-high-risk patients, Myval has been associated with very low rates of peri-procedural mortality, 1-year mortality, minimal residual PVL, and reduced need for PPI.[13] Additionally, another study on low-risk patients with a mean STS score of 2.4% reported favorable hemodynamic performance and short-term outcomes, with a similarly low risk of requiring PPI.[16]

Figure 6A) No significant difference seen in Early safety with Myval compared to Sapien (p=0.14)

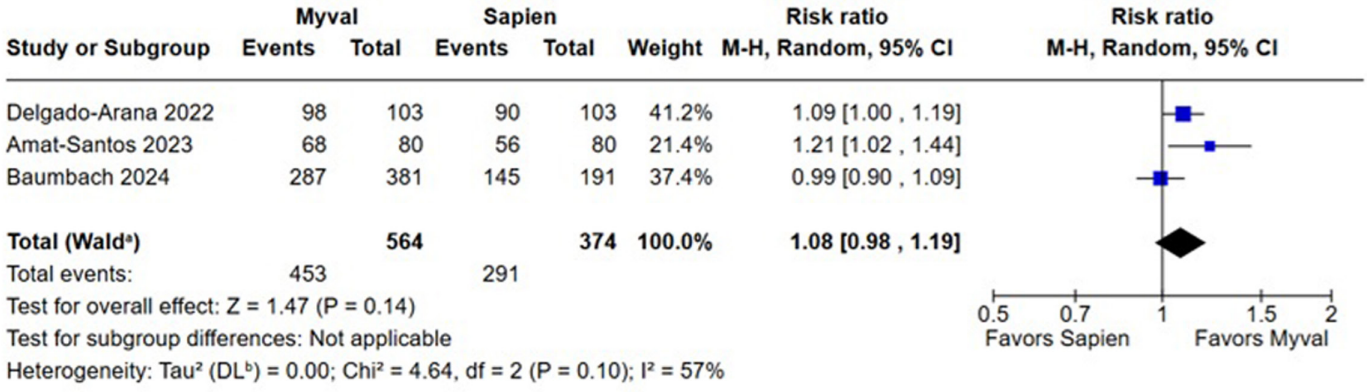

Figure 6B) No significant difference seen in Need for PPI with Myval compared to Sapien (p=0.05)

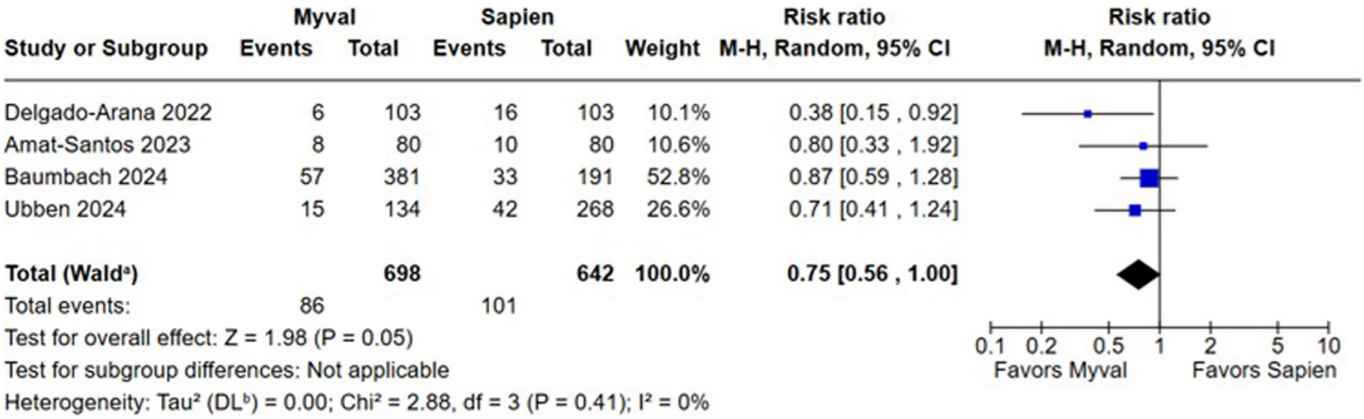

Figure 6. Forest plots for sub group analysis Myval vs. Sapien. (A) No significant difference seen in early safety with Myval compared to Sapien (*P* = .14). (B) No significant difference seen in need for permanent pacemaker implantation with Myval compared to Sapien (*P* = .05).

However, few head-to-head studies have directly compared contemporary THVs.[36-39] The SCOPE II trial, for instance, compared 2 self-expanding THVs (SEVs) and found that the Accurate neo valve failed to meet prespecified non-inferiority criteria and had higher incidences of all-cause mortality and stroke compared to the CoreValve Evolut valve.[36] Similarly, the PORTICO IDE trial showed that the intra-annular SEV Portico valve did not demonstrate advantages over other commercially available THVs, such as the intra-annular BEVs like Sapien, Sapien XT, or Sapien 3, or supra-annular SEVs like CoreValve, Evolut-R, or Evolut-PRO.[37] The SOLVE-TAVI trial compared the Evolut-R SEV with the Sapien 3 BEV and found that all-cause mortality, need for PPI, and PVL were higher in the SEV group, while the incidence of stroke was higher in the BEV group.[38] A recent meta-analysis comparing BEV and self-expandable THVs reported a lower incidence of mortality, shorter hospitalization durations, and reduced need for PPI with BEVs.[39]

In this context, Myval may emerge as a promising option as a BEV and has been compared with contemporary THVs in several studies. However, most of these studies were limited by small sample sizes, non-randomized designs, and short follow-up periods. Hence, large-scale RCTs with long-duration follow-up are warranted to validate these findings.

Transcatheter aortic valve implantation is usually associated with very high cost, and the cost-benefit ratio is skewed. This is the reason it is still not available to a larger part of the global community. Myval could fill this gap by being a safe and effective alternative to contemporary THVs. It also provides drastic cost reduction, making it available to the mass markets at a reduced burden to the healthcare community, especially in resource-limited settings.

Figure 7 A) Funnel plot analysis of early safety outcome showed a symmetrical distribution of study effects per different study weights, indicative of no evidence of publication bias

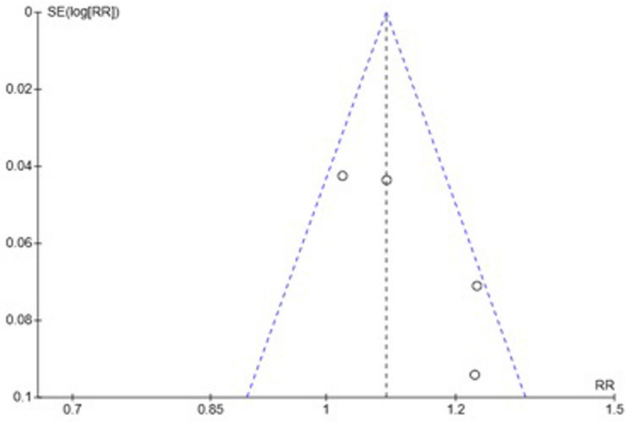

Figure 7 B) Funnel plot analysis of need for PPI outcome showed a symmetrical distribution of study effects per study weights showing no publication bias.

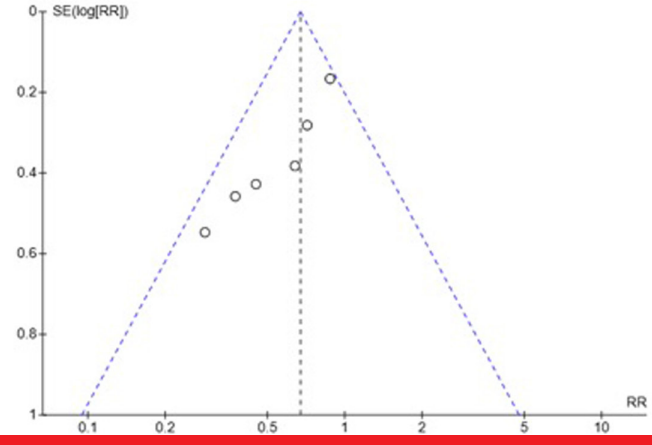

Figure 7. Funnel plots for publication bias for the main analysis of Myval vs. Contemporary thoracic heart valves. (A) Funnel plot analysis of early safety outcomes showed a symmetrical distribution of study effects per different study weights, indicative of no evidence of publication bias. (B) Funnel plot analysis of the need for permanent pacemaker implantation outcomes showed a symmetrical distribution of study effects per study weights showing no publication bias.

With an expanded patient population and consistent results across sensitivity analyses, the authors' findings provide a clearer understanding of the treatment effect of Myval compared to contemporary THVs. Myval may become a valuable therapeutic option for patients with aortic stenosis considering that its efficacy and safety hold true when compared with concurrent THVs. Nevertheless, it is important to emphasize that the current data are insufficient to draw definitive conclusions. These findings lay the groundwork for future, well-designed studies. Larger RCTs are necessary to further test this hypothesis and assess the performance of Myval compared to the latest generations and iterations of contemporary THVs. There are ongoing studies designed to compare Myval THV with contemporary THVs, and although the results are yet to be published, early data have suggested that Myval THV fares well compared to contemporary THVs.[40]

This study has several limitations. Most of the included studies are observational in nature, and only 1 study is an RCT, which limits the generalizability of the data. The heterogeneity in terms of population characteristics (low risk vs. high risk), valve morphology (bicuspid vs. tricuspid), VARC 3 criteria application, THV generations and iterations, follow-up periods, and the underrepresentation of female patients in the observational studies is particularly notable. For instance, Amat-Santos et al included only patients with bicuspid aortic valves, which further increased the heterogeneity of the population. However, even when the authors conducted a leave-one-out analysis excluding this specific study, the overall results remained consistent. Myval Gen 1 and Myval Octacor were used in different studies in different proportions, which may have an impact on the outcomes; however, due to a lack of pre-specified data, a subgroup analysis could not be performed. There was significant heterogeneity in

the application of VARC 3 criteria in all studies. Barki et al,[20] Delgado-Arana et al,[24] Amat-Santos et al,[23] and Baumbach et al[30] reported outcomes that are fully compliant with VARC 3. Halim et al[22] reported outcomes based on VARC 2, whereas Ubben et al[28] reported outcomes in compliance with VARC 3, but there was a lack of 30-day outcome data and early safety parameters.

Additionally, there is only 1 RCT in the authors' review, which was designed to assess non-inferiority, and its findings favored Myval. However, a predefined sub-study from this RCT compared Myval to both the Sapien and Evolut THVs individually and that helped in the authors' subgroup analyses.[41] The authors' assessment of bias found that none of the studies were classified as having a critical or high risk of bias. Still, the authors recognize that some biases may have gone undetected, particularly given the variability in THV iterations and generations across the studies.

There are many limitations of current data and to further improve the scientific integrity and future direction, large and long-term RCTs are needed to fill the gap in current evidence and to validate all the findings observed to date.

CONCLUSION

Systematic review and meta-analysis of 2084 patients suggests that Myval may represent a promising alternative to currently available THVs in TAVI. However, given the predominance of observational data and limited long-term follow-up, larger randomized studies are warranted to confirm these findings.

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