Transcatheter versus surgical aortic valve replacement in patients with aortic stenosis with a small aortic annulus: A meta-analysis with reconstructed time to event data

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ABSTRACT

Background: Aortic stenosis (AS) remains a prevalent and serious global health concern, exacerbated by an aging population worldwide. This valvular disease, when symptomatic and without appropriate intervention, severe AS can drastically reduce life expectancy. In our systematic review and *meta*-analysis, we aim to synthesize available evidence to guide clinical decision-making by comparing the performance of TAVR and SAVR, specifically in patients with severe AS and a small aortic annulus.

Methods: We searched PubMed, EMBASE, Cochrane, Web of Science, and Scopus from inception till May 2024. The risk ratio (RR) and mean difference (MD) with a 95 % confidence interval (CI) are provided as effect size estimates, with all analyses being conducted using RevMan 5.4.

Results: Eleven studies with 3,670 patients were included. TAVR significantly increased the risk of 2-year new permanent pacemaker implantation (PPI) (RR = 2.42; 95 % CI: [1.70–3.44], P < 0.0001) and major vascular complications (RR = 3.73; 95 % CI: [1.98–6.99], P < 0.0001) than SAVR. However, TAVR significantly decreased the risk of patient-prosthesis mismatch (PPM) (RR = 0.56; 95 % CI: [0.48–0.65], P < 0.00001) and new-onset atrial fibrillation (AF) (RR = 0.31; 95 % CI: [0.23–0.41], P < 0.00001). Also, SAVR reduced the risk of paravalvular leak (PVL) (RR = 3.35; 95 % CI: [1.79–6.27], P = 0.0002).

Conclusion: TAVR had a significantly reduced risk of PPM and new-onset AF but with increased PPI and vascular complications. Also, TAVR significantly improved EOA and iEOA. Furthermore, SAVR had less risk of PVL, and better LVEF improvement at predischarge. Therefore, TAVR and SAVR remain valid alternatives, and decisions should be based on anatomy of the annulus and aortic root, operative risk, and comorbidities.

1. Introduction

Aortic stenosis (AS) remains a prevalent and serious global health concern, exacerbated by an aging population worldwide [1–3]. This valvular disease, when symptomatic and without appropriate intervention, severe AS can drastically reduce life expectancy, with an estimated 4-year all-cause untreated mortality of 44.9 % [3]. Surgical Aortic Valve Replacement (SAVR) is the traditional approach to treating AS [3]. In recent years, transcatheter aortic valve replacement (TAVR) has emerged as a formidable alternative, offering less invasive

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intervention with a rapidly expanding body of evidence supporting its efficacy and safety in high-risk and intermediate-risk patient populations [4,5]. Despite this, TAVR's role in younger and lower-risk patients or those with specific challenges like a small aortic annulus (SAA) remains under intense debate, with a preference for SAVR as the standard treatment approach [5,6].

Evidence from observational studies and secondary data from randomized trials show improved prosthetic valve hemodynamics with TAVR compared to SAVR in patients with SAA [6–8]. Data on patients with small aortic annuli are limited, and the choice between TAVR and SAVR remains disputed [9] Given the unique challenges and the critical nature of making the optimal treatment decision, focused research in this subgroup is essential. Therefore, in our systematic review and *meta*-analysis, we aim to synthesize available evidence to guide clinical decision-making by comparing the performance of TAVR and SAVR, specifically in patients with severe AS and a small aortic annulus.

2. Methodology

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [10] and Meta-analyses Of Observational Studies in Epidemiology (MOOSE) [11] guidelines were followed during the conduction of this systematic review and *meta*-analysis. Moreover, our *meta*-analysis was registered on Open Science Framework (OSF) with 10.17605/OSF.IO/XZBCQ.

2.1. Search strategy

We searched PubMed, cochrane library (CENTRAL), EMBASE, Web of Science, and Scopus from inception till May 2024. The following search terms were used: "(TAVR OR Transcatheter Aortic Valve Replacement OR Transcatheter Aortic Valve Implantation OR Transcatheter AVR) AND (SAVR OR Surgical Aortic Valve Replacement OR Surgical AVR) AND (Aortic Stenosis OR Aortic Valve Stenosis) AND (Small Aortic Annulus OR Narrow Aortic Annulus)." Additionally, we reviewed the reference lists of eligible articles to complement the broad search.

2.2. Study selection.

The studies found by our search were uploaded to Covidence, and the duplicates were removed. Four reviewers (M.N.A.Y., F.B.A., Z.B., and H. A.H.) completed title and abstract screening and an autonomously completed full-text screening to determine the included articles according to our eligibility criteria. Conflicts were resolved through discussion.

2.3. Eligibility criteria

Randomized controlled trials (RCTs) and observational comparative studies that investigate the differences between SAVR versus TAVR in the setting of an aortic stenosis and a small aortic annulus, published in peer-reviewed journals reporting separate outcomes data for the two groups, were included. SAA is defined as mean diameter <23 mm or CT scan of aortic annulus showing area ranging from less than 430 mm^2 to less than 400 mm^2 or a CT perimeter of less than 72 mm. We excluded studies that included only severe AS without SAA, conference papers, unpublished articles, letters to the editor, posters, and animal studies. Our PICO was P; Patients with aortic stenosis and small aortic annulus, I; TAVR, C; SAVR, O; primary outcomes: 30 days mortality, all-cause mortality, stroke, myocardial infarction (MI), and major/life-threatening bleed, secondary outcomes: reintervention, permanent pacemaker implantation (PPI), patient-prosthesis mismatch (PPM), change in mean aortic gradient (AS progression degree) and para-valvular regurgitation (PVR).

2.4. Data Extraction and quality assessment

Four reviewers (M.N.A.Y., F.B.A., Z.B., and H.A.H.) extracted the following data from the included studies as baseline characteristics: name of the first author, publication year, country, study design, sex, mean age, body mass index (BMI), body surface area (BSA), STS-PROM score, EuroSCORE, total sample size, left ventricular ejection fraction (LVEF), cardiovascular risk factors, including heart failure, hypertension, diabetes, dyslipidemia, atrial fibrillation, smoking status, renal failure, COPD, peripheral artery disease, previous MI, coronary artery disease, and follow up period, all which were extracted to a standardized Excel spreadsheet to conclude the *meta*-analysis. Finally, for qualitative and quantitative analysis, we extracted 30 days mortality, all-cause mortality after the longest follow-up, overall cardiovascular mortality, aortic reintervention, hospitalization for heart failure, stroke, PPI, PPM, PVR, and AS progression. Conflicts were resolved through discussion.

The risk of bias was assessed using the Cochrane risk of bias-1 (ROB-1) [12] tool for RCTs and the New-Castle Ottawa scale tool [13] for observational studies. Two independent reviewers (H.H. and Z.B.) screened the methodological quality of the included studies. They classified them as low, moderate, or high quality based on the scores after evaluation, and a senior author resolved all discrepancies.

2.5. Data analysis.

The inverse variance method was used to pool study estimates, and the restricted maximum-likelihood estimator was used to estimate between-study heterogeneity. The risk ratio (RR) and mean difference (MD) with a 95 % confidence interval (CI) are provided as effect size estimates. Random-effects *meta*-analysis model was utilized to investigate whether the results were sensitive to model choice and inverse variance method. Forest plots were drawn, the shaded boxes represented the point estimate for each trial, and the horizontal line extending from each box represented the upper and lower limits of the 95 % CI. The diamonds represent the overall effect size. Heterogeneity was evaluated using the Cochrane Q test, Chi-square test, and I^2 statistic. I$^2 > 50$ % denoted substantial heterogeneity in the studies. A p-value less than 0.05 was considered statistically significant with all analyses conducted using RevMan 5.4 [14].

Regarding the reconstructed time-to-event data analysis, we reconstructed individual patient data from the published Kaplan-Meier graphs of all the included studies using the curve approach [15]. We adopted the two-stage approach that Liu et al. [16] outlined using the "IPD-fromKM" R package. First, we extracted raw data coordinates (time, survival probability) of each arm of the included Kaplan-Meier curves. Then, individual patient data were reconstructed based on the raw data coordinates and the number of patients at risk at reported time points. Finally, we merged the reconstructed time-to-event data of all individual studies in a merged data set. We used the Cox frailty regression model to calculate the HR with 95 % CI for the difference between TAVR vs SAVR. We included the γ frailty term to assess the between-studies heterogeneity, where individual studies modeled as a random effect. Then, we used the likelihood ratio test to test the significance of this γ frailty term.

Additionally, we employed a robust variance estimator to accommodate violations of the assumption of homoscedasticity, which assumes equal or similar variances across different groups being compared. We tested the proportional hazard ratio assumption with the Grambsch-Therneau test and diagnostic plots based on Schoenfeld residuals [17]. We calculated Flexible parametric survival models with B-splines to provide HRs with 95 CI% of association between TAVR vs. SAVR and all-cause mortality, allowing a time-varying effect [18]. Finally, using the R package "survRM2″, we analyzed the variation in restricted mean survival times (RMSTs) over time [19].

3. Results

3.1. Literature search

Our search strategy yielded 449 records, which were reduced to 352 articles after removing the duplicates. After full-text screening, eleven studies were included in our systematic review and *meta*-analysis. Fig. 1 shows the PRISMA flow diagram of the present study.

3.2. Characteristics of the included studies

Eleven studies [8,20–29] were included in our systematic review and *meta*-analysis, with 3,670 patients. The mean age was 80.5 years, with most of the patients being females, 2,687 (73.2 %). Five studies (50 %) were conducted in the United States, and six were RCTs or post-hoc RCTs. Further information about our baseline characteristics and a summary of included studies can be found in (Tables 1 and 2), respectively.

3.3. Risk of bias assessment

Assessing the risk of bias of our included observational studies using the NOS tool declared that all of them are of low risk of bias; however, using the ROB-1 tool assessing the risk of bias for RCTs, we found that all of our studies are of low risk of bias except for Head et al. which has high risk of bias due to performance bias. Further information about bias assessment risk can be found in (Fig. 2A.Fig. 2B. **and** Table 3**)**.

3.4. Short-Term clinical outcomes

- 30-day mortality

Our analysis of 30-day mortality included five studies with 1,216 patients and showed a statistically nonsignificant difference between TAVR and SAVR (RR = 0.68; 95 % CI: [0.32–1.45], *P* = 0.31). The pooled studies showed nonsignificant heterogeneity (I^2 = 5 %; *P* = 0.37). Fig. 3A.
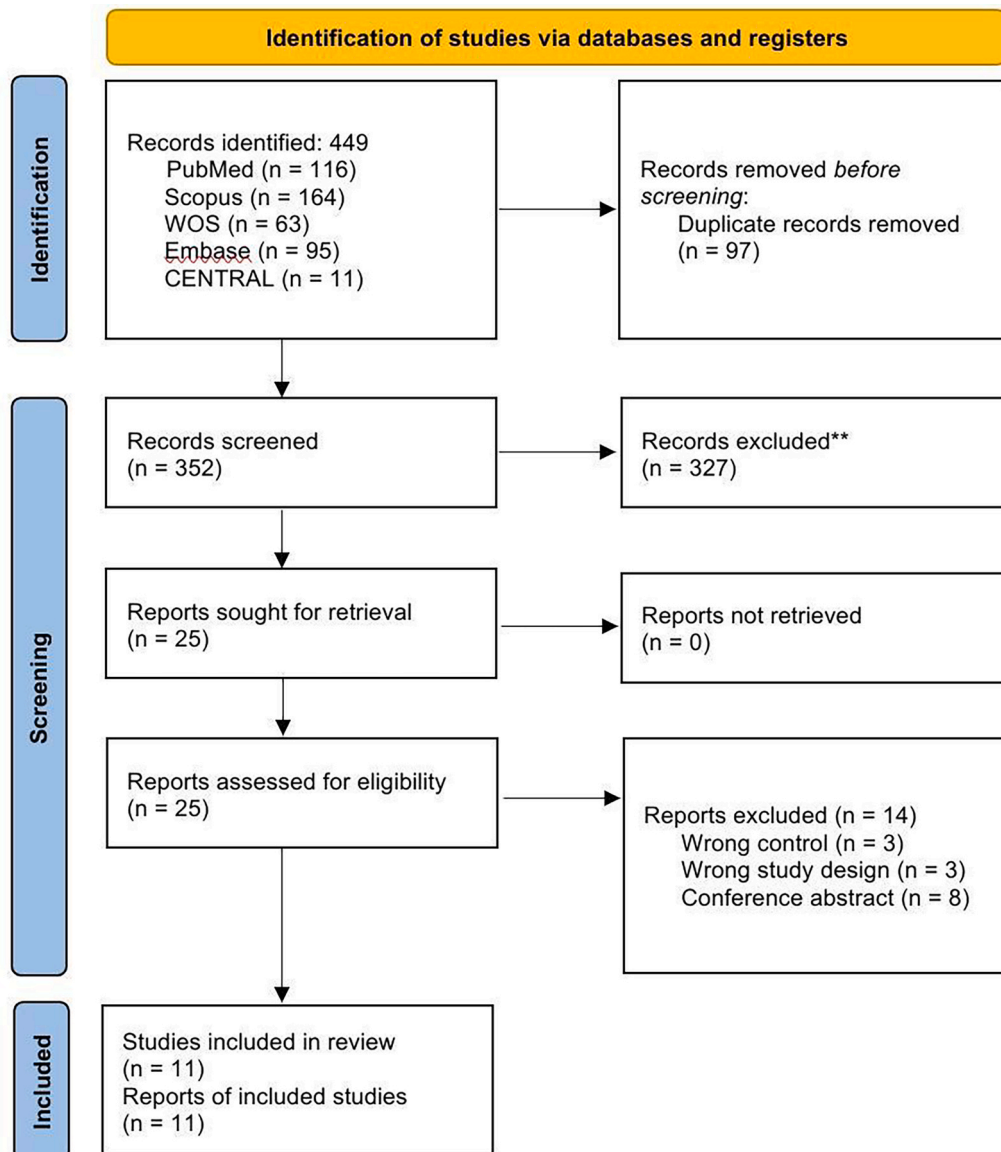
- Stroke

Fig. 1. PRISMA flow diagram.

Table 1
Baseline characteristics of included studies.

Author, year	Study arms	Age, mean (SD)	Sex, female (%)	BMI (kg/m2), mean (SD)	STS-PROM score %, mean (SD)	NYHA functional class III/IV %, (%)	Logistic EuroSCORE %, mean (SD)	Hypertension (%)	Diabetes mellitus (%)	Renal failure (creatinine > 2mg/dL), (%)	Atrial fibrillation (%)	Peripheral arterial disease (PAD), (%)	Coronary artery disease (CAD), (%)	Previous myocardial infarction (MI), (%)	Aortic annulus area (cm2), mean (SD)	Indexed aortic annulus area (cm2/m2), mean (SD)	Aortic annulus diameter (mm), mean (SD)	Mean aortic gradient (mmHg), mean (SD)	Peak aortic gradient (mmHg), mean (SD)	LV ejection fraction %, mean (SD)
Deeb, 2018	TAVR	83.4 (7.4)	104 (88.4)	NA	8.0 (3.1)	86 (82.6)	15.2 (10.0)	NA	NA	1 (1.0)	41 (39.4)	48 (46.2)	70 (67.3)	21 (20.2)	NA	NA	NA	NA	NA	NA
	SAVR	83.4 (6.4)	71 (95.9)	NA	8.3 (3.6)	62 (83.8)	19.2 (13.9)	NA	NA	5 (6.8)	28 (37.8)	31 (41.9)	60 (81.1)	17 (23.0)	NA	NA	NA	NA	NA	NA
Guimaraes, 2020	TAVR	80 (8.0)	285 (80)	27 (7.0)	7.4 (5.1)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	19.2 (0.9)	44 (18)	73 (27)	57 (12)
	SAVR	74 (9.0)	285 (80)	27 (7.0)	3.0 (2.1)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	19.3 (0.9)	42 (18)	71 (27)	57 (10)
Head, 2019	TAVR	77.8 (6.7)	114 (40)	21 (0.2)	4.2 (1.5)	NA	10.7 (6.3)	272 (95.8)	131 (46.1)	NA	NA	91 (32)	169 (59.5)	NA	0.81 (0.22)	0.39 (0.10)	NA	45.9 (11.6)	NA	62.0 (9.1)
	SAVR	76.8 (6.4)	108 (40.9)	21 (0.2)	4.3 (1.7)	NA	10.3 (7.5)	251 (95.1)	124 (47)	NA	NA	85 (32.2)	167 (63.3)	NA	0.80 (0.21)	0.38 (0.10)	NA	46.2 (11.4)	NA	60.7 (10.9)
Kamioka, 2019	TAVR	85.1 (6.0)	32 (91.4)	21.6 (3.4)	6.7 (3.0)	19 (54.3)	18.9 (12.8)	26 (74.3)	16 (45.7)	3 (8.6)	NA	NA	14 (40)	10 (28.6)	0.56 (0.11)	NA	19.1 (0.7)	64.6 (20.1)	NA	60.9 (7.8)
	SAVR	77.4 (8.7)	56 (94.9)	22.7 (4.0)	6.8 (5.0)	18 (30.5)	11.6 (7.3)	42 (71.2)	28 (47.5)	7 (11.9)	NA	NA	15 (25.4)	25 (42.4)	0.58 (0.13)	NA	19.1 (0.6)	58.7 (18.3)	NA	60.6 (9.5)
Nishigawa, 2023	TAVR	84.7 (4.8)	173 (80.8)	NA	NA	34 (15.9)	NA	145 (67.8)	44 (20.6 %)	NA	9 (14.3)	NA	41 (19.2 %)	NA	NA	NA	19.5 (1.3)	53.0 (16.8)	NA	63.7 (4.3)
	SAVR	76.4 (5.3)	50 (79.4)	NA	NA	11 (17.6)	NA	40 (63.5)	9 (14.3 %)	NA	0 (0)	NA	2 (3.2 %)	NA	NA	NA	19.7 (1.3)	61.0 (19.9)	NA	63.4 (3.9)
Pibarot, 2014	TAVR	84.1 (7.0)	127 (41.8)	27.56 (6.9)	11.33 (2.2)	157 (51.6)	26.0 (21.07)	NA	NA	NA	NA	NA	NA	NA	NA	NA	20.07 (2.40)	43.5 (14.6)	NA	51.60 (14.0)
	SAVR	84.6 (6.4)	114 (42.2)	26.84 (5.7)	11.33 (2.3)	138 (51.1)	26.6 (18.2)	NA	NA	NA	NA	NA	NA	NA	NA	NA	20.06 (2.24)	43.4 (14.6)	NA	54.3 (13.0)
Rodés–Cabau, 2014	TAVR	84 (6)	57 (58,2)	26 (6)	11,5 (2,9)	88 (89,8)	NA	89 (90.8)	36 (36.7)	12 (12.4)	49 (50.0)	38 (38.8)	66 (67.3)	NA	0.64 (0.18)	0.36 (0.10)	NA	42.7 (14.7)	NA	56 (12)
	SAVR	85 (6)	50 (60,2)	27 (6)	11,9 (3,2)	79 (95,2)	NA	77 (92.8)	34 (41.0)	11 (13.3)	48 (58.5)	33 (39.8)	62 (74.7)	NA	0.60 (0.20)	0.34 (0.11)	NA	45.8 (14.3)	NA	55 (12)
Rodés–Cabau, 2024	TAVR	75.9 (5.3)	73 (94.8)	27.70 (5.2)	2.54 (1.1)	23 (29.9)	NA	62 (80.5)	23 (29.9)	25 (32.5)	6 (7.8)	NA	17 (22.1)	NA	0.67 (0.18)	NA	21.23 (1.13)	47 (17)	79 (24)	62 (7)
	SAVR	75.1 (4.9)	67 (90.5)	28.68 (5.4)	2.47 (1.5)	24 (32.4)	NA	61 (82.4)	22 (29.7)	26 (35.1)	14 (18.9)	NA	14 (18.9)	NA	0.74 (0.36)	NA	21.13 (1.21)	49 (17)	80 (24)	62 (8)
Salna, 2018	TAVR	84 (80,9)	39 (98)	NA	NA	NA	NA	38 (95)	8 (20)	10 (25)	11 (28)	19 (14.6)	32 (80)	6 (16.2)	0.63 (0.21)	0.40 (0.14)	20.4 (1.4)	42.1 (15.5)	76.6 (25.3)	66.3 (10.7)
	SAVR	82 (75,9)	118 (91)	NA	NA	NA	NA	97 (75)	25 (19)	50 (38)	37 (28)	5 (12.5)	75 (57.7)	13 (10)	0.67 (0.32)	0.43 (0.17)	21.0 (1.0)	47.4 (17.0)	85.0 (27.7)	54.3 (13.5)
Modine, 2024	TAVR	77.5 (6.3)	323 (100)	NA	3.6 (1.7)	NA	NA	289 (89.5)	104 (32.2)	0 (0.0)	53 (16.5)	47 (14.6)	NA	19 (5.6)	NA	NA	NA	47.5 (14.9)	NA	NA
	SAVR	77.5 (6.3)	297 (100)	NA	3.6 (1.7)	NA	NA	252 (85.1)	70 (23.6)	1 (0.3)	45 (15.2)	47 (15.9)	NA	16 (5.4)	NA	NA	NA	48.1 (14.8)	NA	NA
Dionne, 2017	TAVR	83.1 (7.0)	45 (90)	26.5 (6.6)	NA	NA	NA	40 (80)	8 (16)	NA	NA	NA	27 (54)	NA	19.8 (0.9)	NA	NA	48 (19)	69 (30)	60 (9)
	SAVR	79.4 (5.6)	99 (88)	27.5 (4.6)	NA	NA	NA	79 (70)	33 (29)	NA	NA	NA	51 (45)	NA	19.8 (0.9)	NA	NA	47 (18)	73 (26)	61 (6)

NA; not available, SD; satndard deviation, TAVR; transcatheter aortic valve replacement, SAVR; surgical aortic valve replacement.

Table 2
Summary of included studies.

Author, year	Study design	Year	Country	Sample size (n)			Definition of small aortic annulus used for inclusion	Type(s) of device used		Primary outcome(s)
				TAVR	SAVR	Total		TAVR	SAVR	
Deeb, 2018	Prospective Cohort	2018	USA	104	74	178	<23 mm	Self-Expanding CoreValve	Individual Surgeon Preference	Annular size has a significant effect on hemodynamics and the incidence of PPM in SAVR subjects, not observed in TAVR subjects
Guimaraes, 2020	Prospective Cohort	2020	Canada	357	357	714	≤21 mm	Balloon Expandable valves and Self-Expandable valves	Individual Surgeon Preference (Stented, Stentless, Sutureless valves)	TAVR presented superior valve hemodynamics and lower incidence of severe PPM compared with SAVR in SAA patients.
Head, 2019	Secondary Analysis of a Randomized Controlled Trial	2019	USA	284	264	548	9–12 mm/m2	CoreValve or Evolut R	Individual Surgeon Preference	Rates of PPM were significantly lower after TAVR than after SAVR across all groups of indexed annulus size, reflecting better hemodynamic performance of transcatheter versus surgical valves, irrespective of the propensity to develop PPM.
Kamioka, 2019	Retrospective Observational	2019	Japan	35	59	94	≤20 mm	Second-generation THV device, a Sapien XT valve system	Carpentier-Edwards prosthesis Magna Ease valve (Edwards Lifesciences) and a Mosaic Ultra valve (Medtronic, Minneapolis, Minnesota).	TAVR with a Sapien XT exhibited better valve hemodynamics and a lower incidence of PPM than SAVR. In addition, the long-term mortality in SAA patients was similar between the two groups despite the increased age and higher surgical risk in the TAVR population.
Nishigawa, 2023	Retrospective Observational	2023	Japan	214	63	277	≤21 mm	Balloon-Expandable Valve	Bovine Pericardial Bioprosthesis	SAVR provides better LV mass regression than TAVR with a comparable rate of PPM in patients with small aortic annulus.
Pibarot, 2014	Secondary Analysis of a Randomized Controlled Trial	2014	USA (23) CANADA (2) GERMANY (1)	304	270	574	<20 mm	Balloon-Expandable Edwards SAPIEN Transcatheter Heart Valve	Edwards bovine bioprostheses	PPM is more frequent and more often severe after SAVR than TAVR. Patients with PPM after SAVR have worse survival and less LV mass regression than those without PPM. Severe PPM also has a significant impact on survival after TAVR in the subset of patients with no post-procedural aortic regurgitation. TAVR may be preferable to SAVR in patients with a small aortic annulus who are susceptible to PPM to avoid its adverse impact on LV mass regression and survival. aortic annulus.
Rodés-Cabau, 2014	Secondary Analysis of a	2014	USA (23) CANADA (2)	98	83	181	<18 mm	Balloon-Expandable Edwards SAPIEN	Edwards bovine bioprostheses	Patients in the small aortic annulus tertile who underwent transcatheter

Table 2 (*continued*)

Author, year	Study design	Year	Country	Sample size (n)			Definition of small aortic annulus used for inclusion	Type(s) of device used		Primary outcome(s)
				TAVR	SAVR	Total		TAVR	SAVR	
	Randomized Controlled Trial		GERMANY (1)					Transcatheter Heart Valve		aortic valve replacement had a lower incidence of severe prosthesis–patient mismatch (19.7 % versus 37.5 %; P = 0.03) and only a trend toward a higher incidence of moderate-to-severe paravalvular leaks compared with surgical aortic valve replacement (5.7 % versus 0 %; P = 0.06). There were no differences in mortality between transcatheter aortic valve replacement and surgical aortic valve replacement.
Rodés-Cabau, 2024	A Randomized Clinical Trial	2023	15 centers across Canada, Europe, and Brazil	77	74	151	<23 mm	Balloon-expandable SAPIEN 3/Ultra valve (Edwards Lifesciences, Irvine, CA), the self-expandable Evolut R/PRO/PRO+/FX valve (Medtronic, Minneapolis, MN), and the Acurate neo/neo2 valve (Boston Scientific, Boston, MA).	Individual Surgeon Preference	In patients with severe aortic stenosis and SAA (women in the majority), there was no evidence of superiority of contemporary TAVR versus SAVR in valve hemodynamic results. After a median follow-up of 2 years, there were no differences in clinical outcomes between groups.
Salna, 2018	Retrospective Observational	2018	USA	40	130	170	<19 mm	Porcine xenografts (Medtronic CoreValve or Evolut) and Bovine pericardial xenografts (Edwards Sapien	stented porcine xenografts (Mosaic, Medtronic) and stented bovine pericardial xenografts (Magna or Magna Ease, Edwards)	TAVR is a safe and reasonable option for patients with small aortic annuli and is associated with shorter hospital stays and more favorable postoperative hemodynamic outcomes compared with SAVR.
Modine, 2024	Post hoc pooled analysis	2024	Multicenter	323	297	620	≤23 mm	Self-expanding, supra-annular TAVR (CoreValve, Evolut R/PRO, Medtronic)	Surgical best practice at the time the trial was conducted	Women in the TAVR group had better valve hemodynamic performance, with larger EOA, lower mean gradient, and less moderate or severe PPM but higher incidence of new pacemaker implantation than the surgery group. These data suggest that self-expanding TAVR may be the preferred therapy for aortic stenosis in women with small annuli.
Dionne, 2017	Retrospective study	2017	Canada	50	113	163	≤21 mm	SAPIEN-XT bioprosthesis	Perceval sutureless bioprosthesis	There were no significant differences in predischarge effective orifice area (SAPIEN: 1.5 ± 0.5 cm^2 and Perceval: 1.48 ± 0.34 cm^2, P = 0.58) and indexed effective orifice areas

Table 2 (*continued*)

Author, year	Study design	Year	Country	Sample size (n)			Definition of small aortic annulus used for inclusion	Type(s) of device used		Primary outcome(s)
				TAVR	SAVR	Total		TAVR	SAVR	
										(SAPIEN: 0.93 ± 0.32 cm²/m² and Perceval: 0.88 ± 0.22 cm²/m², P = 0.42). Predischarge mean ± SD transaortic gradient was lower with the SAPIEN than with Perceval valves (12 ± 6 and 17 ± 6 mm Hg, respectively, P < 0.001). Rates of moderate and severe prosthesis-patient mismatch were similar (SAPIEN: 44 % and 10 % and Perceval: 50 % and 14 %, P = 0.53 and 0.75, respectively). There were no moderate-severe paravalvular leaks"

N; number; TAVR; transcatheter aortic valve replacement, SAVR; surgical aortic valve replacement.

Fig. 2A. Summary of risk of bias of included studies.

The stroke analysis included six studies with 1,493 patients and showed a statistically nonsignificant difference between TAVR and SAVR (RR = 1.80; 95 % CI: [0.69–4.67], $P = 0.23$). The pooled studies demonstrated nonsignificant heterogeneity ($I^2 = 21$ %; $P = 0.27$). Fig. 3B.

- Myocardial infarction (MI)

The frequency of MI was reported in four studies with 1,122 patients. The analysis showed a statistically nonsignificant difference between TAVR and SAVR (RR = 0.96; 95 % CI: [0.35–2.63], $P = 0.93$). Pooled studies were homogenous ($I^2 = 0$ %; $P = 0.81$). Fig. 3C.

- New permanent pacemaker implantation (PPI)

New PPI was reported in five studies with 1,273 patients. The overall effect estimate favored SAVR over TAVR (RR = 2.49; 95 % CI: [1.64–3.77], $P < 0.0001$). The pooled studies demonstrated no heterogeneity ($I^2 = 0$; $P = 0.81$). Fig. 3D.

- Major vascular complication

The rate of major vascular complication was reported in three studies with 895 patients, and the pooled RR favored SAVR over TAVR (RR = 3.07; 95 % CI: [1.59–5.94], $P = 0.0009$). The pooled studies revealed nonsignificant heterogeneity ($I^2 = 8$ %; $P = 0.34$). Fig. 4A.

- Major/life-threatening bleeding

The frequency of major/life-threatening bleeding in TAVR and SAVR was reported in six studies with 1,493 patients. The overall effect estimate did not favor either of both arms (RR = 0.71; 95 % CI: [0.47–1.07], $P = 0.10$). Pooled studies showed nonsignificant heterogeneity ($I^2 = 44$; $P = 0.11$). Fig. 4B.

- New-onset atrial fibrillation (AF)

The rate of new-onset atrial fibrillation was reported in three studies with a total of 1042 patients. The overall effect estimate favored TAVR over SAVR (RR = 0.31; 95 % CI: [0.23–0.41], $P < 0.00001$). Pooled studies were homogenous ($I^2 = 0$ %; $P = 0.84$). Fig. 4C.
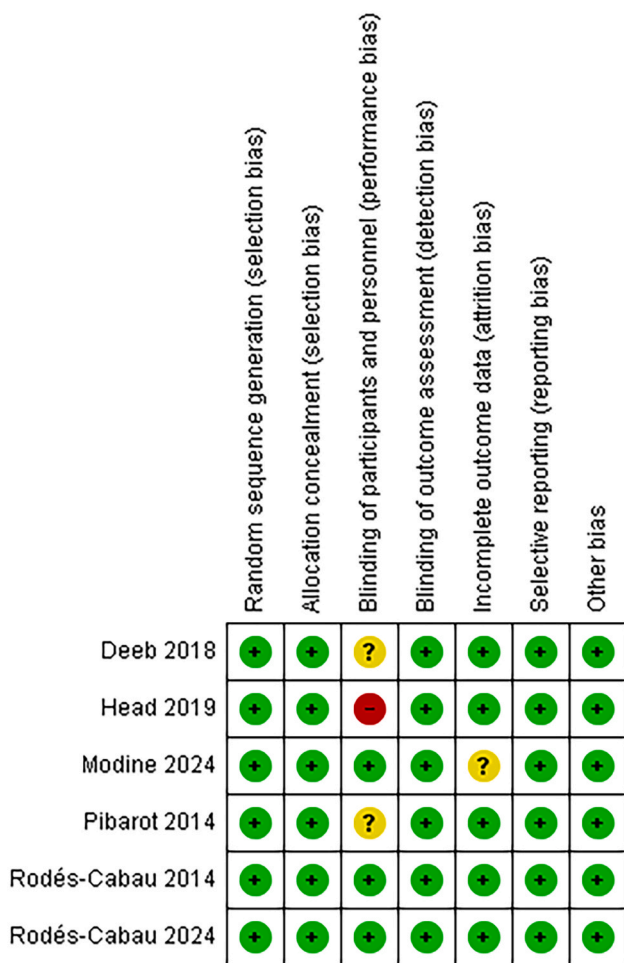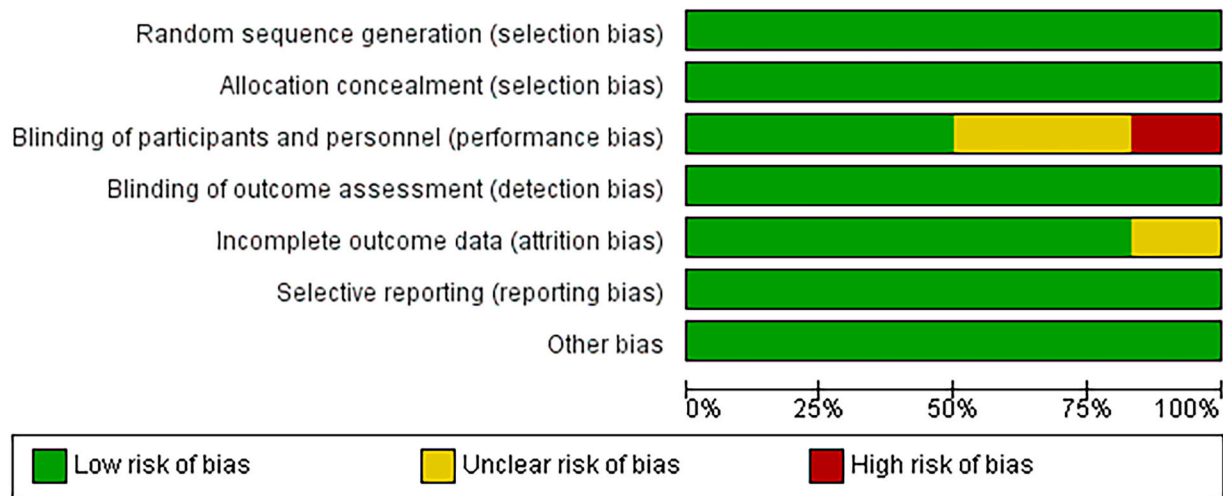
Fig. 2B. Graph of risk of bias of included studies.

Table 3
New Castle Ottawa (NOS) scale of risk of bias of included studies.

Study Author	Year	Selection				Comparability	Outcome			Risk of bias
		Low = ≥ 3, Moderate = 2, High = 0–1 points				Low = ≥ 2, Moderate = ≥ 1 High = 0 points	Low = 3, Moderate = 2, High = 0–1 points			
		Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	
Guimarães	2020	1 (b)	1 (a)	1 (a)	1 (a)	2 (a, b)	1 (b)	1 (a)	1 (b)	Low
Kamioka	2019	1 (b)	1 (a)	1 (a)	1 (a)	2 (a, b)	1 (b)	1 (a)	1 (a)	Low
Nishigawa	2023	1 (b)	1 (a)	1 (a)	1 (a)	2 (a, b)	1 (b)	1 (a)	1 (a)	Low
Salna	2018	1 (b)	1 (a)	1 (a)	1 (a)	2 (a, b)	1 (b)	1 (a)	1 (a)	Low
Repossini	2017	1 (b)	1 (a)	1 (a)	1 (a)	2 (a, b)	1 (b)	1 (a)	1 (b)	Low

Letter in parenthesis refers to selected answer.
A study can be awarded a maximum of one point for each numbered item within the Selection and Outcome categories.
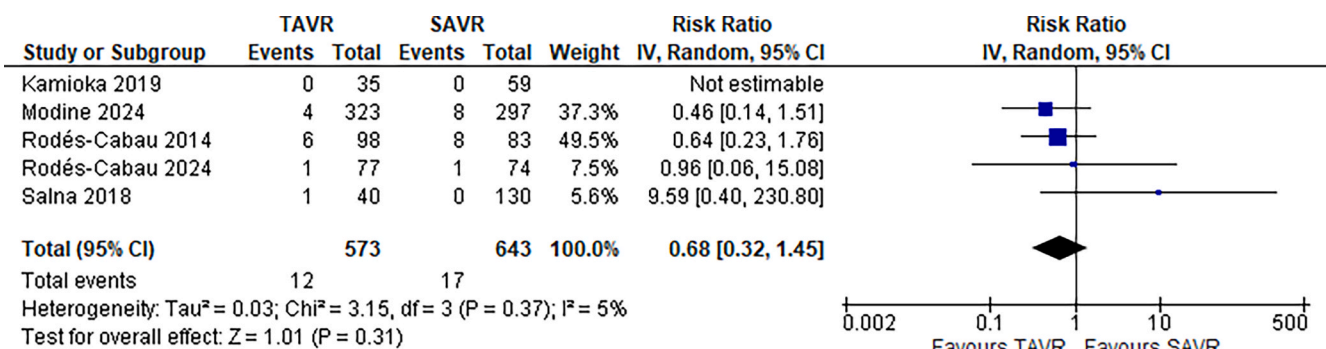A maximum of two points can be given for Comparability.

Fig. 3A. Forest plot for 30 days mortality.

3.5. Long-Term clinical outcomes

- Long-term mortality

The analysis of 2-year mortality included six studies with 1,758 patients and showed a statistically nonsignificant difference between TAVR and SAVR (RR = 0.89; 95 % CI: [0.70–1.13], P = 0.34). The pooled studies demonstrated no heterogeneity (I^2 = 0 %; P = 0.85). Fig. 5A.
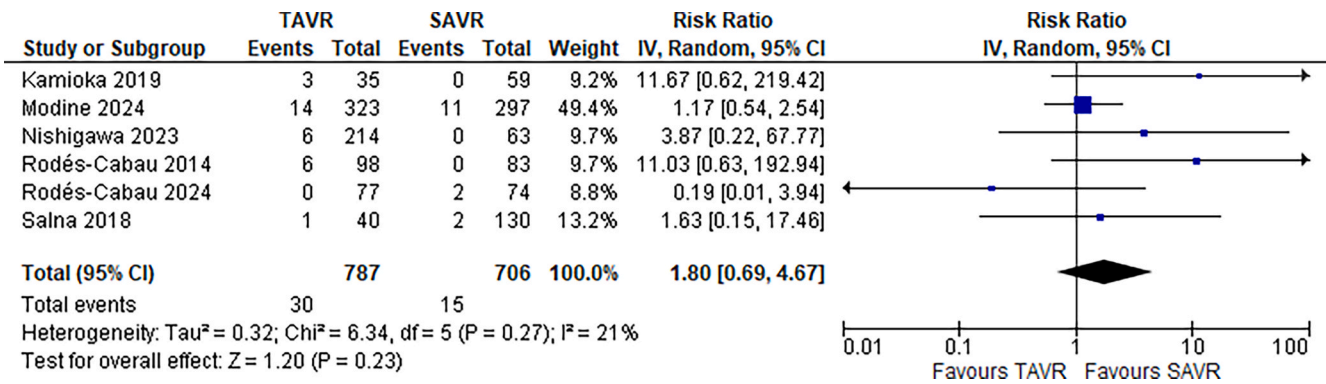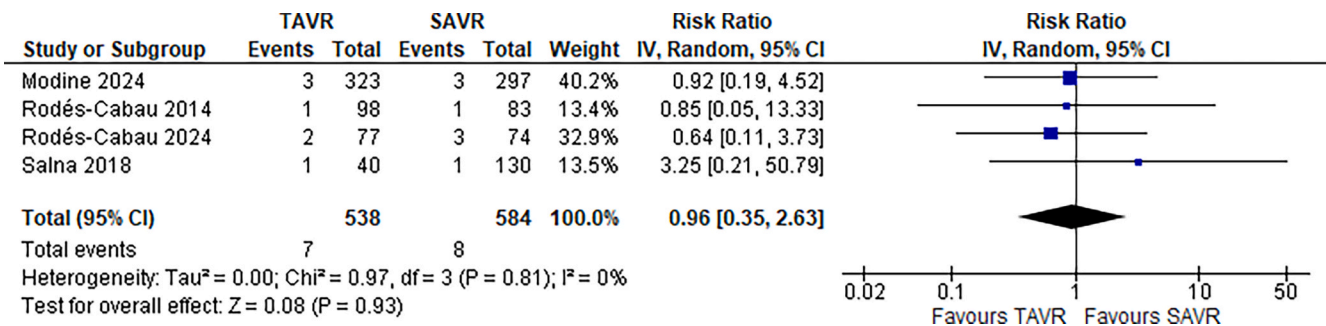
- Long-term stroke

Study or Subgroup	TAVR Events	Total	SAVR Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kamioka 2019	3	35	0	59	9.2%	11.67 [0.62, 219.42]
Modine 2024	14	323	11	297	49.4%	1.17 [0.54, 2.54]
Nishigawa 2023	6	214	0	63	9.7%	3.87 [0.22, 67.77]
Rodés-Cabau 2014	6	98	0	83	9.7%	11.03 [0.63, 192.94]
Rodés-Cabau 2024	0	77	2	74	8.8%	0.19 [0.01, 3.94]
Salna 2018	1	40	2	130	13.2%	1.63 [0.15, 17.46]
Total (95% CI)		**787**		**706**	**100.0%**	**1.80 [0.69, 4.67]**
Total events	30		15			

Heterogeneity: Tau² = 0.32; Chi² = 6.34, df = 5 (P = 0.27); I² = 21%
Test for overall effect: Z = 1.20 (P = 0.23)

Fig. 3B. Forest plot for stroke.

Study or Subgroup	TAVR Events	Total	SAVR Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Modine 2024	3	323	3	297	40.2%	0.92 [0.19, 4.52]
Rodés-Cabau 2014	1	98	1	83	13.4%	0.85 [0.05, 13.33]
Rodés-Cabau 2024	2	77	3	74	32.9%	0.64 [0.11, 3.73]
Salna 2018	1	40	1	130	13.5%	3.25 [0.21, 50.79]
Total (95% CI)		**538**		**584**	**100.0%**	**0.96 [0.35, 2.63]**
Total events	7		8			

Heterogeneity: Tau² = 0.00; Chi² = 0.97, df = 3 (P = 0.81); I² = 0%
Test for overall effect: Z = 0.08 (P = 0.93)

Fig. 3C. Forest plot for MI.

Study or Subgroup	TAVR Events	Total	SAVR Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kamioka 2019	2	35	2	59	4.7%	1.69 [0.25, 11.44]
Modine 2024	49	302	19	279	67.6%	2.38 [1.44, 3.94]
Nishigawa 2023	19	214	0	63	2.2%	11.61 [0.71, 189.62]
Rodés-Cabau 2024	9	77	4	74	13.4%	2.16 [0.70, 6.72]
Salna 2018	5	40	5	130	12.2%	3.25 [0.99, 10.66]
Total (95% CI)		**668**		**605**	**100.0%**	**2.49 [1.64, 3.77]**
Total events	84		30			

Heterogeneity: Tau² = 0.00; Chi² = 1.61, df = 4 (P = 0.81); I² = 0%
Test for overall effect: Z = 4.31 (P < 0.0001)

Fig. 3D. Forest plot for new PPM.

Study or Subgroup	TAVR Events	Total	SAVR Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Kamioka 2019	1	35	2	59	7.6%	0.84 [0.08, 8.96]
Modine 2024	26	323	5	297	43.2%	4.78 [1.86, 12.29]
Rodés-Cabau 2014	18	98	6	83	49.2%	2.54 [1.06, 6.10]
Total (95% CI)		**456**		**439**	**100.0%**	**3.07 [1.59, 5.94]**
Total events	45		13			

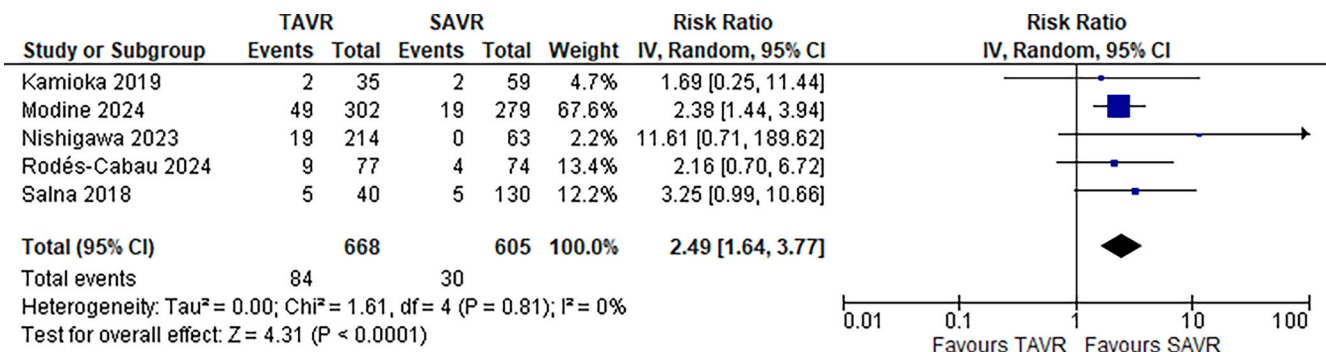Heterogeneity: Tau² = 0.03; Chi² = 2.17, df = 2 (P = 0.34); I² = 8%
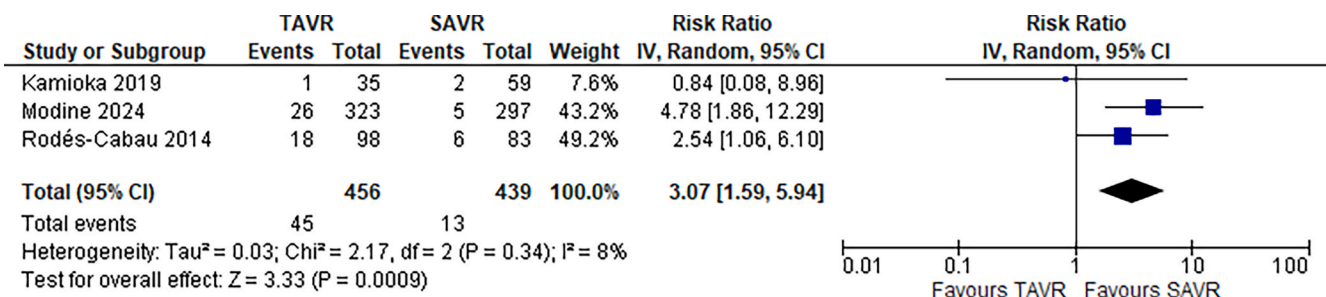Test for overall effect: Z = 3.33 (P = 0.0009)

Fig. 4A. Forest plot for major vascular complication.

The analysis of 2-year stroke included five studies with 1,671 patients and showed a statistically nonsignificant difference between TAVR and SAVR (RR = 1.10; 95 % CI: [0.64–1.90], P = 0.73). The pooled studies displayed non significant heterogeneity (I² = 37 %; P = 0.17). Fig. 5B.

- Long-term MI

Our analysis of 2-year MI included four studies with 1,119 patients and showed a statistically nonsignificant difference between TAVR and SAVR (RR = 0.91; 95 % CI: [0.39–2.12], P = 0.82). The pooled studies
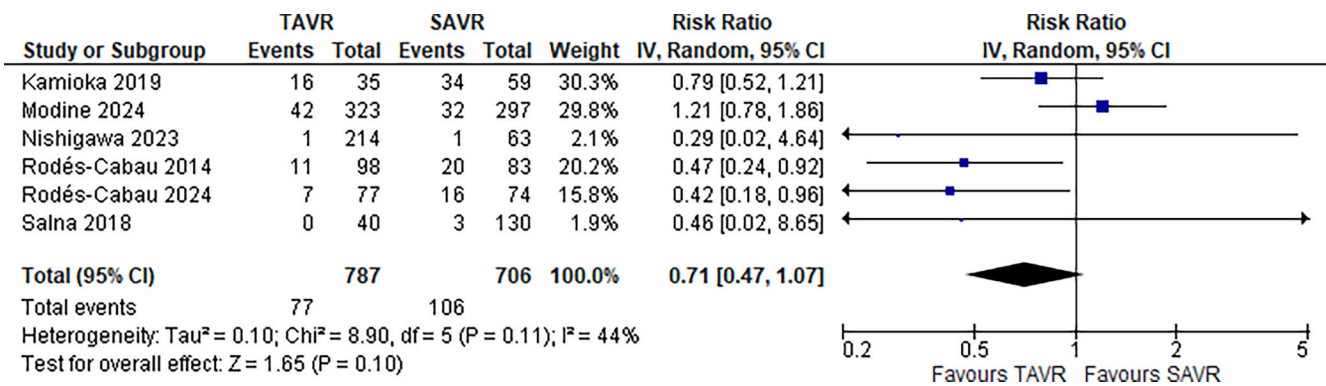
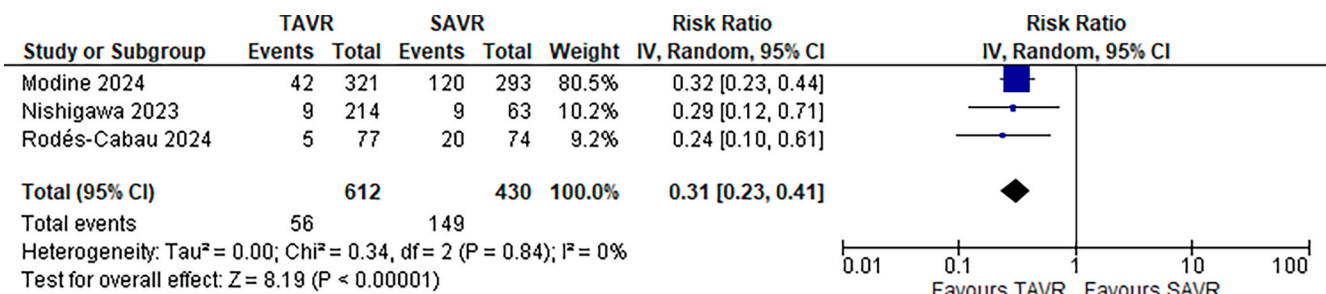**Fig. 4B.** Forest plot for major life-threatening bleeding.

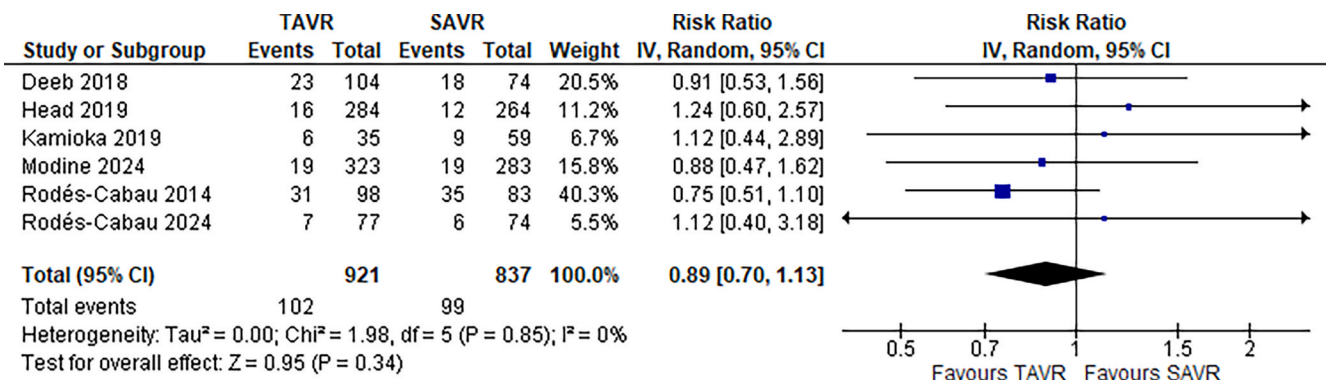**Fig. 4C.** Forest plot for new-onset Afib.

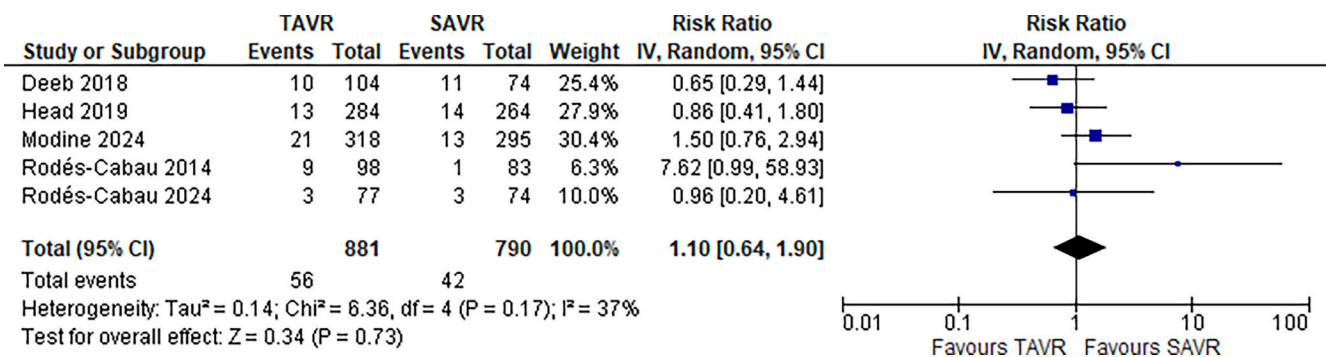**Fig. 5A.** Forest plot for long-term mortality.

Fig. 5B. Forest plot for long-term stroke.

demonstrated no heterogeneity ($I^2 = 0$; $P = 0.63$). Fig. 5C.

- Long-term major or life-threatening bleeding

Our analysis of 2-year major or life-threatening bleeding included four studies with 1,120 patients. Our analysis revealed a statistically nonsignificant brween TAVR and SAVR (RR = 0.75; 95 % CI:

Study or Subgroup	TAVR Events	Total	SAVR Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Deeb 2018	3	104	2	74	23.1%	1.07 [0.18, 6.23]
Modine 2024	6	323	4	286	45.7%	1.33 [0.38, 4.66]
Rodés-Cabau 2014	0	98	2	83	7.9%	0.17 [0.01, 3.49]
Rodés-Cabau 2024	2	77	3	74	23.2%	0.64 [0.11, 3.73]
Total (95% CI)		602		517	100.0%	0.91 [0.39, 2.12]
Total events	11		11			

Heterogeneity: Tau² = 0.00; Chi² = 1.72, df = 3 (P = 0.63); I² = 0%
Test for overall effect: Z = 0.23 (P = 0.82)
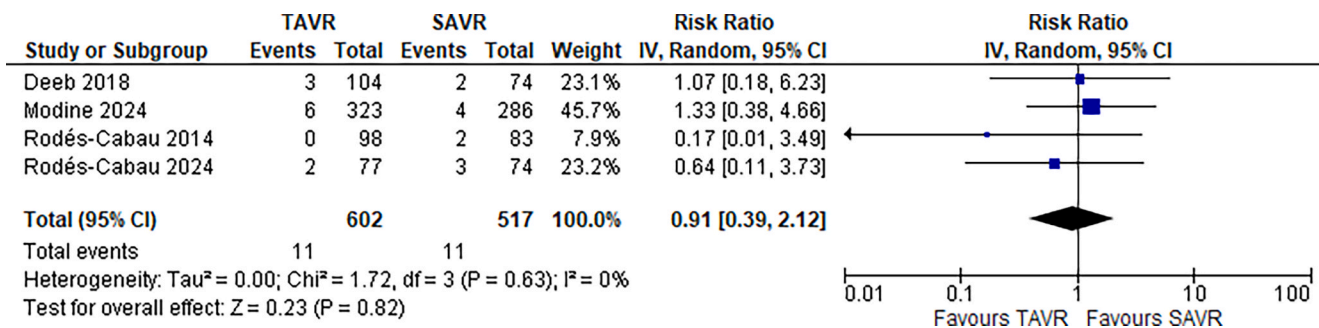
Fig. 5C. Forest plot for MI.

[0.51–1.11], $P = 0.15$. Pooled studies displayed significant heterogeneity ($I^2 = 70$; $P = 0.02$). Heterogeneity was best addressed by excluding the study of Modine *et al.* 2024 ($I^2 = 0$ %; $P = 0.69$). After removing the study of Modine *et al.* 2024 from the *meta*-analysis, the overall RR favored TAVR over SAVR (RR = 0.66; 95 % CI: [0.55–0.80], $P < 0.0001$). Fig. 5D.

- Long-term aortic valve reintervention

Our analysis of 2-year aortic valve reintervention included four studies with 1,497 patients and showed a statistically nonsignificant difference between TAVR and SAVR (RR = 2.64; 95 % CI: [0.71–9.78], $P = 0.15$). The pooled studies showed no heterogeneity ($I^2 = 0$ %; $P = 0.98$). Fig. 6A.

- Long-term new permanent pacemaker implantation (PPI)

The frequency of 2-year PPI was reported in three studies with 933 patients. The overall effect estimate favored TAVR over SAVR (RR = 2.42; 95 % CI: [1.70–3.44], $P < 0.0001$). The pooled studies were homogeneous ($I^2 = 0$; $P = 1.00$). Fig. 6B.

- Long-term major vascular complication

Our analysis of 2-year major vascular complications included three studies with 974 patients, and the pooled RR favored SAVR over TAVR (RR = 3.73; 95 % CI: [1.98–6.99], $P < 0.0001$). The pooled studies revealed nonsignificant heterogeneity ($I^2 = 1$ %; $P = 0.36$). Fig. 6C.

- Long-term aortic valve-related hospitalization

The analysis of 2-year aortic valve-related hospitalization included three studies with a total of 877 patients and showed a statistically nonsignificant difference between TAVR and SAVR (RR = 1.07; 95 % CI: [0.75–1.51], $P = 0.71$). The pooled studies were homogenous ($I^2 = 0$ %; $P = 0.91$). Fig. 6D.

3.6. Echocardiographic outcomes

- Patient-prosthesis mismatch (PPM)

The overall risk ratio was lower with TAVR over SAVR regarding the incidence of PPM (RR = 0.56; 95 % CI: [0.48–0.65], $P < 0.00001$). The pooled studies displayed significant heterogeneity ($I^2 = 62$ %; $P = 0.0002$). A leave-one-out analysis could not address the source of heterogeneity. Supplementary Fig. 1.

TAVR was associated with a significantly lower risk of moderate-to-severe and severe PPM compared with SAVR (RR = 0.61; 95 % CI: [0.50–0.74], $P < 0.00001$) ($I^2 = 75$ %; $P < 0.0001$) and (RR = 0.50; 95 % CI: [0.41–0.60], $P < 0.00001$) ($I^2 = 0$ %; $P = 0.45$), respectively.

- Paravalvular regurgitation (PVR) of leak (PVL)

The overall risk ratio was lower with SAVR over TAVR regarding the incidence of PVL (RR = 3.35; 95 % CI: [1.79–6.27], $P = 0.0002$). The pooled studies were heterogeneous ($I^2 = 64$ %; $P = 0.001$). A leave-one-out analysis could not address the source of heterogeneity. Supplementary Fig. 2.

SAVR was associated with significantly higher risk of mild and moderate-to-severe PVL compared with TAVR (RR = 3.48; 95 % CI: [1.41–8.60], $P = 0.007$) ($I^2 = 81$ %; $P = 0.0003$] and (RR = 3.32; 95 % CI: [1.28–8.64], $P = 0.01$) ($I^2 = 34$ %; $P = 0.17$), respectively.

- Change in effective orifice area (EOA)

The overall mean difference favored TAVR over SAVR regarding the change in EOA (MD = 0.21; 95 % CI: [0.15 to 0.27], $P < 0.00001$). The pooled studies showed nonsignificant heterogeneity ($I^2 = 40$; $P = 0.11$). Supplementary Fig. 3.

SAVR was associated with a comparable 2-month change in EOA with TAVR (MD = 0.14; 95 % CI: [-0.01 to 0.30], $P = 0.07$) ($I^2 = 58$ %; $P = 0.12$). TAVR was associated with significantly favorable change in EOA outcome at predischarge, 1-month, 6-month, and 1-year follow-up periods (MD = 0.21; 95 % CI: [0.09 to 0.34], $P = 0.0006$) ($I^2 = 49$ %; $P =$
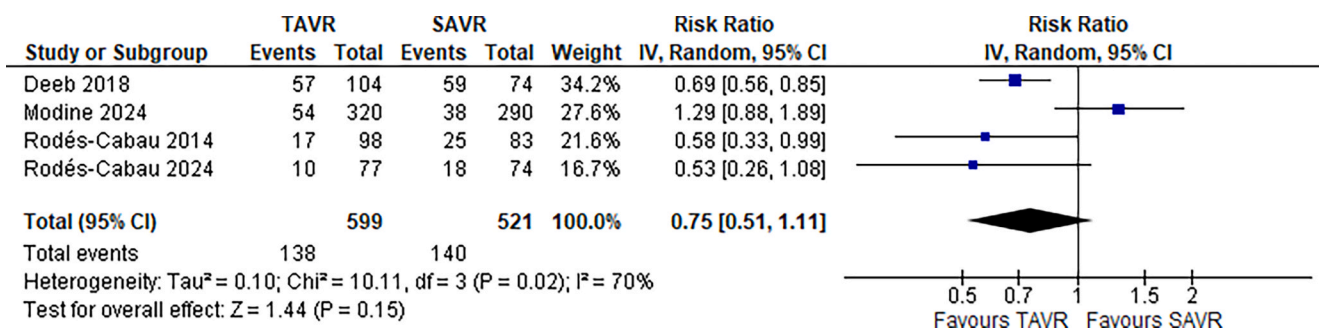

Study or Subgroup	TAVR Events	Total	SAVR Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Deeb 2018	57	104	59	74	34.2%	0.69 [0.56, 0.85]
Modine 2024	54	320	38	290	27.6%	1.29 [0.88, 1.89]
Rodés-Cabau 2014	17	98	25	83	21.6%	0.58 [0.33, 0.99]
Rodés-Cabau 2024	10	77	18	74	16.7%	0.53 [0.26, 1.08]
Total (95% CI)		599		521	100.0%	0.75 [0.51, 1.11]
Total events	138		140			

Heterogeneity: Tau² = 0.10; Chi² = 10.11, df = 3 (P = 0.02); I² = 70%
Test for overall effect: Z = 1.44 (P = 0.15)

Fig. 5D. Forest plot for long-term major life-threatening bleeding.
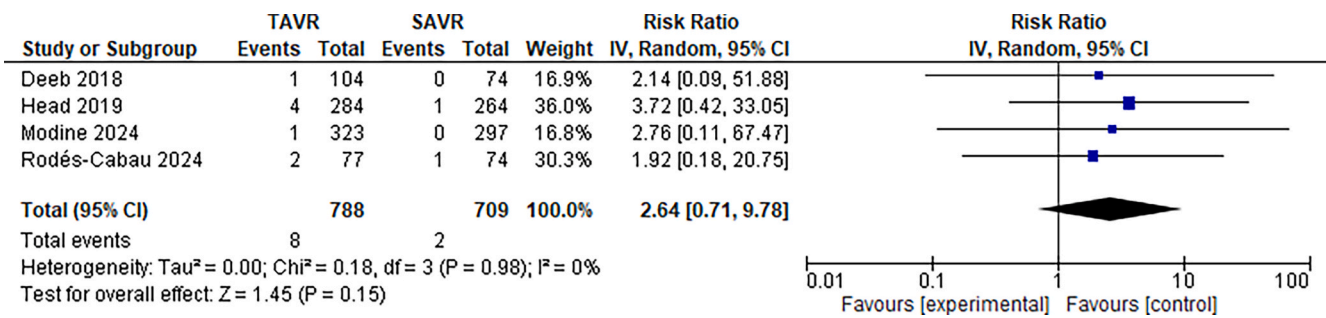
Fig. 6A. Forest plot for long-term aortic valve reintervention.
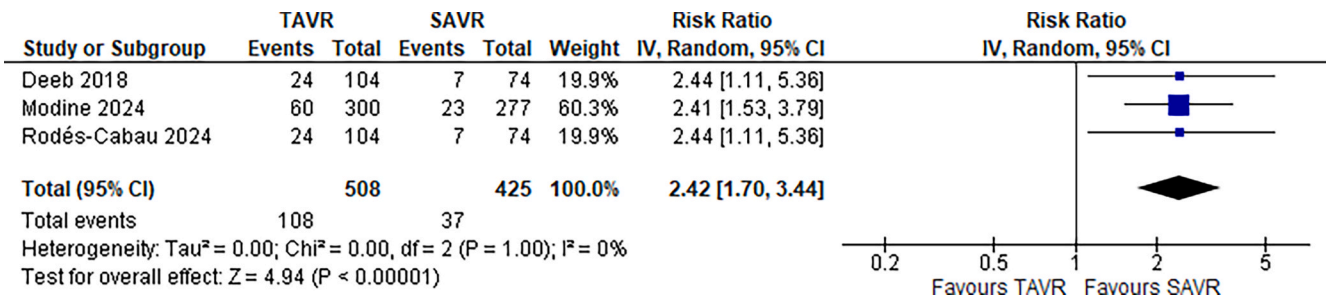

Fig. 6B. Forest plot for long-term new PPM.
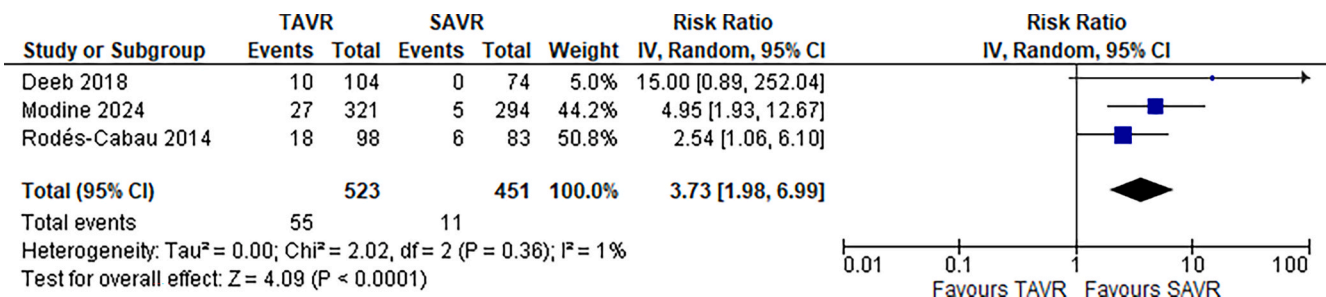

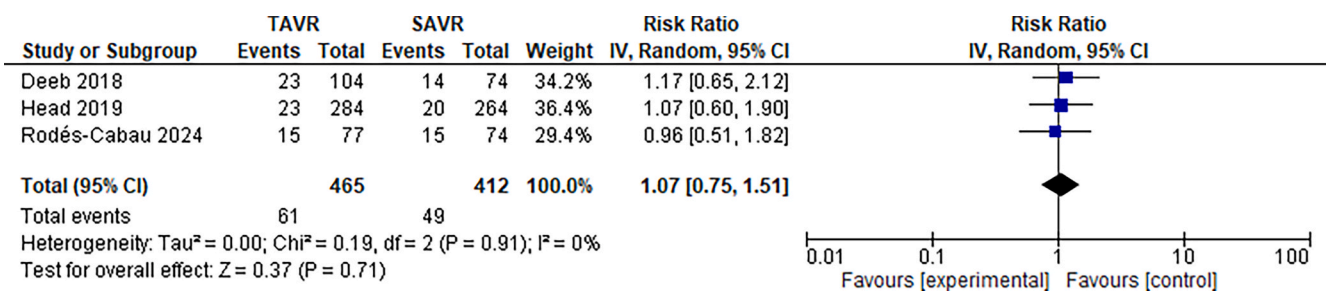**Fig. 6C.** Forest plot for long-term major vascular complication.

Fig. 6D. Forest plot for long-term vascular-related hospitalization.

0.14), (MD = 0.18; 95 % CI: [0.06 to 0.30], $P = 0.003$), and (MD = 0.29; 95 % CI: [0.20 to 0.37], $P < 0.00001$) ($I^2 = 0$ %; $P = 0.48$), respectively.

- Change in indexed effective orifice area (iEOA)

The overall mean difference favored TAVR over SAVR regarding the change in iEOA (MD = 0.13; 95 % CI: [0.09 to 0.16], $P < 0.00001$). The pooled studies showed no heterogeneity ($I^2 = 0$ %; $P = 0.64$). Supplementary Fig. 4.

TAVR was associated with significantly favorable change in iEOA at predischarge and 1-year follow-up durations (MD = 0.11; 95 % CI: [0.06

to 0.16], $P < 0.0001$) ($I^2 = 0$ %; $P = 0.47$) and (MD = 0.15; 95 % CI: [0.10 to 0.20], $P < 0.00001$) ($I^2 = 0$ %; $P = 0.75$), respectively.

- Change in mean aortic gradient

The overall mean difference favored TAVR over SAVR regarding the change in mean aortic gradient (MD = −2.07; 95 % CI: [-3.77 to −0.37], $P = 0.02$). The pooled studies showed significant heterogeneity ($I^2 = 66$ %; $P < 0.0001$). Sensitivity analysis could not address the source of heterogeneity. Supplementary Fig. 5.

A subgroup analysis based on follow-up time showed that TAVR and

SAVR were similar regarding the change in mean aortic gradient at predischarge (MD = −2.20; 95 % CI: [-5.01 to 0.62], *P* = 0.13) (I² = 73 %; *P* = 0.002), at two months (MD = −2.40; 95 % CI: [-7.21 to 2.41], *P* = 0.33) (I² = 54 %; *P* = 0.09), at six months (MD = −4.83; 95 % CI: [-11.63 to 1.97], *P* = 0.16) (I² = 58 %; *P* = 0.12), and at one year of follow-up (MD = −0.69; 95 % CI: [-4.57 to 3.19], *P* = 0.73) (I² = 88 %; *P* = 0.001).

- Change in peak aortic gradient

TAVR was associated with a comparable change in peak aortic gradient with SAVR (MD = −3.71; 95 % CI: [-9.25 to 1.83], *P* = 0.19). The pooled studies showed nonsignificant heterogeneity (I² = 44 %; *P* = 0.15). Supplementary Fig. 6.

TAVR was associated with significantly favorable predischarge change in peak aortic gradient (MD = −7.68; 95 % CI: [-11.75 to −3.62], *P* = 0.0002) (I² = 0 %; *P* = 0.68), albeit not with 2-month change in peak aortic gradient (MD = 1.43; 95 % CI: [-5.30 to 8.15], *P* = 0.68) (I² = 0 %; *P* = 0.81).

- Change in left ventricular ejection fraction (LVEF)

The overall effect estimate did not favor TAVR or SAVR regarding the change in LVEF (MD = −0.01; 95 % CI: [-1.14 to 1.11], *P* = 0.98). The pooled studies displayed significant heterogeneity (I² = 53 %; *P* = 0.03). Heterogeneity was best addressed by excluding Nishigawa *et al.* 2023 study (I² = 40 %; *P* = 0.11). After removing Nishigawa *et al.* 2023 from the *meta*-analysis, the overall MD still did not favor TAVR or SAVR (MD = −0.35; 95 % CI: [-1.45 to 0.75], *P* = 0.53). Supplementary Fig. 7.

SAVR was associated with significantly favorable predischarge change in LVEF (MD = 1.19; 95 % CI: [0.25 to 2.14], *P* = 0.01) (I2 = 0 %;

P = 0.74), whereas TAVR was associated with significantly favorable 1-year change in LVEF (MD = −1.52; 95 % CI: [-2.57 to −0.47], P = 0.005) (I² = 0 %; *P* = 0.63). There were no differences between TAVR and SAVR regarding the 2-month change in LVEF (MD = 0.00; 95 % CI: [-3.33 to 3.33], *P* = 1.00).

3.7. Reconstructed time to event data

We pooled the overall survival from three studies with a total of 426 patients showed no significant difference between TAVR and SAVR along 24 months of follow-up (HR: 0.74 with 95 % CI [0.48, 1.14], P = 0.18) as shown in (Fig. 7). However, upon examining the Schoenfeld residuals plot, there was no visual indication of a violation in the proportionality of the hazard ratio over time. The Grambsch-Therneau test was also not statistically significant (P = 0.79). Supplementary Fig. 8.

Supplementary Fig. 9 shows time-varying hazard ratios (HRs) for survival derived from flexible parametric survival models utilizing B-splines, showing no significant difference between TAVR and SAVR. Moreover, The difference in restricted mean survival time (RMST) over the follow-up period was presented in Supplementary Fig. 10, revealing no significant difference between TAVR and SAVR survival time 0.65 months (95 % CI, −0.756, 2.055, P = 0.365).

4. Discussion

The systematic review and *meta*-analysis compared TAVR and SAVR in patients with severe aortic stenosis and an SAA. The analysis included eleven studies and found that there was no significant difference in 30-day mortality, stroke, myocardial infarction, or major/life-threatening bleeding between TAVR and SAVR. In terms of long-term outcomes,
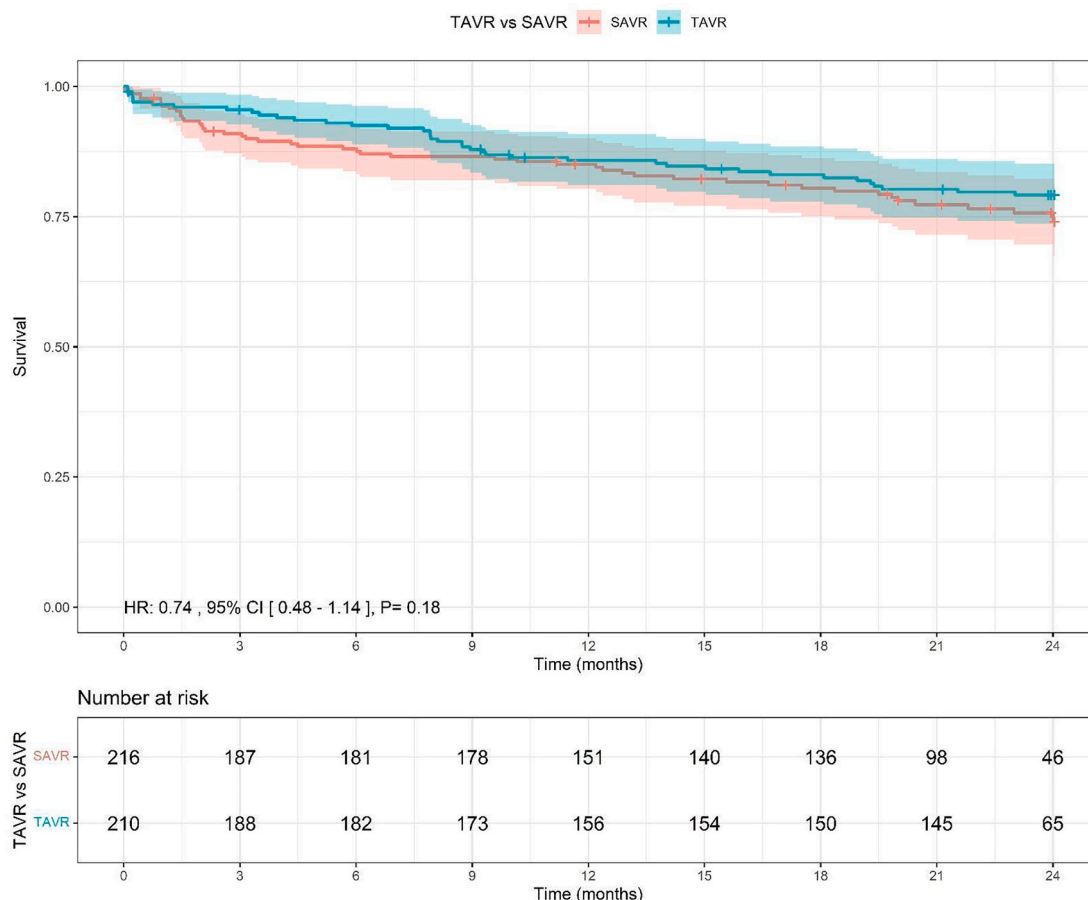

Fig. 7. Kaplan Meier curve of constricted time to event data.

there was no significant difference in 1- or 2-year mortality, stroke, or myocardial infarction between the two procedures. TAVR was associated with a higher risk of 2-year new permanent pacemaker implantation and major vascular complications than SAVR. Echocardiographic outcomes showed that TAVR was associated with a lower risk of moderate-to-severe and severe PPM but a higher risk of paravalvular leak compared to SAVR. Meanwhile, SAVR was associated with a favorable change in EOA, iEOA, and predischarge change in LVEF.

SAA patients pose a challenge when treating AS since this anatomical feature has been associated with worse clinical outcomes. Unlike previous RCTs and observational studies, our study failed to demonstrate the superiority of TAVR over SAVR in terms of both short- and long-term clinical outcomes [21,27]. TAVR and SAVR showed a similar incidence of short-term outcomes: 30-day mortality, stroke, MI, and long-term outcomes: 1- or 2-year mortality, 1- or 2-year stroke, 2-year MI, 2-year aortic valve reintervention, 1- or 2-year aortic valve-related hospitalization. Our findings are consistent with the recent VIVA trial [21]. Arguably, innovations in surgical valve design, such as modern sutureless valves and aortic root enlargement procedures, are bridging the outcome gap between SAVR and TAVR. In this emerging scenario, the alternatives should be based on individual patient characteristics, surgical risk, unique anatomical procedures, and financial bandwidth.

Furthermore, independent of annulus size, the risk of new PPI has remained historically significantly higher with TAVR. Previous reports have suggested an incidence of 5–22 % [30] for conduction abnormalities requiring PPI. The need for a PPI is related to conduction abnormalities arising from anatomic interaction between the valve prosthesis and the atrioventricular node and bundle of His. The risk of post-procedural PPI should be especially considered in young and low surgical-risk patients who prefer SAVR to avoid future complications associated with pacing, such as additional procedures, generator changes, and device upgrades [31]. The risk of PPI is also variable with the used TAVR device; Webb et al. [32], in a multicenter evaluation of balloon-expandable transcatheter balloon expandable aortic valves have reported an incidence of 13.3 % with SAPIEN-3 which is lower than its self-expandable counterparts CoreValve (25.5 %) or EvolutR valve (26.7 %) based on SURTAVI trial for PPI [33]. Hence, SAPIEN-3 can be a viable alternative.

Similarly, our study reported a lower incidence of new-onset atrial fibrillation with TAVR. This is consistent with previous studies, such as the PARTNER trial having found a significant difference in the development of NOAF after TAVR and SAVR 9 % vs 16 % of patients, respectively [27]. The incidence of NOAF after SAVR is attributed to post-procedural inflammation and diuretics [34,35]. The occurrence of arrhythmia has several implications, including increased risk of cerebrovascular accidents, morbidity, mortality, and increased financial burden. Therefore, predicting and managing them with prophylactic antiarrhythmic therapy is important.

Compared to TAVR, SAVR has been associated with fewer major vascular complications both in the short-term and long-term; this can be attributed to its vascular approach compared to SAVR. The risk of the above complications with TAVR has also experienced a downward trend, with the PARTNER trial reporting a 15.7 % to 8.0 % risk in the non-randomized continued access registry for the transfemoral route [36]. This is attributed to the smaller size of transcatheter devices currently in use. However, one point of interest for clinicians is that despite the differences in major vascular complications between SAVR and TAVR, this does not significantly impact the mortality risk of cerebrovascular events or MI, implying that these complications are manageable. Moreover, preoperative optimization with blood transfusions and emphasis on patient selection can reduce the risk and severity of bleeding and vascular complications.

Moreover, our hemodynamic results show a mixed picture, with both TAVR and SAVR having their own merits. TAVR is less likely to cause PPM, is better at reducing mean and peak aortic gradients, and has better LVEF improvement at one year but has a higher risk of PVL.

Managing PPM has challenged clinicians for decades, especially in the subset of the population with SAA, because these patients undergoing SAVR are more prone to receive smaller prostheses, which results in the EOA of a normally functioning prosthetic valve being too small in relation to body size [22]. PPM has several deleterious implications on the prognosis after AVR, including reduced left ventricular mass regression, left ventricular function, and impaired post-surgery normalization of coronary flow reserve and structural valve degeneration [37,38].

In the past decade, the paradigm has shifted towards TAVR in intermediate- to high-risk patients with severe AS [39,40] owing to the superior hemodynamic profile exhibited by TAVR (self- or balloon-expanding valves) compared to SAVR. These findings have been supported by several RCTs, including high- and intermediate-risk patients, which showed lower transvalvular gradients and larger aortic valve areas in TAVR than in SAVR at discharge and during follow-up [39,40]. The incidence of PPM in patients undergoing TAVR tends to be lower than in patients undergoing SAVR and is reported to be between six and 46 % for moderate PPM and between zero and 15 % for severe PPM. In patients treated with SAVR, up to one-half and one-quarter have PPM and severe PPM, respectively [37]. A *meta*-analysis conducted on 745 patients by Takagi et al. described a relative risk reduction of 77 % in the incidence of PPM in patients treated with TAVR compared to SAVR [41]. TAVR achieves this feat by its design, which allows for a larger EOA owing to the absence of a sewing ring and systematic transcatheter valve oversizing. In addition, the supra-annular leaflet position of this SEV subtype of valves further enhances the efficacy [42].

Furthermore, the overall mean difference favored TAVR over SAVR regarding the change in mean aortic gradient. However, this superiority was not replicated in our subgroup analysis based on follow-up time. TAVR was associated with a comparable change in peak aortic gradient with SAVR. TAVR was associated with a significantly favorable predischarge change in peak aortic gradient, albeit not with a 2-month change in peak aortic gradient. The optimistic profile created by favorable aortic gradients and reduced PPM risk is threatened by the paravalvular leakage associated with TAVR. Paravalvular leakage is an area of concern with the use of TAVR devices as moderate/severe PVL has been associated with 2- to 3-times elevation in the risk of all-cause mortality compared to the PVL with SAVR [43]. One mechanism is increased left ventricular overload, which impacts pulmonary circulation [44].

This higher incidence of paravalvular leakage with TAVR can be attributed to the unique anatomy of the aortic annulus, i.e., the device landing zone, which can't be evaluated for size and shape during TAVI, unlike SAVR. Therefore, it is of utmost importance to utilize advanced imaging techniques such as transthoracic echocardiography, transesophageal echocardiography, multirow-detector computed tomography, aortography, or magnetic resonance for pre- and periprocedural evaluation [45,46]. Further, the materialization of newer generation transcatheter heart valves that allow close approximation of valve and aortic annulus is promising. It has resulted in a drop in moderate/severe PVL incidence and has become near that of SAVR [47,48]. Recent refinement in the TAVR technique, including the cusp-overlap technique, has promised to advance the outcomes through the reduction of conduction abnormalities, thereby bringing about a decrease in PPI rates as compared to the traditional three-cusp technique [49]. The enhancement of left ventricular outflow tract visualization allows this technique to place the valve in a very precise manner, thereby aiding in minimizing interference with the conduction system. New-generation self-expanding valves like Evolut PRO+ and FX have already reportedly reduced the incidence of PPI due to design improvements with better radial force distribution [50]. The updated balloon-expandable valve has also provided great success for the SAPIEN 3 Ultra, given its favored positions over the older SAPIEN 3 model [51] for improvements in paravalvular leak prevention and overall procedural success rates. Indeed, these changes reflect further evolution in TAVR technology aimed at optimizing clinical outcomes and procedural safety.

Nevertheless, TAVR was associated with a favorable change in both EOA. A 2-month change in EOA was comparable with SAVR but EOA outcome at predischarge; 1-month, 6-month, and 1-year follow-up periods strongly supported TAVR. Similarly, change in iEOA, especially predischarge and at 1-year follow-up durations, favored TAVR. A favorable change in iEOA correlates with a reduced incidence of PPM which is a decisive factor in choosing intervention for patients with aortic stenosis and SAA. However, findings regarding iEOA should be interpreted cautiously due to a lack of consensus on the iEOA reporting method. Several factors influence the accuracy of both the projected and the measured iEOA for PPM assessment, which leads to a certain number of false assignments to the PPM or no PPM group [52].

There is still a debate on whether measured or predicted iEOA will be used to assess PPM following SAVR and TAVR correctly. Most studies that evaluated the impact of PPM on the outcome following SAVR used the predicted iEOA, whereas more recent TAVR trials used the measured iEOA [52,53]. Predicted iEOA re-classifies a certain proportion of patients toward a lower PPM grade, and the association between gradients and clinical outcomes differs [53]. Therefore, a universal agreement for measuring and reporting iEOA across SAVR and TAVR studies is of utmost importance to establish true comparisons and reduce the incidence of PPM.

Finally, according to our findings, the change in LVEF did not favor either arm; however, SAVR was beneficial in the short-term (favorable predischarge change in LVEF) and TAVR in the long run (favorable 1-year change in LVEF). A *meta*-analysis by Takagi et al. also reports that TAVR is associated with greater LVEF improvement at 6–12 months than SAVR in patients with low EF while reporting similar results with pre-procedural LVEF greater than 50 % [54]. The implication is that TAVR results in faster and enhanced recovery of ventricular function in the SAA population, especially in high-risk candidates.

4.1. Limitations and recommendations

We did not analyze individual patient data; however, we believe this would provide important insights for designing treatments tailored to patients' needs. We did not conduct subgroup analysis for female and young and Asian ethnic populations due to limited data from previous studies; however, future RCTs are warranted, specifically focussing on these subgroups. Ideal valve selection in young patients is more nuanced because of the risk of valve outgrowth associated with congenital heart defects, and bioprosthetic heart valves and homografts are less durable than mechanical valves [55,56]. The ongoing RHEIA trial (NCT04160130) evaluating the safety and efficacy of TAVR in female patients with severe AS will provide further insight. Since TAVR and SAVR are equal contenders in clinical outcomes and hemodynamic profile, cost-effectiveness and feasibility are major factors in clinical decision-making. We believe the results from the Treatment of Aortic Stenosis in Brazil: Cost-Utility Analysis of TAVI vs SAVR (TEAm-BR) (NCT04067089) study will address this issue. Moreover, two major limitaions are lack of consistecny in defination of SAA in the trials as well as PPM which may attributed to divesity and observed high heterogenity.

Additionally, the follow up period was of 1 or 2 years which hinders our ability to have a robust analysis and evidence about the proper long term outcomes of SAVR vs TAVR, thus we call for a longer follow up studies to be conducted. Moreover, the observational studies have hinted at comparable outcomes with novel techniques, such as sutureless or rapid deployment valve and TAVR in patients with severe AS and high operative risk undergoing valve replacement [57,58]; however, this has not been evaluated in RCTs, and we believe that a head-to-head comparison of these intervention arms will enrich our understanding of superior intervention in high-risk population groups.

5. Conclusion

TAVR had a significantly reduced risk of PPM and new-onset AF but with increased PPI and vascular complications. Although, TAVR significantly improved EOA and iEOA, had less risk of PVL, SAVR had better LVEF improvement at predischarge. Therefore, TAVR and SAVR remain valid alternatives, and decisions should be based on differences in anatomy of either aortic annulus or aortic root, operative risk, and associated co-morbidties. Research using newer-generation devices and procedures is likely to provide definitive answers.

CRediT authorship contribution statement

Ahmed K. Awad: Software, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Zina Otmani:** Project administration, Methodology, Investigation. **Mazen Negmeldin Aly Yassin:** Writing – original draft, Resources, Data curation. **Ahmed Mazen Amin:** Writing – original draft, Formal analysis, Data curation. **Farouq Bahaa Alahmed:** Writing – original draft, Methodology, Investigation, Data curation. **Zineddine Belabaci:** Writing – original draft, Resources, Methodology. **Haya A. Hegazy:** Writing – original draft, Resources, Investigation. **Unaiza Ahmad:** Writing – review & editing, Writing – original draft. **Mohamed Abuelazm:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Project administration, Investigation.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2024.101578.

Data availability

The data is available upon reasonable request from the corresponding author.

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