# RESEARCH

# **Open Access**



Ischemic stroke incidence in intermediate or high-risk patients undergoing transcatheter aortic valve replacement versus surgical aortic valve replacement: a comparative systematic review and meta-analysis

Shahzaib Rehman<sup>1</sup>, Mahrukh Ghani<sup>2</sup>, Anshahrah Riaz<sup>3</sup>, Syeda Sadia Masood Raza<sup>4</sup>, Mariam Zahid<sup>5</sup>, Muhammad Hammad Zahid Malik<sup>6</sup>, Arman Amir<sup>7</sup>, Ethuri Lokesh<sup>8</sup>, Kovvuru Ashrita<sup>8</sup>, Meet Popatbhai Kachhadia<sup>9</sup> and Vikash Kumar Karmani<sup>10\*</sup>

# Abstract

**Background and purpose** This comparative systematic review and meta-analysis investigated the incidence of ischemic stroke in intermediate-to-high-risk patients undergoing transcatheter aortic valve replacement versus surgical aortic valve replacement.

**Methods** We conducted a systematic review and meta-analysis following the PRISMA guidelines, searching PubMed, Google Scholar, Embase, Web of Science, and Cochrane CENTRAL databases from their inception to December 2023. The evaluated outcomes were primarily incidence of stroke and transient ischemic attack (TIA), along with other secondary safety end-points at 30 days and 1 year post-procedure. Odds ratios (ORs) with 95% confidence intervals (CIs) were utilized for each study, employing a random-effects model for data synthesis irrespective of heterogeneity. Statistical heterogeneity was assessed using I<sup>2</sup> statistics. All statistical analyses were conducted using Review Manager.

**Results** We screened 8028 articles and included 8 studies consisting of 5 randomized controlled trials and 3 observational studies. The studies examining 30-day and 1-year stroke incidence found no significant difference between TAVR and SAVR patients (OR 0.83, 95% CI 0.59 to 1.17, p = 0.30, OR 0.92, 95% CI 0.64 to 1.33, p = 0.67, respectively). Both TAVR and SAVR also had a comparable risk of having a transient ischemic attack within 30 days (OR 0.93, 95% CI 0.24 to 3.63, p = 0.92,  $l^2$  52%) and 1 year (OR 1.15, 95% CI 0.72 to 1.82, p = 0.56,  $l^2$  0%) following the procedure. Regarding safety endpoints, TAVR had lower rates of all-cause mortality and acute kidney injury at 1 year post-procedure, but a higher incidence of major vascular complications at both 30 days and 1 year compared with SAVR.

**Conclusion** The results suggest that TAVR and SAVR have comparable outcomes for both TIA and stroke incidence at 30 days and 1 year post-procedure, but display varying safety profiles in intermediate-to-high surgical risk patients.

Keywords Aortic valve, Ischemic stroke, Transient ischemic attack, Valve replacement

\*Correspondence: Vikash Kumar Karmani

Vikashkarmani@gmail.com

Full list of author information is available at the end of the article



© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, wisit http://creativecommons.org/licenses/by/4.0/.

# Introduction

Stroke has a significant impact on disability, leading to a decline in the overall health and standard of living of individuals aged 50 years and older and impairing their day-to-day activities. It has consistently been a major contributor to ailments in this age group from 1990 to 2019 [1], with the highest global disease burden persisting to be cardiovascular diseases [2], reporting approximately 19.9 million deaths in 2021 [3].

Aortic valve stenosis (AVS) is considered the most prevalent acquired valvular heart disease [4], carrying a specific risk factor for ischemic stroke [5]. It is currently widespread in the West [6] especially affecting those 60 years of age and beyond, with a prevalence of more than 2% [4]. The etiology of AVS is highly comparable to that of atherosclerosis and is closely linked with cardiac risk factors including age, male gender, smoking, hypertension, high low-density lipoprotein (LDL) cholesterol, and diabetes mellitus [7]. When manifesting symptoms, severe AVS has an intimidating 50% 2-year mortality rate [4], however, the advent of transcatheter aortic valve replacement (TAVR) in 2002 has revolutionized the treatment approach [8].

TAVR offers a good substitute to patients ineligible for surgery while demonstrating comparable, and, in some cases, superior outcomes to SAVR across various risk profiles based on several patient randomized control trials [8]. A 3-year study predominantly directed toward the primary outcome of all-cause mortality or disabling stroke revealed a substantial difference, with an incidence of 7.4% for the TAVR group compared to 10.4% in the SAVR group [8]. Another prospective study conducted over 4 years on 196 individuals, aged 65 and older, who underwent SAVR were assessed by MRI scans and neurological examinations pre- and post-operatively. The results revealed clinical stroke in 17%, transient ischemic attack in 2%, and an in-hospital mortality rate of 5% [9]. This disparity in results led to a discernible increase in the annual performance of TAVR surgeries, indicating its effectiveness and wide acceptance [8].

There has been a consistently higher incidence of stroke with SAVR at 21 per 1000 cases, compared to TAVR which is 16 per 1000 cases, in multiple clinical trials involving 2818 participants with follow-up periods of up to 30 days [10]. The cause of neurological complication post-procedure remains a subject of ongoing debate, with a possible assumption of manipulation of atherosclerotic plaque during aortic valve repair [11]. Additionally, a longer cardiopulmonary bypass time during surgical aortic valve replacement (SAVR) is linked to a higher stroke risk, likely due to hemodynamic changes. A lack of early imaging may contribute to the delayed diagnosis of stroke, in addition to giving time for a thrombus

to form on embolized material, leading to a delayed onset of post-procedural clinical presentation [12]. The prevention of postoperative stroke may be possible with an adequate antithrombotic or anticoagulant regimen, with studies leading the American College of Chest Physicians to recommend the use of aspirin as the preferred antithrombotic therapy after SAVR for  $\geq$  3 months, and the combination of aspirin and clopidogrel after TAVR [11]. This further emphasizes the importance of understanding and mitigating these risks in both procedures. Thus, this study aims to scrutinize the incidence of stroke following TAVR and SAVR procedures in AVS patients, hoping to yield valuable insights into the relative safety and efficacy of these interventions.

# Methods

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and recommendations of the Cochrane Collaboration [13].

#### Search strategy and data sources

A comprehensive electronic search was performed on Medline (PubMed), Google Scholar, Embase, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL) databases from their inception to December 2023 by two independent investigators (V.K. and M.G). The following search strategy was used: ((ischemic stroke) OR (non-hemorrhagic stroke)) AND ((surgical aortic valve replacement) AND (transcatheter aortic valve replacement)). Duplicate references were identified and removed. We included all qualifying randomized controlled trials (RCT) and observational studies without any time restriction but limited our study to English-language research to focus on relevant literature. The detailed search strategy for each database along with the retrieved number of search results is found in Supplementary Table S1.

# **Study selection**

All studies were assessed for eligibility and included if they met the following criteria: (a) participants age  $\geq$  80 years; or age  $\geq$  70 years with intermediate or high operative risk from conventional aortic valve replacement (AVR), as determined by the multi-disciplinary team; (b) patients with severe aortic valve stenosis defined as an effective orifice area < 1 cm<sup>2</sup> or indexed for body surface area < 0.6 cm<sup>2</sup>/m<sup>2</sup> and a mean aortic valve gradient > 40 mmHg or peak systolic velocity > 4 m/s; (c) symptomatic aortic valve stenosis (NYHA Functional Class II or greater); (d) incidence of stroke and/ or transient ischemic attack reported at 30 days and 1-year post-procedure comparing TAVR with SAVR; (e) all patients were evaluated by a heart team consisting of at least an imaging cardiologist, an interventional cardiologist, and a cardiac surgeon; and (e) asymptomatic patients included if they had left ventricular posterior wall thickness of 17 mm, decreasing left ventricular ejection fraction, or new onset Atrial fibrillation (AF). Studies with patients having another severe heart valve disease or coronary artery disease (CAD) requiring intervention or those undergoing SAVR with concomitant coronary artery bypass graft or simultaneous mitral repair/replacement were excluded. Non-English articles and articles not reporting stroke and transient ischemic attack as outcomes were also removed. Detailed exclusion criteria are given in the supplementary appendix.

#### **Data extraction**

Two authors (A.A and M.H) independently assessed the retrieved reports and only studies fulfilling the predefined inclusion criteria were selected. Initially, all studies were screened based on their title and abstract, followed by a comprehensive review of the full-length article to ascertain its relevancy. A third investigator (S.R) was consulted to address any discrepancies. Data including each study's design, inclusion/exclusion criteria, the sample size of each treatment group (SAVR and TAVR), baseline patients' characteristics, and their co-morbids (diabetes, hypertension, cerebrovascular disease, coronary artery disease, and peripheral vascular disease) was extracted using an Excel spreadsheet. The primary outcomes of interest were the risk of stroke and transient ischemic attack (TIA) at 30-day and 1-year follow-ups. All-cause mortality and incidence of periprocedural complications including myocardial infarction (MI), acute kidney injury (AKI), and major vascular complications were also assessed as secondary outcomes at 30 days and 1-year follow-ups. Due to the notable variation in defining disabling versus non-disabling stroke or major versus minor stroke and the limited number of studies included, subgroup analyses were not performed.

#### Risk of bias and quality assessment

The quality assessment of non-randomized cohort and case–control studies was performed using the Newcastle–Ottawa Scale (NOS) (Supplementary Tables S3 and S4) [14]. To estimate the potential bias in the included trials, we used the modified Cochrane Collaboration's risk of bias tool for randomized controlled trials, which assesses the following domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, completeness of outcome data and selective outcome reporting [15]. Two researchers (A.R and M.Z) examined the studies and judged the potential for bias, categorizing each item as having low, unclear, or high risk (Supplementary Table S2). Ultimately, the overall risk of bias for each trial was determined, considering whether bias within specific domains could significantly affect risk estimates.

# Statistical analysis

The risk of stroke, transient ischemic attack (TIA), allcause mortality, and periprocedural complications between groups was presented as odds ratios (ORs) with 95% confidence intervals (CIs) for each study, pooled using the DerSimonian and Laird random effects model [16]. Forest plots were created to visually illustrate the results of pooling. The presence and degree of statistical heterogeneity across studies were assessed using the Chisquare test and Higgins and Thompson's  $I^2$  statistic [17], with p < 0.10 considered statistically significant. I<sup>2</sup> values were interpreted according to the Cochrane Handbook for Systematic Reviews of Interventions, Sect. 10.10 [18]. All statistical analyses were conducted using Review Manager (RevMan, Version 5.4; The Cochrane Collaboration, Copenhagen, Denmark). Assessment of publication bias was not possible due to the limited number of studies included (<10) [27].

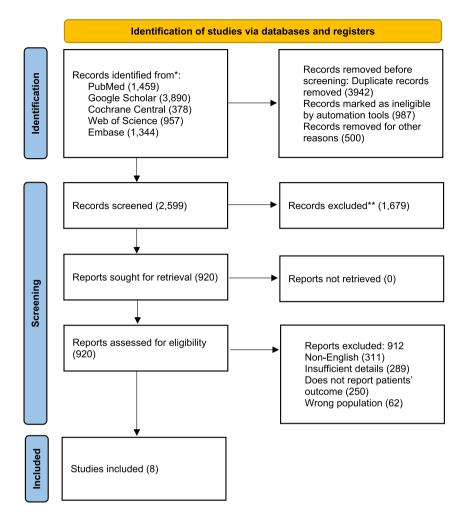
# Results

#### Search results

An initial electronic search of five databases retrieved 378 studies from Cochrane Central, 3890 from Google Scholar, 1459 from Medline (Pubmed), 957 from Web of Science, and 1344 from Embase. After removing duplicates and ineligible studies, 2599 records were screened based on their title and abstracts, and 1679 studies were excluded. We evaluated 920 records in full-text for eligibility and removed most of them for not reporting the desired outcome (n=250), having insufficient details (n=289), not being in the English language (n=311), or assessing the wrong population (n=62). Only 8 studies were identified for inclusion in the review. The flow of studies through the literature search and study selection process is summarised in Fig. 1.

#### Study characteristics

Out of the 8 studies that met the pre-specified inclusion criteria, 5 were randomized controlled trials (RCTs) [19–23], 2 were cohort studies [24, 25] and 1 was a propensity score-matched case–control study [26]. Overall, 6879 patients were randomly assigned to the TAVR group (n=3478) or the SAVR group (n=3401) (Table 1). All studies only recruited patients with severe symptomatic aortic stenosis, with the transfemoral route being the most preferred access site for TAVR across all studies.



\*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).

# \*\*If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

Fig. 1 PRISMA study flow chart. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses. *From*: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. https://doi.org/10.1136/bmj.n71

Assessment of publication bias was not possible due to the limited number of studies included (< 10) [27].

# Risk of bias assessment

In every eligible study, the Newcastle–Ottawa Scale and the Cochrane Collaboration's modified tool assessed the overall risk of bias to be low. However, allocation concealment in two studies was deemed to pose an unclear risk due to inadequate specification. Three randomized trials were rated at a high risk of bias for blinding of participants and medical personnel since it is difficult to conceal the type of intervention performed. These trials also had a high risk of detection bias possibly due to nonblinding of outcome assessors or variation in characteristics of study participants. Tables and graphs summarizing the risk of bias assessment of RCTs and Non-RCT studies are shown in Fig. 2a, b, and Supplementary Tables S2, S3, and S4.

#### Results of the meta-analysis

Eight studies examining the effectiveness of TAVR versus SAVR were included.

Author and year	Latib 2012	Gleason 2018	Tamburino 2015	Thyregod 2015	Toff 2022	Leon 2016	Mack 2018	Schymik 2015
Type of Study	Propensity score matched case– control study	RCT	PCS	RCT	RCT	RCT	RCT	PCS
Sample Size (n) TAVR SAVR	111 111	391 359	650 650	145 135	458 455	1011 1021	496 454	216 216
Age (Years±SD) TAVR SAVR	80.5±6.9 79.4±3.0	83.2±7.1 83.3±6.4	80.3±5.1 80.5±6.2	79.2±4.9 79.0±4.7	81 81	81.5±6.7 81.7±6.7	73.3±5.8 73.6±6.1	78.3±5.2 78.2±4.6
BMI (Kg/m2) TAVR SAVR	25.5±4.6 25.7±3.9	-	26.5±4.8 26.9±4.5	-	27.1 27.7	28.6±6.2 28.3±6.2	$30.7 \pm 5.5$ $30.3 \pm 5.1$	-
Left Ventricular Ejection Fraction (%±SD) TAVR SAVR	53.5±12.5 53.6±10.7	56.9±12.5 56.0±12.2	54.2±11.2 53.6±11.4	-	57 57	56.2±10.8 55.3±11.9	65.7±9.0 66.2±8.6	62.2±11.3 62.0±10.5
NHYA Class III-IV (n) TAVR SAVR	75 77	85 86	385 388	70 61	184 204	782 776	155 108	-
Diabetes Mellitus (n) TAVR SAVR	21 24	136 162	161 165	26 28	-	381 349	155 137	-
Coronary Artery Disease (n) TAVR SAVR	44 51	295 273	-	_	133 145	700 679	137 127	48 48
Cerebrovascular Disease (n) TAVR SAVR	16 20	97 90	-	24 22	-	325 317	-	-
Peripheral Vascular Disease (n) TAVR SAVR	-	159 150	22 18	6 9	-	282 336	34 33	-
Hypertension (n) TAVR SAVR	78 77	-	-	103 103	_	_	_	-
Previous Myocar- dial Infarction (n) TAVR SAVR	16 16	-	72 75	8 6	_	185 179	28 26	_

# Table 1 Baseline Characteristics of Included Studies

BMI Body mass index, NYHA New York Heart Association, PCS Prospective Cohort Study, RCT Randomised Controlled Trial, SAVR Surgical aortic valve replacement, TAVR Transcatheter aortic valve replacement

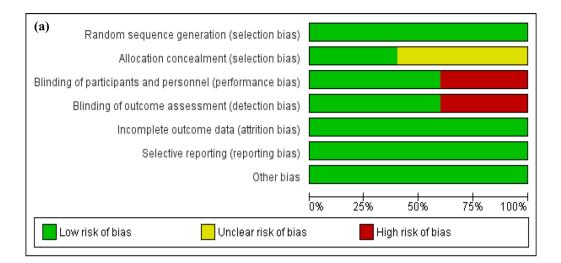
# Stroke

Six studies, involving 4,829 patients, provided data on the 30-day incidence of stroke (Fig. 3A). Leon 2016's research study had the highest weight (68.3%) among the pooled studies with the narrowest 95% CI of 0.91 [0.62, 1.32]. No significant difference was observed in the 30-day risk of stroke among patients who underwent TAVR compared to patients undergoing SAVR (OR 0.83, 95% CI 0.59 to 1.17, p=0.30,  $I^2$  3%). Heterogeneity was low between studies ( $\tau$ 2=0.01,  $I^2$ =3%). (Fig. 3A).

Seven studies (6,439 patients) reported 1-year stroke risk. Patients undergoing TAVR had a comparable 1-year risk of stroke with those undergoing SAVR, OR 0.92 (95% CI 0.64 to 1.33, p=0.67,  $I^2$  52%). Moderate heterogeneity was observed between studies ( $\tau 2=0.11$ ,  $I^2=52\%$ ). (Fig. 3B).

# TIA

Figure 4A represents a meta-analysis of the transient ischemic attack (TIA) risk at 30 days of follow-up.



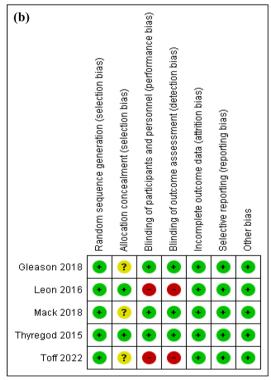


Fig. 2 a, b Risk of bias assessment

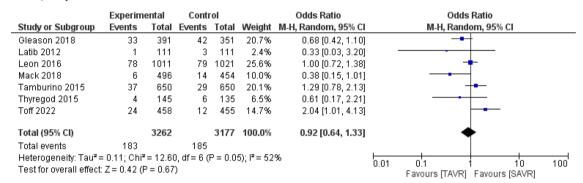
Thyregod 2015's research study has the lowest weight (14.4%) and the largest spread among all the pooled studies with a 95% CI of 4.72 [0.22, 99.24]. There was no evidence of a significant difference between TAVR and SAVR in the risk of having a transient ischemic attack within 30 days following surgery (OR 0.93, 95% CI 0.24 to 3.63, p = 0.92,  $I^2$  52%). Moderate heterogeneity was observed between studies ( $\tau 2 = 0.94$ ,  $I^2 = 52\%$ ).

When the studies were pooled to assess the 1-year TIA risk between TAVR and SAVR, Leon 2016's study was found to have the highest weight (51.4%) and therefore, the greatest influence on the overall effect outcome (Fig. 4B). There was a greater 1-year risk of having a transient ischemic attack in the TAVR group when compared to the SAVR group, OR 1.15 (95% CI 0.72 to 1.82, p = 0.56,  $I^2$  0%), however, this was not a statistically

#### A) 30-day stroke risk

	Experim	ental	Contr	ol		Odds Ratio		Odds	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, Rando	om, 95% Cl	
Latib 2012	1	111	2	111	2.0%	0.50 [0.04, 5.54]				
Leon 2016	55	1011	61	1021	68.3%	0.91 [0.62, 1.32]		-	F	
Mack 2018	3	496	11	454	7.0%	0.25 [0.07, 0.88]				
Schymik 2015	3	216	2	216	3.6%	1.51 [0.25, 9.11]				
Thyregod 2015	2	145	4	135	4.0%	0.46 [0.08, 2.54]				
Toff 2022	11	458	10	455	15.1%	1.10 [0.46, 2.60]				
Total (95% CI)		2437		2392	100.0%	0.83 [0.59, 1.17]		•		
Total events	75		90							
Heterogeneity: Tau <sup>2</sup> =				= 0.40)	); I² = 3%		0.01	0.1 1		100
Test for overall effect	Z = 1.05 (I	P = 0.30	0				0.01	Favours [TAVR]		100

#### B) 1-year stroke risk



**Fig. 3** Random-effects meta-analysis of transcatheter aortic valve replacement vs. surgical aortic valve replacement for (a) 30-day stroke risk and (b) 1-year stroke risk Boxes and horizontal lines depict the odds ratio and its corresponding 95% confidence interval for each study. Values of  $\tau^2$  around 0.04 are considered to indicate low heterogeneity. *TAVR* transcatheter aortic valve replacement, *SAVR* surgical aortic valve replacement, *M-H* Mantel–Haenszel, *CI* confidence interval

significant difference. No heterogeneity was observed between studies ( $\tau 2 = 0.00$ ,  $I^2 = 0\%$ ). Assessment of publication bias was not possible due to the limited number of studies reporting TIA as an outcome.

#### All-cause mortality

Six studies (5,697 patients) compared the rate of death from any cause between TAVR and SAVR patients at 30-days post-procedure. The results indicate that there was no significant difference between the two groups in the death rate at 30 days following the procedure (OR 0.85, 95% CI 0.60 to 1.19, p = 0.34,  $I^2$  19%) (Fig. 5A). However, at 1 year post-procedure, TAVR resulted in a significantly lower rate of all-cause mortality than surgery, OR 0.75 (95% CI 0.60 to 0.95, p = 0.02,  $I^2$  40%). Moderate heterogeneity was observed between studies ( $\tau 2 = 0.04$ ,  $I^2 = 40\%$ ) (Fig. 5B).

# Peri-procedural complications

There was no significant difference between the two groups regarding the incidence of myocardial infarction at 30 days and 1 year following the procedure. However, TAVR had a significantly lower incidence of AKI at 1 year after the procedure compared with surgery (OR 0.59, 95% CI 0.43 to 0.81, p = 0.0009,  $I^2 0\%$ ).

Conversely, major vascular complications after the procedure were significantly higher in the TAVR group as compared to the SAVR group at both 30-day and 1-year follow-ups {(OR 2.90, 95% CI 1.20 to 7.03, p=0.02, I<sup>2</sup> 76%) (OR 2.78, 95% CI 1.34 to 5.75, p=0.006, I<sup>2</sup> 77%) respectively}. Considerable heterogeneity was observed between the studies ( $\tau 2=0.31$ , I<sup>2</sup>=77%) (Supplementary Figures S1-S3).

# Discussion

Amid a major transformation in the treatment of severe aortic stenosis, an emerging option in the form of a transcatheter approach for aortic valve replacement has challenged traditional full sternotomy valve replacement, first in extreme-risk patients and now in high and intermediate-risk groups. Thus, our study aimed to examine the safety and efficacy of TAVR as an emerging option versus conventional SAVR in intermediate and high-risk patients.

Despite diagnostic and treatment advancements, stroke is a common and feared complication for both

# A) 30-day TIA risk

	Experim	ental	Cont	rol		Odds Ratio	Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl	
Latib 2012	3	111	7	111	33.6%	0.41 [0.10, 1.64]		
Leon 2016	9	1011	4	1021	37.0%	2.28 [0.70, 7.44]		
Mack 2018	0	496	3	454	15.0%	0.13 [0.01, 2.52]	• • •	
Thyregod 2015	2	145	0	135	14.4%	4.72 [0.22, 99.24]		
Total (95% CI)		1763		1721	100.0%	0.93 [0.24, 3.63]		
Total events	14		14					
Heterogeneity: Tau <sup>2</sup> = 0.94; Chi <sup>2</sup> = 6.29, df = 3 (P = 0.10); I <sup>2</sup> = 52%						, 6		400
Test for overall effect: Z = 0.11 (P = 0.92)							0.01 0.1 1 10 Favours [TAVR] Favours [SAVR]	100

# B) 1-year TIA risk

	Experim	ental	Cont	rol	Odds Ratio		I Odds Ratio Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl			
Gleason 2018	6	391	5	351	14.9%	1.08 [0.33, 3.57]	<b>_</b>			
Latib 2012	4	111	7	111	13.5%	0.56 [0.16, 1.95]				
Leon 2016	23	1011	16	1021	51.4%	1.46 [0.77, 2.78]	-+ <b>-</b>			
Mack 2018	5	496	5	454	13.7%	0.91 [0.26, 3.18]				
Thyregod 2015	3	145	2	135	6.5%	1.40 [0.23, 8.54]				
Total (95% CI)		2154		2072	100.0%	1.15 [0.72, 1.82]	➡			
Total events	41		35							
Heterogeneity: Tau <sup>2</sup> = 0.00; Chi <sup>2</sup> = 2.01, df = 4 (P = 0.73); l <sup>2</sup> = 0%										
Test for overall effect:	Z=0.58 (	P = 0.56	i)				0.01 0.1 1 10 100 Favours [TAVR] Favours [SAVR]			

**Fig. 4** Random-effects meta-analysis of transcatheter aortic valve replacement vs. surgical aortic valve replacement for (**a**) 30-day TIA risk and (**b**) 1-year TIA risk. Boxes and horizontal lines depict the odds ratio and its corresponding 95% confidence interval for each study. Values of τ2 around 0.04 are considered to indicate low heterogeneity. *TIA* Transient Ischemic Attach, *TAVR* transcatheter aortic valve replacement, *SAVR* surgical aortic valve replacement, *M-H* Mantel–Haenszel, *CI* confidence interval

TAVR and SAVR. It is a major contributor to disability, causing a significant decline in an individual's overall health. Valve placement and implantation during TAVR can elevate the risk of embolic stroke in patients while cross-clamping the aorta during SAVR can increase the likelihood of dislodging loose atheromatous plaque or mural emboli [28, 29]. Our meta-analysis compared the occurrence of stroke and transient ischemic attack (TIA) among patients undergoing transcatheter aortic valve replacement (TAVR) and surgical aortic valve replacement (SAVR) to shed light on the effectiveness of these interventions in preventing such events. Our study's findings, which indicate a comparable 30-day and 1-year stroke risk between TAVR and SAVR patients, align with the 5-year outcomes of the PARTNER trial, as reported by Mack et al. [30]. In this trial, there was no significant difference in stroke rates between the TAVR and SAVR groups at the 5-year follow-up mark.

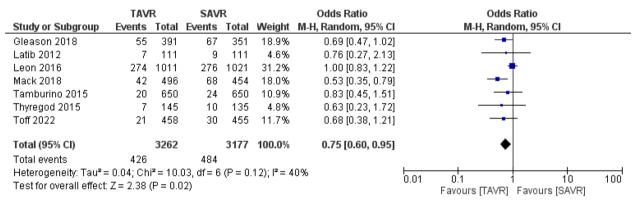
Moreover, consistent with previous studies [28, 31], our findings demonstrated that performing TAVR in intermediate-to-high-surgical risk patients resulted in comparable 30-day and 1-year rates of transient ischemic attack with SAVR. Villablanca et al. [32] also found no significant difference in the risk of disabling stroke between TAVR and SAVR in intermediate-risk patients. These findings suggest that TAVR, despite its advantages, did not reduce stroke incidence in intermediate-to-high-risk patients over the course of one year.

However, undoubtedly TAVR has shifted the paradigm of management of severe, symptomatic AS over the past two decades, with innovations in transcatheter valve design, imaging, and increasing operator expertise collectively boosting safety and minimizing procedural complications [28]. Our findings also reflect this, since TAVR resulted in a significantly lower rate of all-cause mortality than surgery at 1 year post-procedure. This is concurrent with the findings of an NIS study conducted by Algahtani et al. [33] which concluded that TAVR is linked to reduced hospital mortality, lower resource use, and decreased costs compared to SAVR. In contrast, a 2020 study providing an overview of multiple systematic reviews revealed that out of 11 peer-reviewed systematic reviews, 8 reported no differences in mortality between TAVR and SAVR at short and long-term follow-up times, albeit in low-intermediate-risk patients [34].

# A) 30-day all-cause mortality rate

	TAV	R	SAV	R		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
Latib 2012	2	111	2	111	2.8%	1.00 [0.14, 7.23]	
Leon 2016	140	1011	153	1021	56.0%	0.91 [0.71, 1.17]	<b>+</b>
Mack 2018	3	496	11	454	6.4%	0.25 [0.07, 0.88]	
Tamburino 2015	20	650	24	650	22.5%	0.83 [0.45, 1.51]	
Thyregod 2015	3	145	5	135	5.1%	0.55 [0.13, 2.34]	
Toff 2022	8	458	4	455	7.1%	2.00 [0.60, 6.70]	+
Total (95% CI)		2871		2826	100.0%	0.85 [0.60, 1.19]	•
Total events	176		199				
Heterogeneity: Tau² =	0.04; Ch	i² = 6.1	5, df = 5 (	P = 0.2	9); I <sup>z</sup> = 19	%	
Test for overall effect:	Z = 0.96	(P = 0.3	34)				Favours [TAVR] Favours [SAVR]

#### B) 1-year all-cause mortality rate



**Fig. 5** Random-effects meta-analysis of transcatheter aortic valve replacement vs. surgical aortic valve replacement for (**a**) 30-day all-cause mortality rate and (**b**) 1-year all-cause mortality rate. Boxes and horizontal lines depict the odds ratio and its corresponding 95% confidence interval for each study. Values of τ2 around 0.04 are considered to indicate low heterogeneity. *TAVR* transcatheter aortic valve replacement, *SAVR* surgical aortic valve replacement, *M-H* Mantel–Haenszel, *CI* confidence interval

When safety endpoints were compared between the two procedures, our meta-analysis revealed no significant difference in the incidence of MI at 30 days and 1 year after the procedures, however, TAVR was associated with a significantly lower incidence of acute kidney injury (AKI) at the 1-year follow-up compared with surgery. The relationship between AKI and aortic valve replacement is intricate, with multiple risk factors including hypothermia, non-pulsatile blood flow during cardiopulmonary bypass, euvolemic hemodilution during open-heart surgery, and cholesterol embolization during aortic cannulation increasing the likelihood of AKI after SAVR [35]. A meta-analysis conducted in 2018 also showed that the incidence of AKI was 59% significantly lower with TAVR than with SAVR [36].

Arora et al's study assessing national trends in complications after TAVR and SAVR in the States demonstrated that TAVR typically shows lower rates of complications like stroke, cardiogenic shock, AKI, and the need for blood transfusions, but higher occurrences of permanent pacemaker implantation, cardiac arrest, and vascular complications [37]. This is concomitant with Mehmet [38] and Lazkani's [36] studies in which the TAVR group had more vascular complications compared to the SAVR group (17.9% vs. none, 8.78% vs. 3.15% respectively). Our findings also complement data from these studies with major vascular complications seen significantly higher in the TAVR group as opposed to the SAVR group at both 30-day and 1-year follow-ups. Earlier device versions had more frequent aortic injuries and iliac avulsions due to the larger size of the first-generation sheaths. Now, complications are primarily localized to the access site, with dissections, hematomas, and thrombosis being the most common, often treatable with endovascular techniques [36].

The overall results indicating comparable risks of TIA and stroke between TAVR and SAVR patients hold significant implications for clinical decision-making. Clinicians need to carefully consider the risks and benefits of each procedure when determining the most suitable treatment approach for individual patients. Recent research emphasizes the importance of considering patient-specific factors, procedural risks, and long-term outcomes when choosing between TAVR and SAVR. These findings provide valuable insights to clinicians, aiding them in delivering patient-centered care and improving outcomes in the management of aortic valve disease [39–41].

# Limitations

While our meta-analysis offers valuable insights, it is important to recognize several limitations. Firstly, there may be variations among the included studies regarding patient characteristics, procedural methodologies, and follow-up procedures, potentially introducing sources of bias. Moreover, the analysis relies on aggregated data from published studies, lacking individual patient data for a thorough examination, which restricts the ability to control for confounding factors or conduct subgroup analyses.

# Conclusion

The comparison between TAVR and SAVR patients revealed no notable disparities in outcomes for both TIA and stroke incidence at 30 days and 1 year post-procedure. The degree of heterogeneity differed between the two outcomes, with TIA analyses showing moderate heterogeneity and stroke analyses indicating either minimal or no heterogeneity. For patients with intermediate-high surgical risk, both TAVR and SAVR exhibit varying safety profiles, with TAVR having better long-term rates of allcause mortality and AKI, but a higher incidence of major vascular complications post-procedure. Medical professionals should consider this when advising patients, weighing the advantages and disadvantages of each approach, and encouraging patients to make informed, personalized decisions regarding their treatment.

#### Abbreviations

- NYHA New York heart association
- PCS Prospective cohort study
- RCT Randomized controlled trial
- SAVR Surgical aortic valve replacement TAVR Transcatheter aortic valve replace
- TAVR Transcatheter aortic valve replacement

# Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s41983-024-00899-5.

Additional file 1.

#### Acknowledgements

Not applicable.

#### Author contributions

V.K., S.R., A.R., and M.Z., =The concept and design of the study. M.G., E.L., K.A., and M.P. = Data acquisition. A.A., M.H., M.G., and V.K. = Performed the data extraction and interpreted the results. A.R., M.Z., V.K., S.M., S.R. = Analyzed the data and drafted the manuscript. All authors critically revised the manuscript, approved the final version to be published, and agreed to be accountable for all aspects of the work.

#### Funding

The authors have received no funding for this study.

#### Availability of data and materials

All data generated or analyzed during this study are included in this published article and its supplementary information file.

#### Declarations

#### Ethics approval and consent to participate

Ethical approval and patient consent were not necessary as this systematic review involved the synthesis of data from previously published studies.

#### **Consent for publication**

Not applicable.

#### **Competing interests**

The authors declare that they have no competing interests.

#### Author details

<sup>1</sup>Department of Neurology, Jinnah Sindh Medical University, Karachi, Sindh, Pakistan. <sup>2</sup>Department of Internal Medicine, Allama Iqbal Medical College, Lahore, Punjab, Pakistan. <sup>3</sup>Ziauddin University, Karachi, Sindh, Pakistan. <sup>4</sup>Department of Internal Medicine, Karachi Medical and Dental College, Karachi, Sindh, Pakistan. <sup>5</sup>Department of Internal Medicine, Ziauddin University, Karachi, Sindh, Pakistan. <sup>5</sup>Department of Internal Medicine, Jinnah Medical and Dental College, Karachi, Sindh, Pakistan. <sup>6</sup>Department of Internal Medicine, Jinnah Medical and Dental College, Karachi, Sindh, Pakistan. <sup>7</sup>Department of Internal Medicine, Dow University of Health, Karachi, Sindh, Pakistan. <sup>8</sup>Department of Internal Medicine, Osmania Medical College, Hyderabad, Gujarat, India. <sup>9</sup>Department of Internal Medicine, Jinnah Sindh Medical University, Karachi, Sindh, Pakistan.

#### Received: 6 April 2024 Accepted: 29 September 2024 Published online: 15 October 2024

#### References

- Llerena-Velastegui J, Navarrete-Cadena C, Delgado-Quijano F, Trujillo-Delgado M, Aguayo-Zambrano J, Villacis-Lopez C, Marcalla-Rocha M, Benitez-Acosta K, Vega-Zapata J. Frequency of stroke in intermediate-risk patients in the long term undergoing TAVR vs. SAVR: a systematic review and meta-analysis. Cur Prob Cardiol. 2023;21:102099.
- Roth GA, Mensah GA, Johnson CO, Addolorato G, Ammirati E, Baddour LM, Barengo NC, Beaton AZ, Benjamin EJ, Benziger CP, Bonny A. Global burden of cardiovascular diseases and risk factors, 1990–2019: update from the GBD 2019 study. J Am Coll Cardiol. 2020;76(25):2982–3021.
- Martin SS, Aday AW, Almarzooq ZI, Anderson CA, Arora P, Avery CL, Baker-Smith CM, Barone Gibbs B, Beaton AZ, Boehme AK, Commodore-Mensah Y. 2024 heart disease and stroke statistics: a report of us and global data from the American heart association. Circulation. 2024;149(8):e347-913.
- Goody PR, Hosen MR, Christmann D, Niepmann ST, Zietzer A, Adam M, Bönner F, Zimmer S, Nickenig G, Jansen F. Aortic valve stenosis: from basic mechanisms to novel therapeutic targets. Arterioscler Thromb Vasc Biol. 2020;40(4):885–900.
- 5. Andreasen C, Gislason GH, Køber L, Abdulla J, Martinsson A, Smith JG, Torp-Pedersen C, Andersson C. Incidence of ischemic stroke in individuals

with and without aortic valve stenosis: a danish retrospective cohort study. Stroke. 2020;51(5):1364–71.

- Elder DH, McAlpine-Scott V, Choy AM, Struthers AD, Lang CC. Aortic valvular heart disease: is there a place for angiotensin-converting-enzyme inhibitors? Expert Rev Cardiovasc Ther. 2013;11(1):107–14.
- Choi KJ, Tsomidou C, Lerakis S, Madanieh R, Vittorio TJ, Kosmas CE. Lipid interventions in aortic valvular disease. Am J Med Sci. 2015;350(4):313–9.
- Jiang T, Hasan SM, Faluk M, Patel J. Evolution of transcatheter aortic valve replacement| Review of literature. Curr Probl Cardiol. 2021;46(3): 100600.
- Messé SR, Acker MA, Kasner SE, Fanning M, Giovannetti T, Ratcliffe SJ, Bilello M, Szeto WY, Bavaria JE, Hargrove WC III, Mohler ER III. Stroke after aortic valve surgery: results from a prospective cohort. Circulation. 2014;129(22):2253–61.
- Kolkailah AA, Doukky R, Pelletier MP, Volgman AS, Kaneko T, Nabhan AF. Transcatheter aortic valve implantation versus surgical aortic valve replacement for severe aortic stenosis in people with low surgical risk. Cochrane Database Syst Rev. 2019. https://doi.org/10.1002/14651858.CD013319.pub2.
- 11. Waksman R, Minha SA. Stroke after aortic valve replacement: the known and unknown. Circulation. 2014;129(22):2245–7.
- Van Mieghem NM, El Faquir N, Rahhab Z, Rodríguez-Olivares R, Wilschut J, Ouhlous M, Galema TW, Geleijnse ML, Kappetein AP, Schipper ME, de Jaegere pp. Incidence and predictors of debris embolizing to the brain during transcatheter aortic valve implantation. JACC Cardiovasc Interv. 2015;8(5):718–24.
- 13 Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. BMJ. 2021. https://doi.org/10.1136/bmj.n160.
- Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. www.ohri.ca. 2021. https://www.ohri.ca/progr ams/clinical\_epidemiology/oxford.asp
- Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011. https://doi.org/10. 1136/bmj.d5928.
- DerSimonian R, Laird N. Meta-analysis in clinical trials. Cont Clin Trials. 1986;7(3):177–88.
- Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539–58. https://doi.org/10.1002/sim.1186.
- Higgins JP, Green S, editors. Cochrane handbook for systematic reviews of interventions.
- Gleason TG, Reardon MJ, Popma JJ, et al. 5-year outcomes of self-expanding transcatheter versus surgical aortic valve replacement in high-risk patients. J Am Coll Cardiol. 2018;72(22):2687–96. https://doi.org/10.1016/j.jacc.2018.08. 2146.
- Thyregod HG, Steinbrüchel DA, Ihlemann N, et al. Transcatheter versus surgical aortic valve replacement in patients with severe aortic valve stenosis: 1-year results from the all-comers notion randomized clinical trial. J Am Coll Cardiol. 2015;65(20):2184–94. https://doi.org/10.1016/j.jacc.2015.03.014.
- Tavi Trial Investigators UK, Toff WD, Hildick-Smith D, et al. Effect of transcatheter aortic valve implantation vs surgical aortic valve replacement on all-cause mortality in patients with aortic stenosis: a randomized clinical trial. JAMA. 2022;327(19):1875–87. https://doi.org/10.1001/jama.2022.5776.
- Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, Thourani VH, Tuzcu EM, Miller DC, Herrmann HC, Doshi D. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. N Engl J Med. 2016;374(17):1609–20.
- Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med. 2019;380(18):1695–705. https://doi.org/10.1056/NEJMoa1814052.
- Tamburino C, Barbanti M, D'Errigo P, et al. 1-year outcomes after transfemoral transcatheter or surgical aortic valve replacement: results from the Italian observant study. J Am Coll Cardiol. 2015;66(7):804–12. https://doi.org/10. 1016/j.jacc.2015.06.013.
- Schymik G, Heimeshoff M, Bramlage P, et al. A comparison of transcatheter aortic valve implantation and surgical aortic valve replacement in 1,141 patients with severe symptomatic aortic stenosis and less than high risk. Catheter Cardiovasc Interv. 2015;86(4):738–44. https://doi.org/10.1002/ccd. 25866.
- Latib A, Maisano F, Bertoldi L, et al. Transcatheter vs surgical aortic valve replacement in intermediate-surgical-risk patients with aortic stenosis: a

propensity score-matched case-control study. Am Heart J. 2012;164(6):910-7. https://doi.org/10.1016/j.ahj.2012.09.005.

- Sterne JA, Sutton AJ, Ioannidis JP, Terrin N, Jones DR, Lau J, Carpenter J, Rücker G, Harbord RM, Schmid CH, Tetzlaff J. Recommendations for examining and interpreting funnel plot asymmetry in meta-analyses of randomised controlled trials. BMJ. 2011;22:343.
- Avvedimento M, Tang GH. Transcatheter aortic valve replacement (TAVR): recent updates. Prog Cardiovasc Dis. 2021;1(69):73–83.
- 29 Gaudino M, Benesch C, Bakaeen F, DeAnda A, Fremes SE, Glance L, Messe SR, Pandey A, Rong LQ. American heart association council on cardiovascular surgery and anesthesia; stroke council; and council on cardiovascular and stroke nursing considerations for reduction of risk of perioperative stroke in adult patients undergoing cardiac and thoracic aortic operations: a scientific statement from the American heart association. Circulation. 2020. https://doi.org/10.1161/CIR.00000000000885.
- Mack MJ, Leon MB, Smith CR, Miller DC, Moses JW, Tuzcu EM, Webb JG, Douglas PS, Anderson WN, Blackstone EH, Kodali SK. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial. The Lancet. 2015;385(9986):2477–84.
- Shah K, Chaker Z, Busu T, Badhwar V, Alqahtani F, Alvi M, Adcock A, Alkhouli M. Meta-analysis comparing the frequency of stroke after transcatheter versus surgical aortic valve replacement. Am J Cardiol. 2018;122(7):1215–21.
- Villablanca PA, Mathew V, Thourani VH, Rodés-Cabau J, Bangalore S, Makkiya M, Vlismas P, Briceno DF, Slovut DP, Taub CC, McCarthy PM. A meta-analysis and meta-regression of long-term outcomes of transcatheter versus surgical aortic valve replacement for severe aortic stenosis. Int J Cardiol. 2016;15(225):234–43.
- Alqahtani F, Aljohani S, Boobes K, Maor E, Sherieh A, Rihal CS, Holmes DR, Alkhouli M. Outcomes of transcatheter and surgical aortic valve replacement in patients on maintenance dialysis. Am J Med. 2017;130(12):1464-e1.
- Mc Morrow R, Kriza C, Urban P, Amenta V, Amaro JA, Panidis D, Chassaigne H, Griesinger CB. Assessing the safety and efficacy of TAVR compared to SAVR in low-to-intermediate surgical risk patients with aortic valve stenosis: an overview of reviews. Int J Cardiol. 2020;1(314):43–53.
- Thongprayoon C, Cheungpasitporn W, Srivali N, Harrison AM, Gunderson TM, Kittanamongkolchai W, Greason KL, Kashani KB. AKI after transcatheter or surgical aortic valve replacement. J Am Soc Nephrol. 2016;27(6):1854–60.
- Lazkani M, Singh N, Howe C, Patel N, Colón MJ, Tasset M, Amabile O, Morris M, Fang HK, Pershad A. An updated meta-analysis of TAVR in patients at intermediate risk for SAVR. Cardiovasc Revasc Med. 2019;20(1):57–69.
- 37 Arora S, Strassle PD, Qamar A, Kolte D, Pandey A, Paladugu MB, Borhade MB, Ramm CJ, Bhatt DL, Vavalle JP. Trends in inpatient complications after transcatheter and surgical aortic valve replacement in the transcatheter aortic valve replacement era. Circ Cardiovascular Interventions. 2018;11: e007517.
- Yesiltas MA, Haberal İ, Kuserli Y, Yildiz A, Koyuncu AO, Özsoy SD. Comparison of short and mid-term mortality and morbidity in patients with severe aortic stenosis (Intermediate/High Risk) who underwent transcatheter aortic valve replacement and surgical aortic valve replacement. InThe Heart Surgery Forum. 2020. https://doi.org/10.1532/hsf.2913.
- Garcia E, Martinez D, Rodriguez K, et al. Informed consent in aortic valve replacement: a comparative analysis of transcatheter and surgical approaches. Circulation. 2020;142:14872.
- Martinez M, Davis E, Rodriguez K, et al. Perioperative management strategies for reducing neurological complications in aortic valve replacement: insights from a prospective cohort study. J Thorac Cardiovasc Surg. 2021;162(5):1318-1326.e2.
- Patel S, Brown M, Jones A, et al. Long-term follow-up and secondary prevention strategies for patients undergoing aortic valve replacement: a meta-analysis. Eur Heart J. 2020;41:946.

#### **Publisher's Note**

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.