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Transcatheter Aortic Valve Implantation Versus Surgical Aortic Valve Replacement in Low-risk Patients: A Meta-Analysis Based on a 2-Year Follow-Up

ABSTRACT

Background: Previous studies have shown that transcatheter aortic valve implantation is the best alternative therapy to surgical aortic valve replacement in high-risk surgical patients with aortic stenosis. However, it is not clear whether transcatheter aortic valve implantation can be utilized in low-risk surgical patients with aortic stenosis. This study aimed to evaluate the safety and efficacy of transcatheter aortic valve implantation in low-risk patients.

Methods: From the outset of our initiative until April 2022, PubMed, EMBASE, and the Cochrane database were thoroughly searched, yielding the selection of 3 randomized controlled trials including 2644 patients with aortic stenosis, to assess outcome measures at distinct follow-up time.

Results: The mean Society of Thoracic Surgeons Predicted Risk of Mortality score of patients was 2.2. At the 30-day and 1-year follow-up, transcatheter aortic valve implantation was associated with a lower incidence of all-cause mortality, cardiovascular mortality, acute kidney injury (stage 2 or 3), life-threatening or significant bleeding, and new atrial fibrillation but an increased risk of permanent pacemaker implantation. At the 2-year follow-up, transcatheter aortic valve implantation only had an advantage in new atrial fibrillation (relative risk, 0.27; 95% CI, 0.14-0.51; P < .0001), with no significant difference in all-cause mortality or cardiovascular mortality.

Conclusions: For low-risk surgical patients with aortic stenosis, compared to surgical aortic valve replacement, transcatheter aortic valve implantation was associated with lower all-cause mortality at 30-day follow-up and lower cardiovascular mortality at 1-year follow-up. Except for the advantages in new atrial fibrillation, transcatheter aortic valve implantation had no significant impact on mortality at 2-year follow-up.

Keywords: TAVI, SAVR, aortic stenosis, meta-analysis, low risk

INTRODUCTION

Aortic stenosis (AS) is a common heart valve disorder in the elderly with increasing incidence in the aging population.¹ Currently, there is no effective therapy for this condition as valve replacement is the standard of care. Historically, surgical aortic valve replacement (SAVR) is regarded as the gold standard for patients with severe AS.² As a novel modality, transcatheter aortic valve implantation (TAVI) has garnered significant support for its use over the years since its first application in 2002,³ and it is currently the best alternative to SAVR in high-risk surgical patients with AS.⁴

The PARTNER II trial shows that the efficacy of TAVI is non-inferior to that of SAVR in intermediate-risk patients with AS,⁵ prompting the American College of Cardiology to recommend TAVI for intermediate-risk patients (class IIa).⁶ However, complications due to TAVI, such as paravalvular leakage and inadequate durability, are still a cause for concern.⁷ Industry experts are debating whether TAVI can be widely used in low-risk surgical patients with AS. Several randomized controlled trials (RCTs) have been conducted on this matter,^{8,9} but the results from



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META-ANALYSIS

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Figure 1. Flowchart for screening and study selection process.

these experiments and meta-analyses are not consistent. The latest 2020 guideline still lists only SAVR as a class I treatment for low-risk surgical patients without recommending TAVI for this patient subset.¹⁰ The 2-year follow-up results published in the PARTNER III and EVOLUT study did provide some evidence to suggest that further investigation of the efficacy of TAVI in low-risk surgical patients with AS—versus that of SAVR—would be prudent.^{11,12} As a result, we conducted a new meta-analysis to compare TAVI with SAVR to clearly delineate their performance based on different time frames and patient risk stratification.

HIGHLIGHTS

- In low-risk surgical patients with aortic stenosis, compared to surgical aortic valve replacement (SAVR), transcatheter aortic valve implantation (TAVI) is associated with lower all-cause mortality at 30-day follow-up and lower cardiovascular mortality at 1-year follow-up.
- Except for advantages in new atrial fibrillation, TAVI had no significant differences in mortality at 2-year follow-up, compared to SAVR.
- In lieu of 2-year follow-up results and potential valve degradation risks, the decision to use TAVI in patients with a longer life expectancy is yet to be recommended.

METHODS

Eligibility Criteria

The research follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines-P guidelines and is based on those guidelines.^{13,14} The inclusion criteria were as follows: (1) populations of low-risk surgical patients (Society of Thoracic Surgeons Predicted Risk of Mortality (STS PROM) <4%); (2) comparison of TAVI; (3) SAVR as a control; (4) primary outcome—measured over a 2-year period—as all-cause mortality and secondary outcomes as cardiovascular mortality, stroke, transient ischemic attack (TIA), myocardial infarction (MI), acute kidney injury (stage 2 or 3), life-threatening or significant bleeding, permanent pacemaker implantation (PPI), and new atrial fibrillation (NAF)¹⁵; and (5) study designs as RCTs.

Literature Search

From the outset to April 21, 2022, we conducted a comprehensive, systematic search of PubMed, EMBASE, and the Cochrane database. ClinicalTrials.gov trial registries were also reviewed to determine if the available results were reported from ongoing or completed studies. Our supplement details the study strategy.

Data Analyses

Two authors separately collected the required, relevant data—any discrepancies between them were resolved by group consultation. The 2 authors used the Cochrane collaborative risk of bias tool to assess the risk of bias independently in 5 aspects and used the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) to estimate the quality of evidence for each outcome.¹⁶ The results of each RCT were converted to dichotomous data, analyzed using the Mantel-Haenszel method, and presented as relative risk (RR). The summary RR and 95% CI of the survey results were calculated using a random-effect model.¹⁷ $P \leq .5$ was considered statistically significant, and heterogeneity was assessed through I-squared (I²) and Q statistics; I² > 50% was considered substantial.^{18,19} Because fewer than 10 studies were included, we performed neither Egger's nor Begg's tests to evaluate the publication bias of studies.²⁰

RESULTS

Figure 1 details the study selection process, illustrating a total of 2682 retrieved articles with 1039 duplicates, which were deleted by the Endnote X9 software. After reviewing the titles and abstracts, 1629 repetitive literature reviews, case reports, meta-analyses, and unrelated articles were excluded. Eleven items were further excluded based on the inclusion criteria, resulting in the final 3 articles. Table 1 comprises the details of the included studies; 2633 patients with AS across the 3 cohorts were enrolled (EVOLUT,¹² NOTION,¹⁵ and PARTNER III¹¹). In the assessment of deviation risk, due to specific study designs, it is impossible to blind operators or patients (Supplement Figure 1A and B.). The summary of findings and strength of evidence (GRADE) are shown in the supplement (Supplement Tables 1A-D.); the quality of evidence for the most results was evaluated to be high.

The results of the 30-day, 1-year, and 2-year follow-ups are shown in Figures 2, 3, and 4, respectively. There were several patients enrolled at sites in Japan later in the EVOLUT trial who are included in this analysis at the 2-year baseline; thus, the population in the second year of the EVOLUT trial is different from that before. At the 30-day follow-up of the low-risk surgical patients with AS, TAVI was associated with a lower incidence of all-cause mortality (RR: 0.44; 95% CI: 0.20-0.98; P=.04), acute kidney injury (stage 2 or 3) (RR: 0.27; 95% CI: 0.14-0.56; P=.0003), life-threatening or significant bleeding (RR: 0.29; 95% CI: 0.14-0.61; P=.001), and NAF (RR: 0.21; 95% CI: 0.14-0.31; P < .00001) but showed an increased risk of PPI (RR: 3.59; 95% CI, 1.43-9.03; P=.006).

At the 1-year follow-up of the low-risk surgical patients with AS, the cardiovascular mortality (RR: 0.56; 95% CI: 0.33-0.94; P = .03), presence of life-threatening or significant bleeding (RR: 0.32; 95% CI: 0.24-0.42; P < .00001), and the NAF (RR: 0.25; 95% CI, 0.18-0.36; P < .00001) results in the TAVI group were significantly decreased compared to those in the SAVR group. However, the incidence of PPI in the TAVI group

Study		NOTION	PARTNER III	EVOLUT
Number of centers		3	71	86
Recruitment period		2011-2013	2012-2016	2016-2018
Valve type		CoreValve, Evolut R, or Evolut PRO	Sapien 3	CoreValve
Sample size	TAVI	145	496	725
	SAVR	135	454	678
Male, no. (%)	TAVI	78 (53.8)	335 (67.5)	464 (64.0)
	SAVR	71 (52.6)	323 (71.1)	449 (66.2)
Mean year	TAVI	79.2 ± 4.9	73.3 <u>+</u> 5.8	74.1±5.8
	SAVR	79 ± 4.7	73.6 <u>+</u> 6.1	73.6 <u>+</u> 5.9
Mean STS-PROM score	TAVI	2.9 ± 1.6	1.9 ± 0.7	1.9 ± 0.7
	SAVR	3.1 ± 1.7	1.9 <u>+</u> 0.6	1.9 ± 0.7
Prior cerebrovascular accident, n (%)	TAVI	24 (16.6)	17 (3.4)	74 (10.2)
	SAVR	22 (16.3)	23 (5.1)	80 (11.8)
Prior myocardial infarction, n (%)	TAVI	8 (5.5)	28 (5.7)	48 (6.6)
	SAVR	6 (4.4)	26 (5.8)	33 (4.9)
Peripheral vascular disease, n (%)	TAVI	6 (4.1)	34 (6.9)	54 (7.5)
	SAVR	9 (6.7)	33 (7.3)	56 (8.3)
Chronic lung disease, n. (%)	TAVI	17 (11.7)	25 (5.1)	104 (15.0)
	SAVR	16 (11.9)	28 (6.2)	117 (18.0)
Diabetes mellitus, n. (%)	TAVI	26 (17.9)	155 (31.2)	228 (31.4)
	SAVR	28 (20.7)	137 (30.2)	207 (30.5)
Creatinine level >2 mg/dL, no. (%)	TAVI	2 (1.4)	1 (0.2)	3 (0.4)
	SAVR	1 (0.7)	1(0.2)	1 (0.1)

Churche or Sucharoum	Experim	iental Totol	Contr	ol	Mainht	Risk Ratio	Risk Ratio
5tudy of Subgroup	Events	Total	Events	Total	vveight	M-H, Random, 95% CI	M-H, Kandom, 95% CI
T. T. T All-Cause mortal	ity it	735		670	2.70/	0 40 /0 40 4 0 41	
NOTION	4	120	9	1070	3.170	0.42 [0.13, 1.34]	
NUTION	3	145	5	135	3.4%	0.56 [0.14, 2.29]	
Subtotal (05% CD	2	490	5	404	3.0%	0.37 [0.07, 1.88]	
Subtotal (95% Ci)		1500	10	1207	10.170	0.44 [0.20, 0.96]	
Hotorogeneithr Teu? - (9 100-068	-017	19	- 0.021	17 - 0.04		
Testfor everall effect 7	- 2.02.0	-= 0.17, D= 0.04	ui = 2 (P	= 0.92),	1-= 0.%		
Testior overall effect. Z	= 2.02 (P = 0.04;					
112 Cardiovaccular n	ortality						
EVOLUT	a	705	0	070	2.70	0.40 (0.40.4.04)	
NOTION	*	145	3	125	3.7 %	0.42 [0.13, 1.34]	
DADTNED III	2	140	3	155	2.0%	0.50 [0.14, 2.29]	
Subtotal (95% CD	2	490	.4	1267	10 1%	0.47 [0.08, 2.49]	
Total evente	0	1500	10	1207	10.170	0.47 [0.21, 1.05]	
Hotorogeneity Touring	9 100-068	2-010	df= 2 /D	- 0.05)	12-006		
Tect for everall effect 7	- 1 00 /	- 0.10, D - 0.081	ui - 2 (F	- 0.95),	1 = 0 %		
Testili overali ellect. 2	- 1.00 (- 0.00,					
113 Stroke							
EVOLUT	25	725	23	679	4 6%	1 02 (0 59 1 77)	
NOTION	20	145	4	135	3.0%	0.47 0 09 2 501	
PARTNER III	3	496	11	454	3.6%	0.25 (0.07, 0.89)	
Subtotal (95% CI)		1366		1267	11.1%	0.57 [0.22, 1.48]	-
Total events	30		38			eler [eler, itte]	-
Heterogeneity Tau ² = (1.38: Chi	² = 4 36	df=2 (P	= 0.11);	$ ^2 = 54\%$		
Test for overall effect 7	= 1.15 (P = 0.25		\$.11)h			
1.1.4 Transient ischen	nic attac	k					
EVOLUT	4	725	5	678	3.5%	0,75 (0.20, 2 77)	
NOTION	2	145	n	135	1.6%	4 66 (0 23 96 14)	
PARTNER III	ñ	496	3	454	1.6%	0 13 (0 01 2 53)	· · · · · · · · · · · · · · · · · · ·
Subtotal (95% CI)	•	1366	•	1267	6.7%	0.75 [0.17. 3.37]	
Total events	6		8				
Heterogeneity: Tau ² = 0	54 Chi	= 2.74	df = 2 (P)	= 0.25);	$l^2 = 27\%$		
Test for overall effect: Z	= 0.37 (P = 0.71	ui - 2 (i -	0.20%	- 21 70		
1.1.5 Myocardial infar	tion						
EVOLUT	7	725	9	678	4.0%	0.73 (0.27, 1.94)	
NOTION	4	145	8	135	3.7%	0.47 [0.14, 1.51]	· · · · · · · · · · · · · · · · · · ·
PARTNER III	5	496	6	454	3.7%	0.76 [0.23, 2.48]	
Subtotal (95% CI)		1366		1267	11.4%	0.65 [0.34, 1.22]	-
Total events	16		23				
Heterogeneity: Tau ² = 0	0.00; Chř	^z =0.43,	df= 2 (P :	= 0.81);	I ^z = 0%		
Test for overall effect: Z	= 1.34 (P = 0.18)					
1.1.6 Acute kidney inju	ry(stage	e 2 or 3)					
EVOLUT	7	725	19	678	4.2%	0.34 [0.15, 0.81]	
NOTION	1	145	9	135	2.5%	0.10 [0.01, 0.81]	
PARTNER III	2	496	8	454	3.2%	0.23 [0.05, 1.07]	
Subtotal (95% CI)		1366		1267	9.9%	0.27 [0.14, 0.56]	-
Total events	10		36				
Heterogeneity: Tau ² = 0	0.00; Chi	² =1.22,	df=2 (P	= 0.54);	$ ^2 = 0\%$		
Test for overall effect Z	= 3.59 (P = 0.001	03)				
1.1.7 Life-threatening	or disabl	ling blee	ding				
EVOLUT	17	725	51	678	4.6%	0.31 [0.18, 0.53]	
NOTION	16	145	28	135	4.5%	0.53 [0.30, 0.94]	
PARTNER III	18	496	111	454	4.6%	0.15 [0.09, 0.24]	
Subtotal (95% CI)		1366		1267	13.8%	0.29 [0.14, 0.61]	-
I otal events	51		190				
Heterogeneity: Tau ² = 0	1.36; Chi	= 11.99	, df = 2 (F	' = 0.00	2); P= 839	%	
rest for overall effect: Z	= 3.27 (r = 0.00	0				
1 1 9 Dormanant n	maker is	nnlantet	ion				
The remailent pace	anaker if	npantat 705	14	670	4.000	207/207 400	
NOTION	120	145	41	1078	4.8%	2.87 [2.05, 4.02]	· · · · · · · · · · · · · · · · · · ·
PARTNER III	40	140	10	130	3.4%	21.41 [0.30, 80.51]	
Subtotal (05% CD	32	490	18	404	4.0%	3 60 [4 43 0 03]	
Total events	204	1300	61	1207	12.170	5.55 [1.45, 5.05]	
Heterogeneity Tau? - 0	204	= 12 62	o1 df= 2 /0	2 = 0.00	2)· [2 - 940	×.	
Test for overall effect 7	= 2.72.0	= 12.03	-, ui ∠ (F 6)	- 0.00	27,1 = 041	10	
restror overall ellect Z	- 2.12 (0.000	0)				
1 1 9 New atrial fibrilla	tion						
EVOLUT	66	725	240	670	1 9 94	0 22 10 17 0 201	-
NOTION	24	145	240	126	4.0 %	0.22 [0.17, 0.29]	
PARTNER III	24	140	146	150	4 7 94	0.23 [0.20, 0.43]	
Subtotal (95% Ch	21	1366	140	1267	14 2%	0.21 [0.14, 0.34]	•
Total events	101	.500	462	1201		0.2.1 [0.14, 0.3.1]	•
Heterogeneity Tau ² - 0	109:068	= 7 04	df = 2 (P	= 0.03)-	1 ² = 72%		
Test for overall effect 7	= 7.84 (P < 0.00	001)	0.00),			
. sector or or or one of the L		5.00					
							0.01 0.1 1 10 100
							TAVI SAVK

Figure 2. Forest plot for incidence of all-cause mortality, cardiovascular mortality, stroke, transient ischemic attack, myocardial infarction, acute kidney injury, life-threatening or disabling bleeding, permanent pacemaker implantation, and new-atrial fibrillation at the 30-day follow-up.

Etude of Subgroup	xperin	nental	Contr	ol	Maight	Risk Ratio	Risk Ratio
2.1.1 All cause mortalit	vents	rotal	Events	rotal	weight	m-n, random, 95% Cl	m-n, ranuom, 95% Ci
EVOLUT	17	726	20	679	1 704	0 70 10 42 1 601	
NOTION	7	145	10	135	4.7%	0.65 (0.26, 1.66)	
PARTNER III	5	496	11	454	4.0%	0.42 [0.15, 1.19]	
Subtotal (95% CI)	Ū	1366		1267	12.8%	0.66 [0.41, 1.06]	•
Total events	29		41				
Heterogeneity: Tau ² = 0.	00; Chi	² = 1.07,	df = 2 (P)	= 0.59);	I ^z = 0%		
Test for overall effect: Z	= 1.71 (P = 0.09	0				
2.1.2 Cardiovascular m	ortality						
EVOLUT	12	725	18	678	4.6%	0.62 [0.30, 1.28]	
NOTION	6	145	10	135	4.1%	0.56 [0.21, 1.50]	
PARTNER III	4	496	9	454	3.7%	0.41 [0.13, 1.31]	
Subtotal (95% CI)		1366		1267	12.4%	0.56 [0.33, 0.94]	-
Total events	22		37				
Heterogeneity: Tau ² = 0.	.00; Chi	[#] = 0.37,	df= 2 (P:	= 0.83);	$l^2 = 0\%$		
Test for overall effect: Z	= 2.21 (P = 0.03	0				
2 1 3 Stroko							
EVOLUT	20	725	20	670	4 0 %	0.07 (0.60, 1.60)	
NOTION	30	145	29	125	4.970	0.87 [0.59, 1.59]	
PARTNER III	6	496	14	454	4 1 96	0.39 [0.15, 1.01]	
Subtotal (95% Cl)	0	1366	14	1267	12.6%	0.71 [0.40, 1.25]	•
Total events	40	1000	49	1201	121070	0111[0110] 1120]	•
Heterogeneity Tau ² = 0	.08: Chi	² = 2 87	df = 2 (P	= 0.24)	$l^2 = 30\%$		
Test for overall effect Z	= 1,20 (P = 0.23))	0.24/1	. = 50 %		
. Sector of Stan on Sect 2.		. 0.20	<i>,</i>				
2.1.4 Transient ischem	ic attac	k					
EVOLUT	12	725	12	678	4.4%	0.94 [0.42, 2.07]	
NOTION	3	145	2	135	2.7%	1.40 [0.24, 8.23]	
PARTNER III	5	496	5	454	3.6%	0.92 [0.27, 3.14]	
Subtotal (95% CI)		1366		1267	10.8%	0.98 [0.52, 1.83]	+
Total events	20		19				
Heterogeneity: Tau ² = 0.	.00; Chi	² = 0.18,	df=2 (P:	= 0.91);	I ^z = 0%		
Test for overall effect: Z	= 0.07 (P = 0.94)				
2.1.5 Myocardial infarc	tion						
EVOLUT	12	725	11	678	4.4%	1.02 [0.45, 2.30]	
NOTION	5	145	8	135	3.9%	0.58 [0.20, 1.74]	
PARTNER III	ь	496	10	454	4.0%	0.55 [0.20, 1.50]	
Subtotal (95% CI)	22	1300	20	1207	12.3%	0.74 [0.45, 1.27]	
Hotorogonoity Touring 0	23 00: Chi	z_ 1 1 2	29 Af = 2/D	- 0 671.	17 - 00/		
Tect for everall effect 7	- 1 00 /	r = 1.13, 10 - 0.20	ui = 2 (P :	= 0.57);	1-= 0.30		
restion overall effect. Z	- 1.09 (r - 0.20	9				
2.1.6 Life-threatening o	r disab	lina blee	dina				
EVOLUT	23	725	60	678	4 9%	0.36 (0.22, 0.57)	
PARTNER III	38	496	117	454	5.1%	0.30 [0.21, 0.42]	-
Subtotal (95% CI)		1221		1132	10.0%	0.32 [0.24, 0.42]	◆
Total events	61		177				
Heterogeneity: Tau ² = 0.	.00; Chi	² = 0.40,	df=1 (P:	= 0.53);	I ² = 0%		
Test for overall effect: Z	= 8.12 (P < 0.00	001)				
2.1.7 Permanent pacer	naker i	mplanta	tion				
EVOLUT	141	725	45	678	5.1%	2.93 [2.13, 4.03]	-+-
NOTION	51	145	3	135	3.8%	15.83 [5.06, 49.52]	
PARTNER III	36	496	24	454	4.9%	1.37 [0.83, 2.26]	
Subtotal (95% CI)		1366		1267	13.8%	3.42 [1.33, 8.82]	-
Total events	228		72				
Heterogeneity: Tau ² = 0.	.58; Chi	r=17.28	s, af = 2 (F	r = 0.00	UZ); I ^z = 8	8%	
rest for overall effect. Z	= 2.54 (,r = 0.01)				
2.1.8 New, atrial fibrillat	tion						
EVOLUT	71	725	260	679	5.2%	0.26 (0.20, 0.20)	-
NOTION	20	145	200	125	5 1 94	0.20 [0.20, 0.32]	
PARTNER III	20	496	160	454	5.0%	0.18 (0.25, 0.50)	
Subtotal (95% CD	20	1366	150	1267	15.3%	0.25 [0.18, 0.36]	◆
Total events	130		489				
Heterogeneity: Tau ² = 0	07; Chi	z = 7.14	df= 2 (P	= 0.03):	I ^z = 72%		
Test for overall effect Z	= 7.72 (P < 0.00	001)				
							TAM CAMP

Figure 3. Forest plot for incidence of all-cause mortality, cardiovascular mortality, stroke, transient ischemic attack, myocardial infarction, life-threatening or disabling bleeding, permanent pacemaker implantation, and new-atrial fibrillation at the 1-year follow-up.

was significantly increased when compared to that of the SAVR group (RR: 3.42; 95% CI: 1.33-8.82; P = .01).

At the 2-year follow-up of low-risk surgical patients with AS, only the NAF results in the TAVI group were significantly decreased (RR: 0.27; 95% CI: 0.14 to 0.51; P < .0001), compared

to those in the SAVR group. Transcatheter aortic valve implantation was also associated with a higher incidence of PPI (RR: 3.02; 95% CI: 1.31-6.97; P=.01). The differences in all-cause mortality, cardiovascular mortality, stroke, TIA, and MI between the TAVI and SAVR groups were not statistically significant.

	TAV	r	SAVE	٦		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight I	M-H, Random, 95% Cl	M-H, Random, 95% Cl
3.1.1 All-cause morta	lity						
EVOLUT	26	730	30	684	5.7%	0.81 (0.49, 1.36)	
NOTION	11	145	13	135	5.2%	0.79 [0.37, 1.70]	
PARTNER III	12	496	14	454	5.2%	0.78 [0.37, 1.68]	
Subtotal (95% CI)		1371		1273	16.2%	0.80 [0.55, 1.16]	•
Total events	49		57				
Heterogeneity: Tau ² =	0.00; Ch	$i^2 = 0.01$	df = 2(1)	P = 1.0	0); I ² = 0%		
Test for overall effect:	Z = 1.18	(P = 0.2	4)		.,,		
3.1.2 Cardiovascular	mortality	<i>,</i>					
EVOLUT	16	730	23	684	5.5%	0.65 [0.35, 1.22]	
NOTION	9	145	12	135	5.1%	0.70 [0.30, 1.60]	
PARTNER III	8	496	12	454	5.0%	0.61 [0.25, 1.48]	
Subtotal (95% CI)		1371		1273	15.6%	0.65 [0.42, 1.01]	•
Total events	33		47				
Heterogeneity: Tau ² =	0.00; Ch	i ² = 0.05	5, df = 2 (l	P = 0.9	8); I² = 0%		
Test for overall effect: 2	Z = 1.91	(P = 0.0	6)				
3.1.3 Stroke	• -						
EVOLUT	42	730	38	684	5.9%	1.04 [0.68, 1.59]	
NOTION	5	145	7	135	4.4%	0.67 [0.22, 2.05]	
PARTNER III	12	496	16	454	5.3%	0.69 [0.33, 1.44]	
Subtotal (95% CI)		1371		1273	15.6%	0.90 [0.64, 1.28]	T
Total events	59		61	_			
Heterogeneity: Tau ² =	0.00; Ch	i ² = 1.21	, df = 2 (l	P = 0.5	5); I² = 0%		
Test for overall effect: 2	Z = 0.56	(P = 0.5	7)				
3.1.4 Transient ischer	nic atta	ck					
NOTION	8	145	4	135	4.3%	1.86 [0.57, 6.04]	
PARTNER III	5	496	7	454	4.4%	0.65 [0.21, 2.05]	
Subtotal (95% CI)		641		589	8.7%	1.09 [0.39, 3.04]	
Total events	13		11				
Heterogeneity: Tau ² = Test for overall effect: J	0.20; Ch Z = 0.17	i² = 1.57 (P = 0.8	7, df = 1 (l 7)	P = 0.2	1); *= 36%	6	
3 1 5 Mixe ardial infar	ction						
EVOLUT	16	720	11	604	6 206	1 26 /0 64 2 021	
NOTION	7	145		125	4 7 %	0.94 (0.20, 2.10)	
	<i>,</i>	140	12	150	4.7 %	0.01 [0.30, 2.19]	
Subtotal (05% Cl)	9	490	12	404	5.0%	0.09 [0.29, 1.01]	
Total events	22	1571	21	1215	13.070	0.55 [0.56, 1.50]	
Heterogeneity Tour-	0.00°.Ch	2-1.51	df = 2/1	P - 0 4	7) 12 - 0%		
Test for overall effect: 2	Z = 0.18	(P = 0.8)	,ur=∠(i 5)	- 0.4	7,1 = 0.0		
3 1 6 Dormanost room	makari	mplant	ation				
5. 1.0 Permanent pace	154	720	24	604	6 10	2 67 (2 00 2 60)	-
EVOLOT	154	130	54	084	0.1%	2.07 [2.00, 3.58]	
NUTION DADTNED !!!	55	145	5	135	5.0%	10.24 [4.23, 24.81]	
PARTNER III Subtotal (05% CD	44	490	30	454	16.0%	1.34 [0.86, 2.10]	-
Tatal avents	050	15/1	00	1213	10.9%	5.02[1.51, 0.97]	
Liotaregeneity Tou?	253	2-17	89	(D = 0	00043-12	0.000	
Heterogeneity: Tau-=	0.46; Ch	r = 17.8	s_{1} , $\alpha_{1} = 2$	(P = 0.	0001); F=	89%	
rest for overall effect.	2 = 2.59	(P = 0.0	10)				
3.1.7 New-atrial fibrill	ation						
NOTION	32	145	80	135	6.0%	0.37 [0.27, 0.52]	
PARTNER III	33	496	153	454	6.0%	0.20 [0.14, 0.28]	
Subtotal (95% CI)		641		589	12.0%	0.27 [0.14, 0.51]	-
Total events	65		233				
Heterogeneity: Tau ² =	0.18; Ch	I* = 6.80), df = 1 (l	P = 0.0	09); l² = 85	%	
Test for overall effect.	2 = 4.01	(P < 0.0	001)				
							0.01 0.1 1 10 100
							TAV/L GAV/D

Figure 4. Forest plot for incidence of all-cause mortality, cardiovascular mortality, stroke, transient ischemic attack, myocardial infarction, permanent pacemaker implantation, and new-atrial fibrillation at the 2-year follow-up.

DISCUSSION

Since currently established guidelines do not recommend the use of TAVI in low-risk surgical patients with AS, our study aimed to evaluate the efficacy and effectiveness of TAVI in this patient subset by comparing the clinical outcomes of TAVI and SAVR at 30-day, 1-year, and 2-year follow-up time frames. This study included 3 RCTs, comprising 2644 patients, and used a meta-analysis to compare the aforementioned outcomes. Kolte et al²¹ reported that TAVI was associated with a lower risk of cardiovascular and all-cause mortality at 1 year. Our 1-year follow-up had similar results;

however, their study did not report outcomes at other follow-up time intervals. In reviewing the 2-year results of the newly released PARTNER III and EVOLUT trial, we found that the low-risk patients who underwent TAVI at the 30-day and 1-year follow-up outperformed those who underwent SAVR in cardiovascular mortality, acute kidney injury (stage 2 or 3), NAF, and life-threatening or significant bleeding. However, TAVI resulted in a higher risk of PPI during the same time period. Compared with SAVR at the 2-year follow-up, there was no significant difference in cardiovascular and all-cause mortality for patients who underwent TAVI. Therefore, TAVI can reduce mortality and complications at the 30-day and 1-year follow-up; however, at the 2-year follow-up, most of the results demonstrated no significant difference. Most notably, the 5-year follow-up of the PARTNER II trial noted that patients who underwent TAVI had a higher risk of death or disabling strokes.^{22,23} Furthermore, Barili et al²⁴ performed time-interval modeling, incorporating 3 RCTs (including the PARTNER II trial), and found that TAVI was associated with better survival in the first few months after implantation but was a risk factor for all-cause mortality after 40 months. Although these trials were conducted with patients at intermediate and high risk, the results still have important significance to our research conclusions. It reminds us that, over time, the risk of mortality and complications after TAVI may increase rapidly, which corresponds to our discovery in the 2-year clinical results.

The PARTNER III trial using the SAPIEN 3 valve has achieved superior results. According to the analysis of Deharo, the design of SAPIEN 3 is easier to fit the landing zone, which reduces the risk of cardiovascular complications after TAVI.^{25,26} This may also be the reason for the large heterogeneity of TIA and PPI in our findings. Different valves used in various experiments affect the heterogeneity of the analysis. Although the new generation of the valve reduces the incidence of PPI, compared to SAVR, the incidence of PPI after TAVI is still higher. Recent studies have shown that PPI is associated with late all-cause mortality and increased risk of hospitalization due to cardiac failure.²⁷ Therefore, reducing the incidence of PPI after TAVI is an important issue to be considered and an interesting area for valve improvement.

Valve degeneration is another TAVI-associated complication that should be considered. Once it occurs, valve-in-valve implantation is indicated,^{28,29} and it is a complex operative procedure. Postoperatively, device malposition and ostial coronary obstruction are also common TAVI-associated complications. Only the NOTION trial reports data on valve conditions in low-risk surgical patients with AS undergoing TAVI for more than 5 years³⁰; therefore, there are insufficient data to analyze this problem. Moreover, most of the patients undergoing TAVI in the current RCTs are over 75 years old; therefore, their life expectancy is much less than the expected valve use time, hindering the valve durability study. Randomized controlled trials need to be conducted among relatively younger patients to assess long-term follow-up, providing more effective data for future meta-analyses.

Finally, based on the optimal performance of TAVI at the 30-day and the 1-year clinical follow-up and the continuous replacement of the operative valve, TAVI appears to be a very promising procedure in low-risk surgical patients with AS. The eventual use of TAVI in older patients with a shortened life expectancy is reasonable. However, we should also note the changes at the 2-year TAVI follow-up and the potential clinical complications of PPI and valve degeneration. In lieu of these results, the decision to use TAVI in patients with a longer life expectancy is yet to be recommended.

Study Limitations

First, study omissions occurred due to their non-inclusion in the search database, resulting in eventual publication bias.

Second, some inevitable differences in baseline characteristics between studies affect the accuracy of the results. Third, there is significant variability in the literature of the definitions for valve type, surgical risk, and outcomes, leading to possible discrepancies in the results.

CONCLUSIONS

In low-risk surgical patients with AS, compared to SAVR, TAVI was associated with lower all-cause mortality at 30-day follow-up and lower cardiovascular mortality at 1-year follow-up. At the 2-year follow-up, with the exception of decreased NAF risk, there was no significant difference in all-cause mortality, cardiovascular mortality, and mi between TAVI and SAVR. However, potential late TAVIassociated complications, such as valvular degeneration and PPI, are important clinical concerns that must be considered when weighing treatment options for AS.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Union Hospital, Fujian Medical University, (Approval No: 2020KJT091).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – C.G.C., B.B.X.; Design – C.G.C., Q.F.D.; Supervision – L.W.C., Z.H.Q.; Fundings – L.W.C., Z.H.Q.; Materials – C.G.C., B.B.X.; Data collection &/or processing –X.Y.Z., W.C.L.; Analysis &/or interpretation – C.G.C., B.B.X.; Literature search – Z.H.Q.; Writing –C.G.C., B.B.X.; Critical review – L.W.C., Z.H.Q.

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Supplement Figure 1. A. Risk of bias summary: review authors' judgments about each risk of bias item for each included study. B. Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies.

Sup	plement Table 1A. Search Strategy								
Pub	PubMed								
1	"Aortic Valve Stenosis"[Mesh]	48093							
2	((((((Aortic Valve Stenoses[Title/Abstract]) OR (Stenoses, Aortic Valve[Title/Abstract])) OR (Stenosis, Aortic Valve [Title/Abstract])) OR (Valve Stenoses, Aortic[Title/Abstract])) OR (Valve Stenosis, Aortic[Title/Abstract])) OR (Aortic Stenosis[Title/Abstract])) OR (Stenoses, Aortic[Title/Abstract])) OR (Stenosis, Aortic[Title/Abstract])	20267							
3	1OR 2	53638							
4	"Transcatheter Aortic Valve Replacement"[Mesh]	9162							
5	(((((((((((((((((((percutaneous aortic valve implantation[Title/Abstract]) OR (percutaneous aortic valve repla cement[Title/Abstract])) OR (TAVI[Title/Abstract])) OR (trans-apical aortic valve implantation[Title/Abstract])) OR (trans-apical aortic valve replacement[Title/Abstract])) OR (trans-arterial aortic valve implantation[Title/A bstract])) OR (trans-arterial aortic valve replacement[Title/Abstract])) OR (trans-catheter aortic valve implantation [Title/Abstract])) OR (trans-catheter aortic valve replacement[Title/Abstract])) OR (trans-cutaneous aortic valve implantation[Title/Abstract])) OR (trans-cutaneous aortic valve replacement[Title/Abstract])) OR (trans- femoral aortic valve implantation[Title/Abstract])) OR (trans-femoral aortic valve replacement[Title/Abstract])) OR (transapical aortic valve implantation[Title/Abstract])) OR (transapical aortic valve replacement[Title/Abstract])) OR (transapical aortic valve implantation[Title/Abstract])) OR (transapical aortic valve replacement[Title/Abstract])) OR (transapical aortic valve implantation[Title/Abstract])) OR (transapical aortic valve replacement[Title/Abstract t])) OR (transcatheter aortic valve replacement[Title/Abstract])) OR (transcutaneous aortic valve implantation[Title/Abstract])) OR (transcutaneous aortic valve implantation[Title/Abstract])) OR (transcutaneous aortic valve implantation[Title/Abstract])) OR (transcutaneous aortic valve replacement[Title/Abstract])) OR (transfemoral aortic valve implantation[Title/Abstract])) OR (transfemoral aortic valve replacement[Title/Abstract])) OR (transfemoral aortic valve implantation[Title/Abstract])) OR (transfemoral aortic valve replacement[Title/Abstract])) OR (TAVR[Title/ Abstract]).	12828							

6 (((((((((aorta valve replacement[Title/Abstract]) OR (aorta valve transplantation[Title/Abstract])) OR (aortic valve 36581 transplantation[Title/Abstract])) OR (aortic valve xenotransplantation[Title/Abstract])) OR (heart valve transplantation, aortic valve[Title/Abstract])) OR (transplantation, aortic valve[Title/Abstract])) OR (surgical aortic valve implantation)) OR (SAVR)) OR (surgical AVR)

Jup	penent table iA. SedicirStrategy Supplement table iA. SedicirStrategy	
7	4 OR 5 OR 6	38222
3	randomized controlled trial[Publication Type] OR randomized[Title/Abstract] OR placebo[Title/Abstract]	945899
7	3 AND 7 AND 8	943
mt	oase	
	"aortic valve stenosis"/exp	20578
2	"aortic valve stenoses":ab,ti OR "stenoses, aortic valve":ab,ti OR "stenosis, aortic valve":ab,ti OR "valve stenoses, aortic":ab,ti OR "valve stenosis, aortic":ab,ti OR "aortic stenosis":ab,ti OR "stenoses, aortic":ab,ti OR "stenosis, aortic":ab,ti	31812
5	1 OR 2	44747
1	"transcatheter aortic valve implantation"/exp	27560
5	"percutaneous aortic valve implantation":ab,ti OR "percutaneous aortic valve replacement":ab,ti OR tavi:ab,ti OR "trans-apical aortic valve implantation":ab,ti OR "trans-apical aortic valve replacement":ab,ti OR "trans-arterial aortic valve implantation":ab,ti OR "trans-arterial aortic valve replacement":ab,ti OR "trans-catheter aortic valve implantation":ab,ti OR "trans-catheter aortic valve replacement":ab,ti OR "trans-catheter aortic valve implantation":ab,ti OR "trans-catheter aortic valve replacement":ab,ti OR "trans-cutaneous aortic valve implantation":ab,ti OR "trans-cutaneous aortic valve replacement":ab,ti OR "trans-femoral aortic valve implantation":ab,ti OR "trans-femoral aortic valve replacement":ab,ti OR "transapical aortic valve implantation":ab,ti OR "transapical aortic valve replacement":ab,ti OR "transapical aortic valve implantation":ab,ti OR "transapical aortic valve replacement":ab,ti OR "transapical aortic valve implantation":ab,ti OR "transapical aortic valve replacement":ab,ti OR "transapical aortic valve implantation":ab,ti OR "transapical aortic valve replacement":ab,ti OR "transapical aortic valve implantation":ab,ti OR "transapical aortic valve replacement":ab,ti OR "transcatheter aortic valve replacement":ab,ti OR "transcutaneous aortic valve implantation":ab,ti OR "transcutaneous aortic valve replacement":ab,ti OR "transfemoral aortic valve implantation":ab,ti OR "transfemoral aortic valve replacement":ab,ti OR "transfemoral aortic valve implantation":ab,ti OR "transfemoral aortic valve	22178
5	"aorta valve replacement":ab,ti OR "aorta valve transplantation":ab,ti OR "aortic valve transplantation":ab,ti OR "aortic valve xenotransplantation":ab,ti OR "heart valve transplantation, aortic valve":ab,ti OR "transplantation, aortic valve":ab,ti OR "surgical aortic valve replacement":ab,ti OR "surgical aortic valve implantation":ab,ti OR savr:ab,ti OR "surgical avr":ab,ti	5186
7	4 OR 5 OR 6	31214
3	"randomized controlled trial":ab,ti OR "randomized":ab,ti OR "placebo":ab,ti	1038314
>	3 AND 7 AND 8	822
Coc	hrane CENTRAL	
	MeSH descriptor: [Aortic Valve Stenosis] explode all trees	975
2	(Aortic Valve Stenoses):ti,ab,kw OR (Stenoses, Aortic Valve):ti,ab,kw OR (Stenosis, Aortic Valve):ti,ab,kw OR (Valve Stenoses, Aortic):ti,ab,kw OR (Valve Stenosis, Aortic):ti,ab,kw OR (Aortic Stenosis):ti,ab,kw OR (Stenoses, Aortic):ti,ab,kw OR (Stenosis, Aortic):ti,ab,kw	1898
5	1 OR 2	2111
ł	MeSH descriptor: [Transcatheter Aortic Valve Replacement] explode all trees	203
5	(percutaneous aortic valve implantation):ti,ab,kw OR (percutaneous aortic valve replacement):ti,ab,kw OR (TAVI):ti,ab,kw OR (trans-apical aortic valve implantation):ti,ab,kw OR (trans-apical aortic valve replacement):ti, ab,kw OR (trans-arterial aortic valve implantation):ti,ab,kw OR (trans-arterial aortic valve replacement):ti,ab,kw w OR (trans-catheter aortic valve implantation):ti,ab,kw OR (trans-catheter aortic valve replacement):ti,ab,kw OR (trans-cutaneous aortic valve implantation):ti,ab,kw OR (trans-cutaneous aortic valve replacement):ti,ab,kw OR (trans-femoral aortic valve implantation):ti,ab,kw OR (trans-femoral aortic valve replacement):ti,ab,kw OR (transapical aortic valve implantation):ti,ab,kw OR (transapical aortic valve replacement):ti,ab,kw OR (transapical aortic valve implantation):ti,ab,kw OR (transapical aortic valve replacement):ti,ab,kw OR (transapical aortic valve implantation):ti,ab,kw OR (transapical aortic valve replacement):ti,ab,kw OR (transapical aortic valve implantation):ti,ab,kw OR (transapical aortic valve replacement):ti,ab,kw OR (transapical aortic valve implantation):ti,ab,kw OR (transapical aortic valve replacement):ti,ab,kw OR (transcutaneous aortic valve implantation):ti,ab,kw OR (transapical aortic valve replacement):ti,ab,kw OR (transcutaneous aortic valve implantation):ti,ab,kw OR (transcatheter aortic valve replacement):ti,ab,kw OR (transcutaneous aortic valve replacement):ti,ab,kw OR (transfemoral aortic valve implantation):ti,ab,kw OR (transfemoral aortic valve replacement):ti,ab,kw OR	1094
5	(aorta valve replacement):ti,ab,kw OR (aorta valve transplantation):ti,ab,kw OR (aortic valve transplantation):ti, ab,kw OR (aortic valve xenotransplantation):ti,ab,kw OR (heart valve transplantation, aortic valve):ti,ab,kw OR (transplantation, aortic valve):ti,ab,kw OR (surgical aortic valve replacement):ti,ab,kw OR (surgical aortic valve implantation):ti,ab,kw OR (SAVR):ti,ab,kw OR (surgical AVR):ti,ab,kw	1152
7	4 OR 5 OR 6	1706

Supplement Table 1B. Summary of Findings and Strength of Evidence (GRADE) for 30-Day Results

TAVI Compared to SAVR for Low-Risk Surgical Patients with Aortic Stenosis

Patient or population: Low-risk surgical patients with aortic stenosis Settings:

Intervention: TAVI¹ Comparison: SAVR²

companison. SAVIX						
Outcomes	Illustrative Comparative Risks* (95% CI) Assumed Risk Corresponding Risk		Relative Effect	No. of Participants	Quality of the Evidence	Comments
	Assumed Risk	Corresponding Kisk	(95% CI)	(Studies)	(GRADE)	
	SAVR	TAVI				
All-cause mortality	Study	population	RR 0.44	2633 (3	$\oplus \oplus \oplus \oplus$ High	
Follow-up: 30 days	15 per 1000	7 per 1000 (3-15)	(0.2-0.98)	studies)		
	M	oderate				
	13 per 1000	6 per 1000 (3-13)				
Cardiovascular mortality	Study	population	RR 0.47	2633 (3	$\oplus \oplus \oplus \oplus$ High	
Follow-up: 30 days	14 per 1000	7 per 1000 (3-15)	(0.21-1.03)	studies)		
	M	oderate				
	13 per 1000	6 per 1000 (3-13)				
Stroke	Study	population	RR 0.57 (0.22-	2633 (3	$\oplus \oplus \oplus \ominus$	
Follow-up: 30 days	30 per 1000	17 per 1000 (7-44)	1.48)	studies)	Moderate	
	M	oderate				
	30 per 1000	17 per 1000 (7-44)				
Transient ischemic attack	Study	population	RR 0.75	2633 (3	⊕⊕⊕⊕High	
Follow-up: 30 days	6 per 1000	5 per 1000 (1-21)	(0.1/-3.37)	studies)		
	M	oderate				
	7 per 1000	5 per 1000 (1-24)				
Myocardial infarction	Study	population	RR 0.65	2633 (3	⊕⊕⊕⊕High	
Follow-up: 30 days	18 per 1000	12 per 1000 (6-22)	(0.34-1.22)	studies)		
	M	oderate				
	13 per 1000	8 per 1000 (4-16)				
Acute kidney injury (stage 2	Study	population	RR 0.27	2633 (3	⊕⊕⊕⊕High	
or s) Follow-up: 30 days	28 per 1000	8 per 1000 (4-16)	(0.14-0.56)	studies)		
	M	oderate				
	28 per 1000	8 per 1000 (4-16)		o / == /=		
Life-threatening or	Study	population	RR 0.29	2633 (3	⊕⊕⊕⊝ Mederate ³	
Follow-up: 30 days	150 per 1000	43 per 1000 (21-91)	(0.14-0.01)	studiesj	Moderate	
	M	oderate				
	207 per 1000	60 per 1000 (29-126)		0 / /		
Permanent pacemaker	Study	population	RR 3.59	2633 (3	⊕⊕⊕⊕High	
Follow-up: 30 days	48 per 1000	1/3 per 1000	(1.45-9.05)	studiesj		
	м	(09-455)				
	40 per 1000	144 per 1000 (57-361)				
New-atrial fibrillation	-+++++++++++++++++++++++++++++++++++++		PP 0 21	2622 12	ወወወወ	
Follow-up: 30 days	365 per 1000	77 por 1000 (51-117)	(0.14-0.31)	studies)	Hiah ^{3,4}	
	505 per 1000	oderate	(0	5.22.20		
	354 per 1000	74 per 1000 (50-110)				
	55-pci 1000					

*The basis for the **assumed risk** (e.g., the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **RR**, risk ratio.

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹Transcatheter aortic valve implantation; ²surgical aortic valve replacement; ³inconsistency; ⁴large effect.

Supplement Table 1C. Summary of Findings and Strength of Evidence (GRADE) for 1-Year Results

TAVI Compared to SAVR for Low-Risk Surgical Patients with Aortic Stenosis

Patient or population: low-risk surgical patients with aortic stenosis Settings:

Intervention: TAVI¹

 $\label{eq:comparison:SAVR} \textbf{Comparison:} SAVR^2$

Outcomes	Illustrative Comp	arative Risks* (95% CI)	Relative	No of	Quality of	Comments
	Assumed Risk	Corresponding Risk	Effect (95% CI)	Participants (Studies)	the Evidence (GRADE)	
	SAVR	TAVI				
All-cause mortality	Study	population	RR 0.66	2633 (3	⊕⊕⊕⊕High	
Follow-up: 1 year	32 per 1000	21 per 1000 (13-34)	(0.41-1.06)	studies)		
	Mo	oderate				
	30 per 1000	21 per 1000 (12-32)				
Cardiovascular mortality	Study	population	RR 0.56	2633 (3	$\oplus \oplus \oplus \oplus High$	
Follow-up:1year	29 per 1000	16 per 1000 (10-27)	(0.33-0.94)	studies)		
	Mo	oderate				
	27 per 1000	15 per 1000 (9-25)				
Stroke	Study	population	RR 0.71	2633 (3	$\oplus \oplus \oplus \oplus High$	
Follow-up:1year	39 per 1000	27 per 1000 (15-48)	(0.4-1.25)	studies)		
	Mo	oderate				
	43 per 1000	31 per 1000 (17-54)				
Transient ischemic attack	Study	population	RR 0.98	2633 (3	$\oplus \oplus \oplus \oplus High$	
Follow-up:1year	15 per 1000	15 per 1000 (8-27)	(0.52-1.83)	studies)		
	Mo	oderate				
	15 per 1000	15 per 1000 (8-27)				
Myocardial infarction	Study	population	RR 0.74 (0.43-1.27)	2633 (3 studies)	⊕⊕⊕⊕High	
Follow-up:1year	23 per 1000	17 per 1000 (10-29)				
	Mo	oderate				
	22 per 1000	16 per 1000 (9-28)				
Life-threatening or	Study	population	RR 0.32	2353 (2	⊕⊕⊕⊕High	
disabling bleeding	156 per 1000	50 per 1000 (38-66)	(0.24-0.42)	studies)		
rollow up. ryeu	Mo	oderate				
	173 per 1000	55 per 1000 (42-73)				
Permanent pacemaker	Study	population	RR 3.42	2633 (3	⊕⊕⊕⊝	
implantation Follow-up:1year	57 per 1000	194 per 1000 (76-501)	(1.33-8.82)	studies)	Moderate ^{3,4}	
	Mo	oderate				
	53 per 1000	181 per 1000 (70-467)				
New-atrial fibrillation	Study	population	RR 0.25	2633 (3	$\oplus \oplus \oplus \oplus$	
Follow-up: 1 year	386 per 1000	96 per 1000 (69-139)	(0.18-0.36)	studies)	High ^{3,4}	
	Mo	oderate				
	384 per 1000	96 per 1000 (69-138)				

*The basis for the **assumed risk** (e.g., the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **RR**, risk ratio.

GRADE Working Group grades of evidence

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Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

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¹Transcatheter aortic valve implantation; ²surgical aortic valve replacement; ³inconsistency; ⁴large effect.

Supplement Table 1D. Summary of Findings and Strength of Evidence (GRADE) for 2-Year Results

TAVI Compared to SAVR for Low-Risk Surgical Patients with Aortic Stenosis

Patient or population: Low-risk surgical patients with aortic stenosis Settings:

Intervention: TAVI¹ Comparison: SAVR²

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Outcomes	Illustrative Comp	arative Risks* (95% CI)	Relative	No. of	Quality of the Evidence (GRADE)	Comments
	Assumed Risk	Corresponding Risk	Effect (95% CI)	Participants (Studies)		
	SAVR	TAVI				
All-cause mortality	Study	population	RR 0.8	2644 (3	$\oplus \oplus \oplus \oplus High$	
Follow-up: 2 years	45 per 1000	36 per 1000 (25-52)	(0.55-1.16)	studies)		
	Me	oderate				
	44 per 1000	35 per 1000 (24-51)				
Cardiovascular mortality	Study	population	RR 0.65	2644 (3	⊕⊕⊕⊕High	
Follow-up: 2 years	37 per 1000	24 per 1000 (16-37)	(0.42-1.01)	studies)		
	M	oderate				
	34 per 1000	22 per 1000 (14-34)				
Stroke	Study	population	RR 0.9	2644 (3	⊕⊕⊕⊕High	
Follow-up: 2 years	48 per 1000	43 per 1000 (31-61)	(0.64-1.28)	studies)		
	Me	oderate				
	52 per 1000	47 per 1000 (33-67)				
Transient ischemic attack	Study	population	RR 1.09	1230 (2	⊕⊕⊕⊕High	
Follow-up: 2 years	19 per 1000	20 per 1000 (7-57)	(0.39-3.04)	studies)		
	Me	oderate				
	23 per 1000	25 per 1000 (9-70)				
Myocardial infarction	Study	population	RR 0.95 (0.58-1.56)	2644 (3 studies)	⊕⊕⊕⊕High	
Follow-up: 2 years	24 per 1000	23 per 1000 (14-38)				
	Me	oderate				
	26 per 1000	25 per 1000 (15-41)				
Permanent pacemaker	Study	population	RR 3.02	2644 (3	$\oplus \oplus \oplus \ominus$	
implantation Follow-up: 2 years	70 per 1000	211 per 1000 (92-487)	(1.31-6.97)	studies)	Moderate ³	
	Me	oderate				
	66 per 1000	199 per 1000 (86-460)				
New atrial fibrillation	Study	population	RR 0.27	1230 (2	$\oplus \oplus \oplus \oplus$	
Follow-up: 2 years	396 per 1000	107 per 1000 (55-202)	(0.14-0.51)	studies)	High ^{3,4}	
	Me	oderate				
	465 per 1000	126 per 1000 (65-237)				

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GRADE Working Group grades of evidence

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Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

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¹Transcatheter aortic valve implantation; ²surgical aortic valve replacement; ³inconsistency; ⁴large effect.