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ABSTRACT

Background

Stroke is a major cause of morbidity and mortality in trans-aortic valve replacement (TAVR). Despite the relatively high safety profile of newly developed cerebral embolic protection device (CEPDs) and advanced TAVR techniques, recent data on efficacy of CEPDs is still inconclusive. The aim of this meta-analysis is to determine the efficacy of CEPDs in reducing in-hospital mortality, in-hospital stroke, major adverse cardiac and cerebrovascular events, 30-day stroke rate, transient ischemic attack, delirium, vascular complications, in-hospital major bleeding and volume of cerebral lesions on magnetic resonance imaging among patients who underwent TAVR. **Methods:** A comprehensive literature search on CEPDs and TAVR published between January 2015 and June 2022 was done through MEDLINE and Cochrane databases. Full text of eligible articles was obtained and evaluated for final analysis. Statistical analysis was performed using a random-effects model to calculate for the risk ratio (RR).

Results: Seven randomized controlled trials (RCTs) and 6 observational cohort studies (OCSs) involving 126,635 patients were included for analysis. CEPD was associated with a significant reduction of **in-hospital mortality** (RR 0.66; 95% CI 0.54–0.81), **in-hospital stroke** (95% CI 0.69–0.93), and **30-day mortality** (RR 0.72; 95% CI 0.52–0.99). No significant difference was observed in major adverse cardiac and cerebrovascular events, 30-day stroke rate, transient ischemic attack, delirium, vascular complications, in-hospital major bleeding and volume of cerebral lesions on magnetic resonance imaging.

Conclusion

CEPD device use in TAVR is associated with a reduction of in-hospital mortality, in-hospital stroke and 30-day mortality. However, these results are driven mainly by observational studies. The reduction in events are driven mainly by OCSs. Large RCTs are needed to determine efficacy and safety of CEPD use during TAVR.

A.

	With de	vice	Without d	evice		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, Random, 95% Cl
1.2.1 RCT								
Kapadia 2017	21	244	7	119	21.1%	1.46 [0.64, 3.34]		
Lansky 2015	7	46	6	39	14.4%	0.99 [0.36, 2.70]		
Lansky 2021	27	141	5	63	17.6%	2.41 [0.97, 5.98]		
Nazif 2021	22	157	22	157	47.0%	1.00 [0.58, 1.73]		- -
Subtotal (95% CI)		588		378	100.0%	1.26 [0.86, 1.85]		-
Total events	77		40					
Heterogeneity: Tau ² :	= 0.00; Chi	² = 3.05	, df = 3 (P =	: 0.38); P	²= 2%			
Test for overall effect	: Z=1.20 (P = 0.2	3)					
Total (95% Cl)		588		378	100.0%	1.26 [0.86, 1.85]		•
Total events	77		40					
Heterogeneity: Tau ² :	= 0.00; Chi	² = 3.05	, df = 3 (P =	: 0.38); P	²= 2%			
Test for overall effect	: Z = 1.20 (P = 0.23	3)				0.01	0.1 1 1 10 100 Favours with device Favours without device
Teet for subgroup dif	foronco:	Not onn	liooblo					Favours with device Favours without device

Test for subgroup differences: Not applicable

B.

	With de	evice	Without	device		Risk Ratio	Risk Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% Cl	
2.1.1 RCT								
Kapadia 2017	3	234	3	111	1.3%	0.47 [0.10, 2.31]		
Kapadia 2022	41	1501	45	1499	18.4%	0.91 [0.60, 1.38]		
_ansky 2015	1	46	2	39	0.6%	0.42 [0.04, 4.50]		
_ansky 2021	0	141	0	63		Not estimable		
Nazif 2021	3	157	0	57	0.4%	2.57 [0.13, 48.99]		-
Van Mieghem 2016 Subtotal (95% CI)	1	32 2111	0	33 1802	0.3% 20.9%	3.09 [0.13, 73.19] 0.89 [0.60, 1.31]	•	
Total events Heterogeneity: Tau² = Test for overall effect: .				= 0.72); l²	= 0%			
2.1.2 OC \$								
3utala 2021	99	12409	1317	110777	77.3%	0.67 [0.55, 0.82]		
Dona 2022	1	213	1	198	0.4%	0.93 [0.06, 14.76]		
Seeger 2017 Subtotal (95% CI)	2	280 12902	8	280 111255	1.3% 79.1%	0.25 [0.05, 1.17] 0.66 [0.54, 0.81]		
Fotal events Heterogeneity: Tau² = Fest for overall effect: .				= 0.45); l²	= 0%			
Total (95% CI)		15013		113057	100.0%	0.70 [0.59, 0.84]	•	
Total events	151		1376	= 0.61); l²				

C.

	With de	evice	Without	device		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
3.1.1 RCT							
Haussig 2016	5	50	5	50	1.5%	1.00 [0.31, 3.24]	
Kapadia 2017	13	231	10	110	3.2%	0.62 [0.28, 1.37]	
Kapadia 2022	34	1501	43	1499	10.2%	0.79 [0.51, 1.23]	
Lansky 2015	1	46	2	39	0.4%	0.42 [0.04, 4.50]	· · · · · · · · · · · · · · · · · · ·
Lansky 2021	13	141	5	63	2.1%	1.16 [0.43, 3.12]	
Nazif 2021	10	157	3	57	1.3%	1.21 [0.35, 4.24]	
Van Mieghem 2016	0	32	2	32	0.2%		· · · · · · · · · · · · · · · · · · ·
Subtotal (95% CI)		2158		1850	18.9%	0.81 [0.58, 1.12]	•
Total events	76		70				
Heterogeneity: Tau ² =	0.00; Chi	²= 2.61,	df = 6 (P	= 0.86); l²	= 0%		
Test for overall effect:	Z=1.30 (P = 0.20)				
3.1.2 OC S							
Butala 2021	158	12409	1716	110777	77.1%	0.82 [0.70, 0.97]	
Dona 2022	5	213	15	198	2.0%	0.31 [0.11, 0.84]	
Seeger 2017	4	280	13	280	1.6%	0.31 [0.10, 0.93]	
Stamou 2019	1	33	2	50	0.4%	0.76 [0.07, 8.02]	
Subtotal (95% CI)		12935		111305	81.1%	0.53 [0.27, 1.03]	\bullet
Total events	168		1746				
Heterogeneity: Tau ² =	0.23; Chi	² = 6.42,	df = 3 (P	= 0.09); l ^a	= 53%		
Test for overall effect:	Z=1.88 (P = 0.06)				
Total (95% CI)		15093		113155	100.0%	0.79 [0.68, 0.91]	•
Total events	244		1816				
Heterogeneity: Tau ² =	0.00: Chi	² = 9.05.	df = 10 (F	e = 0.53); I	²=0%		
Test for overall effect:				/1 -			0.01 0.1 1 10 100 Favours with device Favours without device
Test for subgroup diff	erences:	Chi ² = 1.	24, df = 1	(P = 0.26)	, l² = 19.8	6%	Favours with device Favours without device

Figure 1: A. Forrest plot showing the risk ratio for major adverse cardiac and cerebrovascular events. **B.** Forrest plot showing the risk ratio for in-hospital mortality as well as subgroup analysis based on study design. **C.** Forrest plot showing the risk ratio for in-hospital stroke as well as subgroup analysis based on study design.