Meta-analysis/Systematic review

Cerebral embolic protection in patients undergoing transcatheter aortic valve implantation: an updated meta-analysis of randomised controlled trials

Moaz Ahmad[1], Yik Ting Chan[2], Obaid Ur Rahman[3], Kevin Vinod Joseph[4], Nimra Zuberi[5], Iqra Safdar[6], Shereen Asghar[6], Danish Ahmed[7], Toqeer Ahmed[8], Umbreen Nadeem[9], Reem Abukhater[10], Ahmad Mesmar[11], Rowena George[6], Haris Khan[12], Syed Muhammad Ali Hassnain[5], Muhammad Sajjad Haider[13], Raheel Ahmed[14,15]

[1]The Rotherham NHS Foundation Trust, UK
[2]Darent Valley Hospital, UK
[3]Department of Cardiology, Midland Metropolitan University Hospital, UK
[4]Department of Medicine, Addenbrooke's Hospital, UK
[5]Department of Medicine, South Tyneside District Hospital, UK
[6]Department of Medicine, Sunderland Royal Hospital, UK
[7]Cardiothoracic Department, Freeman Hospital, UK
[8]Department of Cardiology, Sunderland Royal Hospital, UK
[9]Department of Cardiology, Mid Yorkshire Hospitals NHS Trust, Wakefield, UK
[10]RAK Medical and Health Sciences University, Ras Al Khaimah, UAE
[11]Department of Cardiology, Sheikh Shakhbout Medical City, UAE
[12]Department of Cardiology, William Harvey Hospital, UK
[13]Department of Medicine, Worthing Hospital, UK
[14]Department of Cardiology, Newcastle University, UK
[15]Department of Cardiology, Royal Brompton Hospital, London, UK

***Corresponding author:**
Dr. Raheel Ahmed
Department of Cardiology
Newcastle University, UK
E-mail: Raheel.Ahmed1@newcastle.ac.uk

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Abstract

Introduction: Transcatheter aortic valve implantation (TAVI) has become a standard treatment for patients with severe aortic stenosis. However, periprocedural cerebral embolisation remains a major complication, contributing to the risk of stroke and silent cerebral infarctions. Cerebral embolic protection devices (CEPDs) have been developed to mitigate this risk, but their clinical efficacy remains uncertain.
Methods: A systematic search of the PubMed/Medline, Embase, and Cochrane library databases was conducted for randomised controlled trials (RCTs) comparing CEPD use versus no CEPD in patients undergoing TAVI, from inception to 1 May 2025. The primary outcome was all-cause stroke. Risk ratios (RRs) and mean differences (MDs) were pooled using a random-effects model.
Results: Eight RCTs comprising 11,611 patients (5956 with CEPD and 5655 without CEPD) were included. CEPD use was not associated with a significant reduction in all-cause stroke (RR = 0.92, 95% CI: 0.74–1.15), disabling stroke (RR = 0.80, 95% CI: 0.57–1.12), or non-disabling stroke (RR = 0.82, 95% CI: 0.58–1.16). No significant differences were observed in all-cause mortality (RR = 1.09, p = 0.70), NIHSS worsening (RR = 1.21, p = 0.41), new ischaemic lesions (RR = 0.99, p = 0.70), or lesion volume on DW-MRI (MD = –78.89 mm^3, p = 0.10). Similarly, no significant differences were found in the incidence of acute kidney injury or vascular complications (p > 0.05).
Conclusions: The use of CEPDs during TAVI was not associated with a reduction in stroke, mortality, or other adverse clinical outcomes. Further research may be needed to identify subgroups who could benefit from CEPD use.

Key words: cerebral embolic protection, transcatheter aortic valve implantation, meta-analysis, sentinel.

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Introduction

Transcatheter aortic valve implantation (TAVI) has become a well-established therapeutic intervention for patients with severe aortic stenosis. Despite its widespread implementation and overall procedural success, embolisation of valve-related debris during the procedure can lead to stroke, which remains a major complication associated with significant morbidity and mortality [1, 2]. Stroke incidence ranges from 3.4% to 8%, with most events occurring in the first few days following the procedure, primarily as a result of periprocedural embolisation [3–5]. Beyond clinically apparent strokes, diffusion-weighted magnetic resonance imaging (DW-MRI) studies have demonstrated a high prevalence of silent cerebral infarctions following TAVI [6, 7].

Cerebral embolic protection devices (CEPDs) have been developed to prevent embolic debris released during TAVI from entering the cerebral circulation, hence reducing the risk of embolic stroke and its associated complications [8]. However, the clinical effectiveness of CEPDs remains controversial. A recent analysis of the comprehensive STS–ACC TVT (Society of Thoracic Surgeons–American College of Cardiology Transcatheter Valve Therapy) registry demonstrated a borderline statistically significant reduction in both all-cause stroke and disabling stroke associated with CEPD use [9]. Conversely, previous studies have consistently reported no significant difference in the incidence of severe stroke, disabling stroke, or mortality between patients receiving CEPDs and those in control groups [10, 11].

A recently published randomised controlled trial (RCT), the BHF PROTECT-TAVI study, reported outcomes from a cohort of 7635 randomised patients [12]. In light of these new findings, we conducted an updated systematic review and meta-analysis to evaluate the safety, clinical efficacy, and neuroimaging outcomes associated with the use of CEPD in patients undergoing TAVI.

Methods

This systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [13]. The protocol of review is registered with PROSPERO (CRD420251070225).

Search and screening of studies

Two independent reviewers conducted a systematic literature search across the PubMed/Medline, Cochrane library, and Embase databases. The search included RCTs published from database inception until 1 May 2025, focusing on studies comparing CEPD versus no CEPD in patients undergoing TAVI. Additional relevant studies were identified by manually reviewing reference lists of retrieved articles, prior meta-analyses, and review papers. Duplicate studies were excluded using Rayyan, and no language restrictions were applied. Two reviewers independently screened all articles by title and abstract, followed by full-text assessment for eligibility. Discrepancies were resolved through discussion or consultation with a third reviewer (MA). The detailed search strategy is provided in Supplementary Table SI.

Inclusion and exclusion criteria

Studies were included if they met the following criteria: they were published RCTs, enrolled adult patients (aged 18 years or older) undergoing TAVI, compared CEPD use versus no CEPD, and reported at least one pre-specified efficacy or safety outcome. Studies were excluded if they were non-RCTs, such as observational studies, case reports, reviews, or editorials, or if they presented insufficient or irrelevant data.

Outcomes and data extraction

The primary outcome was the incidence of all-cause stroke. Secondary outcomes included disabling stroke, non-disabling stroke, all-cause death, NIHSS worsening, new ischaemic lesions, acute kidney injury (AKI), major or minor vascular complications, and lesion volume on DW-MRI. We used maximum available follow-up for data extraction of outcomes. Extracted data included study characteristics (author, year, design, sample size, and follow-up duration), patient demographics (age, sex, comorbidities), and clinical outcomes.

Bias assessment

The Cochrane Risk of Bias Tool (RoB 2) was used to evaluate the quality of the included studies [14]. This tool assesses potential bias across several domains, including selection bias, performance bias, detection bias, attrition bias, and reporting bias. Two reviewers independently performed the quality assessment, and any disagreements were resolved through consensus or by involving a third reviewer.

Data analysis

Statistical analyses were conducted using RevMan 5.4. Results were reported as risk ratios (RR) for dichotomous outcomes and as mean differences (MD) for continuous outcomes with corresponding 95% confidence intervals (CIs). Forest plots were used to visualise the results. The DerSimonian Laird random effects model was used for pooled analysis to account for inter-study

variations [15]. Heterogeneity among studies was assessed using the I^2 statistic, where values of less than 25% indicated low heterogeneity, 25% to 75% indicated moderate heterogeneity, and values greater than 75% indicated high heterogeneity. A *p*-value less than 0.05 was considered statistically significant.

Results

A total of 442 studies were identified through database searches. After removing duplicates, 371 articles were reviewed during the title and abstract screening. Twenty-four studies underwent full-text review, and following detailed assessment, 8 studies met the eligibility criteria and were included in this systematic review and meta-analysis (Supplementary Figure S1).

Baseline characteristics and bias assessment

The included studies [10–12, 16–20] reported data for 11,611 patients undergoing TAVI, including 5956 patients receiving CEPD and 5655 patients undergoing TAVI without CEPD. The mean age of patients in the CEPD group was 80.6 years, while it was 80.6 years in the control group. The proportion of male patients was 59.3% in the CEPD group and 61.3% in the control group. Stroke definitions varied among studies, with most using VARC-2 criteria, and some incorporating Neuro-ARC definitions. The most commonly used CEPDs included Sentinel and TriGuard, with one study using the Claret Montage dual filter system. The duration of follow-up ranged from 3 to 60 days. Detailed baseline characteristics for each study are summarised in Table I. Six of the included studies had a low risk of bias while 2 (10, 19) had some concerns mainly related to deviations from intended intervention (Supplementary Figure S2).

Results of meta-analysis

All-cause stroke

Data for the composite outcome for stroke was provided by all 8 studies. Out of total of 11,589 patients, CEPD group (total 5943; events 161) and the control group (total 5646; events 150) were analysed. The pooled analysis did not demonstrate a statistically significant difference for all-cause stroke among patients with CEPD and the control group (RR = 0.92, 95% CI = 0.74–1.15, p = 0.48, Figure 1 A). No heterogeneity was observed among studies included (I^2 = 0%).

Disabling stroke

Data from 8 studies were used to assess the incidence of disabling stroke between the two groups. Out of 11,588 patients, the CEPD group (Total = 5943; Events = 66) and the control group (Total = 5645; Events = 77) were analysed. The pooled analysis did not demonstrate a statistically significant difference in the incidence of disabling stroke between the two groups (RR = 0.80, 95% CI = 0.57–1.12, p = 0.18, Figure 1 B). No heterogeneity was observed among included studies (I^2 = 0%).

Non-disabling stroke

Data from 7 studies were used to assess the incidence of non-disabling stroke between the two groups. Among 3993 participants, the CEPD group (Total = 2146; Events = 68) and the control group (Total = 1847; Events = 63) were analysed. The pooled analysis did not demonstrate a statistically significant reduction in the risk of non-disabling stroke between the two groups (RR = 0.82, 95% CI = 0.58–1.16, p = 0.26, Figure 1 C). No heterogeneity was observed among included studies (I^2 = 0%).

All-cause death

Data from 8 randomised controlled trials was used to assess all-cause mortality between the two groups. Among 11,593 patients, the CEPD group (Total = 5946; Events = 48) and the control group (Total = 5647; Events = 39) were included. The pooled analysis did not show a statistically significant difference in all-cause mortality between the two groups (RR = 1.09, 95% CI = 0.71–1.67, p = 0.70, Figure 2 A). No heterogeneity was observed (I^2 = 0%).

NIHSS worsening

A total of 5 randomised controlled trials, including 595 patients, contributed to the NIHSS worsening outcome. The CEPD group (Total = 331; Events = 41) and the control group (Total = 264; Events = 28) were analysed. The pooled analysis did not show a statistically significant difference in NIHSS worsening between the two groups (RR = 1.21, 95% CI = 0.77–1.91, p = 0.41, Figure 2 B). No heterogeneity was observed (I^2 = 0%).

New ischaemic lesions

Data from 5 studies were used to evaluate the incidence of new ischaemic lesions between the two groups. The CEPD group (Total = 308; Events = 265) and the control group (Total = 250; Events = 221) were analysed. The pooled analysis showed no statistically significant difference in the incidence of new ischaemic lesions between the two groups (RR = 0.99, 95% CI = 0.95–1.04, p = 0.70, Figure 2 C). No heterogeneity was observed (I^2 = 0%).

Table I. Baseline characteristics of included studies

Author/study name	Year of publication	Sample size		Mean age [years]		Male (%)		STS score		TAVR Valve type		Stroke definition	CEPD type	Follow-up [days]
		CEPD	Control	CEPD	Control	CEPD	Control	CEPD	Control	CEPD	Control			
Kharbanda *et al.*/BHF PROTECT-TAVI	2025	3798	3803	81.2 ±6.5	81.3 ±6.5	60.9	61.6	NR	NR	Self-expanding (42.6%), Balloon expandable (57.4%)	Self-expanding (42.7%), Balloon expandable (57.3%)	VARC-2	Sentinel[a]	60
Kapadia *et al.*/ PROTECTED-TAVR	2022	1501	1499	78.9	78.9	58	62.2	3.3	3.4	Edwards SAPIEN 3 (64.3%)	Edwards SAPIEN 3 (63.7%)	NeuroARC	Sentinel[b]	3
Lansky *et al.*/ DEFLECT III	2021	46	39	82.5	82.3	43.5	48.7	6.3	7.4	Edwards SAPIEN/ XT/3 (63.5%), Medtronic CoreValve (31%)		VARC-2	TriGuard	30
Nazif *et al.*/ REFLECT II	2021	157	57	80.3	78.1	54.8	61.4	NR	NR	Edwards SAPIEN (60.5%), Medtronic CoreValve (35.3%)	Edwards SAPIEN (62.4%), Medtronic CoreValve (36.9%)	VARC-2, NeuroARC	TriGuard	30
Kapadia *et al.*/ Sentinel	2017	231	111	83.1	78.1	47.9	51.3	5.6	6.6	Edwards SAPIEN 3 (55.8%), Edwards SAPIEN XT (17.5%), CoreValve Evolut R (24.2%)	Edwards SAPIEN 3 (53.4%), Edwards SAPIEN XT (16.9%), CoreValve Evolut R (23.7%)	VARC-2	Sentinel	30
Van Mieghem *et al.*/ MISTRAL-C	2016	32	33	82	82	53	51	4.6	5.8	Edwards SAPIEN 3 (54%), Edward SAPIEN XT (15%), Medtronic CoreValve (25%)		VARC-2	Sentinel	30
Haussig *et al.*/ CLEAN-TAVI	2016	50	50	80	79.3	42	44	5.6	5.2	Medtronic CoreValve		VARC-2	Claret Montage Dual Filter	30
Lansky *et al.*/ REFLECT-I	2015	141	63	79.8	81.5	56.7	66.7	4.6	4.6	CoreValve (32.4%), Sapien (62.5%)	CoreValve (35.5%), Sapien (59.7%)	VARC-2, NeuroARC	TriGuard	30

[a]Neurological deficit of vascular origin lasting ≥24 h or <24 h with imaging-confirmed infarction. [b]Imaging- or pathology-confirmed CNS infarction, including clinical stroke and silent cerebral infarction. CEPD – Cerebrovascular Event Prevention Device, STS – Society of Thoracic Surgeons, TAVR – transcatheter aortic valve replacement, VARC-2 – Valve Academic Research Consortium 2, NeuroARC – Neurovascular Academic Research Consortium, NR – not reported, SAPIEN – Edwards SAPIEN Valve, XT – Edwards SAPIEN XT Valve, CoreValve – Medtronic CoreValve, CoreValve Evolut R – Medtronic Evolut R CoreValve, TriGuard – Cerebral Embolic Protection Device, Claret Montage Dual Filter – Dual Filter Cerebral Embolic Protection Device.

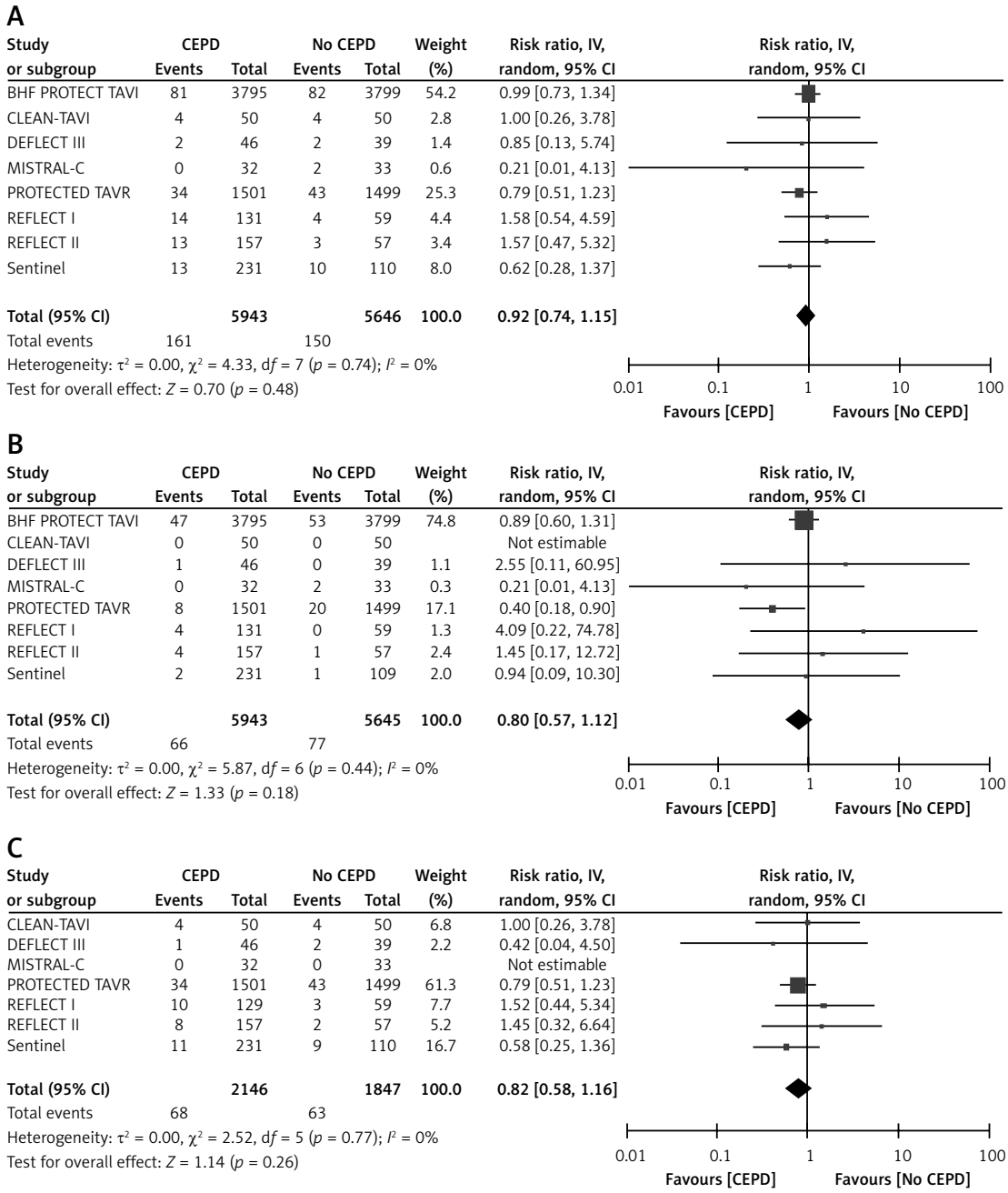


Figure 1. Forest plots for all-cause stroke (**A**), disabling stroke (**B**), and non-disabling stroke (**C**)

Acute kidney injury

Data from 8 studies assessed the incidence of AKI associated with the procedure between the two groups. Out of 10,833 patients, the CEPD group (Total = 5560; Events = 152) and the control group (Total = 5273; Events = 126) were analysed. The pooled analysis did not reveal a statistically significant difference in AKI incidence between the groups (RR = 1.19, 95% CI = 0.94–1.50, p = 0.15, Figure 3 A). No heterogeneity was observed (I^2 = 0%).

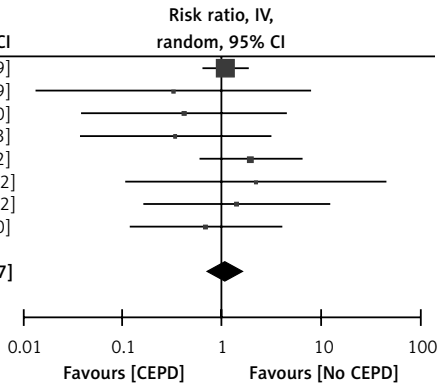
Major or minor vascular complications

A total of 7 randomised controlled trials including 7731 patients were used to assess major or minor vascular complications related to TAVI. The CEPD group (Total = 3996; Events = 182) and the control group (Total = 3735; Events = 133) were analysed. The pooled analysis did not show a statistically significant difference between the two groups (RR = 1.19, 95% CI = 0.73–1.63, p = 0.66, Figure 3 B). Moderate heterogeneity was observed (I^2 = 43%).

A

Study or subgroup	CEPD Events	CEPD Total	No CEPD Events	No CEPD Total	Weight (%)	Risk ratio, IV, random, 95% CI
BHF PROTECT TAVI	29	3795	26	3799	66.4	1.12 [0.66, 1.89]
CLEAN-TAVI	0	50	1	50	1.8	0.33 [0.01, 7.99]
DEFLECT III	1	46	2	39	3.3	0.42 [0.04, 4.50]
MISTRAL-C	1	32	3	33	3.8	0.34 [0.04, 3.13]
PROTECTED TAVR	8	1501	4	1499	12.9	2.00 [0.60, 6.62]
REFLECT I	2	131	0	59	2.04	2.27 [0.11, 46.62]
REFLECT II	4	157	1	57	3.9	1.45 [0.17, 12.72]
Sentinel	3	234	2	111	5.9	0.71 [0.12, 4.20]
Total (95% CI)		**5946**		**5647**	**100.0**	**1.09 [0.71, 1.67]**
Total events	48		39			

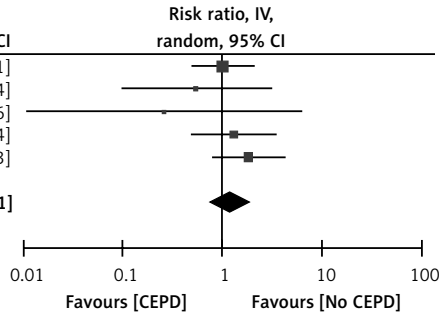
Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 3.70$, d$f = 7$ ($p = 0.81$); $I^2 = 0\%$
Test for overall effect: $Z = 0.39$ ($p = 0.70$)



B

Study or subgroup	CEPD Events	CEPD Total	No CEPD Events	No CEPD Total	Weight (%)	Risk ratio, IV, random, 95% CI
CLEAN-TAVI	11	44	11	45	39.1	1.02 [0.50, 2.11]
DEFLECT III	2	42	3	35	6.8	0.56 [0.10, 3.14]
MISTRAL-C	0	29	1	23	2.1	0.27 [0.01, 6.26]
REFLECT I	14	117	5	56	21.8	1.34 [0.51, 3.54]
REFLECT II	14	99	8	105	30.2	1.86 [0.81, 4.23]
Total (95% CI)		**331**		**264**	**100.0**	**1.21 [0.77, 1.91]**
Total events	41		28			

Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 2.94$, d$f = 4$ ($p = 0.57$); $I^2 = 0\%$
Test for overall effect: $Z = 0.83$ ($p = 0.41$)



C

Study or subgroup	CEPD Events	CEPD Total	No CEPD Events	No CEPD Total	Weight (%)	Risk ratio, IV, random, 95% CI
CLEAN-TAVI	48	49	44	45	62.2	1.00 [0.94, 1.06]
DEFLECT III	19	26	23	26	3.0	0.83 [0.63, 1.08]
MISTRAL-C	16	22	13	15	2.1	0.84 [0.61, 1.16]
REFLECT I	97	111	51	58	15.8	0.99 [0.88, 1.12]
REFLECT II	85	100	90	106	16.8	1.00 [0.89, 1.12]
Total (95% CI)		**308**		**250**	**100.0**	**0.99 [0.95, 1.04]**
Total events	265		221			

Heterogeneity: $\tau^2 = 0.00$, $\chi^2 = 2.90$, d$f = 4$ ($p = 0.57$); $I^2 = 0\%$
Test for overall effect: $Z = 0.38$ ($p = 0.70$)

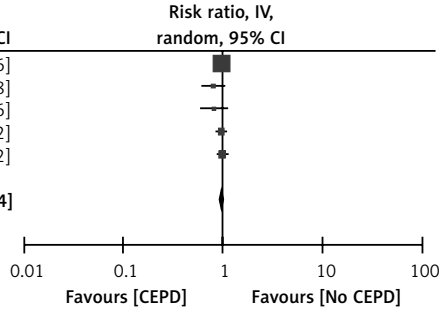


Figure 2. Forest plots for all-cause death (**A**), NIHSS worsening (**B**), and new ischaemic lesions (**C**)

Lesion volume on DW-MRI

A total of 814 patients from 6 randomized controlled trials were included to assess differences in lesion volume on diffusion-weighted MRI. The CEPD group included 448 patients, while the control group included 366 patients. The pooled analysis did not show a statistically significant difference in lesion volume between the two groups (Mean Difference = –78.89, 95% CI = –172.29 to 14.50, $p = 0.10$, Figure 3 C). Substantial heterogeneity was observed ($I^2 = 96\%$).

Discussion

Our meta-analysis of 8 RCTs, with data for 11,611 patients, demonstrated that the use of CEPDs during TAVI was not associated with an improvement in clinical outcomes. CEPDs were developed to mitigate periprocedural cerebral embolisation, aiming to capture or deflect embolic debris during valve deployment [21]. Although earlier studies confirmed the presence of debris captured by these devices, clinical trials have been largely underpowered to detect meaningful differences in neurological outcomes [8, 21]. Our updated meta-analysis sought to resolve this uncertainty by incorporating data from the largest and most recent RCT to date (the BHF PROTECT-TAVI trial), resulting in a pooled cohort of 11,611 patients across eight RCTs [12].

Despite this expanded dataset, our analysis found no statistically significant reduction in all-cause stroke among patients receiving CEPD compared with those undergoing TAVI without protection. Furthermore, the use of CEPDs did not translate into improvements in neurocognitive

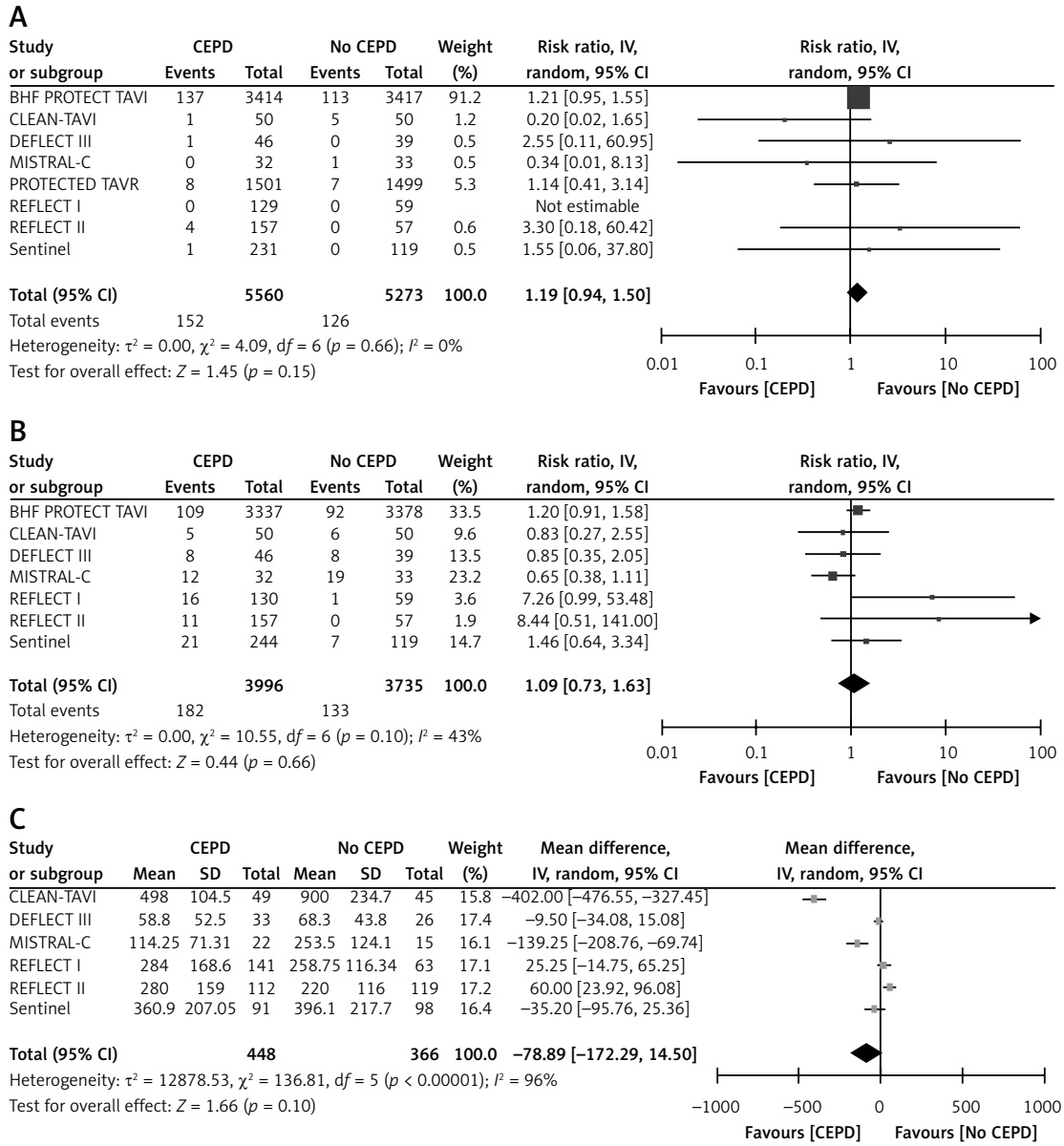


Figure 3. Forest plots for acute kidney injury (**A**), major or minor vascular complications (**B**), and lesion volume (**C**) on DW-MRI

function or neuroimaging endpoints, including the presence of new ischaemic lesions or total lesion volume on diffusion-weighted MRI. Importantly, CEPD use did not lead to increased risk of procedural complications, such as vascular injury or acute kidney injury. It is important to mention that the included trials varied in follow-up duration (3 to 60 days) and stroke definitions, with most using VARC-2 criteria and some adopting NeuroARC definitions. While we used the maximum available follow-up for each trial to capture the broadest outcome data, the shorter follow-up in some studies may have underestimated delayed stroke events. Despite these differences, the consistency of our findings across outcomes, reflected by an I^2 of 0% for all stroke endpoints, suggests that this definitional and temporal heterogeneity did not meaningfully influence the pooled estimates.

A recent meta-analysis that included both randomised trials and observational studies found a reduction in the incidence of all strokes [22]. However, this benefit was primarily observed in the nonrandomised studies and was not evident when the analysis was limited to RCTs. Furthermore, a study involving over 400,000 patients from the STS/ACC TVT registry reported a statistically significant decrease in both all strokes and disabling strokes [23]. These findings raise the question of whether methodological or execution-related differences in RCTs might be obscuring the stroke reduction benefits of CEPD observed in re-

al-world settings. From a trial design perspective, declining stroke rates after TAVI in recent years, currently around 1.6% to 2.3% at 30 days, make it increasingly difficult to detect significant benefit unless extremely large sample sizes are used [24]. Notably, the BHF PROTECT-TAVI trial was appropriately powered with a planned enrolment of over 7000 patients, but it still failed to demonstrate a clear benefit in the primary endpoint of stroke prevention. However, the non-significant findings should be interpreted with caution because they may reflect insufficient statistical power rather than a true absence of effect, particularly given the declining periprocedural stroke rates in contemporary TAVI practice (1.6–2.3% at 30 days), which substantially increase the sample size required to detect clinically meaningful treatment differences.

Multiple factors may explain the limited benefit observed with CEPDs. Patient-related factors such as advanced age, female sex, chronic kidney disease, and prior cerebrovascular disease may independently increase stroke risk and may not be fully addressed by embolic protection alone [6, 25, 26]. Additionally, delayed postprocedural events such as new-onset atrial fibrillation, valve thrombosis, or plaque embolisation may not be preventable by devices used only during the procedure [27–29]. Furthermore, anatomical constraints such as tortuous vasculature or inadequate access can preclude CEPD use in patients who might benefit most.

Device-related limitations also warrant consideration. Current filter-based systems like sentinel typically cover only the brachiocephalic and left common carotid arteries, leaving the left vertebral artery unprotected [12, 22]. While deflection devices such as TriGuard aim to offer full cerebral coverage, they suffer from challenges including incomplete deployment, interference with TAVI delivery systems, and larger sheath sizes, limiting their utility [30]. In the REFLECT I trial, for instance, full cerebral coverage was achieved in only 57% of cases, and delivery interference occurred in 9% [19]. Beyond technical deployment challenges, the included trials evaluated mechanistically distinct devices with differing degrees of cerebral coverage: the Sentinel provides filter-based protection of two vessels, TriGuard offers deflection-based full cerebral coverage, and the Claret Montage employs a dual-filter three-vessel design. These differences in mechanism and coverage represent an important source of clinical heterogeneity, and the pooled estimate should be interpreted as a class-level summary rather than a reflection of any individual device's efficacy.

The substantial heterogeneity observed in lesion volume analyses (I^2 = 96%) probably reflects differences in CEPD type (Sentinel vs. TriGuard vs. Claret Montage), variability in the timing of post-procedural DW-MRI acquisition across trials, and differences in lesion volume quantification methods, all of which can significantly influence measured lesion volumes and limit the interpretability of pooled estimates. Although CEPDs did not significantly reduce new ischaemic lesions or lesion volume on DW-MRI, the clinical significance of these silent cerebral infarctions remains debated. While silent lesions are frequently detected post-TAVI, their correlation with overt stroke outcomes is inconsistent because they may reflect subclinical embolic burden without immediate neurological consequences [31]. However, emerging evidence suggests that cumulative silent infarctions may contribute to long-term cognitive decline and dementia, highlighting the need for trials with extended neurocognitive follow-up to fully evaluate the clinical impact of CEPDs beyond periprocedural stroke prevention [32]. It is important to note that clinical stroke and DW-MRI endpoints are conceptually distinct: DW-MRI lesions reflect acute procedural embolic burden, while clinical stroke additionally integrates delayed postprocedural mechanisms, such as new-onset atrial fibrillation and valve thrombosis, that lie beyond the scope of intraoperative embolic protection. This distinction may explain the observed discordance between neuroimaging and clinical outcomes across CEPD trials.

Although our pooled analysis showed no overall benefit of CEPDs, it is plausible that selected high-risk subgroups such as patients with severe aortic atheroma, prior cerebrovascular disease, or those undergoing valve-in-valve procedures may still derive meaningful neuroprotective benefit from embolic protection. However, the included trials were not individually powered for subgroup analyses, and patient-level data were unavailable, precluding definitive conclusions regarding differential treatment effects. Future adequately powered trials with pre-specified subgroup analyses targeting high-risk populations are needed to determine whether a personalised approach to CEPD use during TAVI may be warranted.

This meta-analysis has several limitations. First, the number of available RCTs remains limited, and although inclusion of the BHF PROTECT-TAVI trial enhances power, a definitive conclusion remains elusive. Second, the included trials varied in device type and follow-up duration, contributing to heterogeneity, especially in procedural complication rates. Third, one trial (REFLECT I) was terminated early due to device discontinuation; however, no inter-study heterogeneity was observed in pooled analysis. Fourth, although a random-effects model was used to account for between-study differences, residual heterogeneity may persist due to variations in TAVI techniques, antithrombotic regimens, patient comorbidities, and endpoint

definitions across trials. Furthermore, as neuroimaging endpoints were derived from a subset of studies and patients based on site availability and eligibility criteria, these findings may be subject to selection bias beyond the limitation of reduced sample size, which may restrict their generalisability to the broader TAVI population. The pooling of outcomes across trials with substantially different follow-up durations (3 to 60 days) is an additional limitation; studies with shorter follow-up may underestimate delayed stroke events, and while the I^2 of 0% suggests no statistical heterogeneity from this variation, residual clinical heterogeneity cannot be excluded. This reduced sample size, compared to the clinical stroke endpoints, increases the risk of type II error and limits the ability to draw definitive conclusions regarding the effect of CEPDs on subclinical cerebral embolisation.

In conclusion, our updated meta-analysis, which incorporates over 11,000 patients including data from the largest RCT to date (BHF PROTECT-TAVI), demonstrates that the use of CEPDs during TAVI is safe but does not significantly reduce the risk of all-cause stroke or improve neurocognitive or neuroimaging outcomes. As newer technologies evolve, the efficacy of comprehensive embolic protection remains a promising yet unproven strategy. Until more definitive evidence becomes available, the decision to employ CEPD during TAVI should be individualised, weighing potential benefits against device-specific limitations, patient anatomy, and procedural complexity.

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Ethical approval

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Conflict of interest

The authors declare no conflict of interest.

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