Title: Routine Cerebral Embolic Protection during Transcatheter Aortic Valve Implantation

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Abstract

Background

Transcatheter aortic valve implantation (TAVI) is associated with procedure-related stroke. Cerebral embolic protection (CEP) devices may reduce embolization to the cerebral circulation and hence the incidence of stroke.

Methods

We conducted a randomized controlled trial across 33 centers in the United Kingdom. We randomly assigned 7635 participants with aortic stenosis in a 1:1 ratio to undergo TAVI with a cerebral embolic protection device (CEP group) or TAVI without CEP (control group). The primary outcome was stroke within 72 hours following TAVI or at the time of discharge from hospital if sooner in the modified intention-to-treat population.

Result

A total of 3815 patients were assigned to the CEP group and 3820 to the control group. In a modified intention-to-treat analysis, the incidence of stroke at 72 hours (or hospital discharge, if sooner) occurred in 81 patients (2.1%) in the CEP group and 82 patients (2.2%) in the control group (difference, -0.02 percentage points; 95% confidence interval [CI], –0.7 to 0.6; P=0.94). Disabling stroke occurred in 47 (1.2%) patients in the CEP group and 53 (1.4%) in the control group. Death occurred in 29 patients (0.8%) in the CEP group and 26 (0.7%) in the control group; access site-related complications appeared similar between groups. There were 24 serious adverse events among 3798 patients (0.6%) in the CEP group and 13 out of 3803 patients (0.3%) in the control group.

Conclusions

Among patients undergoing TAVI, routine use of CEP did not decrease the incidence of stroke at 72 hours.

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INTRODUCTION

Transcatheter Aortic Valve Implantation (TAVI) is an effective and widely used treatment for patients with severe aortic stenosis. Procedure-related stroke remains an unpredictable complication that increases the risk of death and reduces the chance of returning to functional independence.[1,2] Stroke related to the TAVI procedure can be caused by embolism, hemorrhage, or cardiovascular collapse with cerebral hypoperfusion.

Cerebral Embolic Protection (CEP) devices are designed to prevent debris released during the TAVI procedure from reaching the brain, thereby reducing embolic stroke.[3] The Sentinel CEP device (Boston Scientific) is the only CEP device currently approved for clinical use in the United States and Europe. The Stroke Prevention with Sentinel During Transcatheter Aortic Valve Replacement (PROTECTED TAVR) trial investigated the use of CEP to prevent stroke related to the TAVI procedure.[4] The PROTECTED TAVR trial included 51 sites from North America, Europe, and Australia. The trial concluded recruitment after enrolling 3000 patients according to pre-specified stopping rules, but the stroke rate was lower than expected. The incidence of stroke at 72 hours was not significantly different between the CEP and the control groups, but disabling stroke occurred in fewer patients assigned to the CEP group. Hence, the potential impact of CEP on stroke required further evaluation.[5,6]

The British Heart Foundation Randomized Trial of Routine Cerebral Embolic Protection in Transcatheter Aortic Valve Implantation (BHF PROTECT-TAVI) trial was conducted to evaluate whether the routine use of CEP in TAVI procedures would reduce the incidence of clinical stroke.

METHODS

Trial design and oversight

The BHF PROTECT-TAVI trial is a prospective, open-label, blinded outcome-adjudicated multicenter randomized controlled trial conducted in the United Kingdom to evaluate the routine use of a CEP device (Sentinel, Boston Scientific) to prevent stroke in patients with aortic valve stenosis undergoing TAVI. [7]

The study protocol was designed by the academic investigators (for additional information see the Supplementary Appendix available online at NEJM.org with the full text of this article), approved by the UK Health Research Authority (REC 20/WA/0121; IRAS276396), and is available at NEJM.org. The British Heart Foundation (BHF Clinical Study no. CS/20/1/34732) funded the trial and Boston Scientific provided additional support for CEP devices through an investigator-sponsored research grant (ISRCAR00332) but was not involved in design, conduct or reporting of the study. The trial was sponsored by University of Oxford and London School of Hygiene & Tropical Medicine Clinical Trials Unit coordinated the trial and their trial statisticians performed the statistical analyses. A total of 32 of 33 United Kingdom National Health Service centers and one private TAVI center participated in the trial and 29.6% of all TAVI procedures undertaken across National Health Service participating sites were enrolled. Independent Trial Steering and Data Monitoring Committees provided trial oversight. An independent Clinical Events Committee that was blinded to treatment allocation adjudicated the primary outcome of stroke. Research staff at participating sites gathered the data (see the Supplementary Appendix for additional detail). All authors had access to the trial data and vouched for data completeness and

accuracy, and fidelity to the trial protocol. The first author wrote the manuscript, and all authors contributed to subsequent revisions and approved the submission for publication.

Patients

We enrolled trial participants with aortic stenosis who were scheduled to undergo TAVI and in the opinion of the treating physician were clinically and anatomically suitable for treatment with the Sentinel CEP. All participants were over 18 years old and provided written informed consent to join the trial. Full eligibility criteria are described in the Supplementary Appendix.

Randomization

The participants were randomly assigned in a 1:1 ratio stratified by site only using random permuted blocks to undergo TAVI with CEP (CEP group) or without CEP (control group).

Trial procedures

The Sentinel CEP device is usually delivered percutaneously from the right radial artery and deploys filters in the left common carotid (distal filter) and right innominate arteries (proximal filter). Clinical sites were eligible to enroll in the trial after standardized training in the use of the device. A total of 13 sites were using Sentinel in clinical practice prior to the trial starting. Sites with no prior experience with the device were trained by Boston Scientific according to their standard clinical training, and 10 devices were provided for training. There was no formal roll-in period. There was no mandated screening of the aortic arch anatomy and participant eligibility for inclusion in the trial was left to the discretion of the treating physician. Full deployment of the CEP device was defined as correct placement

of both filters for the duration of the TAVI procedure. A participant's stroke-free survival following TAVI was determined using the Questionnaire to Verify Stroke Free Status that was administered daily for the first 72 hours or until discharge.[8] It is a validated structured questionnaire comprised of eight questions where a negative answer to all eight questions accurately predicts stroke-free individuals; a positive response to any of the questions was used to prompt further assessment for a stroke outcome as described in the Supplementary Appendix.

Trial outcomes

The primary outcome was stroke at 72 hours after the TAVI procedure or at hospital discharge if this occurred sooner than 72 hours. Stroke was defined as a new or worsened focal or global neurological deficit of presumed vascular origin, either ischemic or hemorrhagic, occurring after randomization and persisting for more than 24 hours or that led to death within 24 hours of symptom onset. Stroke was not defined by imaging alone. Participants who underwent mechanical thrombectomy for acute ischemic stroke within the 72-hour period after TAVI were classified as having had a stroke, regardless of the success of mechanical thrombectomy procedure. Non-stroke related deaths within the 72-hour period after TAVI were considered as a secondary outcome.

Secondary outcomes included the incidence of all-cause mortality; combined incidence of all-cause mortality or stroke; combined incidence of all-cause mortality, stroke, or transient ischemic attack (TIA) at 72 hours after TAVI or at hospital discharge if this occurred sooner and the incidence of access site vascular complications according to Valve Academic Research Consortium (VARC-2) criteria at 72-hours after TAVI or at hospital discharge if

sooner and at 6 to 8 weeks after the TAVI procedure.[9] For participants with a stroke outcome, stroke severity was assessed according to the National Institutes of Health Stroke Scale (NIHSS) at the time of the initial assessment, and the level of disability after the stroke was assessed using the modified Rankin Scale at 6 to 8 weeks after the TAVI procedure. Severe stroke was defined as a NIHSS score of ≥10.[10] Disabling stroke was defined as a score on the modified Rankin Scale of ≥2 and an increase from the pre-procedure baseline score of at least 1 point.[11,12,13] Participants with a clinical deficit of less than 24 hours in duration were included as part of the secondary outcome analysis as TIA.

Statistical analysis

We estimated that a sample size of 7730 participants would have 80% power at a two-sided 5% significance level to show the superiority of CEP if the incidence of stroke was 3% in the control group and 2% in the CEP group and allowing for a 1% loss to follow-up. An independent Data Monitoring Committee was established and met regularly with formal interim analyses planned at 50% and 70% enrollment to assess efficacy and futility. The Haybittle-Peto approach with $P<0.001$ was used as a guideline to consider stopping early for benefit at each analysis.

The Data Monitoring Committee reviewed the second interim analysis on 5 February 2024 when 5411 participants had been enrolled. The blinded combined stroke rate was 2.0%, and the sample size calculation was revised to 9712 participants to show the superiority of CEP if the incidence of stroke was 2.4% in the control group and 1.6% in the CEP group. The trial protocol was amended accordingly.

The Data Monitoring Committee met for an additional interim analysis when 134 stroke events had accrued. The Data Monitoring Committee recommended to the Trial Steering

Committee that the trial discontinue enrollment as the lower 99% confidence interval excluded a 40% relative risk reduction for the primary outcome and the pre-specified futility criterion had therefore been met. Enrollment was discontinued on 9 October 2024.

The statistical analysis plan (available online at NEJM.org) was finalized before unblinding the trial-group assignments. The primary and secondary outcome measures were assessed on the modified intention-to-treat population. Risk ratios and risk differences were calculated for the primary and other binary outcomes together with 95% confidence intervals using generalized linear models for binomial outcomes. The two-sided P-value for the primary outcome was based on these models.

The modified intention-to-treat analysis included all randomized participants whose TAVI procedure was started, according to the group to which they were assigned, irrespective of whether they received the intervention as allocated. The TAVI procedure was considered to have started once the first arterial puncture was performed.

Complier average causal effect (CACE) analysis was undertaken to address non-compliance with allocated treatment.[14,15] CACE was estimated using two-stage least-squares instrumental variable regression, where the first stage regressed treatment received on randomly assigned treatment, and the second stage regressed the primary outcome on the predicted probabilities of receiving CEP obtained from the first stage.

Prespecified subgroup analyses were performed for the primary outcome by fitting an interaction between the subgroup and randomized treatment using a generalized linear model. A pre-specified secondary analysis for the primary outcome adjusted the modified intention-to-treat population and CACE analyses for age and sex. Given that the primary

outcome does not account for the competing risk of non-stroke-related mortality, a pre-specified unmatched win ratio analysis was also conducted to estimate the effect of CEP on a hierarchical outcome of all-cause mortality, disabling stroke or non-disabling stroke at 72-hours post-TAVI or hospital discharge if this occurred sooner.

Data are presented as mean values with standard deviations or median values with interquartile ranges or counts and percentages as appropriate. Results are reported as point estimates with 95% confidence intervals (CI). There was no adjustment for multiplicity and should not be used to infer treatment effects. Complete case analyses were conducted for all outcomes except for disabling stroke, where missing modified Rankin Scale scores at 6 to 8 weeks were imputed using the last observation carried forward approach. Post-hoc analyses using multiple imputation, best-case and worst-case approaches were also used. All analyses were conducted using Stata software, version 17.0 (StataCorp).

RESULTS

Patients and enrollment

Between October 29, 2020 and October 9, 2024, 7635 participants were randomly assigned to CEP (3815 participants) or the control group (3820 participants) (Figure 1 and Table S1). A total of 17 participants were withdrawn from each group resulting in the modified intention-to-treat population. The baseline demographics, clinical characteristics and procedural details are shown in Table 1 and Table S2 and appeared balanced between the groups. The mean ±SD age of patients was 81.2±6.5 years and 38.7% were female. Overall, the trial cohort was representative of the UK population of patients undergoing TAVI (Table S3).

Both filters of the CEP device were fully and correctly deployed for the duration of the procedure in 3058 of 3768 patients (81.2%) assigned to the CEP group (Table S4). At least one filter (either proximal or distal) of the CEP device was fully and correctly deployed for the duration of the procedure in 87.5% of patients assigned to the CEP group.

Outcomes

The incidence of the primary end point of stroke within 72 hours after TAVI or at the time of hospital discharge if sooner occurred in 81 of 3795 patients (2.1%) assigned to the CEP group and 82 of 3799 patients (2.2%) assigned to the control group (difference, -0.02 percentage points; 95% CI, –0.7 to 0.6; P=0.94). Severe stroke occurred in 18 of 3795 patients (0.5%) in the CEP group and 19 of 3799 patients (0.5%) in the control group (difference, 0.0 percentage points; 95% CI, –0.3 to 0.3). Most strokes occurred within 24 hours of the TAVI procedure (Figure S1). Disabling stroke at 6 to 8 weeks after the TAVI procedure occurred in 47 of 3795 patients in the CEP group (1.2%) and 53 of 3799 patients (1.4%) in the control group (difference, -0.2 percentage points; 95% CI, –0.7 to 0.4) (Table 2 and Supplementary appendix). All-cause mortality within 72 hours after the TAVI procedure or at hospital discharge if sooner occurred in 29 of 3795 patients (0.8%) assigned to the CEP group and 26 of 3799 (0.7%) assigned to the control groups (difference, 0.1 percentage points; 95% CI, 0.3 to 0.5). At 8 weeks after the TAVI procedure, 81 of 3793 patients (2.1%) died in the CEP group and 72 of 3798 (1.9%) in the control group. Additional clinical end points are shown in Table 2 and Tables S5 and S6.

Following CACE analysis, the occurrence of both stroke (difference, -0.1 percentage points, 95% CI, -0.9 to 0.7) and disabling stroke (difference, -0.2 percentage points; 95% CI, -0.8 to 0.5) outcomes were similar (Table S7). The results of the pre-specified age and sex adjusted

analyses of the modified intention-to-treat and CACE analyses are shown in Figure S2. The incidence of stroke at 72 hours or hospital discharge if sooner in predefined subgroups is shown in Figure 2.

Adverse Events

Clinical complications and adverse events appeared similar between the CEP and control groups (Table S8 and Table S9). There were 24 serious adverse events among 3798 patients (0.6%) in the CEP group and 13 out of 3803 patients (0.3%) in the control group.
Access site complication rates at 72 hours or at hospital discharge if sooner occurred in 304 of 3772 patients (8.1%) assigned to the CEP group and 290 of 3776 patients (7.7%) assigned to the control group (difference, 0.4 percentage points; 95% CI, –0.8 to 1.6). Access site complications at the site of arterial access for the aortogram after discharge and at 6 to 8 weeks occurred in 27 of 3347 patients (0.8%) in the CEP group and 13 of 3378 patients (0.4%) in the control group (difference, 0.4 percentage points; 95% CI, 0.1 to 0.8); there were 25 minor access site complications in the CEP group and 12 in the control group (Table S10).

DISCUSSION

In the BHF PROTECT-TAVI trial we tested the effect of routine CEP use on the incidence of stroke among patients undergoing TAVI. The overall stroke rate at 72 hours or at hospital discharge if sooner among patients assigned to receive CEP was 2.1% and 2.2% among patients assigned to the control group. There was no substantial difference among patients assigned to the CEP group and control group with respect to severe stroke, disabling stroke or death.

The results of the BHF PROTECT-TAVI trial are consistent with the reported results of the PROTECTED TAVR trial, which also showed no evidence of a treatment effect with CEP for the primary outcome of stroke. Although our reported stroke rate was lower than what was observed in the PROTECTED TAVR trial, which had an overall rate of 2.6%,[4] we saw no apparent decrease in the rate of disabling stroke with CEP. In our trial, the stroke rate in the control group was 2.2%, which is higher than the in-hospital stroke rate reported in the national UK TAVI registry (2021-2022, 1.9%; 2022-2023, 1.4%), [16,17] suggesting that stroke events were not underreported in our trial population. In addition, we used a clinical definition of stroke (symptom duration greater than 24 hours), rather than one which incorporates imaging with a shorter duration of symptoms. This may explain the difference in stroke rates and the number of outcome events categorized as a TIA in the two trials: 3 in total in PROTECTED TAVR compared to 31 in BHF PROTECT-TAVI.

In contrast to the PROTECTED TAVR trial, our definition of compliance with CEP device deployment required both device filters to be fully deployed for the duration of the procedure. The eligibility criteria for enrollment in our trial were also less restrictive than for the PROTECTED TAVR trial. This suggests that a larger proportion of patients undergoing

TAVI at our centers were enrolled in the trial and may have included those patients with complex access or aortic arch anatomy that would have been ineligible for enrollment in the PROTECTED TAVR trial. These factors may explain some of the differences in rates of device deployment reported in the two trials.

At the start of our trial, one third of participating centers were experienced with Sentinel CEP implantation. We compared the success of device deployment according to our study criteria for the first 100 cases at each site with subsequent cases and found that they appeared similar as did the rate of stroke (Table S11). We also analyzed the rates of successful device deployment across quartiles of recruitment period by site and found that they appeared similar (Table S12). This suggests that the CEP technology was adopted successfully by the centers and there was no sign of center or operator learning effect.

Instrumental variable regression is an established and increasingly used method to adjust for non-compliance to treatment allocation by estimating the complier average causal effect (CACE).[14,15] In BHF PROTECT-TAVI, the CACE analysis did not demonstrate any difference in outcome by treatment group.

Our study has other limitations. While consecutive patient enrollment was encouraged, the trial was ongoing during the COVID–19 pandemic, which impacted clinical research activity in the UK. Despite efforts to promote diverse recruitment, the majority of patients in our study were White and patients from minority ethnic groups were underrepresented in the trial.

In conclusion, among patients undergoing TAVI, routine use of CEP did not decrease the incidence of stroke at 72 hours.

Support Statement:

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Legend

Figure 1: CONSORT - Randomization and Treatment

Figure 2: Incidence of stroke within 72hrs after TAVI (or discharge if sooner) according to subgroups

The confidence intervals are not adjusted for multiplicity and should not be used to infer treatment effect.

Table 1: Demographic and clinical characteristics

Characteristic	CEP Group (n = 3798)	Control group (n = 3803)
Demographics		
Age — yr	81.2±6.5	81.3 ±6.5
Female sex — no./total no. (%)	1484/3798 (39.1)	1461/3803 (38.4)
Ethnicity — no./total no. (%)		
Minority ethnic	60/3798 (1.6)	61/3803 (1.6)
White	3547/3798 (93.4)	3543/3803 (93.2)
Not known	191/3798 (5.0)	199/3803 (5.2)
Clinical		
Hypercholesterolemia treated with drugs — no./total no. (%)	2358/3722 (63.4)	2259/3737 (60.4)
Hypertension treated with drugs — no./total no. (%)	2558/3738 (68.4)	2528/3753 (67.4)
Medically treated diabetes — no./total no. (%)	793/3793 (20.9)	767/3798 (20.2)
Prior TIA — no./total no. (%)	319/3762 (8.5)	291/3754 (7.8)
Prior stroke — no./total no. (%)	217/3763 (5.8)	235/3754 (6.3)
Known dementia or cognitive impairment — no./total no. (%)	31/3762 (0.8)	38/3747 (1.0)
Other neurological disease — no./total no. (%)	112/3764 (3.0)	122/3751 (3.3)
Coronary artery disease — no./total no. (%)	1234/3565 (34.6)	1168/3550 (32.9)
History of congestive heart failure — no./total no. (%)	531/3758 (14.1)	482/3765 (12.8)
Previous TAVI — no./total no. (%)	15/3798 (0.4)	17/3801 (0.4)
History of atrial fibrillation or flutter — no./total no. (%)	1256/3751 (33.5)	1269/3753 (33.8)
History of peripheral vascular disease — no./total no. (%)	262/3424 (7.7)	255/3397 (7.5)
Bovine (or other) head and neck vessel anatomy — no./total no. (%)	491/3684 (13.3)	463/3662 (12.6)
Bicuspid valve anatomy — no./total no. (%)	322/3713 (8.7)	305/3727 (8.2)
EuroSCORE II — IQR	2.4 (1.6 to 4.1), n=2896	2.4 (1.6 to 4.0), n=2921
Aortic valve mean gradient (IQR) — mmHg	43 (35 to 53), n=3589	43 (35 to 52), n=3592
LV function — no./total no. (%)		
Good (LVEF ≥50%)	2803/3679 (76.2)	2835/3688 (76.9)
Fair (LVEF 30-49%)	671/3679 (18.2)	662/3688 (18.0)
Poor (LVEF <30%)	205/3679 (5.6)	191/3688 (5.2)
Aortic valve calcification — no./total no. (%)		
Not severe	1946/3734 (52.1)	1911/3720 (51.4)
Severe	1788/3734 (47.9)	1809/3720 (48.6)
LVOT calcification — no./total no. (%)		
Not severe	3565/3709 (96.1)	3574/3710 (96.3)
Severe	144/3709 (3.9)	136/3710 (3.7)

Plus-minus values are mean ±SD.
CEP denotes cerebral embolic protect, LV left ventricular, LVOT left ventricular outflow tract, TAVI transcatheter aortic valve implantation and TIA transient ischemic attack.

Table 2: Primary and secondary outcomes

Outcome	CEP group (n = 3798)	Control group (n = 3803)	Treatment effect (95% CI)
Stroke at 72 hours post-TAVI or discharge (if sooner) — no./total no. (%)	81/3795 (2.1)	82/3799 (2.2)	RD = -0.02 (-0.7 to 0.6) P-value 0.942
			RR = 0.99 (0.73 to 1.34) P-value 0.942
Ischemic stroke	80/3795 (2.1)	82/3799 (2.2)	
Hemorrhagic stroke	1/3795 (0.0)	0/3799 (0.0)	
Disabling stroke at 6-8 weeks post-TAVI*,** — no./total no. (%)	47/3795 (1.2)	53/3799 (1.4)	RD = -0.2 (-0.7 to 0.4)
			RR = 0.89 (0.60 to 1.31)
Ischemic stroke	47/3795 (1.2)	53/3799 (1.4)	
Hemorrhagic stroke	0/3795 (0.0)	0/3799 (0.0)	
Severe stroke at 72 hours post-TAVI or discharge (if sooner)*** — no./total no. (%)	18/3795 (0.5)	19/3799 (0.5)	RD = 0.0 (-0.3 to 0.3)
			RR = 0.95 (0.50 to 1.80)
Ischaemic stroke	18/3795 (0.5)	19/3799 (0.5)	
Haemorrhagic stroke	0/3795 (0.0)	0/3799 (0.0)	
Death at 72 hours post-TAVI or discharge (if sooner) — no./total no. (%)	29/3795 (0.8)	26/3799 (0.7)	RD = 0.1 (-0.3 to 0.5)
			RR = 1.12 (0.66 to 1.89)
Death or stroke at 72 hours post-TAVI or discharge (if sooner) — no./total no. (%)	108/3795 (2.8)	104/3799 (2.7)	RD = 0.1 (-0.6 to 0.8)
			RR = 1.04 (0.80 to 1.36)
Death	29/3795 (0.8)	26/3799 (0.7)	
Non-fatal stroke	79/3795 (2.1)	78/3799 (2.1)	
Death, stroke or TIA at 72 hours post-TAVI or discharge (if sooner) — no./total no. (%)	126/3795 (3.3)	117/3799 (3.1)	RD = 0.2 (-0.6 to 1.0)
			RR = 1.08 (0.84 to 1.38)
Death	29/3795 (0.8)	26/3799 (0.7)	
Non-fatal stroke	79/3795 (2.1)	78/3799 (2.1)	
TIA	18/3795 (0.5)	13/3799 (0.3)	
CEP denotes cerebral embolic protection, CI confidence interval and TAVI transcatheter aortic valve implantation.			

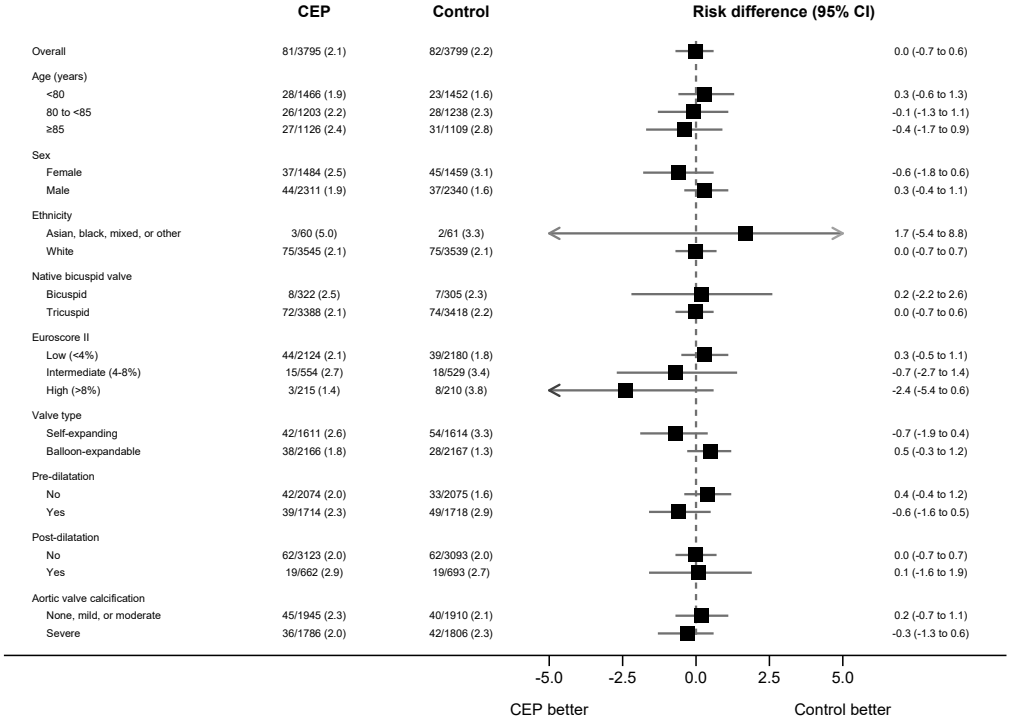
A total of 3 patients withdrew consent before discharge in the CEP group and are excluded; 4 patients withdrew consent before discharge in the Control group and are excluded.

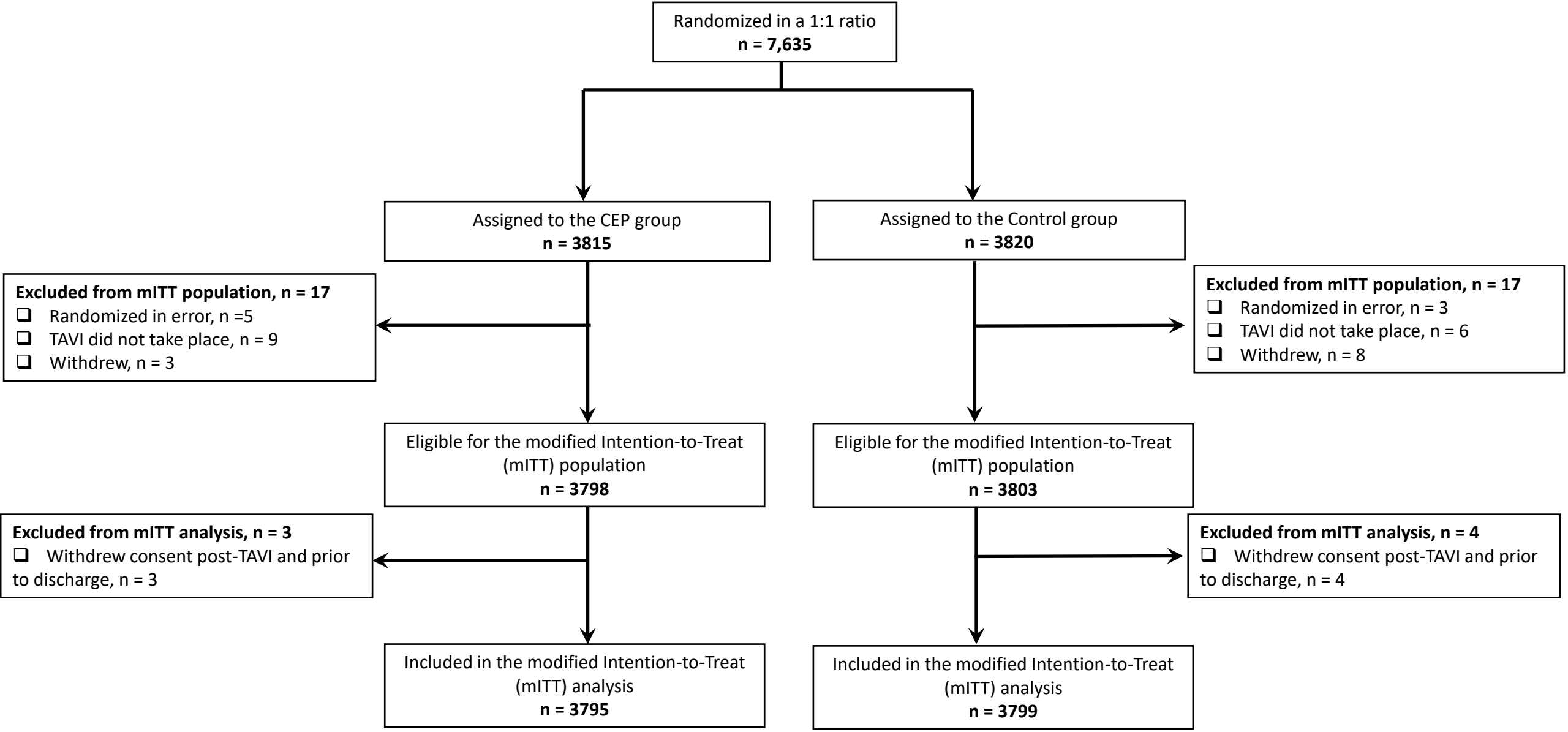
* Disabling stroke was defined as a score on the modified Rankin Scale of ≥2 and an increase of at least 1 point from the pre-procedure baseline modified Rankin Scale score.

**A total of 4 patients required their last observation to be carried forward in the CEP group and 1 required last observation to be carried forward in the control group

***Severe stroke was defined as a NIHSS of ≥10

The confidence intervals are not adjusted for multiplicity and should not be used to infer treatment effect.


CEP
Control
Risk difference (95% CI)
Overall
81/3795 (2.1)
82/3799 (2.2)
0.0 (-0.7 to 0.6)
Age (years)
<80
28/1466 (1.9)
23/1452 (1.6)
0.3 (-0.6 to 1.3)
80 to <85
26/1203 (2.2)
28/1238 (2.3)
-0.1 (-1.3 to 1.1)
≥85
27/1126 (2.4)
31/1109 (2.8)
-0.4 (-1.7 to 0.9)
Sex
Female
37/1484 (2.5)
45/1459 (3.1)
-0.6 (-1.8 to 0.6)
Male
44/2311 (1.9)
37/2340 (1.6)
0.3 (-0.4 to 1.1)
Ethnicity
Asian, black, mixed, or other
3/60 (5.0)
2/61 (3.3)
1.7 (-5.4 to 8.8)
White
75/3545 (2.1)
75/3539 (2.1)
0.0 (-0.7 to 0.7)
Native bicuspid valve
Bicuspid
8/322 (2.5)
7/305 (2.3)
0.2 (-2.2 to 2.6)
Tricuspid
72/3388 (2.1)
74/3418 (2.2)
0.0 (-0.7 to 0.6)
Euroscore II
Low (<4%)
44/2124 (2.1)
39/2180 (1.8)
0.3 (-0.5 to 1.1)
Intermediate (4-8%)
15/554 (2.7)
18/529 (3.4)
-0.7 (-2.7 to 1.4)
High (>8%)
3/215 (1.4)
8/210 (3.8)
-2.4 (-5.4 to 0.6)
Valve type
Self-expanding
42/1611 (2.6)
54/1614 (3.3)
-0.7 (-1.9 to 0.4)
Balloon-expandable
38/2166 (1.8)
28/2167 (1.3)
0.5 (-0.3 to 1.2)
Pre-dilatation
No
42/2074 (2.0)
33/2075 (1.6)
0.4 (-0.4 to 1.2)
Yes
39/1714 (2.3)
49/1718 (2.9)
-0.6 (-1.6 to 0.5)
Post-dilatation
No
62/3123 (2.0)
62/3093 (2.0)
0.0 (-0.7 to 0.7)
Yes
19/662 (2.9)
19/693 (2.7)
0.1 (-1.6 to 1.9)
Aortic valve calcification
None, mild, or moderate
45/1945 (2.3)
40/1910 (2.1)
0.2 (-0.7 to 1.1)
Severe
36/1786 (2.0)
42/1806 (2.3)
-0.3 (-1.3 to 0.6)
-5.0
-2.5
0.0
2.5
5.0
CEP better
Control better


Randomized in a 1:1 ratio
n = 7,635
Assigned to the CEP group
n = 3815
Assigned to the Control group
n = 3820
Excluded from mITT population, n = 17
Randomized in error, n =5
TAVI did not take place, n = 9
Withdrew, n = 3
Excluded from mITT population, n = 17
Randomized in error, n = 3
TAVI did not take place, n = 6
Withdrew, n = 8
Eligible for the modified Intention-to-Treat (mITT) population
n = 3798
Eligible for the modified Intention-to-Treat (mITT) population
n = 3803
Excluded from mITT analysis, n = 3
Withdrew consent post-TAVI and prior to discharge, n = 3
Excluded from mITT analysis, n = 4
Withdrew consent post-TAVI and prior to discharge, n = 4
Included in the modified Intention-to-Treat (mITT) analysis
n = 3795
Included in the modified Intention-to-Treat (mITT) analysis
n = 3799