SENTINEL™ Cerebral Protection System

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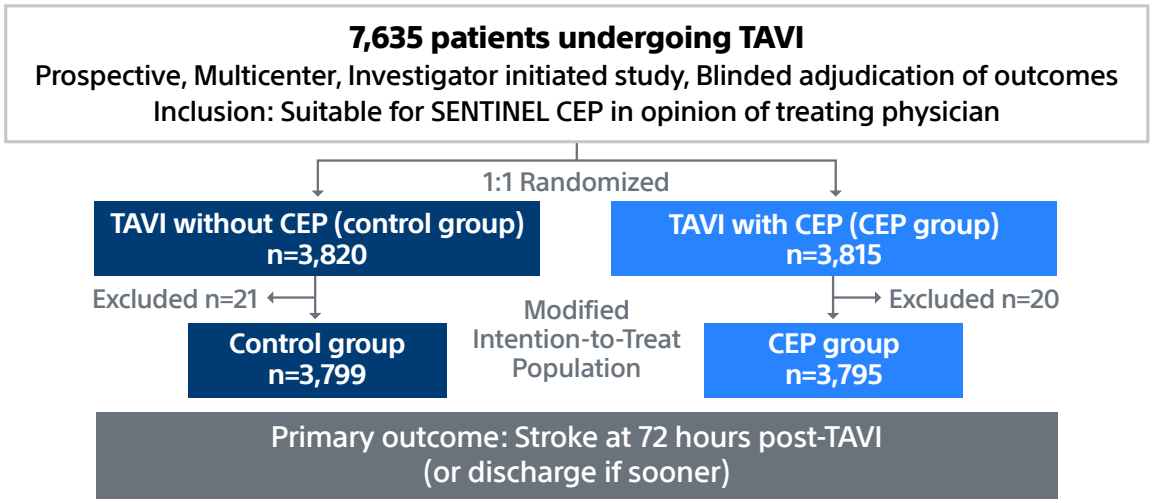
Routine Cerebral Embolic Protection in Transcatheter Aortic Valve Implantation: The British Heart Foundation PROTECT-TAVI Trial[1]

Study Objectives

The British Heart Foundation PROTECT-TAVI (BHF P-TAVI) trial is a United Kingdom-based, prospective, open-label, blinded, outcome-adjudicated, multicenter, randomized, controlled trial that evaluated the routine use of a cerebral embolic protection device – the SENTINEL™ Cerebral Protection System device – to prevent stroke in patients with severe aortic valve stenosis (AS) undergoing TAVI.



BHF PROTECT-TAVI Trial Study Overview

This landmark trial is the largest randomized transcatheter aortic valve implantation (TAVI) trial to date, with 7,635 patients enrolled at more than 30 sites in the United Kingdom who were randomized 1:1 – patients protected with the SENTINEL Cerebral Protection System (CPS) versus no use of the SENTINEL device during TAVI.

- A total of 20 patients from the CEP group and 21 from the control group were withdrawn from the study resulting in the **modified intention-to-treat** (ITT) population (population used to assess the primary endpoint): CEP group n=3,795 and control group n=3,799.
- Standardized training on use of the SENTINEL device was required for sites to be eligible to enroll in the trial.
- The trial enrolled patients with AS who were scheduled to undergo TAVI, and in the opinion of the treating physician, were clinically and anatomically suitable for treatment with the SENTINEL device.
  - o There was no mandated screening of the aortic arch anatomy and patient selection was left to the discretion of the treating physician.
  - o There were no specific exclusion criteria

The **primary outcome** was defined as stroke at 72 hours post-TAVI (or at hospital discharge, if sooner)

- **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 leading to death.
- For patients with a stroke outcome, stroke severity was assessed according to the National Institutes of Health Stroke Scale (NIHSS) at the time of initial assessment; Severe stroke was defined as a NIHSS of 10.
- The level of post-stroke disability was assessed using the modified Rankin Scale (mRS) at 6-8 weeks post-TAVI.
  - o **Disabling stroke** was defined as an mRS of ≥2 and an increase from the pre-procedure baseline mRS of at least 1 point.

Main Study Findings

- Both filters of the CEP device were fully and correctly deployed for the duration of the procedure in 3,058 of 3,768 (81.2%) allocated to CEP group. CEP was not deployed according to the protocol in 710 of 3768 (18.8%) of cases (Table 1).

Table 1

CEP was not deployed according to the protocol	18.8% (710/3768)
• CEP not deployed because of unsuitable anatomy	8.4% (317/3768)
• CEP partially deployed (one filter)	6.3% (239/3768)
• Other including device dislodged or removed before end of the procedure, device failure, emergency complications preventing CEP use, use of the right radial access for the aortogram, lack of trained staff available, and non-specific reasons	4.1% (154/3768)

- The primary and secondary outcomes were assessed in the **modified ITT population** which included **all randomized patients** whose TAVI procedure was started, according to the group to which they were assigned, irrespective of whether they received the intervention as allocated or not.
  - o Baseline demographics, clinical characteristics, and procedural details were balanced between the TAVI with CEP and control groups:
    - Mean age 81.2 years, female sex 38.7%, median EuroSCORE II 2.4%.
  - o The incidence of the primary outcome of stroke at 72 hours post-TAVI or at discharge (if sooner) was comparable among both groups (refer to Figure 1).
  - o The incidence of secondary outcomes of disabling stroke (within 6-8 weeks), as well as death, non-fatal stroke, and transient ischemic attack (TIA) within 72 hours or discharge (if sooner) were also comparable among both groups (refer to Figure 2).

Figure 1

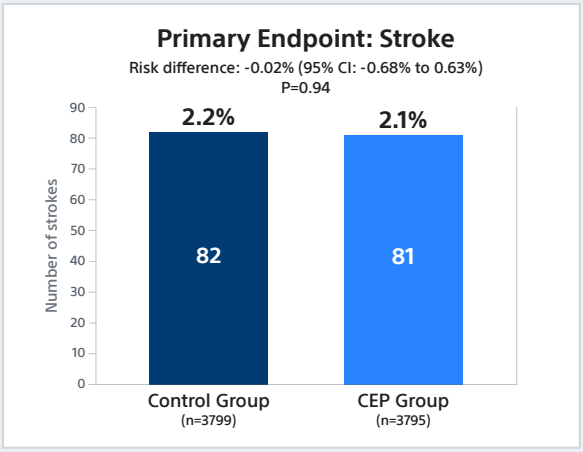
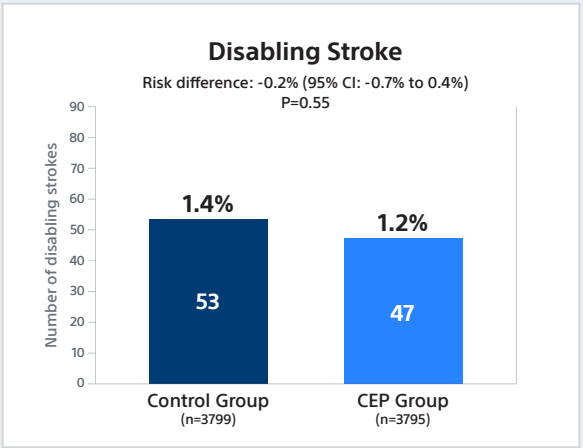
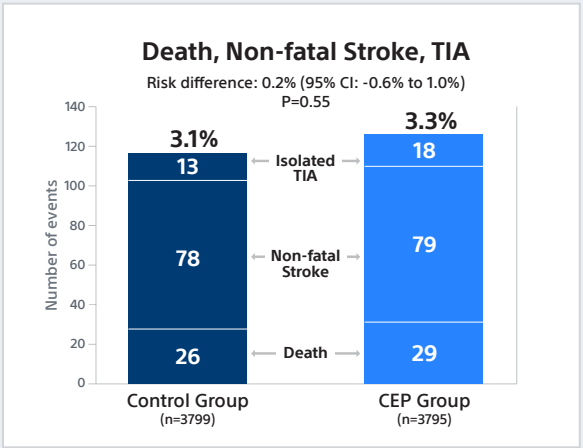


Figure 2





Main Study Findings - Continued

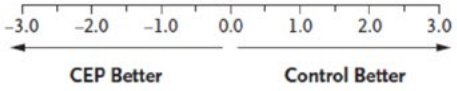
- o Clinical complications and adverse events were similar between the CEP and control groups (refer to Table 2 below).
  - Serious adverse events occurred in 24 of 3,798 patients (0.6%) in the CEP group and 13 of 3,803 patients (0.3%) in the control group.
    - The higher number of adverse events in the CEP group was mainly driven by COVID-19, fall or accidental injury, gastrointestinal or abdominal, infection, procedural complication (4 cases), and respiratory. Only three cases were of cardiovascular-related causes.

Table 2	Control Group (n=3799)	CEP Group (n=3795)	Treatment effect (95% confidence interval)
Access site related complications at 72 hours or at hospital discharge	7.7% (290/3776)	8.1% (304/3772)	0.4 (-0.8 to 1.6)
Access site for CEP (VARC minor) at discharge	0	1.1% (42/3772)	–
Access site related complications between discharge and 6-8 weeks post-TAVI	2.7% (92/3378)	3.3% (109/3347)	0.5 (-0.3 to 1.3)
Access site for CEP (VARC minor) between discharge and 6-8 weeks	0	0.7% (24/3347)	–

- To address non-compliance with the allocated treatment (being use CEP or no CEP), researchers used a method called **Complier Average Causal Effect (CACE)** where they predicted how likely patients were to receive treatment based on their original assignment (receive CEP or not receive CEP), and used this prediction to measure the treatments' actual effect on the primary outcome (will use of CEP reduce or not reduce stroke). This method helps to provide a more accurate estimate of the treatments' real impact.
  - o The CACE analysis did not demonstrate any difference in outcome between the two treatments groups.
    - Occurrence of all-stroke (difference -0.1%, 95% confidence interval – 0.9% to 0.7%).
    - Occurrence of disabling stroke (difference -0.2%; 95% confidence interval -0.8% to 0.5%).

- A pre-specified subgroup analysis was performed to identify an interaction between the randomized treatment and any specific patient subgroup (including an adjudication for age and sex). Results showed that the incidence of stroke at 72 hours, or hospital discharge if sooner, was similar between both groups.

Subgroup	CEP	Control	Risk Difference (95% CI)
	no. of events/no. of participants (%)		*percentage points*
All participants	81/3795 (2.1)	82/3799 (2.2)	0.0 (–0.7 to 0.6)
Age			
<80 yr	28/1466 (1.9)	23/1452 (1.6)	0.3 (–0.6 to 1.3)
80 to <85 yr	26/1203 (2.2)	28/1238 (2.3)	–0.1 (–1.3 to 1.1)
≥85 yr	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)
Race or ethnic group			
White	75/3545 (2.1)	75/3539 (2.1)	0.0 (–0.7 to 0.7)
Asian, Black, multiracial, or other	3/60 (5.0)	2/61 (3.3)	1.7 (–5.4 to 8.8)
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 to 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)
Type of valve			
Self-expanding valve	42/1611 (2.6)	54/1614 (3.3)	–0.7 (–1.9 to 0.4)
Balloon-expanding valve	38/2166 (1.8)	28/2167 (1.3)	0.5 (–0.3 to 1.2)
Predilatation procedure			
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)
Postdilatation procedure			
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)



Study Conclusions

- In the study population, routine use of the SENTINEL device in patients undergoing TAVI was not effective in reducing stroke.
- Additional clinical data is needed to identify which patient sub-groups are at a higher risk of stroke.

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1. Kharbanda RK. Et al. Routine Cerebral Embolic Protection during Transcatheter Aortic- Valve Implantation. *NEJM*. 2025.

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