Transcatheter aortic valve replacement (TAVR) is a minimally invasive procedure to treat severe aortic stenosis in patients with intermediate or high risk for complications from surgical aortic valve replacement. Despite continuing advancements to this increasingly popular procedure, post-TAVR stroke remains a major source of safety concern for patients undergoing implantation, occurring in between 4.3 to 8.2% of cases within one-year of follow-up (Bjursten, H., Norrving, B. & Ragnarsson, S, 2021). The Sentinel cerebral embolic protection device (EPD), (Boston Scientific,) was given FDA De Novo clearance in 2017.

Although its goal is to decrease risk of procedural stroke by capturing calcific embolized debris, preventing them from escaping into cerebral circulation, Sentinel device has failed to show benefit in preventing stroke. In the SENTINEL RCT trial of 363 patients undergoing TAVR, there was no difference in lesion volume or in rate of major adverse cardiac/cerebrovascular event between the device and no-device arm. Despite the lack of any RCT showing benefit for the Sentinel device in stroke prevention, Sentinel wascleared by the FDA as a cerebral embolic protection device. Several other similar devices are currently being developed, including Embrella (Edwards Lifescience) and TriGUARD (Keystone Heart Ltd).

Additional post marketing data from use of Sentinel EPD, finds lack of benefit for risk of post-procedure stroke for patients undergoing TAVR. Observational data of 10,985 patients who underwent TAVR showed that the stroke or transient ischemic attack occurred in 2.2% of the patients in the no-EPD group and 1.8% of patients in the EPD group (p=0.15) (Alkhouli, et al., 2020). While mean length of stay was found to be longer in the no-EPD group (5.0 vs 4.1 days, p<0.001), the mean burden of procedural costs and total costs were higher for patients in the EPD group. These results are particularly concerning considering the growing use of these devices during TAVR procedures, with the proportion of hospitals using EPDs expanding from 8.6% in quarter 3 of 2017 to 32.4.3% in quarter 4 of 2018 and proportion of TAVR patients receiving EPD implantation increasing from 2.8% to 17.3% between that same time period (Alkhouli, et al., 2020). Additionally, an analysis from the Transcatheter Valve Therapy Registry found no association between the use of embolic protection devices and in-hospital stroke when using an instrumental variable model (adjusted relative risk, 0.90 [95% CI, 0.68–1.13]; absolute risk difference, −0.15% [95% CI, −0.49 to 0.20])

TriGUARD 3 is the newest EPD currently seeking FDA 510(k) clearance. This device, designed to block all three of the cerebral vessels during TAVR procedures has stark and concerning similarities to its predicate device, the Sentinel, in the lack of evidence for clinical outcome benefit. In the REFLECT II trial, the 30-day stroke rate was 8.3% in the EPD-group vs 5.3% in the control group (P = 0.57) and bleeding and major vascular complications occurred at 5.7% and 7.0% in the EPD-group, with none occurring in the control group. Patients in the EPD-group saw no benefit for all-cause 30-day mortality and stroke (combined mortality and stroke rate of 9.8% in device-group vs 6.7% in control group; P = 0.475), as well as worse scores on the NIH Stroke Scale prior to discharge (14.1% vs 7.6%; P = 0.176) and no significant difference in cerebral lesion volume (215.39 vs 188.09 mm^3; P = 0.405). Efficacy analysis of the data showed that the use of TriGUARD 3 resulted in no advantage over non-EPD protected TAVR procedure, with results showing absence of improvement in adverse event rate, stroke symptoms, and burden of cerebral lesions. Given that the Sentinel device has not demonstrated a benefit on clinical

outcomes, there is significant concern about similar devices, such as the TriGUARD 3, providing clinical benefit.

With the results from the REFLECT II trial demonstrating no evidence for clinical outcome benefit in TAVR patients, and numerically higher rates for stroke risk, mortality, bleeding risk, and other dangerous adverse complications among those treated, it is concerning and dangerous for patient safety that the TriGUARD 3 cerebral embolic protection device is being considered for FDA 510(k) clearance. Data showing clinical outcome benefit (not on surrogate imaging endpoints) from embolic protection devices are unequivocally necessary to justify its FDA authorization – which should not be through 510(k) clearance - and any clinical use. Currently, patients are exposed to harms of insertion without any realistic expectation of benefit. For patient interest, all cerebral embolic protection devices should only reach market after showing clinical benefit in stroke reduction at one year post procedure. And these devices should be correctly classified as Class III, as they are high-risk devices with serious adverse events, including death, associated with their use.

References:

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