“All patients” should receive cerebral protection when undergoing TAVI procedures

Data indicate that patients who undergo TAVI with the Sentinel Cerebral Protection System (Claret Medical) have a significantly higher rate of stroke-free survival than do patients who undergo TAVI without the device. Furthermore, data also suggest Sentinel captures debris in 99% of patients; for this reason, Sanjir Kapadia (Cleveland Clinic, Cleveland, USA) believes that the device should be used in all patients.

The risk of stroke after TAVI is an ongoing concern. While newer generation TAVI devices are associated with a lower risk of stroke than are first-generation devices, the risk of stroke after TAVI is still higher than it is after surgery (in inoperable/high-risk patients). Kapadia observes that this risk is now a “still significant” 3.5% (major stroke 2%).

Kapadia and colleagues1 report in the Journal of the American College of Cardiology that stroke “remains a concerning complication”. They add that clinically “silent” brain infarctions—as seen on MRI—occur in “as many as 80% of patients” after TAVI. They observe that these “are associated with neurocognitive function changes”. “Although the aetiology of strokes and MRI perfusion abnormalities is multifactorial, most are the result of embolisation of debris during the procedure,” the authors add.

The Sentinel device, which is now both CE marked and US FDA cleared, was designed to provide cerebral protection when undergoing TAVI procedures. The Sentinel device, which has been demonstrated in several studies. Evidence base

In CLEAN TAVI1 100 surgically high-risk patients undergoing TAVI at the Heart Center, Leipzig, Germany were randomised to receive cerebral protection (50 patients) or no cerebral protection (50 patients). The primary endpoint was the numerical difference in new positive post-procedure diffusion-weighted MRI (DW-MRI) two days after TAVI in protected territories. The investigators, writing in the Journal of the American Medical Association, Stephan Haussig (University of Leipzig, Heart Center, Leipzig, Germany) and others report that the Sentinel device was associated with a significantly fewer new lesions: 4 vs. 10 for the no cerebral protection group (p=0.001). New lesion volume (a secondary endpoint) was also 54% lower: 242 mm³ vs. 527 mm³ for the control group (p<0.01).

Concluding their findings, Haussig et al observe that the use of the SENTINEL device did reduce the frequency of ischaemic cerebral lesions in protected areas. However, they do state that larger studies “are needed to assess the effect of a cerebral protection device on neurologic and cognitive function after TAVI”.

The aim of the Sentinel randomised controlled trial,1 therefore, was to further examine the safety and efficacy of the SENTINEL device in a larger patient population. In this study, patients were randomised into one of three groups: a safety arm (123; all received the Sentinel device), a device imaging arm (121; all received the Sentinel device), and a control imaging arm (119; no patients received the Sentinel device). Unlike the patients in the two imaging arms, the patients in the safety arm did not undergo MRI after the TAVI procedure. Kapadia et al comment that the patients in this arm did not undergo MRI to allow the investigators to “assess safety without increasing the cost of the trial”.

There were no significant differences in the primary safety endpoint—the rate of major adverse cardiac and cerebrovascular events (MACCE) at 30 days—between the device groups and the control. A secondary clinical primary endpoint was reduction in new lesion volume in protected brain territories (on MRI two to seven days after TAVI) and there were no significant differences between the device-imaging arm and the control-imaging arm in this endpoint.

However, mean new lesion volume was lower in the device-imaging arm compared with the control—imaging arm 102.8 mm³ vs. 178 mm³, respectively. This finding meant that the Sentinel device was actually associated with a 42% reduction in new lesion volume. It was also associated with a significant 63% reduction in all-strokes at 5372 hours (p=0.05).

According to Kapadia et al, several study limitations “likely contributed to the lack of statistical significance” in the reduction of new lesion volume. These include “considerable variance” in MRI-procedure outcomes, few benchmark MRI data on which to base control arm assumption, and the observed new lesion volume and number were less than predicted from CLEAN TAVI. Kapadia summarises these observations by saying “the primary endpoint was underpowered and we did not have enough power to conclusively determine the clinical importance of this endpoint was also unclear”.

In an accompanying editorial2 to the Sentinel study, Azeem Latib (San Raffaele Scientific Institute, Milan, Italy) and Matteo Pagnesi (EMO-GVM, Centro Cuore Columbus, Milan, Italy) note that “idiosyncrasies” may have led to the study not meeting its surrogate imaging endpoint.

They add that pooling study-level data from three randomised controlled trials reviewing the Sentinel device (SENTINEL, CLEAN-TAVI, and MISTRAL-C) provides a total of 314 patients undergoing TAVI with (165) or without the device (149) and cerebral DW-MRI before and after the procedure. “This meta-analysis suggests that the Sentinel dual-filter device significantly reduces total new lesion volume in protected regions by approximately 100mm³ of damaged brain,” Latib and Pagnesi write.

Furthermore, in the Sentinel study, debris was found in filters in 99% of patients, with Kapadia et al reporting that the debris components included “acute thrombus with tissue elements, artery wall, calcification, valve tissue, and foreign materials”. They add: “On average, one in four patients had 25 distinct pieces of debris larger than 0.5 mm in size. Those are visible to the naked eye and can potentially block mid and distal cerebral arteries downstream.” Also, 16% of the patients had debris larger than 2 mm.

Following the publication of the SENTINEL study, Gian Giusto (The Zen and Michael A Wiener Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, New York, USA) published—ina the Journal of American College of Cardiology—an updated systematic review and aggregate data meta-analysis of five randomised controlled trials (including SENTINEL) of embolic protection during TAVI. Of 625 patients included in the meta-analysis, 376 had been randomised to embolic protection (various devices) and 249 had not. Giustino et al found that embolic protection was associated with a significantly lower risk of stroke or death, corresponding to an approximate 4% absolute reduced risk of stroke (with a number needed to treat of 22). The authors conclude: “The totality of the data suggests that use of embolic protection during TAVI appears to be associated with a significant reduction in death or stroke.”

A real-world study,3 also published after SENTINEL, provided further insights into the safety and efficacy of the device. It showed that using the Sentinel device alongside TAVI is associated with a significantly higher rate of stroke-free survival than is performing TAVI without the device. Overall, the device was associated with a 70% relative risk reduction in stroke/death.

On the basis of the current evidence base, Kapadia told CardioVascular News that identifying a “high-risk” population that would benefit the most from cerebral protection is difficult. Therefore, he says, “all patients need the device” given that debris was found in filters of nearly all patients—regardless of valve type or STS risk score—who received a device in the SENTINEL study.

References

Sarrir Kapadia

ADVERTORIAL
SENTINEL Cerebral Protection System (CPS)

INDICATIONS FOR USE: The Sentinel Cerebral Protection System is indicated for use as an embolic protection device to capture and remove thrombus/debris while performing transcatheter aortic valve replacement procedures. The diameters of the arteries at the site of filter placement should be between 9 – 15 mm for the brachiocephalic and 6.5 – 10 mm in the left common carotid. CONTRAINDICATIONS • Do not use in patients for whom anticoagulant and antiplatelet therapy is contraindicated. • Do not use in patients with a known hypersensitivity to nickel-titanium. • Do not use in vessels with excessive tortuosity. • Do not use in patients with uncorrected bleeding disorders. • Do not use in patients with compromised blood flow to the right upper extremity. • Do not use in patients who have arterial stenosis >70% in either the left common carotid artery or the brachiocephalic artery. • Do not use in patients whose brachiocephalic or left carotid artery reveals significant stenosis, ectasia, dissection, or aneurism at the aortic ostium or within 3 cm of the aortic ostium. WARNINGS • Carefully read all instructions and labeling prior to use. Observe all warnings, cautions, and precautions noted throughout these instructions. Failure to do so may result in complications. • Refer to the instructions for use supplied with any interventional devices to be used in conjunction with the Sentinel System for their intended uses, sizing, warnings, and precautions. • The safety and effectiveness of the Sentinel System have not been demonstrated with transcatheter aortic valves other than the SAPIEN XT, SAPIEN 3, CoreValve,® and CoreValve-Evolut R®. • The appropriate antiplatelet/anticoagulation therapy should be administered pre- and post-procedure in accordance with standard medical practice. • Prior to use, the packaging and product should be inspected for signs of damage. Never use a damaged product or product from a damaged package. • Never advance or withdraw the Sentinel System without proper fluoroscopic guidance or against resistance until the cause is determined. Advancing with such resistance may lead to embolization of debris, and vessel and/or device damage. • It is recommended that the patency of the right radial or brachial artery be assessed prior to the introduction of the Sentinel System. • It is recommended that the patient be tested for occlusion of the radial or brachial artery prior to device introduction. • Do not use the device in left radial or left brachial access. • Do not use the Sentinel System to deliver any type of fluid to the patient e.g. contrast media, heparinized saline, etc. due to risk of air embolization and comprise to device performance. • Minimize movement of the Sentinel System after initial placement and stabilize the patient’s right arm by their side. Excessive movement of filters may lead to embolization of debris, vessel and/or device damage. • Do not deploy the filters within a previously repaired artery, an artery that has been used for dialysis purposes, or an AV fistula. • Observe the Sentinel System under fluoroscopy and monitor the patient to verify the filters have not become occluded with debris resulting in slow or no flow. The filters should be recovered if they become occluded or if flow is compromised (See Procedural Use – Retrieval). • Indwell time of the Sentinel System is not to exceed 90 minutes as occlusion could occur, resulting in slow or no flow. • Failure to adequately close off the Flush Ports (Front Handle, Rear Handle) may result in air embolism. • Do not undersize or oversize the filters in relation to the selected vessel diameter. This may result in inadequate vessel wall apposition or incomplete deployment of the filters. (Refer to Sizing Guide, Table 1 in IFU). • Do not apply excessive force to the Sentinel System. This may lead to distal embolization of debris, and vessel and/or device damage. PRECAUTIONS • Do not forcefully bend or reshape the Articulating Sheath of the Sentinel System. This may cause device damage. • A guidewire with excessive stiffness may alter the shape of the Articulating Sheath curve and make cannulation of the left common carotid difficult. • Use of a guidewire with an intermediate coil may result in compromised guidewire movement. • Improper bending of the Sentinel System may damage the catheter. • Do not re-sterilize or reuse on another vessel or patient. ADVERSE EVENTS Possible adverse events associated with Sentinel System use and application procedure include, but are not limited to, the following: • Access site complications • Angina • Aortic dissection • Arrhythmia • Arteriovenous fistula • Atelectasis • Bleeding, operative or post-operative • Cardiac Tamponade • Cardiogenic Shock • Conduction system injury • Congestive Heart Failure (CHF) • Death • Endocarditis • Embolism, including air • Gastrointestinal (GI) bleed • Hematoma • Ischemia (coronary, limb, carotid) • Infection (local or systemic) • Myocardial Infarction (MI) • Nerve injury • Pericardial effusion • Pneumonia • Pulmonary edema • Pulmonary embolism • Respiratory failure • Respiratory insufficiency • Stroke • Vessel injury (e.g., dissection, rupture, perforation, pseudoaneurysm) Adverse events experienced during clinical studies are presented in the Clinical Study Overview section of the Instructions For Use (IFU). Rx Only, CAUTION: Federal Law (USA) restricts this device to sale by or on the order of a physician. SH-608920-AB