Cerebral Protection During Structural Heart Interventions

A discussion on who, when, and why to use cerebral embolic protection.

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Transcatheter aortic valve replacement (TAVR) has matured into a viable treatment for selected patients with severe, degenerative aortic valve stenosis (AS) destined to receive a bioprosthetic valve irrespective of the estimated surgical risk.[1-3] As indicated by recent low-risk trials, TAVR may also serve younger patients (< 75 years old).[3,4] The incidence of TAVR-related neurologic events has waned over time. Yet, an estimated 2.5% risk of disabling stroke remains important given the dreadful consequences for outcome, quality of life, and overall health care expense.[5] Moreover, postprocedural MRI can detect new (often silent) ischemic brain lesions in up to 80% of TAVR patients.[6] This sobering reality should not be trivialized because it is linked to premature neurocognitive decline that may particularly haunt younger patients with fewer comorbidities and longer life expectancy.[7]

Early neurologic events occur predominantly in the first 48 hours after TAVR and are strongly related to procedural factors, such as catheter manipulation and navigation through the arch and ascending aorta, crossing the degenerated stenotic aortic valve, and transcatheter valve deployment.[8] Origin of debris is not only limited to what is liberated from interactions with the aortic valve. Aortic atheroma burden extending into the ascending aorta and arch have been linked to neurologic events in patients with severe AS in general—and undergoing TAVR in particular.[9,10] Histopathologic studies with material captured during TAVR support the sobering reality that dislodgment of debris and embolism to the brain is ubiquitous after TAVR. Its origin is heterogeneous and varies from tissue-derived material (eg, amorphous calcium), collagenous material originating from either the aortic valve or aortic wall, frank valve leaflet and atherosclerotic particles, thrombotic material, myocardial tissue (from wire manipulation in the left ventricle), and foreign body material derived from delivery catheters.[11]

CEREBRAL EMBOLIC PROTECTION DEVICES

Cerebral embolic protection (CEP) devices may reduce the incidence of procedural stroke during TAVR. Deflectors are deployed in the outer curve of the aortic arch to deviate debris away from the brain into the descending aorta. Filters capture debris en route to the brain and allow for its removal from the body. Arguably, most CEP data have been acquired from studies using the Sentinel cerebral protection system (Boston Scientific Corporation). The safety, feasibility, and efficacy of CEP have been tested in multiple randomized trials with surrogate endpoints based on brain MRI and transcranial Doppler ultrasound but have so far been inconclusive for hard clinical neurologic endpoints.[12-14]

The randomized trials of the Sentinel system showed consistent safety and successful deployment ranging from 89% to 100%, including numeric reductions in new ischemic brain lesions by brain MRI. Yet, these studies proved to be underpowered to establish significant reductions in clinical neurologic events or new ischemic brain lesions due to dropout rates for MRI follow-up and overall insufficient sample size. A pooled analysis by Seeger et al, including the three randomized controlled trials using the Sentinel dual-filter system, showed significant reductions in both neurologic events and new ischemic brain lesions. This analysis showed a relative risk reduction for stroke in the range of 70%.[15] Comparable results with a significant reduction in new ischemic brain lesions and better neurocognitive function testing have

also been demonstrated in another, more extensive, meta-analysis.[16]

The filter-based Sentinel system contains a basket filter in the brachiocephalic trunk to protect the right vertebral and common carotid artery and another filter in the left common carotid artery. The left vertebral artery, therefore, remains uncovered but may account for up to 20% of total brain perfusion.[17] Randomized Sentinel trials have indeed suggested that the treatment effect of reduction in new brain injury was restricted to the so-called protected areas and excluded those brain areas at least partially dependent on the left vertebral artery (Figure 1).[12-14]

A mechanistic study that added a third filter to protect the left vertebral artery demonstrated similar types and amounts of debris in the additional filter in all patients treated with TAVR, thereby supporting the concept that additional protection provides complete filter protection to all areas of the brain supplied by the extracranial arteries.[17,18]

Contemporary deflectors promise to protect all routes to the brain by deflecting debris away from the brain. The TriGuard device (Keystone Heart) is the best studied in this regard. The DEFLECT III trial randomized 83 patients in 13 centers in Europe and Israel to TriGuard protection versus no protection. Complete brain protection with coverage of the entire aortic arch was achieved in 88.9% (40/45) of cases. In patients with established complete three-vessel coverage, TriGuard reduced new ischemic brain lesions (26.9% vs 11.5%), fewer new neurologic events, and better results in selected neurocognitive performance metrics at 30 days.[19] The REFLECT trial (NCT02536196) randomized 478 patients 2:1 to the latest TriGuard iteration (TriGuard 3) versus no embolic protection, and it completed study enrollment in June 2019. Trial results are anticipated later in 2020.

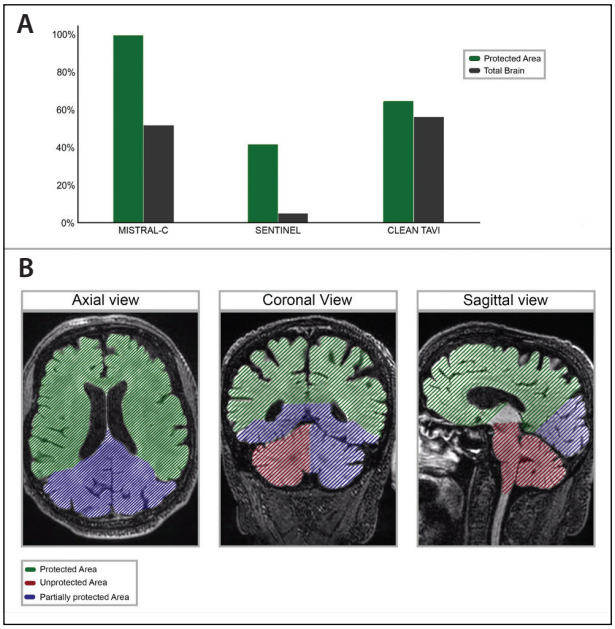

Figure 1. Partial versus complete brain protection. An overview of the reduction in new ischemic brain lesions between the protected area and the total brain in the three studies using the Sentinel device (A). An MRI overview of the protected, partially protected, and unprotected areas of the brain (B).

CURRENT PERSPECTIVES

Global TAVR adoption and expansion to new patient populations—notably, low-risk patients who are younger with fewer comorbidities and longer life expectancy—demands enhanced procedural safety. Although rates of stroke have decreased over the last decade, its implications are devastating.[8] In addition, the almost universal appearance of brain injury after TAVR, as demonstrated by MRI, is particularly worrisome because at first glance, these silent lesions may be linked to postprocedural delirium and premature neurocognitive decline.[7,20] The mechanistic concept of using CEP to prevent debris from reaching the brain using filters or deflectors is sound and undisputed. However, the clinical implications of these procedure-related emboli seem more controversial. The current evidence relies on retrospective clinical data and meta-analyses of underpowered randomized trials with surrogate MRI endpoints. The lack of randomized trials that are properly powered for hard clinical endpoints impedes the adoption of CEP in clinical practice and divides the clinical community into believers and nonbelievers in this technology.

In an attempt to settle the debate, the PROTECTED TAVR trial (NCT04149535) will randomize 1:1 approximately 3,000 patients undergoing TAVR to filter-based Sentinel CEP or control arms and seems appropriately powered for clinically relevant neurologic endpoints. ■

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