EDITORIAL COMMENT

How Embolism Proof Is the Embrella Embolic Deflector System?*

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Updated guidelines on valvular heart disease from both sides of the Atlantic have endorsed transcatheter aortic valve replacement (TAVR) for treatment of symptomatic patients with severe aortic valve stenosis (AS) at (very) high risk for post-operative mortality (1,2). Following the publication of the PARTNER (Placement of AoRtic TraNs cathETer Valves) Cohorts A and B randomized trial results, the stigma of excessive cerebrovascular events was associated with TAVR (3,4). Of note, the difference in major or disabling stroke between TAVR and surgical aortic valve replacement (SAVR) never was significant, and after 3 years, the overall number of cerebrovascular events in both treatment arms converged. Earlier this year, the U.S. CoreValve High Risk Study wiped this apparent inaccuracy away because there appeared numerically even fewer cerebrovascular events in the TAVR arm as compared with SAVR at both 30 days and 1 year (5). Case closed? Probably not! Major or disabling stroke rates of 3.8% and 5% in PARTNER Cohorts A and B, respectively, and 2.3% and 3.9% in the U.S. CoreValve Extreme Risk and High Risk studies should not be taken for granted, and efforts to reduce stroke rates to an absolute minimum should be encouraged (3–6).

Crossing a degenerated aortic valve with any kind of guidewire or catheter is associated with a definite risk of mostly subclinical cerebral embolization, and systematic diffusion-weighted brain magnetic resonance imaging (DW-MRI) examination after TAVR revealed new ischemic brain lesions in approximately 80% of patients, double what is reported after SAVR (7–9). These, at first glance, subclinical events may not be so innocent because neurocognitive decline and premature dementia are linked to silent brain infarcts (10). Especially because the TAVR technology is shifting to lower-risk and thus younger patient populations, these astronomical numbers of MRI-detected brain (micro-)infarcts post-TAVR can hardly be acceptable. The disclosure of the histopathology of what exactly embolizes to the brain during TAVR could help focus research efforts (11). Intuitively, it makes sense to install a barrier at the origin of the major brain arteries and filter or deflect debris stemming from atherosclerotic plaques or the aortic valve.

This issue of JACC: Cardiovascular Interventions features the PROTAVI-C pilot study (12), which assessed procedural safety, technical feasibility, and efficacy of the Embrella Embolic Deflector (EED) system (Edwards Lifesciences, Irvine, California). The study follows prior publications on safety and feasibility of other embolic protection devices (13,14). A total of 42 patients underwent TAVR while receiving the EED device and were compared with 12 patients who underwent TAVR without EED. The EED appeared user friendly. All attempts to implant the device were successful without extending the overall TAVR procedure time (median time to deploy the EED system was just 2 min). The target ostia of the brachiocephalic trunk and left common carotid were covered in all but 1 patient.

All but 2 patients had a DW-MRI at baseline and per-procedural transcranial Doppler (TCD) monitoring. The high rate of successful TCD recordings is remarkable and somewhat unexpected, given the mean age of the study population (well above 80 years of age). In our TAVR practice, suboptimal acoustic windows preclude interpretable TCD signals in a considerable number of octogenarians.

*Editorials published in JACC: Cardiovascular Interventions reflect the views of the authors and do not necessarily represent the views of JACC: Cardiovascular Interventions or the American College of Cardiology.

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Nonetheless, the TCD data corroborated previous TCD insights that transcatheter valve positioning and implantation were associated with the majority of high-intensity transient signals (HITS). The impact of EED use on TCD findings is sobering: the total number of HITS was significantly higher in patients with EED, and the introduction of the EED was associated with more HITS than specific TAVR-related maneuvers such as balloon valvuloplasty or the navigation of the transcatheter valve delivery system across the aortic arch.

Follow-up DW-MRI within 7 days was performed in 80% (34 of 42) of patients in the EED cohort and in 50% (6 of 12) of the control group and in 62% and 42% at 30 days, respectively. MRI findings within 1 week of the procedure confirm previous reports that cerebral embolization is simply ubiquitous in patients undergoing TAVR. EED had no impact on the overall ischemic cerebral lesion volume and was associated with at least numerically more new lesions per patient (7.5 vs. 4). Conversely, the median volume per lesion was smaller, but the mean lesion volume per patient was similar. Of note, timing of the first brain MRI post-TAVR varied with a median interval of 3 days (IQR: 2 to 5 days). This may have considerable impact on study results and is a fundamental limitation to the study findings because size and number of lesions could change considerably between 1 and 7 days post-procedure. Also the field strength of the MRI scanners was not mentioned. It would make a difference if a 1.5-T or a 3-T scanner was used. A 3-T scanner is more sensitive and would yield an even higher lesion detection rate.

Remarkably, all lesions had vanished as documented by follow-up MRI at 30 days. How to explain this discrepancy? The MRI compliance rate at 30 days was low, especially in the no-device arm, and precludes any firm conclusions. Indeed Kahlert et al. (9) demonstrated that acquired lesions were still visible by brain MRI 3 months post-TAVR in 20% of patients undergoing TAVR. Conceivably, the high dropout rate in this study may explain why detectable new (micro-) infarcts could have been missed. It’s also important to realize that DW-MRI is highly sensitive in identifying cerebral ischemia, yet it may not be easy to discern transiently ischemic brain tissue from completely infarcted tissue at a relatively early stage. Other MRI techniques, for example, perfusion weighted imaging with intravenous gadolinium and transversal fluid-attenuated inversion recovery, can assess cerebral blood dynamics (volume, flow, and so on) and uncover hypoperfusion in much larger areas of tissue than suggested by DW-MRI and thus identify a larger area of tissue at risk for infarction. Most probably, the new brain lesions in this study were relatively small (median lesion volume 30 mm³, IQR: 20 to 50 mm³) and represented brain ischemia, but not infarction, and therefore, not surprisingly, most of the lesions had disappeared by 30 days.

The value of embolic protection in other areas of medicine, for example, carotid stenting is conflicting and definitely not globally accepted. Yet TAVR arguably comes with more thorough tissue instrumenta- tion that could lead to dislodgment of considerable pieces of debris as shown in recent histopathologic studies (11). This may justify some sort of barrier protection. Broadly, 2 embolic protection concepts are under study. The EED and the Triguard (Keystone Heart, Tel Aviv, Israel) are embolic deflectors. The Sentinel cerebral protection system (Claret Medical, Santa Rosa, California) consists of 2 separate filters in the brachiocephalic trunk and the left common carotid artery, respectively, and is an embolic capture device. It has the additional feature of not only capturing debris, but also removing it from the body. The question remains whether use of embolic protection devices during TAVR reduces cerebral embolization and whether embolic deflection would be different from filter-based embolic protection.

One may wonder whether this pilot study on cerebral protection with EED has spurred more controversy than proof of concept. Indeed, the fact that EED did not affect total new brain lesion volume nor changed the mean lesion volume per patient, yet was associated with more HITS by TCD, may suggest futility. The EED may generate a paradoxical increase in microembolic load by disintegrating macroemboli into smaller microemboli that can pass through the pores of the device (100 μm) or through gaps between the EED and the vessel wall. Also, thrombus may form on the device or secondary to arterial wall damage induced by the device, and slow-flow distal to the EED may occur if the pores are obstructed and normal antegrade flow is hampered. Furthermore, the confirmation that these new brain lesions documented by DW-MRI seemed transient does not mean that these lesions are negligible and irrelevant. The truth of the matter is that the brain experienced an ischemic insult, and its definite impact is uncertain.

Rightfully, the authors of the PROTAVI-C Pilot study (12) alluded to the need for larger randomized studies to settle the verdict on EED because for the time being, it is not clear how embolism proof EED really is.

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REFERENCES


KEY WORDS embolic protection, stroke, transcatheter aortic valve replacement