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Embolic protection devices during TAVI – the "proof of the pudding"

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Over the past decade the technique of transcatheter aortic valve implantation (TAVI) has matured into a viable, less invasive treatment option for patients with symptomatic severe aortic stenosis (AS). Arguably, TAVI saves lives in patients with a prohibitive operative risk, promises to reduce post-procedural recovery times and may improve quality of life in selected patients. Given the suboptimal performance of current risk models in predicting an individual patient's operative mortality risk, local Heart Teams carry a responsibility in preserving this rather expensive technology to those patients who would benefit most given their operative risk profile, but also keeping in mind an estimated life expectancy of at least one year.

Multiple registries and the randomised PARTNER trial have consistently demonstrated TAVI may come with an increased risk for post-procedural stroke as compared to surgical aortic valve replacement (SAVR). PARTNER cohorts A and B report TAVI related stroke rates of 5 and 6% respectively, which was consistently higher than the comparator[1,2]. A pooled analysis of 53 studies comprising over 10,000 patients undergoing TAVI showed a procedural stroke (<24 h) rate of 1.5±1.4% with an 3.3±1.8% overall 30-day stroke/TIA and the majority being major strokes (2.9±1.8%)[3]. Brain

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imaging studies with magnetic resonance imaging pre- and post-TAVI have shed additional light on the stroke conundrum by demonstrating new ischaemic brain lesions in the majority of patients undergoing TAVI regardless of which transcatheter access strategy (transfemoral or transapical) is selected[4-6]. Whereas a major stroke can have an immediate devastating impact on a patient's wellbeing, and is associated with increased 1-year mortality, the fate of newly acquired subclinical brain defects as detected by MRI is unclear. Data from the cardiac surgery literature suggest a direct correlation between cognitive decline and the number of such new brain defects[7].

The pathophysiology of ischaemic brain defects after TAVI is multifactorial. Apart from intrinsic patient characteristics such as age, previous stroke, AF and left ventricular dysfunction instrumentation on the way towards as well as in the aortic root, can mobilise debris or stimulate clot formation. Furthermore, cerebral hypoperfusion may result from intraprocedural tachy-pacing manoeuvres, transient low output states or hypovolemia. Insights in 30-day stroke events post-TAVI suggest that half of all neurological events occur more than 24 hours after the procedure[8]. This feeds into the idea that the cause of stroke could be related to a specific patient's susceptibilities and acquired risk factors (e.g., new onset atrial fibrillation) as opposed to mobilisation of atherosclerotic material by wire and catheter manipulations, or calcified valve particles during balloon valvuloplasty or actual bioprosthesis implantation.

Since per-procedural stroke will be predominantly caused by embolisation of various debris into the cerebral circulation, embolic protection devices have been developed to reduce such events. Three different technologies are currently being tested in humans: the Embrella (Edwards Lifesciences, Irvine, CA, USA), the SMT-Shimon Embolic protection Filter or SHEF (SMT Medical, Herzliya Pituach, Israel) and the Claret (Claret Medical, Inc. Santa Rosa, CA, USA). Embrella and SMT-SHEF are so-called embolic deflection devices as their effect is based on a protective shield that deflects embolisms away from the cerebral arteries, the Claret is an

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embolic "capture" device. The Embrella contains a nitinol frame with a heparin coated polyurethane porous membrane mainly covering the brachiocephalic trunk and the left common carotid artery (and partially also the left subclavian artery). The system is 6 Fr compatible and is introduced through right radial/brachial access. The SHEF embolic Deflector consists of a nitinol frame and mesh that is deployed in the aortic arch and covers the main cerebral arteries. The device is 9 Fr compatible and requires femoral arterial access.

In this issue of the Journal, Naber et al report on the first experience with the Claret CE Pro™ (Claret Medical, Inc. Santa Rosa, CA, USA) embolic protection device, the concept of which is familiar to those devices used in percutaneous saphenous vein graft and carotid interventions[9]. The device is introduced via right radial

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or brachial arterial access, and contains two filter baskets attached in series. The proximal filter is deployed first in the truncus brachiocephalicus followed by the distal filter in the left common carotid artery. The authors describe improved technical success with the second generation of the device. Yet there is clear room for improvement since in 13% of procedures the Claret CE Pro™ could not be completely installed and strikingly, despite the fact the device is 6 Fr compatible, the operators preferred brachial over radial access, which led to the need for surgical intervention in two cases of access related brachial pseudoaneurysms. Proof of concept was at least partly illustrated by the macroscopic evidence of captured debris in the retrieved baskets in over half of the patients. Undoubtedly, systematic microscopic analysis of these filters might have yielded a more extensive "catch" of debris. An important limitation of the study is the absence of systematic and protocolised MRI neuro-imaging at baseline and follow-up to discover new TAVI related brain lesions.

Several questions remain unanswered: what is the aetiology of the debris that is captured by the Claret CE Pro™? Will the use of Claret CE Pro™ translate into a reduction of new brain lesions by neuro-imaging? Is there an effect on neurocognitive function? And ultimately, would systematic use of Claret CE Pro™ result in lower incidence of clinical stroke post-TAVI since embolic protection devices like the Claret CE Pro™ can only impact true procedure related embolic neurological events. The relative contribution of procedure induced neuro-embolic events to the global stroke burden in TAVI patients is far from elucidated and therefore the overall impact of embolic protection devices in general and the Claret CE Pro™ remains to be established.

The stroke conundrum associated with TAVI is not trivial, especially if this technology would shift to lower risk and younger patient populations and an increasing number of centres want to offer TAVI to their patients. First, we need to have a better understanding of the pathophysiology of neurological events after TAVI. Second, we may want to know whether the implementation of embolic protection devices and the continuous refinement of the TAVI technology can reduce clinical stroke events to the level of conventional SAVR and third, we need a better understanding on how to minimise the detrimental effects of the learning curve in future centres willing to embark doing TAVI procedures.

Regulatory instances (e.g., the FDA in the USA) and academic research organisations (e.g., Valve Academic Research Consortium – VARC) acknowledge the importance of stroke and advocate for a closer involvement of neurologists to TAVI activities[10]. A thorough neurological assessment should be part of baseline and postoperative care for each TAVI patient. A neurologist should thus be involved before the patient enters the operating room/cathlab. This expert involvement seems essential to getting a better perspective on the true scope of the TAVI-Stroke issue. With respect to this philosophy, a case can be made to invite neurologists to the Heart Team decision-making process to further improve patient selection.

Since randomised data has demonstrated TAVI is associated with more neurological events compared to SAVR, every effort should be made to reduce such devastating complications like major stroke, which dramatically impact on a patient's quality of life. Postoperative new onset atrial fibrillation seems to be associated with neurological events post-TAVI, and warrants careful documentation and appropriate therapeutic action (anticoagulation and cardioversion, if possible). Further downsizing of TAVI device systems, the introduction of next generation antiplatelet and anticoagulant therapies and the systematic use of embolic protection devices may help reduce TAVI related cerebral embolisations.

As always, the best tool we have to understand the true impact of embolic protection devices in preventing TAVI related strokes – and to evaluate whether these devices would justify the additional cost to the already impressive financial price tag of TAVI – is the creation of carefully designed randomised clinical trials.

As always, the "proof of the pudding" will be in the eating…

Conflict of interest statement

The authors have no conflict of interest to declare.

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