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Review article

Embolic Protection Devices During TAVI: Current Evidence and Uncertainties

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ABSTRACT

Transcatheter aortic valve implantation (TAVI) is now the principal therapeutic option in patients with severe aortic stenosis deemed inoperable or at high surgical risk. Implementing TAVI in a lower risk profile population could be limited by relatively high cerebrovascular event rates related to the procedure. Diffusion-weighted magnetic resonance imaging studies have demonstrated the ubiquitous presence of silent embolic cerebral infarcts after TAVI, with some data relating these lesions to subsequent cognitive decline. Embolic protection devices provide a mechanical barrier against debris embolizing to the brain during TAVI. We review the current evidence and ongoing uncertainties faced with the 3 currently available devices (Embrella, TriGuard and Claret) in TAVI. Studies evaluated neurological damage at 3 levels: clinical, subclinical, and cognitive. Feasibility and safety were analyzed for the 3 devices. In terms of efficacy, all studies were exploratory, but none demonstrated significant reductions in clinical event rates. The Embrella and Claret devices demonstrated significant reductions of the total cerebral lesion volume on diffusion-weighted magnetic resonance imaging. Studies evaluating the effects on cognition were also somewhat inconclusive. In conclusion, despite embolic protection devices demonstrating reductions in the total cerebral lesion volume on diffusion-weighted magnetic resonance imaging, the clinical efficacy in terms of preventing stroke/cognitive decline requires confirmation in larger studies.

Dispositivos de protección embólica durante el TAVI: evidencias e incertidumbres actuales

Palabras clave:
Implante percutáneo de la válvula aórtica
Ictus
Resonancia magnética

RESUMEN

El implante percutáneo de válvula aórtica (TAVI) es actualmente la principal opción terapéutica para los pacientes con estenosis aórtica grave considerados inoperables o de alto riesgo quirúrgico. La extensión de las indicaciones del TAVI a una población con un perfil de riesgo inferior puede verse limitada por las tasas relativamente altas de eventos cerebrovasculares asociados a la intervención. Estudios realizados con resonancia magnética cerebral con ponderación de difusión demuestran una alta incidencia de infartos cerebrales subclínicos de probable origen embólico tras el TAVI. Algunos estudios han relacionado estas lesiones con un deterioro cognitivo posterior. Los dispositivos de protección embólica nacen como una protección mecánica para impedir la embolización de partículas de material diverso hacia el cerebro durante la intervención. Se presenta una revisión de la evidencia y las incertidumbres existentes respecto a los tres dispositivos actuales (Embrella, TriGuard y Claret) diseñados específicamente para TAVI. Los estudios realizados tienen carácter exploratorio y evalúan el daño neurológico en tres aspectos: clínico, subclínico y cognitivo. El implante de los tres dispositivos parece viable y seguro. Por lo que respecta a la eficacia, ninguno ha mostrado una reducción significativa de las tasas de eventos clínicos. Sin embargo, los dispositivos Embrella y Claret han mostrado reducciones significativas del volumen total de lesión cerebral en las imágenes de resonancia magnética con ponderación de difusión. Los estudios que han evaluado los efectos en la capacidad cognitiva han mostrado resultados poco concluyentes. En conclusión, a pesar de que los dispositivos de protección embólica muestran reducciones del volumen total de lesión cerebral en la resonancia magnética con ponderación de difusión, la eficacia clínica en prevención del ictus/deterioro cognitivo deberá confirmarse en estudios más amplios.

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Abbreviations

CD: Claret device
CVE: cerebrovascular events
DWI: diffuse weighted magnetic resonance imaging
ED: Embrella Embolic Deflector device
TAVI: transcatheter aortic valve implantation
TG: TriGuard
TIA: transient ischemic attack
TLV: total lesion volume

INTRODUCTION

During the last decade, transcatheter therapies have revolutionized the management of patients with valvulopathy.[1] Currently, transcatheter aortic valve implantation (TAVI) is the principal therapeutic option in patients with severe aortic stenosis considered inoperable or at high risk for open-heart surgery,[2–4] thus having progressively increased the rates of its use with this indication.[5–7] Increasing evidence points toward the effectiveness of TAVI in patients considered at intermediate or even at low surgical risk.[8–10] However, further implementation of TAVI in lower risk patients is limited by the relatively high incidence of neurological events related to TAVI. Despite significant device improvements achieved in recent times, clinical cerebrovascular events (CVEs) remain one of the most dreaded complications post-TAVI. Stroke represents an important source of morbidity and mortality, multiplying by more than 3.5-fold the risk of 30-day mortality and consumption of finite health resources.[11,12]

Earlier TAVI studies highlighted the relevance of neurological events during the peri-procedural period. The PARTNER trial demonstrated a greater incidence of 30-day stroke/transient ischemic attack (TIA) in the TAVI group compared with medically-treated (6.7 vs 1.7%, $P = .03$) and surgical groups (5.5 vs. 2.4%, $P = .04$).[13,14] The U.S. Pivotal CoreValve trial reported a 30-day incidence of stroke/TIA of 4.9% with the CoreValve Self-expanding prosthesis.[15] Eggebrecht et al.[12] published a meta-analysis with more than 10 000 patients who underwent TAVI between 2004 and 2011. The overall 30-day stroke/TIA rate was 3.3%, with the majority being major strokes (2.9%). In addition, TAVI in the intermediate surgical risk population was not associated with a significant reduction in neurological event rates. The recently published PARTNER 2 trial showed the 30-day rate of stroke/TIA to be 6.4% with the use of a second generation SAPIEN XT balloon expandable valve.[10]

Timing of Cerebrovascular Events During TAVI

Cerebrovascular events appear in 2 different scenarios in patients undergoing TAVI: *a)* during the acute phase related to the procedure, and (*b)* during the chronic phase, with a constant rate of new episodes during follow-up. Although the pathogenesis of the acute phase of stroke or TIA following TAVI is likely multifactorial, given the arterial distribution and temporal pattern of peri-procedural brain infarctions, embolization is likely to be the dominant mechanism.[16–18] Nombela-Franco et al.[17] found that 50% of acute phase stroke/TIAs appear within the first 24 hours post-TAVI, suggesting that catheter manipulation in the setting of atherosclerotic-laden aortas and severely calcified aortic valves might play an important role. The remainder of strokes in the acute phase appears after the first 24 hours of the procedure, with a vulnerable period of up to 2 months. In this setting, thromboembolism originating directly from the native-transcatheter heart valve complex *per se*, or as a result of chronic or new atrial fibrillation, likely further contributes to strokes early post-TAVI. Vascular complications, and an increased atherosclerotic burden are other proposed mechanisms. On the other hand, the stroke rate incidence during the chronic phase post-TAVI is similar in patients treated surgically or medically, suggesting that the risk of neurological events in this period is determined by the underlying baseline risk profile of patients with aortic stenosis rather than by factors associated with the procedure.[18–22]

DWI Studies

Clinically overt stroke simply represents the tip of the iceberg in terms of cerebral embolization. The spectrum of cerebrovascular damage following TAVI also involves subclinical cerebral infarcts detected by diffuse weighted magnetic resonance imaging (DWI), which have been related to a potential cognitive decline in the long-term.[23–31]

Cerebral DWI is a technique providing in vivo insights allowing the differentiation of acute from chronic stroke as well as nonspecific white-matter lesions. It is sensitive to changes in the mobility of water molecules from the extracellular to intracellular compartment seen in the early phases of the cascade of ischemic tissue changes. Therefore, DWI provides temporal information, because acute lesions become increasingly hyperintense during the first few days but then attenuate during the subsequent weeks (Figure 1). In addition, DWI has high sensitivity in identifying small ischemic lesions. Moreover, certain imaging patterns, such as multiple cortical or/and subcortical acute infarctions affecting both hemispheres, or anterior and posterior cerebral circulations, strongly suggest a cardiac or aortic source of embolism. However, it is important to keep in mind that such findings do not necessarily prove cerebral ischemia, given that other mechanisms, such as prothrombotic, inflammatory or infectious processes could also provide a similar distribution.[23]

Several studies have demonstrated the near ubiquitous presence of subclinical or silent cerebral lesions detected by DWI following TAVI with a cerebral pattern highly suggestive of an embolic process (Table 1).[24–30] Similarly, transcarotid Doppler studies have shown a high incidence of high-intensity transient signal (HITS) during TAVI, especially during valve positioning and implantation, thus suggesting the importance of embolization during these procedural steps.[31,32] For these reasons, some authors have suggested a likely common origin of these cerebral DWI lesions with those generated by macroemboli that usually result in a clinically overt stroke. Importantly, the scanner potency used (ie, 1.5 T or 3 T), as well as the time point for performing DWI post-TAVI could affect the sensitivity for detecting silent cerebral infarcts, as these lesions tend to disappear over time, being totally absent at 30 days following the procedure.[23,31–33] Therefore, in embolic protection device (EPD) studies, change in the cerebral DWI ischemic total lesion volume (TLV) has been proposed as a surrogate endpoint of clinical stroke.[34,35] However, even though the biological plausibility and cost-rationale of this assumption, it should be confirmed in larger studies. In fact, the current American Heart Association guidelines do not recommend the use of silent cerebral infarcts detected on brain imaging as a surrogate endpoint for stroke studies, unless all study patients undergo standardized imaging at specific time points according to the study protocol.[36,37]

Origin of DWI Cerebral Lesions

Gaseous embolization, an inflammatory state related to cardiac instrumentation, thrombus, or embolization of debris from the

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