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STATE-OF-THE-ART REVIEW

Cerebral Embolic Risk During Transcatheter Mitral Valve Interventions

An Unaddressed and Unmet Clinical Need?

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ABSTRACT

As new transcatheter mitral valve (MV) interventions continuously evolve, potential procedure-related adverse events demand careful investigation. The risk of cerebral embolic damage is ubiquitous in any left-sided structural heart intervention (and potentially linked to long-term neurocognitive sequelae); therefore, efforts to evaluate these aspects in the field of catheter-based MV procedures are justified. Given the peculiarities of MV anatomy, MV disease, and MV procedures, the lessons learned from other transcatheter heart interventions (i.e., transcatheter aortic valve replacement) cannot be directly translated to MV applications. Through a systematic assessment of available evidence, the authors present and discuss procedure- and patient-related factors potentially associated with cerebral embolic risk during catheter-based MV interventions. Given the paucity of available data in this field, future large, dedicated studies are needed to understand whether cerebral embolic injury represents a real clinical issue during MV procedures. (J Am Coll Cardiol Intv 2018;11:517–28) © 2018 by the American College of Cardiology Foundation.

Mitral valve (MV) disease is the most common heart valve disorder, and its most frequent manifestation, mitral regurgitation (MR), affects more than 10% of subjects above the age of 75 years (1). Although open-heart surgery represents the gold standard for the treatment of severe MR, transcatheter MV interventions are emerging as less-invasive options for patients who are inoperable or at high surgical risk (2). These new percutaneous techniques allow both repair/replacement of the native diseased MV and replacement of a degenerating surgical bioprosthesis or failed annuloplasty.

Over the past 10 years, transcatheter aortic valve replacement (TAVR) has become established as a valuable catheter-based option for patients with

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ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

CEP = cerebral embolic protection

DW-MRI = diffusion-weighted magnetic resonance imaging

MAC = mitral annular calcification

MoCA = Montreal Cognitive Assessment

MR = mitral regurgitation

MV = mitral valve

TAVR = transcatheter aortic valve replacement

THV = transcatheter heart valve

TMVI = transcatheter mitral valve implantation

TMVR = transcatheter mitral valve repair

VIR = valve-in-ring

VIV = valve-in-valve

severe aortic stenosis. Rationally, lessons learned during this "TAVR revolution" should be strongly considered when approaching MV treatment and should guide future evaluation of percutaneous MV therapies. As with any other cardiac endovascular procedure, catheter-based MV interventions may be associated with overt or covert cerebral injury, the latter being more frequent and likely linked with long-term neurocognitive disturbances (3,4). Besides the risk of clinically apparent neurological events (5), silent cerebral infarcts are present in the majority of patients (75% to 80%) undergoing TAVR (6); furthermore, when performing TAVR with filter-based cerebral embolic protection (CEP) devices, embolic debris is captured in most (90% to 95%) patients (7,8). These observations should not be overlooked when moving to transcatheter MV procedures, as similar risks are likely associated with any left-sided structural heart intervention.

The aim of this review is intended to analyze and discuss the available evidence concerning cerebral embolic injury during transcatheter MV interventions (repair, replacement, valve-in-valve [VIV], and valve-in-ring [VIR]) in an effort to better understand this potential future clinical need.

TRANSCATHETER MITRAL VALVE REPAIR

Edge-to-edge transcatheter mitral valve repair (TMVR) with the MitraClip device (Abbott Vascular, Menlo Park, California) is the most widely adopted catheter-based strategy to treat MR, with more than 40,000 patients treated worldwide. **Figure 1** shows the rate of clinically overt stroke at short-term (in-hospital or 30-day) follow-up reported in major MitraClip studies (9–17). Details of these studies are reported in **Table 1**. Reported clinically apparent stroke occurs in a very small percentage of patients after MitraClip implantation, with rates ranging from 0.2% to 1.2% and 0.7% to 2.6% for in-hospital and 30-day stroke, respectively.

COVERT CENTRAL NERVOUS SYSTEM INJURY DETECTED BY NEUROIMAGING. Despite the low rate of clinically overt stroke after MitraClip implantation, the risk of covert central nervous system injury detected by neuroimaging (according to the recent definition of the Neurologic Academic Research Consortium [18]) is not negligible. Indeed, a recent study by Blazek et al. (19) evaluated the incidence and features of new cerebral embolic lesions detected by brain diffusion-weighted magnetic resonance imaging (DW-MRI) after MitraClip implantation. This prospective, single-center study included 27 patients with severe, symptomatic MR (functional MR in 67%) undergoing TMVR with the MitraClip device and DW-MRI within 2 days before and 2 to 6 days after the procedure. The study population represented a high-risk cohort with multiple comorbidities (most notably atrial fibrillation [AF] in 67%). Interestingly, new DW-MRI lesions were observed in 23 patients (86%), with 19 (70%) showing multiple lesions in different neurovascular territories of both cerebral hemispheres, strongly suggesting an embolic mechanism. Device time (a marker of procedural complexity) independently predicted a higher number of new lesions in multivariate analysis. No patients showed a significant decline in post-procedural neurocognitive function (as assessed by the Montreal Cognitive Assessment [MoCA] score) compared with baseline; furthermore, although MV calcification on echocardiography and the presence of >3 new DW-MRI lesions were univariate predictors of lower post-procedural MoCA score, pre-procedural MoCA score was the only independent predictor after multivariate analysis. The lack of statistical significance may be related to the small number of patients; nevertheless, this study did not identify a clear relationship between new brain DW-MRI lesions after MitraClip and early neurocognitive impairment.

The study by Blazek et al. (19) allows us to perform a comparison between cerebral DW-MRI lesions detected after MitraClip and those (more extensively studied) after TAVR (6). As shown in **Table 2**, new cerebral lesions are very common after both procedures (MitraClip 86%, TAVR 77.5%) with similar numbers of new lesions per patient. Although such lesions seem to affect both cerebral hemispheres more frequently after MitraClip, total lesion volume is higher after TAVR.

HISTOPATHOLOGIC ANALYSIS OF DEBRIS CAPTURED BY CEP SYSTEMS. An elegant means of investigating neurological risk during transcatheter heart interventions is provided by histopathologic analysis of debris captured by CEP filters used during the procedure. Detailed analysis of debris traveling to the brain allows a logical understanding of the pathophysiology of procedure-related cerebral embolic phenomena. In this context, the recent pioneering study by Frerker et al. (20) reports the first experience of CEP during MitraClip implantation and provides histopathologic analysis of embolic debris potentially responsible for cerebrovascular damage. This