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Cutting-Edge Trials in Structural Heart Disease at The Texas Heart Institute

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Introduction

Mitral and tricuspid valvular disease have been managed surgically; however, multiple transcatheter technologies have diversified the therapeutic arsenal and expanded the number of patients eligible for treatment. These new technologies and active trials currently being performed at The Texas Heart Institute will be highlighted.

Transcatheter Mitral Valve Repair

Transcatheter edge-to-edge repair (TEER) with MitraClip (Abbott Structural Heart) plays an important role in the management of degenerative and functional mitral regurgitation (MR). Despite its success, the limitations of MitraClip include challenging anatomy that may not be amenable to TEER, the common need for multiple devices, risk of device-related mitral stenosis, and a not-trivial rate of residual MR.[1] Delivered via a 22F sheath, the PASCAL device (Edwards Lifesciences) offers several improvements.[2] Its 3-catheter system (including a guide, steerable, and implantation catheter) offers easy maneuverability in 3 independent planes. It has a spacer that fills the interleaflet area, helping reduce regurgitation. Additionally, its relatively larger "clasps" are designed to reduce leaflet stress by better distributing tension. Similar to the latest generation of MitraClip, PASCAL has independent gripper action.

The CLASP IID and CLASP IIF trials randomized patients with degenerative and functional MR, respectively, to PASCAL vs MitraClip. The CLASP IID trial, which has completed enrollment, reported noninferiority of the PASCAL device with relation to procedural safety and effectiveness.[3] It also showed durable reductions in MR to ≤1+ (87.2% at discharge and 83.7% at 6 months in the PASCAL arm; 88.5% at discharge and 71.2% at 6 months in the MitraClip arm). The CLASP IIF trial is currently enrolling.

Transcatheter Mitral Valve Replacement

Compared with TEER, transcatheter mitral valve replacement (TMVR) theoretically offers treatment for complex mitral valvular anatomies, including mixed valvular disease and the potential for lower rates of residual regurgitation.[4] The Intrepid valve (Medtronic) is a promising transcatheter device being studied in the APOLLO trial. Intrepid is designed as a double stent composed of a nitinol mesh, with an inner stent containing a bovine, trileaflet valve and a larger, outer stent that fixates onto the mitral annulus. It is available in 42- and 48-mm outer diameter sizes, with a 54-mm size currently in development.[5] The APOLLO trial initially began as a randomized controlled

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trial comparing transapical TMVR to surgery, but because of developments in TEER technology, has evolved into a single-arm trial of patients who are not candidates for TEER or conventional mitral valve surgery. More recently, a 35F transfemoral delivery platform for the Intrepid system has been developed.

One particularly important complication of TMVR is left ventricular outflow tract obstruction that is caused by displacement of the anterior mitral valve leaflet. Multiple efforts have been made to prevent this complication, including sophisticated computed tomography–based prediction of the neo–left ventricular outflow tract that help guide patient selection and the use of interventional techniques including leaflet laceration and alcohol septal ablation.[6]

Early results of the Intrepid valve show excellent procedural success (96%) with mild or less MR in 100% of patients at a median 173-day follow-up.[5] Whereas the early experience with transapical delivery of the Intrepid valve in a high-risk patient cohort was associated with high mortality (14% at 1 month),[5] the development of a transfemoral delivery platform promises to reduce procedural morbidity and mortality.

Transcatheter Tricuspid Valve Repair

Often labeled the "forgotten valve," tricuspid valvular regurgitation (TVR) is common and associated with substantial morbidity and mortality—as low as 34% survival at 5 years.[7] However, late patient presentation, high comorbidity burden, and a high associated surgical mortality preclude many patients from receiving surgical treatment. Additionally, whether tricuspid valve intervention can improve patient outcomes is unclear because TVR is usually secondary to right ventricular dysfunction rather than being primary valvular disease. Therefore, it may often be a marker of severe disease rather than a pathophysiologic mediator.

Nonetheless, transcatheter technologies are being studied for their potential to improve clinical outcomes of patients with severe TVR. The CLASP-TR trial, in which patients are being randomized to TEER with the PASCAL device vs medical therapy, should provide insight into the natural history of TVR and the utility of intervention.[8] One of the major challenges is imaging. Owing to its more anterior position, clear transesophageal windows of the tricuspid valve are more difficult to obtain than are those with the mitral valve. Whereas the tricuspid valve has traditionally been viewed as trileaflet, tricuspid anatomy is actually quite diverse, often consisting of 4 or even 5 leaflets.[9] New structural imaging guidelines aid in the evaluation of tricuspid valve disease and procedural guidance.[10]

Abbreviations and Acronyms

MR	mitral regurgitation
TEER	transcatheter edge-to-edge repair
TMVR	transcatheter mitral valve replacement
TVR	tricuspid valvular regurgitation

Conclusion

New transcatheter valve repair devices and transcatheter valve replacement technologies hold the promise of increasing the number of patients with structural heart disease who are eligible for transcatheter technologies and may permit more complete, durable responses to treatment; this will hopefully translate into better long-term patient outcomes.

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