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EDITORIAL COMMENT

Transcatheter Mitral Valve Replacement Clears the First Hurdle*

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The impetus for the development of transcatheter therapies for valvular heart disease arises from 2 major factors. First is the expectation that a transcatheter therapy can avoid the risks and discomfort associated with surgery, particularly the use of cardiopulmonary bypass and sternotomy or thoracotomy. Second is the patient's desire to avoid the slower recovery associated with major surgery. However, these factors must be balanced with the efficacy of the transcatheter approach. A transcatheter approach that is less invasive, provides faster patient recovery, and has similar efficacy will always be preferred to a surgical approach. However, a less efficacious approach, even if safer and associated with faster recovery, will require more complex decision-making that takes into account the patient's age, frailty, comorbidities, and goals of care.

The search for a less invasive alternative to surgery for mitral regurgitation (MR) is more than a decade old. The results of this effort have been both disappointing and sobering with only a single device, MitraClip (Abbott Vascular, Santa Clara, California), approved by the Food and Drug Administration for use in selected high-risk patients with primary MR (1).

By contrast, over a similar time period, transcatheter aortic valve replacement (TAVR) has moved rapidly from concept to approval for an increasingly wide spectrum of patients. Fueled by the success of TAVR, those interested in the nonsurgical therapy of MR have gravitated to the hope that transcatheter mitral valve replacement (TMVR) might offer a more efficacious solution than transcatheter repair for the more divergent anatomic etiologies of MR (2).

Initial reports of success with TAVR devices in previously placed annuloplasty rings and surgical prostheses confirmed the feasibility of treating MR with a valve-in-valve approach (3), prompting others to successfully implant TAVR prostheses in a native calcified mitral annulus (4,5). However, a subsequent registry raised the specter of an early mortality as high as 30% and complications including valve embolization, thrombosis, and left ventricular (LV) outflow tract obstruction (6).

On the basis of this background, >30 dedicated TMVR devices are under development with novel insertion, folding, fixation, sealing mechanisms, and deployment approaches (7). Five are being evaluated in U.S. early feasibility studies. Initial results from the largest study to date, investigating the safety and efficacy of 1 of these devices, are reported in this issue of the *Journal* (8).

Muller et al. (8) treated 30 patients at 8 sites who were at high risk for surgery with a transcatheter transapical self-expanding nitinol prosthesis supporting a trileaflet porcine pericardial valve (Tendyne Mitral Valve System, Abbott Vascular, Roseville, Minnesota). The device is reminiscent of the first surgical mitral valve replacement done by Nina Braunwald and Andrew Morrow at the National Institutes of Health in 1960 in which a valve cuff was attached surgically to the annulus and tethers were sewn into individual papillary muscles. Novel aspects of the Tendyne device include an outer D-shape

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with an asymmetric sealing cuff and a braided polyethylene tether that helps to anchor the prosthesis to an apical epicardial pad.

All patients (mean age 76 years, 83% male) had severe or moderately severe MR and a mean Society of Thoracic Surgery predicted risk of mortality at 30 days of 7.3%. The majority (77%) had secondary MR and nearly one-half had LV ejection fractions of <50%. The device was successfully implanted in 28 patients (93%) and was retrieved without complications in the other 2 patients. Grade 0 MR is reported in all but 1 patient. There were no device embolizations, no strokes, and no LV outflow tract obstruction. At 30 days, there was 1 death due to pneumonia and only 1 patient had mild MR. Overall freedom from major adverse events was 83%, and there was significant improvement in New York Heart Association functional class, walk time, and quality of life (8).

These short-term results can be considered remarkable and contrast with case reports of other first-generation devices having worse outcomes, albeit often in compassionately treated subjects with multiple comorbidities. Nonetheless, several warning signals and issues in the present series deserve additional comment. These include 1 case of leaflet thrombosis, a fall in mean LV ejection fraction from 47% to 41%, and paravalvular leak in 1 patient.

The transapical approach has been shown in TAVR trials to affect outcomes adversely (9). One might anticipate even greater unfavorable effects of a transapical incision in patients with a dysfunctional and less hypertrophied LV. Despite the excellent results reported by Muller et al. (8), it is likely that the search will continue for a less invasive (e.g., transseptal or direct atrial) approach, which, if successful, could become a preferred access.

The reported fall in LV ejection fraction requires further investigation. Although it could certainly be the result of MR elimination and increased afterload, the possibility of a reduction in myocardial contractility cannot be excluded. Mitral valve replacement, even with full chordal sparing, is associated with worse LV reverse remodeling than repair. In a recent randomized comparison of mitral valve replacement and repair, LV remodeling was best in patients who received successful repairs as compared with replacement (10). This could be due to less favorable effects of replacement compared with repair on normal LV vortex flow that is aided by the rudder-like effect of the anterior leaflet (11). The apical incision, tether, or prosthesis could also adversely affect the normal LV twisting contraction pattern or, conversely, improve remodeling by shortening the ventricular long axis. How subsequent ventricular remodeling affects tension on the tether over time is unknown. Additional considerations that will require longer follow-up include prosthesis durability, the effects of paravalvular leak, which has been associated with greater mortality in the mitral as compared with the aortic position (12), and the incidence of leaflet and valve thrombus formation. The duration and long-term consequences of anticoagulation will need to be determined.

Even with the early success demonstrated in this report, issues relating to study design and patient population will need to be solved before TMVR can become clinically relevant (13). Phase 2 study investigators will wrestle with the fact that most patients with secondary MR do not have high short-term mortality and, therefore, are frequently medically managed. Overcoming procedural complications of TMVR will be essential to realize the symptomatic benefits in comparison to medical care. Patient comorbidities, both cardiac and noncardiac, could hamper and confound comparative evaluations. For example, the treatment of concomitant tricuspid regurgitation, present in the majority of MR patients, will confound a surgical comparison group that also undergoes a tricuspid annuloplasty. It will be difficult to improve on the efficacy of current surgical repair results for primary MR if such patients are also included in the study population. Finally, the safety of transcatheter mitral repair with the MitraClip for suitable anatomic candidates with primary MR and high surgical risk will be hard to beat.

The multidisciplinary heart team, now established as a Class I indication for the evaluation of complex patients with valvular heart disease, should play a central role in the use of this new technology. This study demonstrates the impressive progress that has occurred in transcatheter mitral valve therapy and sets a high bar for competing technology, but it is only the first hurdle. The opportunity for cardiologists and surgeons to learn from each other, practice together, and improve patient outcomes makes us confident that together we will be able to clear the remaining hurdles in front of us.

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