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EDITORIAL COMMENT

Transcatheter Tricuspid Valve Intervention

The Next Frontier*

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The pioneering work of Dr. Alan Cribier (1) in 2002 ushered in a new era for the treatment of valvular heart disease. In the past decade, transcatheter aortic valve replacement (TAVR) has gone from a difficult, moderately successful procedure (2,3) to a widely adopted intervention that rivals surgical AVR (4,5). Because untreated critical aortic stenosis (AS) is such a lethal condition, a survival advantage of TAVR to the medical therapy was accomplished with 1-year follow-up (6).

The success of TAVR has stimulated attempts at transcatheter mitral valve replacement (TMVR) for percutaneous treatment of mitral regurgitation (MR). This has proven to be far more complex than TAVR. The "D" shape of the mitral annulus, the large width of the orifice, and the potential interaction with the aortic outflow tract have been challenging. Currently, first-in-human testing has begun, and this year will bring forth the first moderately sized trials of transcatheter TMVR (7). Alternately, attempts at transcatheter mitral valve repair have occurred. One such device (MitraClip, Abbott Vascular, Santa Rosa, California) recently received U.S. Food and Drug Administration approval (8). Mitral annulus plication with another device (Mitralign, Tewksbury, Massachusetts) is currently being tested in Europe. This device lacks the precise visualization required to place the pledgets in proper anatomic location. The advances in three-dimensional (3D) transesophageal echocardiographic (TEE) imaging may overcome this problem. A recent trial in Europe investigated the use of the Mitralign device for functional MR in 61 patients, and follow-up data are being collected.

Apart from the daunting technical challenges, proof of efficacy for interventions in chronic, moderate, or severe MR is far more difficult than critical AS. Mechanical reduction or elimination of regurgitation alone is insufficient. Mortality trials will need to study hundreds if not thousands of patients and conduct at least 5 years of follow-up to show benefit. Safety endpoints, such as symptom status and heart failure readmissions, are subject to the placebo effect, and skeptics may demand sham procedures with strict double blinding. Despite these challenges, there is such a large pool of high-risk/inoperable patients with severe MR that within 10 years, it is likely that effective transcatheter therapy will emerge. With transcatheter aortic valve intervention proven and mitral valve intervention emerging, attention will soon turn to the third heart valve that malfunctions in adults: the tricuspid valve.

Tricuspid regurgitation (TR) remains an undertreated problem with substantial morbidity. In the United States alone, <1% of patients with moderate or severe TR undergo surgery annually (9). This is despite a 1-year mortality rate of 36.1%, which has been reported in a Veterans Affairs retrospective study of patients with severe TR (10). For those patients who undergo surgery, recurrence of moderate or severe TR can be as high as 60% at 5 years (11). Therefore, it is not surprising that only 16% of patients with isolated severe TR underwent surgery at 5 years in a recent study (12). Currently, transcatheter interventions for tricuspid valve disease have been restricted primarily to patients with a degenerating bioprosthesis, with mixed results (13,14). The mechanical and clinical challenges of

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tricuspid intervention for severe TR are as daunting as those of severe MR. First, cardiologists do not attempt to quantify the severity of TR during right heart catheterization. Second, imaging with contrast ventriculography or echocardiography has not been standardized and widely promulgated. Standardized methods of quantifying improvement of TR will be required for testing efficacy of interventions. Finally, isolating the impact of TR in the setting of pulmonary hypertension, atrial fibrillation, and left heart pathology is problematic. Despite these challenges, our aging population, the increasing prevalence of atrial fibrillation, the increase in iatrogenic TR from transvenous pacemaker leads, and the likely increase in life expectancy of patients with effectively treated AS and MR will mandate development of transcatheter therapy. Schofer et al. (15) began this long journey with a first step.

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In this issue of the *Journal*, the authors present the first-in-human experience with percutaneous tricuspid valve repair for functional TR (Mitralign system). The procedure was performed with the use of an 8-F deflectable catheter that was advanced into the right ventricle through the internal jugular vein. With the use of 3D TEE guidance, previously a limitation to accurately image the tricuspid valve, a radiofrequency wire was advanced through the tricuspid valve annulus that allowed the placement of two pledgeted sutures around the posterior leaflet. Through direct plication of these sutures with a locking device, the authors performed a modified Kay bicuspidalization of the tricuspid valve. In-hospital results were favorable, with dramatic reductions in right atrial pressures and annular area as measured by means of TEE, with the patient being discharged from the hospital within 5 days (15).

Although off-label use of TAVR technology has been applied to the failing bioprosthesis in the tricuspid valve position (14), percutaneous therapies for direct native tricuspid valve intervention are currently lacking; this is due in part to the lack of a rigid landing zone for valve deployment such as in AS, as well as the variety of annular dimensions that may occur in severe TR. This has recently led to some experience with heterotopic placement of transcatheter aortic valves in the inferior vena cava in those patients with refractory ascites and lower-extremity edema (16,17). Short-term results demonstrating reduction in ascites, hepatic congestion, and peripheral edema are encouraging. Long-term follow-up is needed. Finally, investigators are currently exploring the transjugular use of the MitralClip system to attempt leaflet tethering and decrease functional TR (B. Maini, personal communication, January 2015).

While we enthusiastically wait for effective transcatheter therapy, an increasing population of patients with severe TR exists. In our experience, clinicians may fail to appreciate that severe TR causes portal hypertension and bowel edema, which make oral furosemide therapy ineffective (18). Addition of bumetanide in twice-daily doses of 2 to 10 mg can effectively decrease peripheral edema. Simple measures, such as insisting that patients lie with legs elevated above the heart level, also can be helpful. Finally, recognition that transvenous procedures can cause severe TR in up to 30% of implants may prompt our electrophysiologist colleagues to develop better implant techniques to avoid severe TR. Severe TR is finally getting the recognition that it deserves, and a once-ignored valve pathology may succumb to transcatheter therapy.

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REFERENCES

1. Cribier A, Eltchaninoff H, Bash A, et al. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. Circulation 2002;106:3006–8.

2. Laborde J, Borenstein N, Behr L, et al. Percutaneous implantation of the CoreValve aortic valve prosthesis for patients presenting high risk for surgical valve replacement. EuroIntervention 2006;1:472–4.

3. Schofer J, Colombo A, Klugmann S, et al. Prospective multicenter evaluation of the direct flow medical transcatheter aortic valve. J Am Coll Cardiol 2014;63:763–8.

4. Adams DH, Popma JJ, Reardon MJ, et al., for the US CoreValve Clinical Investigators. Transcatheter aortic-valve replacement with a self-expanding prosthesis. N Engl J Med 2014;370:1790–8.

5. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 2011;364:2187–98.

6. Leon MB, Smith CR, Mack M, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010;363:1597–607.

7. Cheung A, Webb J, Verheye S, et al. Short-term results of transapical transcatheter mitral valve implantation for mitral regurgitation. J Am Coll Cardiol 2014;64:1814–9.

8. Feldman T, Foster E, Glower D, et al. Percutaneous repair or surgery for mitral regurgitation. N Engl J Med 2011;364:1395–406.

9. Stuge O, Liddicoat J. Emerging opportunities for cardiac surgeons within structural heart disease. J Thorac Cardiovasc Surg 2006;132:1258–61.

10. Nath J, Foster E, Heidenreich PA. Impact of tricuspid regurgitation on long-term survival. J Am Coll Cardiol 2004;43:405–9.

11. Kim JB, Jung SH, Choo SJ, et al. Clinical and echocardiographic outcomes after surgery for

severe isolated tricuspid regurgitation. J Thorac Cardiovasc Surg 2013;146:278–84.

12. Topilsky Y, Nkomo VT, Vatury O, et al. Clinical outcome of isolated tricuspid regurgitation. J Am Coll Cardiol Img 2014;7:1185–94.

13. Bentham J, Qureshi S, Eicken A, et al. Early percutaneous valve failure within bioprosthetic tricuspid tissue valve replacements. Catheter Cardiovasc Interv 2013;82:428–35.

14. Roberts PA, Boudjemline Y, Cheatham JP, et al. Percutaneous tricuspid valve replacement in congenital and acquired heart disease. J Am Coll Cardiol 2011;58:117–22.

15. Schofer J, Bijuklic K, Tiburtius C, et al. First-in-human transcatheter tricuspid valve repair in a patient with severely regurgitant tricuspid valve. J Am Coll Cardiol 2015;65:1190–5.

16. Lauten A, Ferrari M, Hekma K, et al. Heterotopic transcatheter tricuspid valve implantation: first-in-man application of a novel approach to tricuspid regurgitation. Eur Heart J 2011;32:1207–13.

17. Laule M, Stangl V, Sanad W, et al. Percutaneous transfemoral management of severe secondary tricuspid regurgitation with Edwards Sapien XT bioprosthesis: first-in-man experience. J Am Coll Cardiol 2013;61:1929–31.

18. Wargo KA, Banta WM. A comprehensive review of the loop diuretics: should furosemide be first line? Ann Pharmacother 2009;43:1836–47.

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