

# Percutaneous Valve Repair and Replacement Challenges Encountered, Challenges Met, Challenges Ahead

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This issue of *Circulation* contains reports on the acute results of 2 approaches for percutaneous heart valve treatment.<sup>1,2</sup> The introduction of nonsurgical, catheter-based approaches to the management of valvular heart disease is in a phase of rapid development. These 2 reports highlight both challenges and successes in phase I experience with these innovative therapies.

### Articles pp 842 and 851

Percutaneous valve therapy developed initially with aortic valve replacement, described by Andersen et al<sup>3</sup> in 1992 in a swine model. These investigators fabricated a stent-mounted bioprosthetic valve and demonstrated that percutaneous implantation is feasible. Bonhoeffer et al<sup>4</sup> reported the use of a stent-mounted bioprosthesis for pulmonic valve replacement in 2000. This achievement clearly marked the beginning of the era of percutaneous valve replacement therapy in patients. Pulmonic valve replacement with this percutaneous approach has been remarkably successful. To date, >100 patients have been treated, with only a single procedure-related mortality and good results in a population of pediatric patients with congenital heart disease who otherwise would face third or fourth open heart procedures. Percutaneous aortic valve replacement with a stent-mounted bioprosthetic valve device was initially reported by Cribier et al<sup>5,6</sup> in 2002, with a growing experience since then.

### Challenges Encountered

Numerous technical and clinical challenges have been encountered during phase I procedures for percutaneous heart valve therapy. The patient population for aortic valve replacement has been a group of patients considered high risk for surgery or nonsurgical candidates with numerous comorbid conditions. These patients have come to the cardiac catheterization laboratory with hypotension and low cardiac output. Under the best circumstances, they represent a great management challenge, even without the demands of new, complex percutaneous procedures. Early mortality in this group has been high, but there have also been stunning successes.

Percutaneous aortic valve replacement was initially accomplished by an antegrade approach, with implantation of the

valve via transseptal delivery through the left atrium, left ventricle, and into the aortic root. The antegrade approach is technically challenging and has been tolerated poorly by some patients. A stiff wire must be delivered via the femoral vein, through the right atrium, across the transseptal puncture, looped in the left ventricle, passed across the aortic valve, and exteriorized from the femoral artery. The degree of mechanical support needed to deliver these large-caliber prostheses is substantial. The transcatheter guidewire may prop open the mitral or aortic valves, causing valvular insufficiency and hemodynamic instability during the procedure. In addition, this therapy has been initially used for patients with end-stage aortic valve disease, who are often in shock or receiving cardiopulmonary resuscitation. There have been poor outcomes from the antegrade procedure in a significant number of patients as a result of this constellation of challenging circumstances.

Therapy for the mitral valve has been complex as well. There is no single therapeutic approach for repair for every etiology of mitral regurgitation. Surgical mitral valve repair represents a group of techniques that are applied depending on the etiology and anatomy of the mitral regurgitation. The first report of mitral valve repair with the use of a percutaneous leaflet technique in humans has recently been published.<sup>7</sup> The development of annuloplasty therapies is now under way, with coronary sinus–based approaches.<sup>8</sup> The coronary sinus parallels the mitral annulus and has been recognized as a conduit for delivery of annuloplasty devices. A number of different percutaneous coronary sinus annuloplasty devices have been used as temporary intraoperative implants. In some cases, despite favorable results in animal testing, intraoperative results have been disappointing and have led to redesign and ongoing testing of some of these devices. This initial effort by Webb et al highlights the challenges to device deployment in patients. It documents negative results due to fracture of the device bridge element in the first reported permanent human implants of coronary sinus annuloplasty devices. The article is especially important because it reports negative results. Fortunately, no complications resulted from device failure. It is important to applaud both the physician team and study sponsor for being forthright in reporting these negative results. Reporting and understanding negative results such as this are critical to guide the safe and ultimately effective progress in the development of coronary sinus annuloplasty technologies.

In contrast to these percutaneous efforts, the early development of surgery for valvular heart disease was performed in a different era. There was no scrutiny of the protocols or methods used to develop early heart valve prostheses and heart-lung machines. There have been almost no randomized

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trials to evaluate any of the surgical approaches in current use. The degree of oversight involved in contemporary percutaneous heart valve trials is substantial. All of the percutaneous trials are being conducted with core laboratory assessment of the echocardiographic and hemodynamic outcomes, data safety monitoring committees, and, for trials in the United States, oversight by the Food and Drug Administration.<sup>9</sup>

### Challenges Met

Mitral valve repair for mitral regurgitation has been performed successfully with the use of a leaflet plication method to create a double-orifice mitral valve.<sup>7</sup> Reduction in the degree of mitral regurgitation and improvement of symptoms have been achieved with this catheter-based, nonsurgical approach. Pulmonic and aortic valve replacement has been accomplished as well.<sup>4–6</sup> A variety of bridges have been crossed to reach this point.

The reports in this issue of *Circulation* describes a retrograde approach for aortic valve replacement with the use of a stent-mounted prosthesis. The ability of patients to tolerate the retrograde approach is clearly better than for the antegrade technique. The major limitation of the approach is the large-caliber arterial access that is required, which requires femoral arterial anatomy that will accommodate a 24F introducer sheath.

Efforts to accomplish percutaneous mitral annuloplasty with other devices are also under way. The Pilot Safety Study of the Cavillon Mitral Contour System for the Treatment of Mitral Regurgitation (COMPETENT) has begun to enroll patients to test experience with the Carillon coronary sinus annuloplasty device, which is fundamentally different in design than the device described in this report by Webb et al. The Carillon has been used successfully in some patient implants. The device described in this issue of *Circulation* by Webb et al has been redesigned, and implantation has resumed. It will obviously require a larger experience to determine the safety, efficacy, and appropriate patient populations for all of these devices under development for mitral repair.

### Challenges Ahead

Aortic valve replacement therapy has advanced slowly, with improvements in both technique and technology. Other percutaneous products are under development in this field. The early human experience with a self-expanding aortic implant, the CoreValve device, was initially poor but has improved rapidly, as both the device and delivery approaches have been modified.<sup>10</sup>

The early results from aortic valve replacement and mitral valve repair procedures illustrate some of the challenges in selecting an appropriate patient population for development of these new devices. The initial patients selected for aortic valve therapy were “no option” patients and in many ways ensured poor clinical outcomes.

Mitral valve leaflet therapy with Evalve MitraClip is now in a phase II randomized trial in comparison with mitral valve repair or replacement surgery. In the Endovascular Valve Edge-to-Edge Repair Study (EVEREST), the surgical arm

allows either valve repair or valve replacement. There is no requirement in the trial for prospective identification of which surgical therapy might be the optimal surgical approach in a given patient. In addition to evaluating the Evalve clip, EVEREST is the first-ever prospective, core laboratory-monitored evaluation of surgical therapy for mitral regurgitation. Prior reports regarding the outcomes of mitral valve repair have not included intention-to-treat analyses. The proportion of patients in whom repair is planned but who ultimately receive mitral valve replacement is not well known. Furthermore, the results of repair are generally reported from single-center experiences and do not have core laboratory- or criteria-based evaluation of mitral regurgitation before and after repair. The American Society for Echocardiography guidelines for evaluation of mitral regurgitation are being used in core laboratories in trials now under way for mitral valve repair technologies.<sup>11</sup> In these controlled trials, the use of echo core laboratories may change the way we understand results from surgical mitral repair in the same way that angiographic core laboratories changed our view of coronary interventional results.

An interesting consideration for percutaneous stent-mounted bioprosthetic implants for valve replacement is the potential for multiple replacements. The durability of a surgically implanted valve must be great. Percutaneous stent-mounted valves have already been re-replaced in the Bonhoeffer experience.<sup>4</sup> Some of these patients initially had a bioprosthetic valve in a Fontan conduit for congenital heart disease. A Bonhoeffer valve was implanted within the initial bioprosthetic valve. A few patients have already undergone re-replacement with a third valve sandwiched inside of this conduit. Thus, the potential for re-replacement on a more frequent basis than we might expect for surgical valve prosthesis is possible, without requiring the same durability of surgical implants. Sequential or staged or combined procedures are conceivable as well for mitral valve repair. It is easily imaginable that a patient might have a leaflet repair with the Alfieri approach with creation of a double-orifice mitral valve and that at the same or a later time the patient might additionally have a percutaneous annuloplasty. Repeated annuloplasty with similar or differing approaches is also possible.

### Conclusion

It is sometimes said that all that is needed for a new device company is a drawing on a cocktail napkin, a patent, and an animation. At that stage of concept and early design development, all new devices appear to offer novel, definitive solutions to important clinical problems. The first stages of animal testing typically amplify the excitement of the design phase. It is only when initial human experience begins that the real limitations of new approaches become apparent. It is unavoidable that unanticipated challenges will arise in the first patients treated with a new device. It is only at this stage that problems can be solved. It is the solution of these problems that ultimately leads to successful therapies. These 2 reports in the current issue of *Circulation* highlight the fact that problems are being solved in this new and exciting field.

## Disclosures

None.

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