During the last 2 decades, percutaneous endovascular therapies have revolutionized the treatment of coronary artery disease. However, the development and dissemination of percutaneous approaches to heart valve disease have been less rapid. Whereas rheumatic mitral stenosis and congenital aortic stenosis are effectively managed by balloon valvuloplasty in many instances,\(^1\,^2\) and pulmonary regurgitation can be treated by percutaneous pulmonary valve insertion,\(^3\) progress with more common valvular lesions—mitral regurgitation and acquired aortic stenosis—requires development of new techniques and technology. Recent advances promise to facilitate application of endovascular therapies for these lesions. Although technological challenges remain, it is likely that many patients with mitral regurgitation and aortic stenosis will soon be candidates for percutaneous heart valve repair or replacement.

**Surgical Management of Heart Valve Disease**

Percutaneous approaches to heart valve disease are modeled upon successful surgical techniques for valve repair and replacement. Since the development of cardiopulmonary bypass, open-heart surgery has been the standard definitive treatment for heart valve disease. The most common valvular lesions—mitral regurgitation and aortic stenosis—are effectively treated by cardiac surgery, extending longevity and improving quality of life in hundreds of thousands of patients annually. Mortality associated with primary heart valve disease has dropped from nearly 10% in the 1960s to less than 3% today, and patients awaiting heart valve replacement can expect to live up to 8 years following surgery.

**Percutaneous Heart Valve Repair and Replacement**

Endovascular therapies for heart valve disease may reduce risk and offer new options for poor surgical candidates.

**BY A. MARC GILLINOV, MD, AND DELOS M. COSGROVE, III, MD**

Figure 1. Surgical annuloplasty to treat mitral regurgitation. In functional mitral regurgitation, the leaflets fail to coapt, allowing central regurgitation (A). The annuloplasty band reduces the distance between the anterior and posterior leaflets, increasing leaflet coaptation (B).
Valve surgery is 1% to 3%, and minimally invasive, isolated heart valve operations can be performed through small chest wall incisions.\(^4\)

Mitral regurgitation is the most common valve lesion encountered in clinical practice. Valve dysfunction in patients with mitral regurgitation may be caused by a variety of disorders, including degenerative, rheumatic, endocarditic, congenital, ischemic, or functional processes. Degenerative, rheumatic, congenital, and endocarditic processes affect the valve leaflets and/or chordae, causing structural damage that results in mitral regurgitation. In contrast, patients with ischemic and functional mitral regurgitation usually have a normal-appearing mitral apparatus; the regurgitation is caused by changes in left ventricular and mitral annular geometry that prevent normal leaflet coaptation. Patients with congestive heart failure (CHF) are particularly prone to ischemic or functional mitral regurgitation. It is estimated that 15% of patients with CHF have clinically important mitral regurgitation, meaning that worldwide there are approximately 3 million CHF patients with mitral regurgitation. Because of the morbidity and mortality rates associated with the operation, few of these CHF patients undergo surgery, and they represent a logical target for percutaneous therapies.

Regardless of etiology, mitral regurgitation is best treated by mitral valve repair. The cornerstone of surgical mitral valve repair is annuloplasty. An annuloplasty is a band or ring placed along the mitral valve circumference; it increases leaflet coaptation by reducing annular size, reduces tension on suture lines, and prevents future annular dilatation (Figure 1). In patients with functional or ischemic mitral regurgitation, annuloplasty constitutes the entire mitral valve repair procedure.

Although mitral regurgitation is the most common heart valve lesion in the general population, aortic stenosis is the condition most frequently encountered by surgeons. Without surgical therapy, symptomatic aortic stenosis is generally fatal within 3 years. Aortic stenosis is treated by aortic valve replacement; repair of stenotic aortic valves is generally not feasible. Replacement prostheses may be biologic or mechanical. Biologic prostheses, such as the bovine pericardial valve, generally last 10 to 15 years and are recommended in most patients with aortic stenosis.\(^5\) Mechanical prostheses, which require chronic anticoagulation, rarely undergo structural failure and are placed in selected younger patients with aortic stenosis.

Mitral valve repair and aortic valve replacement are extremely effective means of treating heart valve disease. However, because they currently require a chest wall incision and cardiopulmonary bypass, they are usually associated with a 1-week hospitalization and a 4- to 6-week recovery period. The development of percutaneous techniques for valve repair and replacement promises to offer effective, safe, and minimally invasive therapy to large numbers of patients with heart valve disease.

**Percutaneous Mitral Valve Repair**

Investigators are pursuing two novel, percutaneous techniques for mitral valve repair—percutaneous annuloplasty and percutaneous edge-to-edge repair.
Percutaneous Annuloplasty

As noted previously, annuloplasty can be used to reduce mitral regurgitation in patients with CHF. Although surgical annuloplasty is quite effective, high operative mortality in CHF patients (5% to 8%) is responsible for limited application in this group.6 Nonetheless, recent data suggest that correction of mitral regurgitation in CHF patients improves clinical status.7 These data confirm that anatomic correction of mitral regurgitation by annuloplasty is beneficial in CHF patients with ischemic or functional mitral regurgitation.

The feasibility of percutaneous mitral annuloplasty is based upon the favorable anatomic relationships of the coronary sinus and mitral annulus (Figure 2A). The coronary sinus is the largest vein in the heart; it courses in the atrioventricular groove in direct proximity to the posterior mitral annulus.8-10 Preclinical experience from two groups of investigators demonstrates that placement of an annuloplasty device in the coronary sinus can alter mitral valve geometry such that mitral regurgitation is reduced or eliminated.8,9 The effect of a coronary sinus-based percutaneous annuloplasty is to increase mitral leaflet coaptation by reducing the septal-lateral (anterior-posterior) dimension of the valve,8 and may be accomplished using a device that cinches the coronary sinus and mitral annulus or by a device that straightens or flattens the arc of the posterior mitral annulus (Figure 2B). In experimental models, both approaches are effective.8,10 These devices are placed in the coronary sinus via the internal jugular or subclavian vein using standard guidewire-based techniques. Issues under investigation include patient selection, device fixation, long-term efficacy, and long-term safety. It is noteworthy that instrumentation of the coronary sinus and long-term placement of coronary sinus pacing leads have resulted in favorable safety profiles in humans.

“The feasibility of this approach has been demonstrated in animal models, and clinical trials are now underway.”

Percutaneous Edge-to-Edge Repair

Popularized by Alfieri, the edge-to-edge repair reduces mitral regurgitation by fixation of the middle of the anterior mitral valve leaflet to the middle of the posterior mitral leaflet.11 Like annuloplasty, the edge-to-edge repair is a technique that has been validated in cardiac surgical practice. Generally accomplished with a mattress suture in open surgical procedures, the edge-to-edge repair may be used to increase leaflet coaptation in functional mitral regurgitation or to prevent leaflet prolapse in patients with degenerative mitral valve disease and ruptured or elongated chordae. Surgical results suggest that the addition of an annuloplasty improves durability of the edge-to-edge repair.11

Percutaneous edge-to-edge repair entails transseptal puncture, stabilization of the anterior and posterior mitral valve leaflets, and fixation of the leaflets to one another by a clip, screw, or stitch. The feasibility of this approach has been demonstrated in animal models, and clinical trials are now underway.12,13

Percutaneous Aortic Valve Replacement

Percutaneous aortic valve replacement has been applied clinically in more than one dozen patients, and preliminary results are encouraging (Figure 3). Currently, the technique involves percutaneous placement of a tissue valve mounted on an expandable stent; the native aortic valve is not resected. Potential challenges associated with percutaneous aortic valve replacement include (1) resection of the native valve, (2) intravascular filtering, including filtering of the coronary arteries, (3) hemodynamic support during the procedure, (4) positioning of the new prosthesis, and (5) fixation of the new prosthesis. If resection of the native valve is not required, procedural complexity will be greatly reduced. In addition, long-term durability and safety of the bioprostheses used for percutaneous aortic valve replacement must be demonstrated. Taken individually, each of these challenges has several potential solutions, offering encouragement for the future development of percutaneous aortic valve replacement.

Figure 3. Stented prosthesis for percutaneous aortic valve replacement (Edwards Lifesciences, LLC, Irvine, CA). The aortic prosthesis is placed percutaneously without resection of the native valve.
CONCLUSIONS

Percutaneous treatment of heart valve disease represents a logical step in the evolution of the management of heart valve disease. With advances in technology and endovascular technique, it is likely that certain surgical procedures can be duplicated with percutaneous approaches. These new approaches will enable extension of therapy to large numbers of patients who are not surgical candidates and will encourage earlier treatment in patients with moderate or moderately severe valvular dysfunction. Such strategies will greatly expand the therapeutic impact of valve repair and replacement.

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