The development of catheter-based therapy for heart valve disease, in particular aortic stenosis, is rapidly evolving. Building on previous experience with balloon aortic valvuloplasty from decades ago, new technology involving stent valves mounted on a catheter delivery system promises to be a potential treatment strategy for high-risk patients with severe aortic stenoses. The approach through the apex of the left ventricle (the transapical approach) has propelled the collaboration of cardiac surgeons and interventional cardiologists (Figure 1).

We summarize the current status of surgical aortic valve replacement (AVR), describe currently available transcatheter heart valves for aortic valve implantation (AVI), suggest perceived benefits of the transapical approach for AVI (TA-AVI), outline the experimental animal research that led to the initial human trials for TA-AVI, and conclude with future directions of TA-AVI.

CURRENT STATUS OF AVR

AVR via a median sternotomy using cardiopulmonary bypass and cardioplegic arrest is the treatment of choice for patients with severe, symptomatic aortic stenosis.1 Data from previous eras have shown improved survival of patients after surgical AVR as compared to unoperated patients despite a 7% operative mortality rate at that time (3-year survival rate of 87% vs 21%).2 The Society of Thoracic Surgeons database shows that the operative mortality rate for isolated AVR has continued to decline since the 1980s to 2.5% in 2006, whereas the percentage of patients older than 75 years has increased to 37%.3

Patients deemed high risk secondary to advanced age, comorbid risk factors, or less tangible factors such as frailty and an unclampable aorta are often not considered for AVR. A prospective, multicenter European survey suggested that only 47% of patients with severe aortic stenosis underwent surgical intervention.4 In a retrospective study conducted at the University of Michigan, approximately half of patients with severe aortic stenosis underwent a surgical intervention confirming similar findings in North America.5 Another study found that 61% of patients with severe aortic stenosis were treated medically with a 1-year survival rate of only 62%.6 These patients, particularly the elderly, are often considered too sick to undergo an open heart operation. Current retrospective studies involving the octogenarian population show an operative mortality rate of approximately 10%, which is certainly not prohibitive but is higher than most subpopulations.2,7,11 Nevertheless, a therapeutic gap exists...
for these elderly patients who are otherwise offered only medical management, which is ineffective, or balloon aortic valvuloplasty, which is only palliative.

**TRANSCATHETER HEART VALVES**

Experimental work on stent valves for AVI in animals was first described separately by Anderson and Pavcnik in 1992. Cribier performed the first AVI in humans using a transfemoral venous antegrade approach. This technique required transseptal passage of the device, traversing both the mitral and aortic valves in an antegrade fashion. Technically challenging, this procedure was complicated by catheter-induced mitral regurgitation that caused significant hemodynamic instability, precluding widespread adoption.

The two devices with the most worldwide experience are the Sapien transcatheter heart valve (Figure 2) and the ReValving System (CoreValve Inc., Irvine, CA) (Figure 3). Both devices employ a bioprosthetic design with a trileaflet xenograft valve attached to a metal stent. The Sapien valve was based on the original Cribier-Edwards valve (Edwards Lifesciences), which employed an equine pericardial valve but now uses a bovine pericardial valve. The stainless steel stent requires balloon expansion for deployment. The CoreValve is constructed with a porcine pericardial valve, but it is attached to a nitinol stent that is self-expandable.

Both valves have received CE Mark approval in Europe and are therefore available for commercial use. The feasibility trial for the Edwards valve has been completed in the US, and the pivotal study (the PARTNER trial) is currently being conducted in multiple centers across the country. As of this writing, the pivotal trial for the CoreValve device has not yet been approved by the FDA.

**DELIVERY SYSTEM AND PERCEIVED BENEFITS OF THE TRANSAPICAL APPROACH**

Hanzel and colleagues described the first human case using the femoral retrograde arterial approach (transfemoral approach) after a failed transseptal approach. This approach is an intuitive extension of balloon aortic valvuloplasty familiar to cardiologists. In addition, a steerable delivery system permits safe retrograde passage of the device around the transverse aortic arch. Webb and colleagues recently reported their series using the transfemoral approach. The benefits are an approach that is familiar to cardiologists and the possibility of percutaneous access when smaller-profile delivery systems become available. The disadvantages are a learning curve associated with the new device, femoral access site complications, and frequently associated aortoiliac disease limiting retrograde delivery of these devices, which requires up to a 24-F sheath.

The transapical approach involves direct cannulation of the left ventricular apex via a small left anterolateral thoracotomy. Several perceived benefits over the transfemoral approach are:

- The size of the delivery system is not limited by aortoiliac occlusive disease.

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**Figure 2.** The Edwards Sapien valve (Edwards Lifesciences, Irvine, CA). A pericardial valve is attached to a balloon-expandable stainless steel stent.

**Figure 3.** The CoreValve ReValving system. A pericardial valve is attached to a self-expandable nitinol stent.
• Passage through the transverse aortic arch, which is thought to be a cause of embolic stroke, is avoided.
• The working distance in the transapical approach is much shorter and improves the accuracy of valve deployment.
• Antegrade passage of wires, catheters, and sheaths through the stenotic aortic valve simplifies the procedure.

Disadvantages of the transapical approach include:
• Pain from the thoracotomy site contributing to postoperative respiratory compromise.
• Bleeding complications from the left ventricular apical site.

Animal Studies Using a Transapical Approach
Building on their experience with transventricular implantation of stent valves in the pulmonary position,17 Huber and colleagues published their experience with implantation of custom-made aortic stent valves in 17 pigs.18,19 The biologic valve was sutured into a scaffold constructed of self-expandable linked nitinol Z stents (Figure 4). The device was introduced through the apex of the left ventricle via a left minithoracotomy and deployed using both fluoroscopy and intracardiac echocardiography. Eleven (64%) stented valves were implanted successfully. Of the six failed implantations, three were deployed supra-annularly, causing fatal coronary obstruction, and three were placed too low with subsequent dislodgment into the left ventricle. Three cases had perivalvular leak after implantation of the valve.

Dewey and colleagues described their experience with implantation of another stent valve in 24 pigs.20,21 In the Cribier-Edwards aortic prosthesis, an equine pericardial valve was mounted on a stainless steel stent (Figure 5). The device was similarly introduced through the apex of the left ventricle via a left minithoracotomy and deployed using both fluoroscopy and either intracardiac or epicardial echocardiography. Sixteen (67%) stented valves were implanted successfully. Of the eight failed implantations, two embolized into the distal aorta, and six migrated in a retrograde fashion into the left ventricle. This stented valve differed from the previous valve in that balloon inflation was needed to expand the steel stent. Deployment of their first two valves resulted in distal embolization; therefore, the remaining cases were performed with ventricular unloading via either rapid ventricular pacing or transfemoral cardiopulmonary bypass. Also attributed to the rigid steel stent were the 14 cases with perivalvular leak after implantation of the valve.

A problem specific to both of these experimental results is the implantation of stent valves in normal, nonstenotic aortic valves, obviously a different situation than the intended human use in calcific aortic stenosis. The researchers concluded that the high rate of embolization and migration may be less during implantation into a severely calcified valve. Also, an important observation was that the institution of ventricular unloading via cardiopulmonary bypass and, later, rapid ventricular pacing for the stainless steel stented valve was required to enhance precise deployment of the valve. Finally, both groups confirmed that the sutureless nature of these valves was associated with some degree of perivalvular leak in the experimental model.

Initial Human Experience Using a Transapical Approach
Ye and colleagues reported the first case of TA-AVI in humans using the Cribier-Edwards valve.22 Two cardiac surgeons deemed that this patient had inoperable severe aortic stenosis and was not a candidate for the transfemoral approach due to severe aortoiliac disease. An equine pericardial valve within a balloon-expandable stainless steel stent, the Cribier-Edwards aortic prosthesis, which was also used for their transfemoral cases,23 was implanted via a small anterolateral thoracotomy through the sixth interspace. Unlike the previously described ani-

Figure 4. The aortic stent valve used for direct access antegrade implantation is constructed of three linked nitinol Z stents housing a tissue valve. (Reprinted with permission from Huber CH, et al. Eur J Cardiothorac Surg. 2006;29:380-385.)
mal experience, a balloon valvuloplasty was performed to permit passage of the mounted valve through the stenotic valve. Rapid ventricular pacing was performed during balloon expansion of the stent valve without the need for cardiopulmonary bypass.

Lichtenstein and colleagues from the same group reported their 1-month follow-up with seven patients using their technique. The average age of this group was 77 years, with an estimated operative mortality rate based on the logistic EuroSCORE of 35%. All TA-AVIs were technically successful, and the 30-day mortality rate was 14%. Average valve area (AVA) increased from 0.7 mm² preoperatively to 1.8 mm² immediately after the procedure, and mean aortic gradient decreased from 31 mm Hg to 9 mm Hg. All patients had some degree of perivalvular leak (grade 1 to 2), but no patients were considered clinically significant. Problems associated with previous nonstenotic animal models, such as device embolization and coronary artery obstruction, were not observed for these patients with calcified aortic stenosis. Yeo and colleagues recently reported their 6-month follow-up that included two additional late deaths. The four remaining patients had durable hemodynamic results with an average AVA of 1.5 mm², mean gradient of 11, and no worsening of perivalvular leak.

Walther and colleagues from Leipzig reported their single-center results with 30 patients as well as expanded results from a multicenter experience including Leipzig, Vienna, Frankfurt, and Dallas with 59 patients receiving a bovine pericardial valve in a balloon-expandable stainless steel stent (the Sapien transcatheter heart valve). The technique for implantation was similar to that described by the Vancouver group and based on their previous experimental procedure performed in animals. Approximately half of the patients were placed on cardiopulmonary bypass instead of rapid ventricular pacing for ventricular unloading during valve deployment. In the multicenter experience, the average age was 81 years, and the estimated 30-day mortality rate based on the logistic EuroSCORE was 27%. TA-AVI was successful in 93%, and the 30-day mortality rate was 13.6%. Of the four unsuccessful patients, two had valves deployed too high, and two were deployed too low. All four patients required conversion to conventional sternotomy with AVR, and two subsequently died in the hospital. Preoperative AVA was 0.5 cm², and the postoperative mean aortic gradient was 9 mm Hg. Morbidity was significant and included stroke, tracheostomy, reoperation, pleural effusion, arrhythmia, hemofiltration, cardiopulmonary resuscitation, and pericardial effusion. Sixty-three percent of patients were able to be extubated on the same day, and 18% were free from any complication.

Concern about postoperative bleeding from the left ventricular apex was not substantiated in these two series, with only one patient requiring a return to the operative room. Surgeons with experience implanting ventricular assist devices or apicoaortic conduits will be familiar with operating through the left ventricular apex.

**FUTURE DIRECTIONS**

Currently, transcatheter heart valves for AVI are being evaluated in patients with high surgical risk or in inoperable patients. The Society of Thoracic Surgeons score and EuroSCORE can quantify operative mortality rates based on the patient’s risk profile. The current pivotal trial using the Sapien valve includes high-risk surgical patients defined as having an operative mortality rate of >15%. As this technology progresses from clinical trial to eventual widespread use, the challenge for physicians is to avoid
off-label use in lower-risk patients until results from yet-undesigned trials become available.

Percutaneous therapy for aortic valve implantation is already possible in the transfemoral approach using techniques employed in endovascular stent grafting for aortic pathology. However, the goal of a truly percutaneous transapical approach for aortic valve implantation remains to be realized. Instrumentation of the heart is essentially performed with wires, catheters, and sheaths. However, no device exists to close the access point in the ventricular apex; such a device must be secure and completely reliable because a device failure would lead to a catastrophic outcome. Nevertheless, such a device would allow the combination of a truly percutaneous therapy with the advantages associated with direct antegrade access to the aortic valve.

**CONCLUSION**

Transcatheter heart valve therapy lends a unique opportunity to combine the expertise of cardiac surgery and interventional cardiology. Implications for training programs are substantial as residencies must adapt to assimilate this new technology. Transcatheter heart valve technology is an exciting development for both surgeons and cardiologists. This combined expertise will benefit the significant number of patients who would otherwise not be offered an intervention. Although morbidity and mortality rates in this high-risk or inoperable patient group are currently high, the valve hemodynamics are excellent, and further procedure refinements should reduce risk.

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