The only effective treatment for severe aortic stenosis is aortic valve replacement (AVR), which requires thoracotomy and cardiopulmonary bypass, with its associated morbidity and mortality. The advent of a percutaneous approach to AVR offers a new option to patients who are at high risk for surgery and to those who cannot have surgery. This article reviews the present state of the Percutaneous Valve Replacement Program with the Sapien valve (Edwards Lifesciences, Irvine, CA).

BACKGROUND
Aortic stenosis is a common valvular degenerative process in the adult population, with increased prevalence in advanced age. It is estimated that 300,000 patients have severe aortic stenosis in the US, and approximately 60,000 undergo aortic valve replacement every year.

Aortic stenosis of old age is most often a degenerative process. The etiology is unclear: it has been suggested that it is similar to the atherosclerotic disease seen in arterial vessels, and new research has found a possible genetic basis for it.¹

Patients with aortic stenosis have a long period of asymptomatic course. Within 3 years of the onset of angina, syncope, or congestive heart failure, 75% of patients die (2% per month mortality) unless treated with aortic valve replacement. The 3-year survival rates were reported to be 87% and 21% for operated and nonoperated patients, respectively.²

Even in apparently asymptomatic patients, when the valve area is 0.8 cm² or less, the mortality rate is high without AVR.³

The mortality rate for AVR is approximately 3% to 4% in the US, but it increases with higher baseline risk factors, reaching 20% to 50% in the highest risk groups.⁴ Patients in the highest risk group are considered inoperable.

Many patients with severe aortic stenosis do not undergo AVR because of the physician's reluctance to recommend it or reluctance of the patient and the family to go along with the recommendation for AVR surgery.
introduction of a percutaneous option for AVR offers a potential solution for these patients who are at high risk for surgery.

PERCUTANEOUS AORTIC VALVE REPLACEMENT

Andersen\(^5\) completed the original animal work for a stent-mounted, balloon-expandable aortic valve prosthesis, and Cribier,\(^6\) after testing large stents in human cadavers, worked with Percutaneous Valve Technologies (now Edwards Lifesciences) and developed a balloon-expandable valve on a stent that was successfully tested in sheep. This led to the first human implantation of a percutaneous aortic valve by Cribier in April 2002. Subsequent modifications of the original valve have led to improved performance. The Sapien Valve (Figure 1) is composed of a balloon-expandable, stainless steel frame with an integrated trileaflet bovine pericardial valve. The pericardial leaflet material is treated with a similar process to the one used for the surgical Carpentier-Edwards Perimount Magna pericardial valves (Thermafix anticalcification treatment, leaflet deflection testing for matched elasticity, and proprietary tissue processing). Bench testing of the Sapien valve has, to date, established a durability of >5 years.

The valve is available in two sizes (23 mm and 26 mm) to achieve optimal matching with the aortic annulus dimensions. The valve is crimped on a balloon just before implantation with a specially designed mechanical crimper (Figure 2) to achieve a symmetrical low profile and ensure retention onto the delivery system.

The balloon, with the crimped valve, is advanced with a delivery catheter (the RetroFlex catheter, Edwards Lifesciences). The RetroFlex catheter has an 18-F shaft that increases in the distal end to 22 F or 24 F for the 23-mm and 26-mm valve, respectively. The newest version of this catheter is the RetroFlex II, which integrates a nose cone in the distal end (Figure 3) to facilitate advancing the delivery system around the aortic arch and to eliminate any resistance in crossing the native aortic valve. The tip of this catheter is deflectable, to facilitate advancement through the aortic arch and the native aortic valve. The RetroFlex catheter with the Sapien valve is advanced through a hydrophilic 22-F or 24-F sheath. The next-generation catheters from Edwards Lifesciences are being designed to achieve a truly percutaneous profile.

PROCEDURE

The procedure is performed preferentially in a hybrid catheterization lab/operating room. High-quality imaging is required for good visualization of the native aortic calcification. The patient is placed under general anesthesia in most centers, although some hospitals in Europe, as well as the Washington Hospital Center, in Washington, DC, use conscious sedation without intubation.

As part of the protocol, transesophageal echocardiography (TEE) is used in all patients during the procedure. TEE could help with valve positioning and is important to evaluate for any residual aortic regurgitation after deployment of the valve. A second inflation of the balloon after initial deployment has shown to be effective to decrease perivalvular leak in cases in which it is observed.\(^7\) Introduction of the 22-F or 24-F femoral sheath is completed by direct surgical exposure of the common femoral artery or by percutaneous entry.

After crossing the aortic valve, an extra stiff Amplatz wire (Cook Medical, Bloomington, IN) is placed in the left ventricle. The diseased native valve is first dilated by means of balloon valvuloplasty with rapid right ventricular pacing to facilitate subsequent entry of the crimped valve assembly and to allow for flow while the new valve position is adjusted for optimal delivery location.

An optimal fluoroscopy projection is selected with the three aortic sinuses well aligned. This is completed with sequential
aortograms using low contrast dose: 10 mL of 50% diluted contrast.

The 22-F or 24-F sheath is placed after predilatation with hydrophilic dilators (16, 18, 20, 22, and 25 F). The RetroFlex catheter with the crimped valve is advanced gently up the aorta and around the aortic arch under fluoroscopic guidance. The native aortic valve is crossed. The RetroFlex catheter is withdrawn into the ascending aorta. The Sapien valve is then pulled to its optimal position with two thirds of the assembly on the ventricular side of the aligned sinuses. Aortography helps confirm the final optimal position. The pigtail used for aortography is withdrawn, rapid right ventricular pacing is initialized, and the valve is deployed by inflating its balloon. Only after full deployment is rapid pacing terminated; this is important to prevent displacement of the valve before full expansion of the stent. A final aortogram is obtained, and TEE images are carefully analyzed for any residual aortic insufficiency. The delivery assembly is withdrawn, the access site is closed (surgically or percutaneously), and the patient is monitored in the intensive care unit for 24 hours.

**Transapical Approach**

For patients without adequate femoral access, the transapical approach was developed. A minimal left thoracotomy allows exposure of the left ventricle apex. A purse-string suture is placed in the apex of the left ventricle, and the left ventricle is entered with a needle and wire. The valve is dilated with a balloon, and the percutaneous valve is delivered through a specially designed sheath, similar in concept to the transfemoral system.

**Patient Selection**

The Edwards Sapien aortic valve is only available in the US to patients randomized in the PARTNER (Placement of AoRtic TraNs cathetER Valves) IDE Pivotal Trial. The valve is available commercially in Europe. PARTNER IDE’s basic inclusion and exclusion criteria are listed in Table 1. Figure 4 is an overview of the trial’s design.

In the PARTNER IDE trial, patients with critical aortic stenosis who are at high surgical risk are randomized to surgery or percutaneous treatment (cohort A), and patients who are inoperable because of a surgical mortality >50% are randomized to continued medical therapy or percutaneous valve placement (cohort B). Patients assigned to medical therapy usually have aortic valvuloplasty as part of their treatment. The primary endpoint of the trial is mortality at 1 year.

**Iliac Analysis**

An evaluation of the iliac and common femoral arteries is important to make certain that these vessels will allow the delivery of the 22-F or 24-F sheath. A minimum diameter of 7 mm and 8 mm is required for the 22-F and 24-F sheaths, respectively. A detailed quantitative angiogram and CT are performed and analyzed for diameter, tortuosity, and calcification; occasionally, IVUS of these vessels is performed for further clarification. At this time, patients with borderline measurements are not included because of the major risk of morbidity and mortality if there is a complication from vascular access.

**Results of Percutaneous Valve Replacement**

**Hemodynamics**

The Sapien valve implanted in patients has a valve area of at least 1.7 cm² for the 23-mm valve and 1.9 cm² for the 26-mm valve. The residual gradient is usually 0, and always <15 mm Hg. Because of improved outflow efficiencies, mitral regurgitation and pulmonary pressures decrease and cardiac output increases. To date, more than 1,000 patients have been treated worldwide with the Sapien percutaneous valve (EuroPCR 2008).
Inclusion Criteria (Cohort A)
- Predicted operative mortality is 15% and STS score ≥10
- Surgeon and cardiologist joint assessment
- Severe degenerative AS with mean gradient >40 mm Hg and/or jet velocity >4 m/s, or AVA <0.8 cm²
- NYHA class II, III, or IV
- Informed consent
- Subject agrees to return for all required postprocedure follow-up

Inclusion Criteria (Cohort B)
- All of cohort A criteria are met and
- Medical factors preclude operation; probability of death or serious, irreversible morbidity should exceed 50%

Exclusion Criteria
- Evidence of AMI ≤1 month before intended treatment
- Aortic valve is congenital unicuspid or bicuspid or is noncalcified
- Mixed aortic valve disease (AS and AR with predominant AR >3+)
- Any therapeutic invasive cardiac procedure, other than BAV, within 30 days of index procedure; 6 months if DES implantation
- LVEF <20%
- Untreated, clinically significant CAD requiring revascularization
- Primary hypertrophic obstructive cardiomyopathy
- Native aortic annulus size, estimated by LVOT on baseline echo, <16 mm or >24 mm

Functional Status
Most patients improve from functional class 3-4 to functional class 1-2 (Figure 5).9

Mortality of the Procedure
In the REVIVE II trial, REVIVAL II IDE trial, and Vancouver experience, the 30-day mortality rates associated with the placement of the Sapien valve were 12.1%, 7.8%, and 10.6%, respectively. These results reflect the early experience in patients at very high risk. In the most recent experience published by Webb, the 30-day mortality rate was 0%.10 A significant component of trial mortality has been related to vascular access complications. Better screening of patients and newer, smaller-sized devices will certainly minimize this cause of morbidity and mortality.

The PARTNER IDE Trial
The PARTNER IDE trial is an FDA-approved study to evaluate the safety and efficacy of the Sapien percutaneous aortic valve in the treatment of patients with critical aortic stenosis and those who are at high risk for surgery or who are inoperable. Three groups are eligible for the trial:

(1) Patients at high risk for surgical AVR, as determined by an STS score >10 (Society of Thoracic Surgeons), are randomized to surgery or percutaneous treatment.

(2) Patients who are inoperable because the surgical risk of mortality or serious, irreversible morbidity (estimated by two independent surgeons) is >50%. Such patients are randomized to percutaneous treatment or continued medical therapy.

(3) Patients who do not have access through their femoral vessels are randomized to the transapical approach with the Sapien valve or surgical AVR.

Fifteen centers are currently enrolling patients in the trial.

Additional information about the trial and enrolling centers can be found at www.clintrials.gov.

CONCLUSION
Percutaneous AVR is now a reality. Its safety and effectiveness are being evaluated in the current PARTNER randomized trial for patients who are at high risk for surgical AVR. Future advances in technology may expand the indications for percutaneous valve replacement.

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