

Balloon-Expandable Transcatheter Aortic Valve Implantation

How the Edwards Sapien valve is changing the treatment of aortic stenosis.

BY UYGAR C. YUKSEL, MD; SAMIR R. KAPADIA, MD; AND E. MURAT TUZCU, MD

Aortic stenosis is the most common valvular heart disease in the Western World and the third leading cause of cardiovascular disease after hypertension and coronary artery disease.¹ Calcific aortic stenosis affects 2% to 4% of adults over age 65 in the United States.^{2,3} Until 2002, the only option for patients with severe symptomatic aortic stenosis was open heart surgery for valve replacement. Unfortunately, surgery carries a high risk for some elderly patients—particularly those with multiple severe comorbidities.⁴ The prognosis of symptomatic aortic stenosis patients who are not referred to surgery is poor.⁵ Although balloon aortic valvuloplasty provides some relief for symptomatic patients, it is almost always a temporary palliative procedure.⁴ Transcatheter aortic valve implantation (TAVI) emerged to be an answer to the limitations of open heart surgery and balloon valvuloplasty as a nonsurgical method with long-lasting efficacy.

The first successful percutaneous transcatheter implantation of an aortic valve was accomplished by Alain Cribier, MD, in April 2002.⁶ The first-generation balloon-expandable aortic valve was named after him. The Cribier-Edwards valve (Edwards Lifesciences Corporation, Irvine, CA) had three leaflets made from equine pericardial tissue that was sutured inside a balloon-expandable stainless steel 14-mm stent. The aortic valve prosthesis was mounted over a 3-cm-long balloon catheter using a specially designed mechanical crimping device. After many modifications, based on a fairly large experience, the current valve, called the Edwards Sapien valve (Figure 1), was developed.

EDWARDS SAPIEN BIOPROSTHESIS

The Edwards Sapien valve, a modification of the initial Cribier-Edwards valve, is a trileaflet bioprosthesis fabricated from bovine pericardial tissue that has been preserved in low-concentration solutions of buffered glutaraldehyde to fully crosslink the tissue and maintain flexibility and strength. The leaflets are treated with

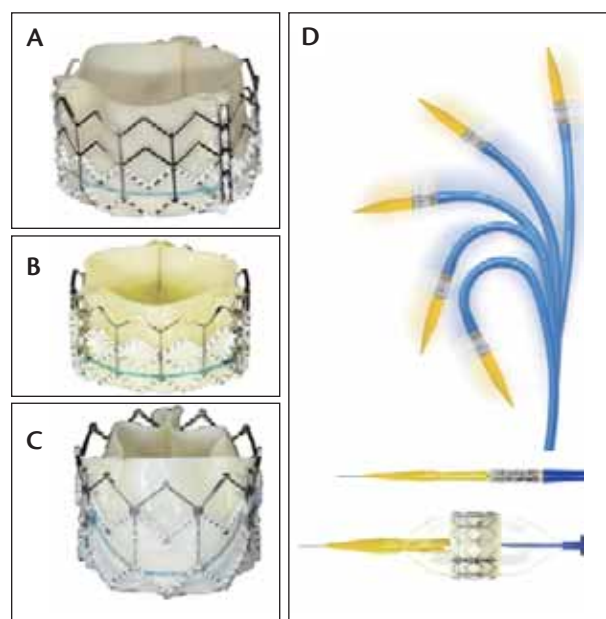


Figure 1. The first-generation Cribier-Edwards valve (A), the Edwards Sapien valve (B), and the new-generation cobalt chromium low-profile Sapien XT valve (C). The RetroFlex transcatheter valve delivery system (D).

ThermaFix (Edwards Lifesciences), which renders the leaflets more resistant to calcification.⁷ ThermaFix advanced tissue processing extracts the phospholipids and residual glutaraldehyde molecules from the leaflets, thereby providing a more durable anticalcification effect. The Edwards Sapien valve also contains a polyethylene terephthalate fabric cuff mounted on a tubular, radiopaque, stainless steel, balloon-expandable stent. Currently, two different sizes (expanded maximum diameter) of the valve are available: a 23-mm valve (14.5 mm in height) and a 26-mm valve (16 mm in height).

Transcatheter implantation of the Edwards Sapien valve can be done by a retrograde transfemoral approach or by a small transapical thoracotomy. The transfemoral approach is the preferred method. The transapical approach is reserved for patients whose iliofemoral anatomy is unfavorable for a peripheral vascular access with a large sheath. Because the transapical approach is discussed separately in this issue (See page 56 by John C. Alexander, MD), we will focus on the transfemoral approach.

PATIENT SELECTION

Patient selection is a critical step for the success of the percutaneous aortic valve replacement procedure. Candidates considered for transcatheter aortic valve replacement must have severe symptomatic aortic stenosis and very high or prohibitive risk for operative mortality. The procedure should be offered to patients who have a potential for functional improvement after valve replacement. Patients with heavily calcified, small, tortuous arteries should undergo placement through a transapical approach to prevent vascular complications.

PREPROCEDURAL IMAGING

The aortic valve annular diameter must be precisely determined to avoid valve embolization and to minimize paravalvular aortic regurgitation. Oversizing may cause coronary obstruction or aortic injury. Preoperative echocardiographic examination is essential in the preliminary assessment. If transthoracic echocardiography (TTE) windows yield suboptimal images, transesophageal echocardiography (TEE) may be needed.

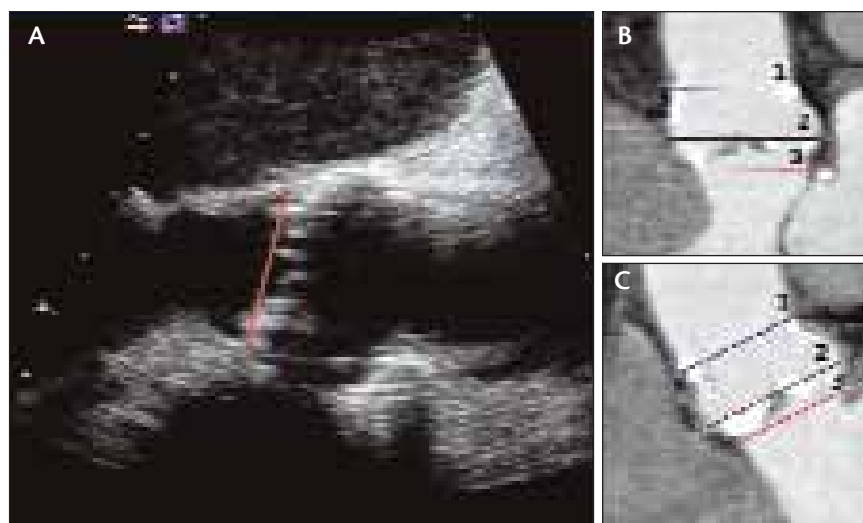


Figure 2. Annulus measurement by transthoracic echocardiography (A). Aortic root measurements at the level of (1) the sinotubular junction, (2) the annulus, and (3) the valve by computed tomography (CT) (B, C).

Initial assessment with TTE may deem some patients with too small (< 18 mm) or too large (> 26 mm) annulus size unsuitable for the procedure. Annulus measurement is performed in the parasternal long-axis view at the point of insertion of the right and noncoronary aortic cusps into the aortic annulus (Figure 2). Multiple repeated annulus diameter measurements should be obtained before the final decision is made.

Because TEE guidance is routinely used throughout the procedure, annular dimensions can be measured before the procedure with TEE, which can yield better image quality. Moss et al reported that TEE yields larger annular dimensions than TTE.⁸ In their study, the mean difference in aortic annulus dimension was 1.36 mm larger with TEE. The success rate of the procedure was found to be similar between the TTE and TEE assessed groups.

Because the aortic annulus has an oval shape rather than circular, assessment with multislice CT (MSCT) may provide more precise anatomic information. The oblique sagittal view on MSCT is equivalent to the parasternal long-axis view on TTE and the midesophageal long-axis view on TEE, whereas the coronal view is equivalent to the anteroposterior view on aortic root angiography.⁹

Recent advances in echocardiography introduced real-time three-dimensional TEE imaging into clinical practice. Real-time three-dimensional TEE allows visualization of the complete left ventricular outflow tract and the aortic valve for accurate positioning of the transcatheter valve.¹⁰ The incremental value of three-

dimensional echocardiography in TAVI is currently being assessed.

VALVE SIZE

The transcatheter heart valve must be slightly larger than the aortic annulus to decrease the amount of perivalvular aortic insufficiency and achieve appropriate valve anchoring. Currently, only patients with an aortic annulus of 18 to 24 mm in diameter can be considered for placement of an Edwards Sapien prosthesis. A 23-mm valve is used when the annulus diameter is between 18 to 21 mm, whereas a 26-mm valve is used for an annulus measuring 21 to 24 mm.

The valve is packaged unfolded and preserved in glutaraldehyde to preserve the function of the pericardial leaflets. The valve is crimped on the balloon at the time of the procedure. To facilitate the crossing of the severely narrowed aortic valve by the delivery catheter, predeployment balloon aortic valvuloplasty is performed.

ACCESS

The iliofemoral anatomy must be evaluated thoroughly before the procedure. The size of the artery, tortuosity, calcification, and the presence of peripheral vascular disease should be evaluated by angiography, CT angiography, or both. In borderline cases, some operators perform intravascular ultrasound for more accurate assessment of the vessel size and extent of calcification. Minimal arterial diameter, vessel tortuosity, and vessel calcification are still the major limiting factors.

A 22-F introducer sheath is used for the 23-mm valve, whereas a 24-F introducer sheath is used for the 26-mm valve. Due to large sheath sizes, many operators prefer to gain vascular access via surgical cutdown. Alternatively, a percutaneous approach with a suture-mediated closure device is used by others.¹¹

The Edwards Sapien valve is currently introduced with a steerable retrograde transfemoral delivery system (RetroFlex delivery catheter system, Edwards Lifesciences) (Figure 1). The steerable characteristic of the RetroFlex catheter facilitates navigating the tortuous vessels and the aortic arch. The RetroFlex II catheter with a fixed cone at the tip makes crossing the stenotic valve easier. The position of final deployment of the prosthetic valve is determined by the patient's native

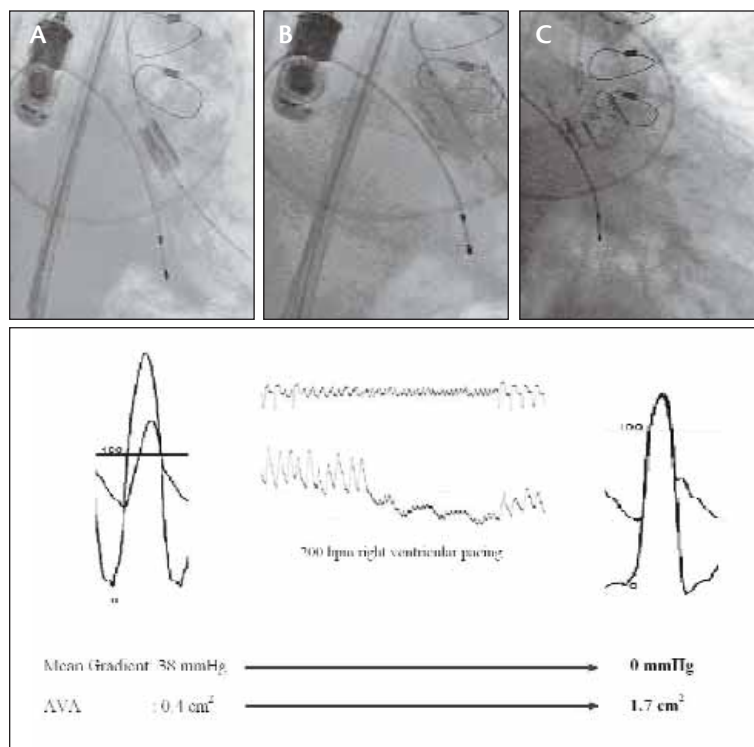


Figure 3. Implantation of the Edwards Sapien valve during temporary high-rate cardiac pacing. The Edwards Sapien valve is advanced with the RetroFlex catheter delivery system at the level of the native valve (A), and the balloon-expandable stent is deployed during high-rate right ventricular pacing (B). Successfully deployed transcatheter valve (C).

AVA, aortic valve area.

valvular structure and anatomy and is optimized by using fluoroscopic imaging of the native aortic valve calcification as an anatomic marker. Supra-aortic angiography and TEE also guide the deployment process.¹²⁻¹⁴

The aortic valve prosthesis should be placed at mid-position in the patient's aortic valve, taking care to not to impinge on the coronary ostia or to impede the motion of the anterior mitral leaflet. The deployment is carried out during temporary high-rate right ventricular apical pacing, with a ventricular rate of 180 to 220 bpm. This leads to an immediate decrease in the forward stroke volume, which in turn facilitates the positioning of the prosthetic valve by diminishing balloon movement (Figure 3).

TRIAL RESULTS

The first transcatheter aortic valve implantation trials are composed of multicenter registries from the United States (REVIVAL II, transcatheter Endovascular Implantation of Valves II), Europe (REVIVE II, Registry of

Endovascular Implantation of Valves in Europe II), and Canada, and included patients with a valve area < 0.8 cm² and a high predicted operative mortality rate (logistic EuroScore > 20%). Their aim was to evaluate procedural safety and efficacy.

REVIVE consists of 106 patients with transfemoral percutaneous aortic valve replacement with a mean age of 83.9 ± 5.4 years. The mean logistic EuroScore was 28.9 ± 13.4 . The implantation was successful in 88% of the cases. Freedom from death and stroke was 87% and 97%, respectively, at 30 days. The incidence of conduction disturbance requiring permanent pacemaker implantation was 3.8% at 30 days.

REVIVAL II consists of 55 patients with transfemoral percutaneous aortic valve replacement with a mean age of 83.7 ± 5.2 years. The mean logistic EuroScore was 34.1 ± 18 . In the REVIVAL registry, the Society of Thoracic Surgeons mortality risk score (STS score) was also used in patient selection, and the mean STS score was 13.1 ± 7.2 . In 48 cases (87.3%), the implantation was successful. Freedom from death and stroke was 92.7% and 90.7% at 30 days, respectively. The 30-day pacemaker implantation rate was 7.3% in the transfemoral TAVI patients.

In their first 50 patients of retrograde transfemoral implantation, Webb et al¹⁴ reported initial procedural success of 78%, which increased to 96% after the first 25 cases, reflecting an important learning curve.¹² The observed 30-day mortality rate was 12%. In the latter half of this first-in-man percutaneous retrograde transarterial balloon-expandable valve experience, 30-day mortality decreased further to 8%.

PARTNER EU (Placement of Aortic Transcatheter Valve) was a feasibility study conducted in Europe before the Edwards Sapien valve was granted CE Mark approval. The transfemoral cohort of the study included 61 patients with a mean age of 82.3 ± 5.2 . Mean logistic EuroScore was 25.7 ± 11.5 , and the mean STS score was 11.3 ± 6.1 . The procedural success was 91%. The stroke and mortality rates were 3.2% and 8.1% at 30 days, respectively. The 30-day pacemaker implantation rate was 1.6% in transfemoral TAVI patients.

In September 2007, the Edwards Sapien valve achieved the CE Mark in Europe. The SOURCE registry is a postmarket registry of the Edwards Sapien valve. The SOURCE registry included 1,038 patients from 32 centers across Europe.¹⁵ A total of 463 patients with a mean age of 81.7 underwent transfemoral TAVI. The mean logistic EuroScore was 25.7. Acute procedural success was 95.6%. The 30-day stroke and mortality rates were 2.4% and 6.3%, respectively. The 30-day pacemaker implantation rate was 6.7% in the transfemoral TAVI cohort.

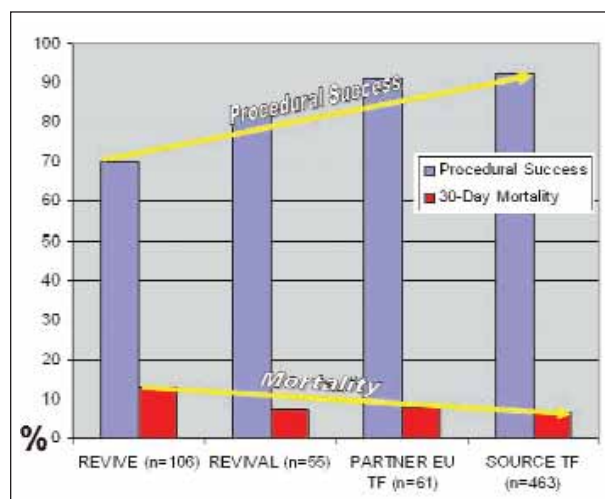


Figure 4. The effect of the learning curve on the procedural success.

PARTNER US (Placement of Aortic Transcatheter Valve), a multicenter randomized trial with a primary endpoint of 1-year mortality, is currently enrolling patients in the United States, Canada, and Europe. The aim of this prospective randomized clinical trial is to enroll 1,040 patients in two separate treatment arms. The primary endpoint in both arms is death at 1 year; secondary endpoints focus on long-term (1 year) composite cardiovascular events, valve performance, and quality-of-life indicators. Cohort A of the trial is to compare the Edwards Sapien valve with standard surgical aortic valve replacement, with the objective of showing noninferiority in patients with an STS score of 10 or higher. Cohort B, which enrolled patients who were deemed inoperable by two experienced cardiac surgeons, is comparing percutaneous valve replacement against medical therapy or balloon valvuloplasty, with the aim of showing superiority.

The most recent report published by Webb et al¹⁶ includes 168 cases (113 transfemoral, 55 transapical) with transcatheter aortic valve implantation by the Edwards Sapien valve. This series also includes the first-in-human transarterial and off-pump transapical case series.¹⁴ Their overall intraprocedural mortality rate was 1.2%, and operative 30-day mortality was 11.3%. The 30-day mortality was insignificantly lower in the transarterial group than the transapical group (8% vs 18.2%; $P = .07$). The need for permanent pacemaker implantation was 4.4% in the transfemoral TAVI group. In this study, maximum follow-up was > 3 years, and the median follow-up was 221 days; no structural valve failure was observed during the follow-up period. After TAVI, substantial improvement in the patients' functional class was observed within the

first month. The most improvement occurred in patients who were in class III and IV at baseline, of whom 88.6% and 100%, respectively, had improved by at least one functional class. This latest report again highlighted the importance of the learning curve. The mortality rate for the last half of this series was 3.6% compared to 12% in the first reported series.¹⁴ The strong effect of the learning curve is evident throughout the study.

CONCLUSION

The clinical trial results revealed that transfemoral TAVI is an effective and feasible method for treating patients with severe symptomatic aortic stenosis who have prohibitive risks for surgical replacement. Surgical aortic valve replacement remains the gold standard treatment for patients with symptomatic aortic stenosis. At present, the use of this procedure in younger patients, patients at low surgical risk, patients with long life expectancy, and in asymptomatic patients is strongly discouraged because of the uncertainty regarding long-term durability and clinical outcomes compared to conventional aortic valve replacement.

Learning curve remains one of the most important predictors of procedural success and mortality. From the older REVIVE to the more recent SOURCE registry, every new study conducted in this field revealed higher success rates and lower mortality rates with increasing experience (Figure 4).

Future advances in transcatheter valves and delivery systems may improve the clinical results. Aortic valve regurgitation is still an important issue that must be solved. Imaging modalities providing precise annulus measurements and availability of different valve sizes may decrease the incidence of aortic regurgitation. Another challenging issue is peripheral vascular complications due to large-bore access and difficulty in traversing the aortic arch with bulky devices. Edwards' next-generation balloon-expandable pericardial tissue valve features a cobalt chromium alloy frame (Sapien XT) that reduces the profile by 4 to 5 F (Figure 1). A thinner cobalt chromium frame permits thinner and more open struts, allowing for tighter crimping of the valve. This next-generation valve is expected to reduce the delivery profile to 18 F. The Sapien XT valve also has a scalloped leaflet geometry that showed superior durability by in vitro testing. Even though the midterm clinical results provided excellent durability with no reported structural failure to date with the Edwards Sapien valve, future advances in tissue engineering may provide superior durability. These further advances in the field will considerably change our clinical practice for severe aortic stenosis. ■

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