The Sapien 3 Valve

Current use in United States TAVR practice.

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Transcatheter aortic valve replacement (TAVR) has become the standard for treatment of aortic stenosis in patients who are at high or prohibitive risk for conventional surgical aortic valve replacement, although its role in patients who are at intermediate risk for surgery is currently being studied. For TAVR to be considered equivalent to surgical valve replacement, it is vital that the performance of transcatheter valves improve; in the past 10 years, the technology of transcatheter valves has advanced tremendously. One of the most important predictors of clinical outcomes in patients undergoing TAVR is residual paravalvular leak (PVL), and newer valve designs have concentrated on reducing PVL. In addition, newer-generation valves have been designed to improve deliverability and safety, including reducing periprocedural mortality, stroke, and vascular complications. The Sapien 3 valve (Edwards Lifesciences), which builds upon the Sapien platform (Edwards Lifesciences), has recently been approved for use in the United States. The valve was designed to improve on its predecessors, the Sapien and the Sapien XT transcatheter heart valves (Edward Lifesciences), in terms of vascular injury, stroke, positioning, and PVL. This article reviews the features of this device, as well as the early data that have led to its approval.

FEATURES
The Sapien 3 valve retains the basic structure of the Sapien and Sapien XT, with a cobalt chromium frame and bovine pericardial tissue leaflets (Figure 1A). The valve itself is a balloon-expandable system that is crimped onto a delivery catheter prior to implantation. Much like the Sapien XT, the Sapien 3 valve is positioned onto the balloon in the descending aorta and then unsheathed after the valve is positioned across the aortic annulus. The frame design has been updated to include wider strut angles and an increase of rows and columns between the valve commissures. This frame has been designed to improve radial strength, decrease delivery profile, and improve access to coronary arteries after valve implantation. Although the frame height remains low, it is slightly higher than its predecessor, the Sapien XT. As a result, the Sapien 3 valve will foreshorten to a greater extent than the Sapien XT valve upon deployment. The improved delivery profile has reduced the French size of the Sapien 3 introducer sheath. The 20-, 23-, and 26-mm
valves are now delivered through a 14-F sheath, while the 29-mm valve is delivered through a 16-F sheath. This smaller sheath has expanded the patient population in which transfemoral access can now be safely utilized. The suggested minimal diameter of the femoral/iliac arterial system has been decreased to 5.5 mm with the 20- to 26-mm valves, and 6 mm with the 29-mm valve.

An adaptive outer skirt made of polyethylene terephthalate has been added to the ventricular aspect of the valve. This skirt has been designed to improve the rates of significant PVL (as subsequently described). The delivery system of the Sapien 3 valve (Sapien 3 Commander Delivery System; Edwards Lifesciences) has been modified as well. There is an increased ability to distally retroflex the delivery system as it traverses the aortic arch into the ascending aorta (Figure 1B). A fine-control knob has been added to the handle to provide microcontrol of valve positioning while in the aortic annulus (Figure 1C). In addition, a central balloon marker has been added to be used as the primary landmark for valve positioning. These changes are designed to improve deliverability and allow more precise valve positioning.

**INITIAL DATA**

The initial feasibility data, published in 2013, were based on implantation in 15 patients, in whom all 15 implantations were successful; there were no major complications, and one patient required a new pacemaker. These data were followed by the European CE trial of 150 patients. The initial 50 patients were high risk, and the subsequent 100 were deemed intermediate risk. The average age was 84 years with an average Society of Thoracic Surgery (STS) score of 7.4%. Ninety-nine percent of the valves were implanted at the intended site, and mortality at 30 days was 2.1% in those patients in whom transfemoral access was used, whereas the mortality was 11.1% in those who required alternative (transapical or direct aortic) access. The 30-day stroke rate in the transfemoral group was 1%, whereas the stroke rate in the alternative access group was 5.6%. Vascular complications were low, with a major complication rate of 4.2% in the transfemoral group. Pacemaker rates were higher than previously reported with the Sapien XT, with 13.3% of patients requiring a new pacemaker. Only 6.6% of patients had New York Heart Association class III/IV symptoms at 30 days. The average effective orifice area at 30 days was 1.5 cm², and the mean gradient was reduced to 10.6 mm Hg, with only 3.5% of patients having more than mild PVL. This low rate of PVL has also been reported in several other small registry trials. During this early experience, it was evident that the valve sizing of the Sapien 3 was different than its predecessors. It was found that the same degree of oversizing for Sapien XT was not required, and subsequent sizing algorithms allowed up to 5% undersizing of the valve with no increase in PVL, which allows for easier and safer sizing of the Sapien 3 valve. Small comparative data...
registry data have found marked improvements in PVL and vascular complications with the Sapien 3 valve compared to the Sapien XT valve.\textsuperscript{6}

As explained previously, early data found that while the Sapien 3 valve reduced significant PVL and vascular complications, the rate of pacemaker implantation was higher than expected. Subsequent analyses of these patients found that lower implantation of the valve, which was initially suggested due to the foreshortening of the valve, was associated with higher pacemaker rates. A higher implantation seemed to be associated with lower pacemaker rates, similar to that of the Sapien XT, without affecting the rate of paravalvular leak.\textsuperscript{7} These early trials have found that the optimal annulus sizing can be anywhere from 5% undersized to 20% oversized, and the valve should be implanted with the bottom of the middle marker at the base of the annulus.

The large PARTNER II S3 trial was designed to study the performance of the Sapien 3 valve in the United States. The trial consisted of two, single-arm, nonrandomized trials. One arm included patients who were deemed high risk or inoperable by a heart team, while the other arm contained patients who were deemed intermediate risk. The trial was designed to compare the Sapien 3 valve against historical controlled studies (PARTNER IA for high-risk patients and the PARTNER IIA for intermediate-risk patients).

Although no published data have been presented from these trials, the results have been presented at national meetings. The initial 30-day results were presented in March 2015, at the annual meeting of the American College of Cardiology.\textsuperscript{8} In the high-risk cohort, the average STS score was 8.6%, and the average age was 83 years. The 30-day mortality was 2.2%, and the rate of any stroke was 1.5%. The 1-year data were recently presented at the 2015 TCT meeting demonstrating an overall 1-year mortality rate of 14.4% (10.7% in high-risk patients, 15.7% in inoperable patients).\textsuperscript{9} The Sapien 3 intermediate-risk cohort had an average STS of 5.3% (average age, 82 years). The 30-day mortality was 1.1%, with a stroke rate of 2.6%. Vascular complications rates were low, with a major vascular complication rate of 5% in the high-risk cohort and 5.6% in the intermediate-risk cohort. Coronary obstruction and annular rupture were very uncommon. There was a marked improvement in symptoms, with New York Heart Association class III/IV symptoms in 13% of the high-risk patients and 6% in the inoperable-risk patients at 30 days. Only 3.8% of patients had more than mild PVL at 30 days.

**CLINICAL IMPLICATIONS**

Although the full results of the PARTNER II and the PARTNER II Sapien 3 results have not been fully released, the collective early experience utilizing the Sapien 3 valve suggests an excellent safety profile, with the lowest 30-day mortality rates seen to date with a balloon-expandable TAVR (Figure 2), very low rates of significant PVL (Figure 3), and few vascular complications. Pacemaker implantation appears to occur at similar rates as with the Sapien XT valve with proper positioning and
sizing. Based on these data, the Sapien 3 valve has been approved for use in patients with high-risk features for conventional surgical aortic valve replacement.

Given the improvements in the Sapien 3 valve and the Sapien 3 valve delivery system, the Sapien 3 valve has supplanted the Sapien XT as the balloon-expandable transcatheter valve of choice. The improved deliverability and need for only a 14-F sheath (with the 20–26-mm valve) has also made the need for alternative access (transaortic or transapical) a much less common occurrence, likely further improving patient outcomes and recovery. Although some valvular anatomy may be more suitable for a self-expanding transcatheter valve, the Sapien 3 valve has proven to be reproducibly implantable in many different anatomies. As indications for TAVR are being broadened to patients at lower risk for surgical aortic valve replacement, it is imperative that newer-generation transcatheter valves achieve exceedingly low rates of procedural complications and PVL. The new design iterations of the Sapien 3 valve appear to have lowered these specific metrics to levels potentially comparable to surgical valve replacement.

FURTHER AREAS OF INTEREST

Further study of long-term, follow-up data is needed in the field of TAVR. It is still unclear how well these transcatheter valves will perform upon later follow-up and, as we try to make decisions on whether to offer TAVR to younger patients, these clinical data will be of utmost importance. The original trials utilizing the Sapien valve were performed on patients with extreme comorbidities, with the majority not surviving for long-term follow-up. However, recent trials have enrolled lower-risk patients, and along with the advent of large national databases (such as the TVT registry), data on the longevity and durability of the new transcatheter valves should become available as soon as the valves have been used in clinical practice long enough.

It appears that the Sapien 3 valve has an excellent safety profile and provides excellent early echocardiographic and clinical outcomes. The earlier-generation transcatheter valves have been shown in randomized trials to be at least equivalent, if not superior, to conventional aortic valve surgery. The next question will be whether the improvements made in the latest-generation Sapien 3 valve will lead to long-term improvements in clinical outcomes in patients who are at lower risk for surgical aortic valve replacement. The PARTNER IIA trial results along with the PARTNER II S3 data will provide key information on the role of the Sapien 3 valve in those deemed intermediate risk for surgical aortic valve replacement. The SURTAVI trial will provide further information in this key patient group. Given the marked improvement in the Sapien 3 valve, further studies are being planned in low-risk patients, including the recently approved PARTNER III study comparing TAVR to surgical aortic valve replacement in low-risk patients.

CONCLUSIONS

The Sapien 3 has a lower profile, improved deliverability, more precise positioning, and appears to improve rates of procedural complications. Importantly, rates of stroke, death, and severe PVL appear to be reduced with the Sapien 3 valve compared to previous Sapien valves. Given these improvements, it has become the balloon-expandable valve of choice for patients undergoing TAVR. Further investigation is ongoing to see if the improvements made in the valve design will translate into long-term clinical benefits for patients with aortic stenosis. As trials that will compare TAVR to conventional aortic valve replacement in low-risk patients are just beginning, improvements to valve design are critical to help achieve equivalent, and perhaps superior, outcomes.

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