Sapien 3: A Triple Threat to Aortic Stenosis*

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Transcatheter aortic valve replacement (TAVR) is an established treatment for patients with severe aortic stenosis (AS) deemed to be at high risk for surgery (1,2). The first-generation balloon-expandable SAPIEN (Edwards Lifesciences, Irvine, California) transcatheter heart valve (THV) was the first device to be approved by the U.S. Food and Drug Administration (FDA) for inoperable, and subsequently, high-risk patients with AS. Limitations of the first-generation SAPIEN device included access-site related vascular complications, inconsistent positioning, paravalvular aortic valve regurgitation, and periprocedural strokes. Subsequent iterations of the SAPIEN THV included modifications in device design translating to improved performance and clinical outcomes. The Edwards-SAPIEN 3 (S3) is the fifth-generation balloon-expandable THV device. The valve and delivery system contain a number of improvements designed to reduce the risk of access site vascular injury, facilitate consistent and accurate positioning, and mitigate paravalvular regurgitation. The valve comprises a cobalt chromium stent, bovine pericardial leaflets, and an inner and outer polyethylene terephthalate sealing cuff. The unique cell design of the frame allows an ultra-low delivery profile while maintaining radial strength for circularity. The outer sealing skirt acts to minimize paravalvular regurgitation. The delivery system allows distal flex to help cross in challenging anatomies and control coaxiality, and has a handle that reflects degree of articulation, to ensure precise deployment. The valve comes in 4 sizes (20, 23, 26, and 29 mm), enabling treatment of a greater range of native aortic annular sizes. All valves aside from the 29-mm device are compatible with a 14-F sheath. The low profile characteristics of the sheath and catheter allow passage through femoral arteries as small as 5.5 mm in diameter with significantly fewer vascular complications. Previously, patients with small-caliber femoral vessels were subject to alternative access, such as transaortic or transapical approaches, with worse clinical outcomes compared with those undergoing the transfemoral approach (3).

The SAPIEN 3 THV received approval for high-risk patients with AS in Europe in January 2014 (CE Mark) and in the United States in June 2015 (FDA). The CE Mark was based on results from 1 nonrandomized study (4). The excellent clinical outcomes observed with SAPIEN 3 were further confirmed by the results of subsequent clinical studies, including 1 study assessing intermediate-risk patients (5). FDA approval was based on the results of the PARTNER (Placement of AoRTic TranScatheter Valve) II S3 trial, the largest TAVR trial to date (6). The trial comprised 2 single-arm, multicenter, nonrandomized studies assessing outcomes in high-risk/inoperable and intermediate-risk/operable patients compared with outcomes in the historical SAPIEN and SAPIEN XT groups. Excellent clinical outcomes were seen in both groups at 30 days and at 1 year. Longer-term follow-up is awaited.

In this issue of JACC: Cardiovascular Interventions, Husser et al. (7) report 30-day outcomes of 250 patients treated with the SAPIEN 3 valve at a single center. The authors should be congratulated on the sample size of their study, meticulous recording of clinical data in accordance with the updated Valve Academic Research Consortium 2 criteria, and excellent overall clinical outcomes. This study population

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was similar to those in previously published studies, with advanced age, multiple comorbidities, and an intermediate risk profile based on Society of Thoracic Surgeons risk score. All procedures were performed via a transfemoral approach using a 23-mm valve in the majority of cases, with a high overall device success rate (97.4%). A total of 5 (2%) patients were left with grade 3 aortic regurgitation, with one patient requiring a second valve implantation to treat severe paravalvular regurgitation.

There were no in-hospital deaths, and only 1 death within 30 days. There were 4 cases of major disabling stroke (1.6%), with an overall stroke rate of 3.2% at 30 days. Major vascular complications occurred in 3.6%, and the rate of new pacemaker implantation was 15.2%. Although these findings are generally consistent with previously published SAPIEN 3 experience, the stroke and pacemaker rates appear to be slightly higher in this real-world series.

The slightly elevated stroke rate in this series may be attributable to 2 causes. First, the higher than usual rate of post-dilation in this study compared with previous studies may have contributed to embolic events. Second, following the procedure, there may have been thrombus formation on the valve with subsequent embolization. The antithrombotic therapy administered in this series was not discussed. It is possible that the routine use of cerebral protection devices in conjunction with better post-procedure antithrombotic therapy might help in further reduction of neurological events. The results of ongoing clinical trials to explore the effect of cerebral protection devices and the optimal antiplatelet or anticoagulation regimen are eagerly anticipated.

Despite advances in THV technology, the requirement for permanent pacemakers remains an issue. In this series, the slightly elevated rate of permanent pacemaker implants may have been related to a combination of relative oversizing, increased depth of implantation, and the use of post-dilation in over one-third of cases.

Despite enrolling a relatively large sample size with excellent overall clinical outcomes, this study does have certain limitations. Although this series reflects a real-world application of the SAPIEN 3 device, outside of the rigorous constraints of a clinical trial, the absence of independent adjudication of data may lead to under-reporting of clinical events. A further limitation of a single-center study, particularly at an experienced center, is the inability to reproduce and extrapolate the degree of clinical success to a larger population at other institutions.

There have been major advances in THV therapy since the inception of TAVR. The emergence of new devices coupled with the evolution of existing technologies has helped catalyze the rapid progression of the THV field. Once limited to large, tertiary centers participating in multicenter clinical trials, TAVR is now available in over 60 countries to centers with appropriate infrastructure that can demonstrate adequate procedural experience. The SAPIEN 3 THV, with its excellent safety and efficacy profile, particularly low mortality, low stroke, and minimal paravalvular leak, has set a new benchmark against which all other THV devices should be compared. Further advances in device technology and delivery methods will no doubt further reduce the incidence of stroke and pacemaker requirement. It is only a matter of time before TAVR will be the standard therapy for aortic stenosis, irrespective of a patient’s risk profile.

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REFERENCES


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