

Transcatheter Aortic Valve Replacement: A Review of Current Indications and Outcomes

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ABSTRACT

In patients with symptomatic severe aortic stenosis, surgical aortic valve replacement (SAVR) improves survival, quality of life, and functional status compared with medical therapy. Based on the results of the randomized PARTNER Trial, Transcatheter Aortic Valve Replacement (TAVR) using the Edwards Sapien balloon expandable valve is now available in the United States for patients who are either inoperable due to anatomic concerns or severe medical co-morbidities, or as an alternative in patients considered high risk for SAVR. Fifty-six patients have been treated with TAVR at Rhode Island Hospital from March 2012 through October 2013 with similar outcomes to The PARTNER Trial and several large European registries. Second-generation valves and lower profile delivery systems designed to reduce the incidence of vascular complications, stroke, and paravalvular leak; and extension of TAVR to intermediate risk surgical patients, are under investigation.

KEYWORDS: Aortic Stenosis, Transcatheter Aortic Valve Replacement

INTRODUCTION

When patients with severe calcific aortic stenosis (AS) develop symptoms, survival at 2 years is less than 50%, and by five years less than 10% of these patients are alive.^{1,2} Surgical aortic valve replacement (SAVR) improves symptoms, quality of life, and mortality.³ However, there are patients with severe AS with coexisting morbidities or anatomical concerns who have a prohibitive operative risk for SAVR. In the late 1980s, balloon aortic valvuloplasty was developed as an alternative to surgery, but this procedure did not improve mortality; it suffered from high restenosis rates, and thus remained a palliative treatment for inoperable patients.⁴ TAVR has been shown to improve mortality and relieve symptoms in patients deemed to have a prohibitive operative risk for SAVR compared to medical management.⁵ Since the first TAVR was performed in 2002, over 60,000 patients have been treated worldwide, either with a balloon expandable Edwards Sapien valve (Edwards Lifesciences Corp., Irvine, CA) or the self-expanding Medtronic CoreValve (Medtronic, Inc., Minneapolis, MN). Increased operator and institutional

experience along with improved technology has led to procedural success rates greater than 95% with reduction in early mortality, vascular complications and stroke rates.

The PARTNER Trial

The PARTNER (Placement of Transcatheter Aortic Valves) Trial was the first, and to date, only randomized controlled trial of TAVR in patients with aortic stenosis. It thus remains a pivotal study guiding current practice. This was a two-armed trial in which patients with severe symptomatic aortic stenosis considered high risk for SAVR were randomized to either TAVR or SAVR (cohort A). If they were deemed inoperable (cohort B) by two cardiac surgeons and had adequate access for transfemoral TAVR, patients were randomized to TAVR or medical therapy.

Three hundred and fifty-eight patients were randomized in the inoperable arm of the trial (cohort B). Among those cohort B patients treated with TAVR, there was a 20.0% absolute reduction in mortality at 1 year compared with patients treated medically (30.7% vs. 50.7%, $p < 0.001$), despite 85% of the medically treated patients receiving at least one balloon aortic valvuloplasty. Mortality continued to diverge with a 24.7% (43.3% vs. 68.0%) and 26.8% (54.1% vs. 80.9%) absolute reduction for the TAVR treated patients at years 2 and 3 ($p < 0.001$), respectively. The number needed to treat was less than 4 patients to save one life. There were also significantly lower readmission rates for recurrent congestive heart failure (CHF), improved New York Heart Association functional class (75% vs. 42% NYHA class 1 or 2), and improved quality of life in TAVR treated patients.^{5,6} The very high mortality at 2 and 3 years in the medically treated patients in this contemporary trial confirms the poor prognosis for patients with symptomatic aortic stenosis, with no long-term symptomatic or mortality benefit from palliative balloon valvuloplasty.

Complications from TAVR included an increased risk of stroke in the TAVR-treated patients at 30 days (6.7% vs. 1.7%) and 2 years (13.8% vs. 5.5%), with the majority of early strokes occurring during the procedure from aortic atheroembolic or valvular particulate embolization. Due to the large diameter delivery sheaths (22 or 24 French requiring iliac artery diameter ≥ 7 or 8mm), major vascular complications were higher with TAVR (16.2% vs. 1.1%) as compared with medical therapy with or without balloon valvuloplasty.^{5,6}

Figure 1. [L] Edwards Sapien Valve, [R] Sapien Valve on balloon and Delivery System



In cohort A of the trial, 688 high-risk operable patients were randomized 1:1 to either TAVR (transfemoral or transapical from a left thoracotomy if iliofemoral access was not adequate) or SAVR. Mortality was similar in each group at 30 days (TAVR 3.4% vs. SAVR 6.5%), 1 year (TAVR 24.2% vs. SAVR 26.8%), 2 years (TAVR 33.9% vs. SAVR 35%) and 3 years (TAVR 44.2% vs. SAVR 44.8%). Combined stroke or transient ischemic attacks were more frequent after TAVR than SAVR at 30 days (5.5% vs. 2.4%), 1 year (8.7% vs. 4.3%) and 2 years (11.2% vs. 6.5%). At 30 days, TAVR was associated with more frequent vascular complications (11.0% vs. 3.2%), but SAVR was associated with more frequent major bleeding (19.5% vs. 9.3%) and new onset atrial fibrillation (16.0% vs. 8.6%). More TAVR patients experienced early symptomatic improvement at 30 days, but by 1 year, symptoms and exercise tolerance were similar in both groups.^{7,8}

Based largely on the results of the PARTNER Trial, the United States FDA first approved TAVR from a transfemoral approach using the Edwards balloon expandable Sapien Valve (Figure 1) in late November 2011 for patients deemed inoperable for SAVR, followed by approval of transfemoral or transapical TAVR as an alternative to SAVR in high-risk patients in October 2012. Since FDA approval of the Edwards Sapien heart valve two years ago, more than 13,500 patients in the United States have undergone TAVR. All patients treated with TAVR are enrolled in the Transcatheter Valve Registry. In a report of the first 7,710 patients (20% inoperable and 80% high risk, with 64% treated transfemorally), device success was 92% with a 30-day mortality of 5.5% and stroke rate of 2.0%.⁹

PATIENT SCREENING

The Valve Academic Research Consortium (VARC) has produced guidelines for effective implementation of TAVR across the United States.^{10,11} Patients with symptomatic aortic stenosis who are considered high risk for SAVR or inoperable are seen by a multidisciplinary team including at least two cardiac surgeons and an interventional cardiologist. The Society of Thoracic Surgery (STS) score is used to risk stratify patients for AVR; however, there are some comorbidities not accounted for in the STS score that

prohibit SAVR. These include severe lung disease, severe liver disease with Child-Pugh B or greater cirrhosis, severe pulmonary hypertension with right ventricular dysfunction, and prior mediastinal radiation. Some frail and elderly patients may fail to pass a surgeon's "eyeball test." Anatomic considerations that carry a prohibitive surgical risk include severe kyphoscoliosis, a heavily calcified or "porcelain" ascending aorta, and one or more prior median sternotomies

with dense adhesions, prior sternal wound infection, or bypass graft anatomy such as a left internal mammary graft coursing anteriorly under the sternum.

Complications

There are several serious procedural complications that may occur during TAVR. Patients may transiently develop shock and low cardiac output states following rapid pacing, required to prevent movement during valve deployment. This may require temporary hemodynamic support. Rarely, coronary artery obstruction may occur (1%-2%) – especially with low coronary ostia heights < 10mm, small coronary sinuses, or with bulky displaced native leaflet calcification.¹² Annular rupture, aortic dissection, or valve embolization (< 1%) are rare, but may require pericardiocentesis or emergency median sternotomy with open surgical repair. Complete heart block requiring permanent pacemaker placement (especially with a preexisting right bundle branch block) occurred in 5-10% of patients.¹³

Vascular complications occur in approximately 10% of patients, including iliac artery dissection, perforation or avulsion.^{5,7,13} Most can be treated percutaneously with stents or stent grafts, but with proper procedural planning and vessel sizing, many vascular complications can be avoided. Major vascular complications are associated with an increase in late mortality.^{6,8}

Perivalvular regurgitation occurs in nearly 85% of TAVR patients as a result of incomplete apposition of the valve prosthesis within the aortic annulus due to inadequate inflation and expansion of the prosthesis or calcific deposits that prevent proper seating. In the PARTNERS Trial, moderate or severe perivalvular aortic regurgitation was more frequent after TAVR compared with SAVR at 30 days and out to 2 years (6.9% vs. 0.9%). Any more than trivial perivalvular regurgitation is associated with an increased late mortality at 2 years (hazard ratio 2.11, 95% CI 1.43-3.10), but it is uncertain if the aortic insufficiency itself is a cause of late mortality or just a marker of increased risk.^{6,8}

Stroke occurs in 4%-8% of patients, with the majority occurring early due to aortic or valvular atheroemboli. The rate of stroke has fallen over time with improved procedural technique, improved delivery systems, and more aggressive

anticoagulation. MRI-detected “silent” embolic events occur in nearly 85% of TAVR procedures.¹⁴ Embolic protection filter devices delivered from the radial artery to shield the aortic arch vessels are being tested in clinical trials.

RHODE ISLAND HOSPITAL OUTCOMES

From March 2012 through October 2013, 56 patients have undergone TAVR using the Edwards Sapien balloon expandable valve, 30 from a transfemoral approach and 26 from a transapical approach. During the same time period, 157 patients underwent SAVR and 89 patients underwent combined CABG and AVR for aortic stenosis (TAVR performed in 23% of the total AVR procedures). Procedural success has been 100%, with one annular perforation from displacement of bulky calcification that resulted in tamponade treated with pericardiocentesis. There have been 3 vascular complications in transfemoral TAVR patients (10%) from iliac artery dissections managed with stenting. We have had 2 major periprocedural strokes resulting in death at 34 and 60 days, and one minor stroke without residual neurologic deficit – an overall 5.4% stroke rate. Four patients died within 30 days (7.1% mortality), with 7 more deaths after 30 days for a total mortality of 20%. Of the first 14 patients with more than 1-year follow-up, 2 patients have died (14% mortality).

FUTURE DIRECTIONS

Next-generation lower profile valve and delivery systems are available and have replaced the first-generation Edwards Sapien valve outside of the United States.^{15,16} The Edwards Sapien XT balloon expandable valve (Edwards Lifesciences Corp., Irvine, CA) made of cobalt-chromium is delivered through an 18 or 19 French delivery system. In the PARTNER 2 Trial, 560 inoperable or extreme-risk patients with adequate iliofemoral access for TAVR were randomized to either the current FDA-approved Edwards Sapien valve or the lower profile Sapien XT valve. There was no difference in 1-year mortality (23.7% vs. 22.5%) or stroke (4.6% vs. 4.5%) between the devices. However, procedural times were

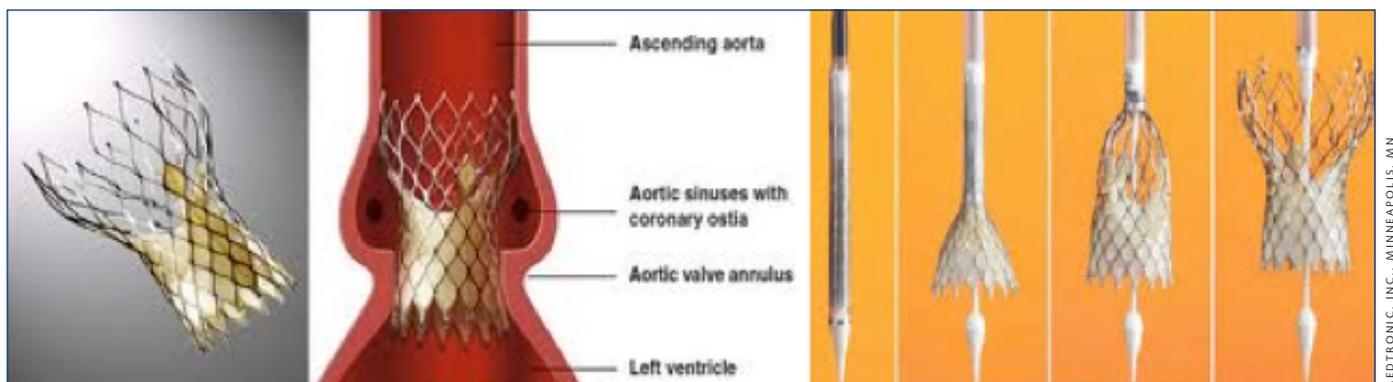
shorter with Sapien XT, and major vascular complications were significantly reduced at 30 days (15.5% vs. 9.6%).¹⁷

The Medtronic CoreValve is a self-expanding valve with bovine pericardial leaflets sewn to a nitinol cage that extends from the left ventricular outflow tract to the proximal ascending aorta (**Figure 2**). Four valve sizes range from 23-31 mm in diameter. This valve is used in approximately 50% of the TAVR procedures outside of the United States. The 18 French delivery system allows for transfemoral access through a minimum 6mm iliac artery. Multiple large registries using both the Edwards Sapien XT and Medtronic valves show procedural success is greater than 95%, with stroke rates reduced to 4-5% and vascular complications reduced to 5%.^{15,16} The need for permanent pacemaker is higher with the Corevalve (25.8%) compared with the Sapien XT valve (6.5%) due to extension of the self-expanding nitinol cage within the left ventricular outflow track.¹⁸

The 1-year outcomes for the CoreValve SURTAVI Trial (Surgical Placement and Transcatheter Aortic Valve Implantation) were recently released in October 2013. This was a non-randomized registry of extreme-risk patients with aortic stenosis (Society of Thoracic Surgery predicted combined morbidity and mortality > 50%). Four hundred and seventy-one patients were enrolled and treated with transfemoral TAVR using the CoreValve; 30-day mortality was 7.9%, with all cause mortality at 1 year of 24%. The 30-day stroke rate was 4.1%. While perivalvular leak was common, 80% of patients with a moderate or less perivalvular leak post procedure improved by 1 year.¹⁹ This was likely due to the self-expanding nature of this valve conforming to the aortic annulus over time.

TAVR has been extended to intermediate-risk patients in Europe with similar late 1- and 3-year mortality to SAVR in propensity-matched cohorts.²⁰ Extension to intermediate-risk patients is being tested in the randomized PARTNER 2 and SURTAVI Trials. In PARTNER 2, operable patients are randomized to TAVR with the second-generation Sapien XT valve or SAVR. Patients with significant obstructive CAD are included in this trial (percutaneous intervention with TAVR vs. CABG and AVR). In the SURTAVI trial, intermediate-risk

Figure 2. [L] Medtronic CoreValve, [R] Self-Expanding CoreValve and Delivery System



MEDTRONIC, INC., MINNEAPOLIS, MN

patients are randomized to TAVR with the CoreValve (femoral or direct aortic approach) or SAVR.

The direct transaortic retrograde approach from a small incision to the right of the upper sternum with a sheath placed in the ascending aorta is being developed as an alternative to the transapical approach in patients who are not candidates for transfemoral TAVR. In small-matched series, there were fewer bleeding complications compared with the transapical approach,²¹ and it may be a better alternative in patients with severe lung disease who may not tolerate a left thoracotomy. Within the PARTNER 2 trial, the direct aortic approach is being compared to transapical TAVR in a subset of patients.

With lower profile second-generation valves, some centers have been performing TAVR procedures in catheterization laboratories under conscious sedation without transesophageal echocardiography using percutaneous suture closure devices with excellent outcomes.²² This approach significantly lowers ancillary costs and hospital lengths of stay, with many patients being discharged 1 day post procedure. The PARTNER 3 trial is about to begin enrollment testing an even smaller diameter 14F delivery system with a third-generation balloon expandable valve with a self-sealing cuff to reduce the incidence of perivalvular leak.

SAVR remains the treatment of choice in most patients with severe symptomatic aortic stenosis. At present, TAVR remains an alternative to surgery in high-risk or inoperable patients. As technology improves to lower stroke rates, vascular complications, and perivalvular leak, TAVR likely will be extended to lower-risk patients with comparable outcomes to SAVR.

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