JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 8, NO. 7, 2015

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jcin.2015.03.014

STRUCTURAL

Comparison of Self-Expanding and Mechanically Expanded Transcatheter Aortic Valve Prostheses

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ABSTRACT

OBJECTIVES The aim of this study was to determine whether transcatheter aortic valve replacement (TAVR) with the mechanically expanded Lotus valve (Boston Scientific, Natick Massachusetts) offers potential benefits over treatment with the self-expanding CoreValve (Medtronic, Minneapolis, Minnesota).

BACKGROUND New-generation transcatheter aortic valve systems are emerging in clinical trials and practice with design features aimed at improving safety and efficacy. To date, these devices have not been compared systematically with current-generation devices.

METHODS A total of 100 patients (83.4 ± 4.8 years of age, 44% male, Society of Thoracic Surgeons Predicted Risk of Mortality score of 5.5 ± 2.4) were assessed. Fifty consecutive patients undergoing a Lotus transcatheter aortic valve replacement were enrolled and compared with 50 matched patients treated with a CoreValve. An independent core laboratory reviewed all echocardiographic data, and an independent clinical events committee adjudicated all events.

RESULTS Valve Academic Research Consortium 2-defined device success was 84% and 64% in the Lotus and CoreValve cohorts, respectively ($p = 0.02$). This difference was driven by lower rates of moderate or greater aortic regurgitation (4% vs. 16.7%, respectively; $p = 0.04$) and higher rates of successfully implanting a single device in the correct anatomic position (100% vs. 86%, respectively; $p = 0.06$). Cardiovascular mortality rate (0% vs. 4%, respectively; $p = 0.32$), major stroke rate (4% vs. 2%, respectively; $p = 0.56$), and permanent pacemaker insertion rate (28% vs. 18%, respectively; $p = 0.23$) were not different at 30 days in the Lotus and CoreValve cohorts.

CONCLUSIONS In this matched comparison of high surgical risk patients undergoing transcatheter aortic valve replacement, the use of the Lotus device was associated with higher rates of Valve Academic Research Consortium 2-defined device success compared with the CoreValve. This was driven by higher rates of correct anatomic positioning and lower incidences of moderate paraprosthetic regurgitation. The clinical significance of these differences needs to be tested in a large randomized, controlled trial. (J Am Coll Cardiol Intv 2015;8:962–71) © 2015 by the American College of Cardiology Foundation.

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Transcatheter aortic valve replacement (TAVR) has proved to be a safe and effective treatment for severe aortic stenosis in appropriately selected high and extremely high surgical risk patients (1,2). Since its inception in 2002 (3), TAVR has gained wide acceptance and clinical approval in many countries on the basis of a rapidly growing body of evidence. As a result, adoption of the technology and implant rates have grown nearly exponentially (4,5).

Most global TAVR experience has been obtained with either the Edwards SAPIEN or SAPIEN XT (Edwards Lifesciences, Irvine, California) or the Medtronic CoreValve device, (Minneapolis, Minnesota); however, a growing number of next-generation prostheses are now entering clinical trials and routine practice (6–9). Most of these devices incorporate novel features designed to reduce the modest yet important complications identified with current-generation devices. Data supporting enhanced safety and efficacy of new-generation devices, however, are modest and derived from single-arm studies.

The CoreValve Revalving System (Medtronic) is a self-expanding device fashioned from nitinol wire. The distinctive frame has a flared inflow portion to anchor in the native annulus, a constrained midsegment to avoid coronary obstruction, and a flared outflow portion to improve coaxial alignment to the aortic flow plane. In a U.S. pivotal trial, the CoreValve was found to have a significantly higher survival rate at 1 year than surgical valve replacement in a high-risk cohort (10). These results mirror favorable safety and efficacy data from large single-center (11,12), national (13–15), and multinational (16) registries.

The Lotus device (Boston Scientific, Natick, Massachusetts) is a new TAVR device that uses a unique mechanical expansion mechanism. It is made of a single braided nitinol wire and 3 bovine pericardial leaflets. The outer surface of the lower half of the frame is covered with an adaptive seal, essentially a polymer membrane that concertinas as the device is expanded and, in doing so, occupies any small residual interstices, sealing the frame against the native aortoventricular interface (8,17). This has been reported to reduce the rate of paraprosthetic aortic regurgitation (PAR). The device is fully repositionable and resheathable, even in the completely expanded position, allowing for fine control and the potential for removal should the device position or size be deemed suboptimal. The Lotus device was studied in the REPRISE I (Repositionable Percutaneous Replacement of Stenotic Aortic Valve Through Implantation of Lotus™ Valve System—Evaluation of Safety and Performance) (19), and REPRISE II Extension single-arm trials.

Although there has been an adoption of new devices such as the Lotus at some centers, to date, there have been no systematic head-to-head comparisons, with independent core laboratory assessments, of devices to accurately determine their relative safety and efficacy.

ABBREVIATIONS AND ACRONYMS

EOA = effective orifice area

MDCT = multidetector computed tomography

PAR = paraprosthetic aortic regurgitation

TAVR = transcatheter aortic valve replacement

TTE = transthoracic echocardiography

VARC2 = Valve Academic Research Consortium 2

METHODS

STUDY POPULATION. A total of 100 patients (mean age, 83.4 ± 4.8 years, 44% male) with symptomatic severe aortic stenosis were included in this study. Fifty consecutive and prospectively enrolled patients receiving a Lotus transcatheter device were compared with 50 matched patients who had undergone TAVR with the CoreValve device during the same period.

All patients were treated at a single Australian center. All patients were deemed to be at high or extremely high surgical risk because of an increased Society of Thoracic Surgeons Predicted Risk of Mortality score (higher than 8) and/or the collective opinion of the institution's Heart Team after a comprehensive history, examination, and frailty assessment (dominant hand-grip strength, 5-m gait speed, and serum albumin). Patients were eligible for inclusion if they had severe aortic stenosis based on echocardiographic criteria (mean transaortic gradient ≥40 mm Hg or aortic velocity ≥4 m/s and an aortic valve area ≤1 cm^2 or indexed aortic valve area ≤0.7 cm^2/m^2) and reported symptoms attributable to severe aortic stenosis (**Table 1**).

All patients were assessed in a systematic and standardized manner beginning with their attendance and clinical evaluation at our Structural Heart Disease Clinic. All patients underwent multidetector computed tomography (MDCT), transthoracic echocardiography (TTE), invasive angiography, and right heart catheterization before inclusion. Only patients who had MDCT annular sizing that allowed for treatment with either device (according to the respective instructions for use) and were treated via the femoral access route were considered suitable for the study. Patients were matched on age, sex, Society of Thoracic Surgeons score, and frailty indexes.

JACC: CARDIOVASCULAR INTERVENTIONS VOL. 8, NO. 7, 2015
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TABLE 1 Inclusion and Exclusion Criteria

Inclusion criteria
1. Severe aortic stenosis
Mean aortic gradient ≥40 mm Hg or aortic velocity ≥4 m/s
AVA ≤1 cm^2 or indexed AVA ≤0.7 cm^2/m^2
2. Symptoms consistent with aortic stenosis
NYHA functional class II–IV dyspnea
Exertional angina
Exertional syncope or pre-syncope
3. High or extreme surgical risk
STS PROM ≥8 or heart team agreement that patient is at high surgical risk
4. Suitable aortic root anatomy for placement of either a Lotus* or CoreValve† prosthesis
MDCT-derived annular dimension ≥19 mm and ≤27 mm
5. Suitable peripheral vasculature for passage of an 18-/20-F sheath
Exclusion criteria
1. Inability to consent

*Boston Scientific, Natick, Massachusetts. †Medtronic, Minneapolis, Minnesota.
AVA = aortic valve area; NYHA = New York Heart Association; STS PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; MDCT = multidetector computed tomography.

320-MDCT imaging of the aortic root at baseline. All scans were performed on a Toshiba Aquilion One 320-detector row scanner (Toshiba Medical Systems, Otawara, Japan). No heart rate control was used. Collimation was individualized to achieve a z-axis that encompassed the entire aortic root. Slice thickness was 0.5 mm. Gantry rotation speed was 275 ms per rotation, tube voltage was 100 to 120 kV, and the tube current was individualized to body habitus. Intravenous contrast (Omnipaque 350, GE Healthcare, Little Chalfont, Buckinghamshire, United Kingdom) was administered via an 18-gauge antecubital vein as a 70-ml bolus followed by a 50-ml saline solution bolus at a rate of 6 ml/s. Systolic phase images (20) were acquired after manual triggering by monitoring for contrast density in the descending aorta to ensure adequate contrast opacification.

All MDCT scans were analyzed by an experienced computed tomography cardiologist using the 3Mensio valve analysis program (3Mensio Medical Imaging, Bilthoven, the Netherlands). The annular plane was identified as the short axis through the nadir of each coronary cusp, and diameters, perimeter, and area were measured. The eccentricity was calculated using the eccentricity index (eccentricity index = 1 − minimal diameter/maximal diameter). Further measurements were taken in the left ventricular outflow tract 4 mm below the annular plane, sinus of Valsalva,

Sizing of TAVR devices was guided by the 3-dimensional MDCT measurements and strictly conformed with the respective manufacturer's instructions for use. The degree of oversizing for each device was calculated based on annular plane perimeter (perimeter oversizing = (device perimeter − annular perimeter)/annular perimeter × 100) and annular plane area (area oversizing = (device area − annular area)/annular area × 100).

PRE-PROCEDURAL TTE ASSESSMENT. TTE was performed using an iE33 machine (Philips, Best, the Netherlands) before enrollment. All scans were assessed by an experienced echocardiologist with severity of aortic stenosis graded based on European Association of Echocardiography and American Society of Echocardiography joint guidelines (21). An independent echocardiography core laboratory subsequently reviewed these studies with these results used for study analysis.

PRE-PROCEDURAL INVASIVE ANGIOGRAPHIC ASSESSMENT. All patients underwent invasive coronary and peripheral angiography to confirm access site suitability and to identify significant coronary artery disease warranting treatment before TAVR. Treatment of concomitant coronary artery disease was at the discretion of the implanting cardiologist. Right heart catheterization was performed to exclude significant primary pulmonary hypertension and corroborate ultrasound-based hemodynamic measurements.

TREATMENT. All TAVR procedures were performed in the cardiac catheterization laboratory with patients under general anesthesia or conscious sedation. Three experienced TAVR cardiologists performed all procedures with 2 operators present at each procedure. The femoral artery was used for device access in all cases with an 18-F Cook sheath (Cook Medical, Bloomington, Indiana) used for all CoreValve procedures, whereas an 18-F Lotus Introducer (Boston Scientific) was used for 23-mm Lotus cases and 20-F Lotus Introducer for those receiving a 27-mm Lotus valve. The femoral access site was managed uniformly in all patients. The designated femoral access was routinely "pre-closed" with either a single Prostar or 2 Proglide devices (Abbott Vascular, Abbott Park, Illinois), and final access site closure was performed using a crossover balloon occlusion technique (22).

Balloon valvuloplasty was performed in all patients under rapid ventricular pacing to enable maximal balloon stability. Valvuloplasty balloons

Deployment of the respective devices was performed in strict accordance with manufacturer's guidelines and current best practices (8,16,17).

Aortic regurgitation was assessed by aortography after final deployment using 20 ml of iodinated contrast delivered at 20 ml/s and 800 psi by automated injector through a 5-F pigtail catheter positioned above the prosthesis leaflets. Moderate or greater aortic regurgitation, identified at the time of deployment by either imaging modality and/or haemodynamic assessment, was treated by post-dilation in the CoreValve cohort and repositioning in the Lotus cohort. Aortography was repeated after final device manipulation to reassess final degree of PAR and to exclude the need for further manipulation.

INDEPENDENT CORE LABORATORY ECHOCARDIOGRAPHIC ASSESSMENT. All patients had a TTE study performed on day 7 to 10 or on the day of discharge, if this occurred earlier, and again at 30 days after TAVR. The independent core laboratory assessed prosthesis function, degree, and location of aortic regurgitation, severity of mitral regurgitation, left ventricular function, and pulmonary artery pressure. Prosthetic regurgitation was assessed in accordance with Valve Academic Research Consortium 2 (VARC2) (23) recommendations.

CLINICAL REVIEW. A study investigator reviewed patients at the time of each echocardiogram, and a detailed history was taken and an examination performed. New York Heart Association functional class was determined on the basis of the patient's self-reporting of symptoms.

ENDPOINTS. The primary endpoint of the trial was VARC2-defined device success (23). This is a composite endpoint that includes the absence of procedural mortality, correct positioning of a single prosthesis in the correct anatomic position, and intended prosthesis function (no prosthesis-patient mismatch, mean aortic valve gradient <20 mm Hg, peak velocity <3 m/s, and no moderate or greater aortic regurgitation on TTE at time of discharge). Prosthesis function was determined by core laboratory assessment of the discharge echocardiogram.

Secondary endpoints were all-cause and cardiovascular mortality at 30 days, minor and major bleeding, minor and major vascular injury, new pacemaker insertion, and disabling and nondisabling stroke.

STATISTICAL ANALYSIS. Categorical variables were compared using a chi-square test, whereas nonparametric continuous variables were compared using the Mann-Whitney or independent-sample *t* test. A 2-sided p value <0.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS Statistics version 22.0 (IBM Corporation, Armonk, New York).

RESULTS

BASELINE CHARACTERISTICS. The baseline demographic and clinical characteristics are described in Table 2. In brief, there were no clinically significant differences between the 2 study populations other than a higher proportion of patients with NYHA functional class IV symptoms in the Lotus cohort and more patients with pre-existing atrial fibrillation in the CoreValve cohort. Baseline Society of Thoracic Surgeon scores, Charlson Comorbidity Index, and frailty index were similar.

Baseline echocardiographic parameters of aortic stenosis severity were not significantly different between the Lotus and CoreValve cohorts, with average mean gradients of 44.9 ± 12.9 mm Hg and 47.3 ± 12.5 mm Hg, respectively (p = 0.34). There

TABLE 2 Baseline Characteristics

	Lotus* (n = 50)	CoreValve† (n = 50)	p Value
Age, yrs	84.0 ± 5.2	82.7 ± 4.5	0.19
Male	18 (36)	26 (52)	0.11
Height, cm	161.4 ± 10.0	163.8 ± 8.9	0.20
Weight, kg	72.9 ± 17.2	73.9 ± 14.6	0.75
Body mass index, kg/m^2	28.1 ± 6.6	27.5 ± 4.8	0.62
STS PROM, %	5.80 ± 2.40	5.21 ± 2.47	0.23
STS M&M	26.21 ± 7.44	23.97 ± 6.08	0.10
Charlson Comorbidity Index	2.7 ± 2.0	2.6 ± 1.4	0.65
Hand grip strength	16.6 ± 7.0	16.0 ± 6.3	0.73
5-m gait speed	9.9 ± 3.0	9.5 ± 2.9	0.55
Serum albumin	33.9 ± 5.6	32.1 ± 5.8	0.12
NYHA functional class			
II	7 (14)	13 (26)	
III	36 (72)	36 (72)	
IV	7 (14)	1 (2)	0.05
Creatinine, μmol/l	97.6 ± 57.3	103.2 ± 28.4	0.54
Type 2 diabetes mellitus	10 (20)	12 (24)	0.63
Existing coronary artery disease	29 (58)	33 (66)	0.41
Previous coronary bypass surgery	7 (14)	15 (30)	0.05
Peripheral vascular disease	3 (6)	6 (12)	0.30
Chronic pulmonary disease	14 (28)	16 (32)	0.66
Atrial fibrillation	5 (10)	14 (28)	0.02
Existing permanent pacemaker	5 (10)	7 (14)	0.54

Values are mean ± SD or n (%). *Boston Scientific, Natick, Massachusetts. †Medtronic, Minneapolis, Minnesota.
STS M&M = Society of Thoracic Surgeons Morbidity and Mortality; other abbreviations

were no differences in the proportion of patients with mild, moderate, or severe aortic regurgitation at baseline. MDCT annular dimensions, whether diameter, perimeter, or perimeter-derived metrics, were well matched. The basal plane was slightly more eccentric among the CoreValve cohort (eccentricity index: 0.20 ± 0.06 vs. 0.23 ± 0.06, p = 0.02). Left ventricular outflow tract, sinus dimensions, and height of the coronary arteries above the basal plane were similar. Full baseline anatomic dimensions are shown in Table 3.

PROCEDURAL DETAILS. Twenty-six patients (52%) in the Lotus cohort were treated with the smaller Lotus device (23 mm), whereas 22 patients (44%) in the CoreValve group received the smaller CoreValve prosthesis (26 mm) (p < 0.001). There was greater perimeter oversizing (3.6 ± 5.7% vs. 14.0 ± 6.2%, p < 0.001) and area oversizing (13.0 ± 12.3% vs. 36.6 ± 15.4%, p < 0.001) in the CoreValve cohort. All patients left the catheterization laboratory with a functioning TAVR prosthesis. There were no differences in procedure duration (Table 4).

TABLE 3 Pre-procedural Echocardiographic and Computed Tomographic Imaging Assessment

	Lotus* (n = 50)	CoreValve† (n = 50)	p Value
Transthoracic echocardiography			
Mean gradient	44.9 ± 12.9	47.3 ± 12.5	0.34
AVA	0.70 ± 0.17	0.67 ± 0.16	0.35
AVA indexed	0.41 ± 0.10	0.39 ± 0.07	0.41
Dimensionless index	0.23 ± 0.05	0.22 ± 0.05	0.39
Pulmonary artery pressure	41.3 ± 11.4	39.1 ± 9.8	0.34
Left ventricular ejection fraction	56.4 ± 9.1	54.9 ± 9.2	0.51
Mitral regurgitation			
None/trivial	29 (58)	25 (50)	
Mild	14 (28)	25 (50)	
Moderate	7 (14)	0	0.01
Tricuspid regurgitation			
None/trivial	22 (44)	30 (60)	
Mild	23 (46)	17 (34)	
Moderate	5 (10)	2 (4)	
Moderate/severe	0	0	
Severe	0	1 (2)	0.22
Aortic regurgitation			
None/trivial	21 (42)	20 (40)	
Mild	23 (46)	28 (56)	
Moderate	6 (12)	2 (4)	0.28
Multidetector computed tomography			
Basal plane			
Minimal diameter	21.2 ± 1.9	21.0 ± 2.0	0.68
Maximal diameter	26.5 ± 2.1	27.3 ± 2.2	0.09
Eccentricity index	0.20 ± 0.06	0.23 ± 0.06	0.02
Perimeter	75.6 ± 5.5	76.5 ± 5.8	0.42
Area	435.7 ± 63.4	447.1 ± 68.9	0.40
Left ventricular outflow tract			
Minimal diameter	19.2 ± 2.6	19.5 ± 2.4	0.59
Maximal diameter	27.4 ± 2.7	27.7 ± 2.8	0.54
Eccentricity index	0.30 ± 0.09	0.30 ± 0.07	0.99
Perimeter	74.6 ± 6.8	75.8 ± 6.8	0.36
Area	405.8 ± 80.5	424.9 ± 77.3	0.23
Sinus of Valsalva			
Area	776.8 ± 122.2	831.3 ± 136.2	0.04

Values are mean ± SD or n (%). *Boston Scientific, Natick, Massachusetts. †Medtronic, Minneapolis, Minnesota.

The primary outcome measure of VARC2-defined device success was achieved in 84% of the Lotus cohort and 64% of the CoreValve cohort (p = 0.02). The components of this outcome measure were the absence of procedural mortality (100% vs. 96%; p = 0.15), correct positioning of a single prosthesis (100% vs. 86%; p = 0.06), mean gradient across the prosthesis <20 mm Hg (96% vs. 100%; p = 0.16), absence of prosthesis-patient mismatch (92% vs. 86%; p = 0.68), and no more than mild aortic regurgitation (96% vs. 83.3%; p = 0.04) in the Lotus and CoreValve cohorts, respectively (Figure 1).

All-cause death was 0% in the Lotus cohort and 4% in the CoreValve cohort at 7 days. At 7 days, 1 death in the CoreValve cohort was due to ischemic colitis after a partially deployed prosthesis was retrieved through the aorta, whereas the other death was due to progressive congestive cardiac failure in the setting of severe PAR that was refractory to post-dilation. There was 1 additional death in the Lotus cohort at 30 days due to a hemorrhagic stroke, and 1 additional death in the CoreValve cohort due to pneumonia and respiratory failure.

There was no significant difference in the rates of acute kidney injury, minor or major vascular injury, disabling or nondisabling stroke, or periprocedural myocardial infarction. The rate of new pacemaker insertion was greater in the Lotus cohort (28% vs. 18%), although not statistically different (p = 0.23) (Figure 2).

CORE LABORATORY DISCHARGE ASSESSMENT. The mean transprosthetic gradients were 12.4 ± 4.2 mm Hg and 8.5 ± 2.9 mm Hg (p < 0.001) for the Lotus and CoreValve cohorts, respectively. The mean effective orifice areas (EOAs) were similar in both cohorts (1.6 ± 0.3 cm^2 vs. 1.7 ± 0.4 cm^2, p = 0.07). There were no differences in the severity of mitral regurgitation, pulmonary artery pressure, or left ventricular function (Table 5).

Core laboratory-adjudicated PAR was mild in 14% and 56.2% (p < 0.001) and moderate in 4% and 16.7% (p = 0.04) of the Lotus and CoreValve

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