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

Robert P. Gooley, MD,*† Andrew H. Talman, MD,*† James D. Cameron, MD,*† Siobhan M. Lockwood, MD,*† Ian T. Meredith, AM, MD*†

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.

From *MonashHeart, Monash Health, Clayton, Victoria, Australia; and the †Monash Cardiovascular Research Centre, Monash University, Clayton, Victoria, Australia. Dr. Gooley, Dr. Lockwood, and Prof. Meredith receive modest consulting fees from Boston Scientific. Prof. Meredith serves on the Strategic Advisory Boards of Boston Scientific and Medtronic. Dr. Gooley receives a research scholarship from the National Health and Medical Research Council of Australia. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

Manuscript received February 23, 2015; revised manuscript received March 20, 2015, accepted March 26, 2015.

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) (18), the REPRISE II (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.

PRE-PROCEDURAL MDCT ASSESSMENT. All patients underwent prospectively electrocardiography-gated,

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, ascending aorta, and height of the coronary arteries.

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 were sized so as to not exceed the minimal diameter of the left ventricular outflow tract.

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 expressed as frequencies and percentages, whereas continuous variables were expressed as means and SDs. 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 as in Table 1.

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.
AVA = aortic valve area.

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 cohorts, respectively. Although 1 patient in the CoreValve cohort died of complications of severe

PAR before the discharge TTE time point, there were no further cases of severe PAR in those patients alive at 7 days.

CORE LABORATORY 30-DAY ASSESSMENT. There was no deterioration in valve function as assessed by TTE at 30 days by mean transprosthetic gradient or EOA. The mean transprosthetic gradient remained significantly higher in the Lotus cohort than the CoreValve cohort (12.6 ± 6.5 mm Hg and 8.2 ± 2.6 mm Hg, respectively; $p < 0.001$), with no difference in the prosthesis EOA (1.7 ± 0.4 cm^2 vs. 1.8 ± 0.4 cm^2, respectively; $p = 0.17$).

Moderate PAR occurred in 0% and 10.6% ($p = 0.02$) of patients in the Lotus and CoreValve cohorts, respectively, with no cases of severe PAR at 30 days. The percentage of patients with mild AR was similar to that at discharge: 14.3% and 66% ($p < 0.001$), respectively (Table 5).

FUNCTIONAL ASSESSMENT. There was a significant improvement in New York Heart Association score in both cohorts with 79.2% of patients in the Lotus group and 82.9% in the CoreValve group, improving by 1 class or more (Figure 3).

TABLE 4 Procedural Characteristics

	Lotus* (n = 50)	CoreValve† (n = 50)	p Value
Device size			<0.001
Small (23-mm Lotus, 26-mm CoreValve)	26 (52)	22 (44)	
Large (27-mm Lotus, 29-mm CoreValve)	24 (48)	28 (56)	
Sheath size, Fr			<0.001
18	26 (52)	50 (100)	
20	24 (48)	0 (0)	
Prosthesis oversizing			
Perimeter	3.6 ± 5.7	13.0 ± 12.3	<0.001
Area	14.0 ± 6.2	36.6 ± 15.4	<0.001
No. of devices used	1.12 ± 0.32	1.14 ± 0.40	0.79
Post-dilation	0 (0)	13 (26)	<0.001
Procedure duration, min	118.0 ± 39.2	114.2 ± 35.8	0.62

*Boston Scientific, Natick, Massachusetts. †Medtronic, Minneapolis, Minnesota.

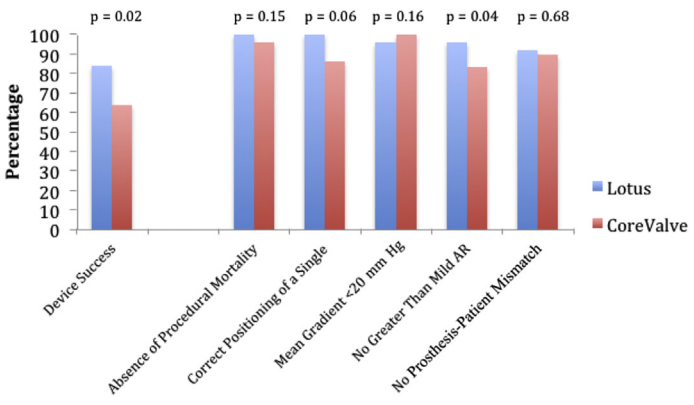
DISCUSSION

There is a substantial body of evidence supporting the efficacy and safety of TAVR as an alternate treatment to surgical valve replacement in high-risk patients (1,10) and its superiority to medical therapy in patients denied surgery due to extreme risk (2). Despite improvements in patient selection, the utility of 3-dimensional computed tomography image-based sizing algorithms and deployment techniques, a number of limitations remain with the current technologies. These include vascular access complications (24,25), need for permanent pacemaker after implantation (26,27), PAR (28), and stroke (29,30). Although second-generation devices, designed to address some of these limitations, are emerging in both clinical trials and clinical practice, the evidence supporting their safety and efficacy is limited. This study was designed to systematically compare a widely accepted and well-studied current-generation device, the CoreValve, with an emerging new-generation device, the Lotus valve.

In this nonrandomized, single-center study, we observed that both the Lotus and CoreValve devices were associated with high rates of procedural success, although the VARC2-defined primary composite outcome of device success was higher in the Lotus cohort. Device success was 84% and 64% in the Lotus and CoreValve arms, respectively, driven by higher rates of correct positioning of a single device and lower rates of moderate PAR in the Lotus group. Importantly, the rates of procedural mortality and transprosthesis gradient greater than 20 mm Hg and prosthesis patient mismatch were not different.

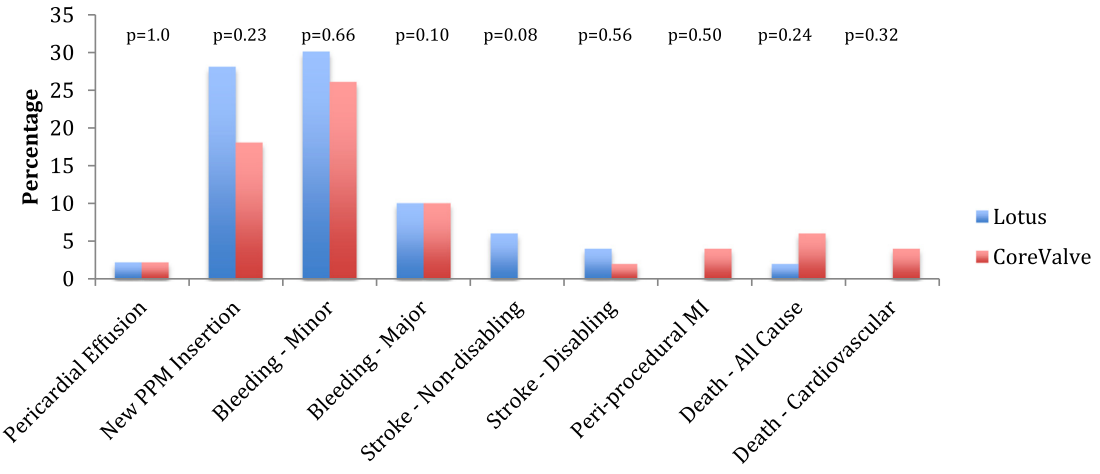
It could be argued that the difference we observed was due to a lower than expected VARC2 device success rate in the CoreValve group; however, the rate was comparable to that observed in the CoreValve arm of the CHOICE trial (Comparison of balloon-expandable vs. self-expandable valves in patients undergoing transcatheter aortic valve replacement) —77.5% (31)—if the same VARC definition is used. The CHOICE trial used the first VARC

FIGURE 1 Device Success and Composites



Primary outcome measure of Valve Academic Research Consortium 2–defined device success and its composites. AR = aortic regurgitation.

FIGURE 2 Secondary Outcome Measures



Comparison of Valve Academic Research Consortium 2 defined outcome measures between the valve types. MI = myocardial infarction; PPM = permanent pacemaker.

definition of device success, which, unlike VARC2, does not include prosthesis-patient mismatch in the composite endpoint. If the prosthesis-patient mismatch is not included in the composite, the rates of device success in our study are 92% and 74% in the Lotus and CoreValve cohorts, respectively. Moreover, the rate of moderate PAR observed in this study was comparable, if not lower, than that observed in

TABLE 5 Core Laboratory-Adjudicated Echocardiographic Assessment

	Discharge			1 Month		
	Lotus* (n = 50)	CoreValve† (n = 48)	p Value	Lotus (n = 49)	CoreValve (n = 47)	p Value
Paraprosthetic aortic regurgitation						
None/trivial	41 (82)	13 (27.1)	<0.001	42 (85.7)	11 (23.4)	<0.001
Mild	7 (14)	27 (56.2)		7 (14.3)	31 (66)	
Moderate	2 (4)	8 (16.7)	<0.001	0	5 (10.6)	<0.001
Moderate/severe	0	0		0	0	
Severe	0	0	0.04	0	0	0.02
Valvular aortic regurgitation						
None/trivial	46 (92)	44 (91.7)	0.95	44 (89.8)	45 (95.7)	0.26
Mild	3 (6)	4 (8.3)	0.65	5 (10.2)	2 (4.3)	0.26
Moderate	1 (2)	0	0.33	0	0	
Moderate/severe	0	0		0	0	
Severe	0	0		0	0	
Mean transprosthetic gradient	12.4 ± 4.2	8.5 ± 2.9	<0.001	12.6 ± 6.5	8.2 ± 2.6	<0.001
Effective orifice area	1.6 ± 0.3	1.7 ± 0.4	0.07	1.7 ± 0.4	1.8 ± 0.4	0.17
Pulmonary artery pressure	41.4 ± 10.8	34.8 ± 8.9	0.03	40.4 ± 10.1	37.0 ± 8.8	0.11
Left ventricular ejection fraction	55.3 ± 10.1	54.5 ± 8.7	0.70	56.0 ± 8.9	55.3 ± 6.0	0.68
Mitral regurgitation						
None/trivial	25 (50)	16 (33.3)		27 (55.1)	20 (42.6)	
Mild	22 (44)	29 (60.4)		18 (36.7)	22 (46.8)	
Moderate	3 (6)	3 (6.3)		4 (8.2)	5 (10.6)	
Moderate/severe	0	0		0	0	
Severe	0	0	0.24	0	0	0.68

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

other core laboratory-adjudicated trials (10,16). The rate of post-dilation in the CoreValve cohort (26%) was also comparable to the rate reported in the CoreValve United States Investigational Device Exemption trial (20.3%) (10). Importantly, the apparent difference in device success in the current study was not reflected in differences in mortality nor clinical efficacy to 30 days.

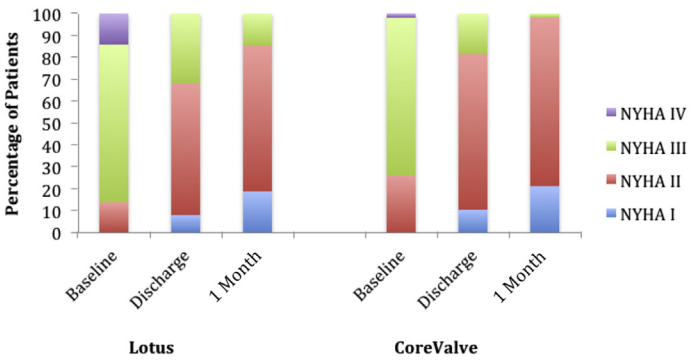
Significant PAR after TAVR deployment has been shown to correlate with increased morbidity and mortality (32,33). Factors contributing to regurgitation include baseline annular eccentricity (34), the depth of device implantation (35), and the degree of prosthesis oversizing (36), whereas the degree of calcification has been an inconsistent predictor in various studies (37–39). In this study, the native basal plane was slightly more eccentric in the CoreValve cohort, although whether this contributed to the device success differences is unclear. The degree of prosthesis oversizing was greater in the CoreValve cohort, although this reflected differences in the manufacturer sizing recommendations for the 2 devices.

The novel features of the Lotus valve may potentially explain the differences observed in device success. The Lotus is totally repositionable, even when fully expanded in the final position by virtue of its deployment and coupling mechanism. This enables detailed interrogation of the device function, degree of PAR, and device stability before uncoupling and release. In addition, the presence of an adaptive seal around the outer aspect of the lower valve frame appears to reduce PAR by occupying residual interstices between the frame and native annulus (17–19). Placement of the CoreValve, on the other hand, relies on accurate initial positioning and oversizing of the device to increase device/annular interaction.

A nonsignificant reduction in the degree of PAR was noted between the discharge and 30-day time points. In the CoreValve cohort, 3 patients with moderate PAR at discharge had only mild PAR at 30 days. Similarly, 2 patients in the Lotus cohort had a reduction from moderate to mild PAR. Detailed interpretation of the mechanism of this improvement is difficult given the small numbers but may represent further device expansion, occupation of residual interstices by fibrous tissue, or sampling error due to different echocardiographic windows.

Secondary procedural outcome measures including vascular injury, stroke, myocardial infarction, and mortality (all-cause and cardiovascular) were not different between the cohorts and consistent with previously reported rates (10,19). There was a numerically but not statistically higher rate of permanent pacemaker insertion after Lotus device placement. This study was not powered to identify the cause of increased pacing; however, in the REPRISE II trials, pacemaker insertion was found to correlate with the degree of prosthesis oversizing (40), which was greater than anticipated because only 2 valve sizes were available.

FIGURE 3 Change in New York Heart Association Functional Class



New York Heart Association (NYHA) functional class change at discharge and at 1 month.

Core laboratory assessment of the echocardiographic studies at discharge and 30 days showed that the prosthesis EOA was similar in both cohorts but that the mean transprosthesis gradient was greater in the Lotus cohort. Despite well-matched baseline annular dimensions, a significantly larger number of small prostheses were inserted in the Lotus cohort due to manufacturer sizing recommendations of less oversizing with this device. It is possible that the smaller average device size contributed to a higher mean gradient.

The results of this well-matched study suggest that placement of either the CoreValve device or Lotus device, in appropriately selected high surgical risk patients, results in acceptable procedural outcomes with good safety and efficacy profiles. The higher rate of VARC2-defined device success observed in the Lotus cohort, driven by higher rates of correct positioning and less PAR, supports the efficacy of the device's novel design features.

STUDY LIMITATIONS. This was a small, single-center, nonrandomized study not powered for major clinical endpoints such as death, stroke, and MI. Although every attempt was made to match patients, it is possible that unrecognized differences between the study cohorts may have contributed to the

results. The results should be viewed as hypothesis generating.

CONCLUSIONS

In this well-matched, single-center, nonrandomized study, both the CoreValve and Lotus devices demonstrated comparable procedural safety and efficacy results. Independent core laboratory assessment of all echocardiograms suggested greater device success with the second-generation Lotus valve driven by higher rates of correct anatomic positioning of a single prosthesis and lower rates of moderate paraprosthetic regurgitation. The clinical significance of these differences will need to be tested in larger randomized trials such as the REPRISE III trial.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Ian T. Meredith, Monash Heart, Monash Health, 246 Clayton Road, Clayton, Victoria, 3168 Australia. E-mail: ian.meredith@myheart.id.au.

PERSPECTIVES

WHAT IS KNOWN? TAVR is an accepted treatment modality for appropriately selected patients with symptomatic severe aortic stenosis, yet modest complication rates remain.

WHAT IS NEW? New-generation TAVR devices, with new design features, are entering clinical practice with potential safety and efficacy advantages over current devices. We have shown that the mechanically expanded Lotus device results in higher rates of device success than the self-expanding CoreValve device in a matched cohort.

WHAT IS NEXT?The clinical significance of these differences will need to be tested in a larger randomized trial such as the currently recruiting REPRISE III study.

REFERENCES

1. Smith CR, Leon MB, Mack MJ, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med 2011;364:2187–98.

2. Makkar RR, Fontana GP, Jilaihawi H, et al. Transcatheter aortic-valve replacement for inoperable severe aortic stenosis. N Engl J Med 2012;366:1696–704.

3. Cribier A, Eltchaninoff H, Bash A, et al. Percutaneous transcatheter implantation of an aortic valve prosthesis for calcific aortic stenosis: first human case description. Circulation 2002;106:3006–8.

4. Osnabrugge RL, Mylotte D, Head SJ, et al. Aortic stenosis in the elderly: disease prevalence and number of candidates for transcatheter aortic valve replacement: a meta-analysis and modeling study. J Am Coll Cardiol 2013;62:1002–12.

5. Mylotte D, Osnabrugge RL, Windecker S, et al. Transcatheter aortic valve replacement in Europe: adoption trends and factors influencing device utilization. J Am Coll Cardiol 2013;62:210–9.

6. Binder RK, Rodes-Cabau J, Wood DA, et al. Transcatheter aortic valve replacement with the SAPIEN 3: a new balloon-expandable transcatheter heart valve. J Am Coll Cardiol Intv 2013;6:293–300.

7. Freeman M, Rodé3s-Cabau J, Urena M, et al. First-in-man transfemoral transcatheter aortic valve replacement with the 29 mm Edwards SAPIEN XT valve. Catheter Cardiovasc Interv 2013;82:664–70.

8. Gooley R, Lockwood S, Antonis P, Meredith IT. The SADRA Lotus Valve System: a fully repositionable, retrievable prosthesis. Minerva Cardioangiol 2013;61:45–52.

9. Manoharan G, Spence MS, Rodes-Cabau J, Webb JG. St Jude Medical Portico valve. EuroIntervention 2012;8 Suppl Q:Q97–101.

10. Adams DH, Popma JJ, Reardon MJ, et al. Transcatheter aortic-valve replacement with a self-expanding prosthesis. N Engl J Med 2014;370:1790–8.

11. Godino C, Maisano F, Montorfano M, et al. Outcomes after transcatheter aortic valve implantation with both Edwards-SAPIEN and CoreValve devices in a single center: the Milan experience. J Am Coll Cardiol Intv 2010;3:1110–21.

12. Grube E, Buellesfeld L, Mueller R, et al. Progress and current status of percutaneous aortic valve replacement: results of three device generations of the CoreValve Revalving system. Circ Cardiovasc Interv 2008;1:167–75.

13. Meredith IT, Walton A, Walters DL, et al. Mid-term outcomes in patients following transcatheter aortic valve implantation in the CoreValve Australia and New Zealand study. Heart Lung Circ 2015;24:281–90.

14. Barbanti M, Ussia GP, Cannata S, Giarratana A, Sgroi C, Tamburino C. 3-year outcomes of self-expanding CoreValve prosthesis—The Italian Registry. Ann Cardiothorac Surg 2012;1:182–4.

15. Hamm CW, Mollmann H, Holzhey D, et al. The German Aortic Valve Registry (GARY): in-hospital outcome. Eur Heart J 2014;35:1588–98.

16. Linke A, Wenaweser P, Gerckens U, et al. Treatment of aortic stenosis with a self-expanding transcatheter valve: the International Multi-centre ADVANCE Study. Eur Heart J 2014;35:281–90.

17. Meredith IT, Hood KL, Haratani N, Allocco DJ, Dawkins KD. Boston Scientific Lotus valve. EuroIntervention 2012;8 Suppl Q:Q70–4.

18. Meredith IT, Worthley SG, Whitbourn RJ, et al. Transfemoral aortic valve replacement with the repositionable Lotus Valve System in high surgical risk patients: the REPRISE I study. EuroIntervention 2014;9:1264–70.

19. Meredith Am IT, Walters DL, Dumonteil N, et al. Transcatheter Aortic Valve Replacement for Severe Symptomatic Aortic Stenosis Using a Repositionable Valve System: 30-Day Primary Endpoint Results From the REPRISE II Study. J Am Coll of Cardiol 2014;64:1339–48.

20. Bloomfield GS, Gillam LD, Hahn RT, et al. A practical guide to multimodality imaging of transcatheter aortic valve replacement. J Am Coll Cardiol Img 2012;5:441–55.

21. Baumgartner H, Hung J, Bermejo J, et al. Echocardiographic assessment of valve stenosis: EAE/ASE recommendations for clinical practice. Eur J Echocardiogr 2009;10:1–25.

22. Genereux P, Kodali S, Leon MB, et al. Clinical outcomes using a new crossover balloon occlusion technique for percutaneous closure after transfemoral aortic valve implantation. J Am Coll Cardiol Intv 2011;4:861–7.

23. Kappetein AP, Head SJ, Genereux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. J Thorac Cardiovasc Surg 2013;145:6–23.

24. Tchetche D, Dumonteil N, Sauguet A, et al. Thirty-day outcome and vascular complications after transarterial aortic valve implantation using both Edwards Sapien and Medtronic CoreValve bioprostheses in a mixed population. EuroIntervention 2010;5:659–65.

25. Van Mieghem NM, Nuis RJ, Piazza N, et al. Vascular complications with transcatheter aortic

valve implantation using the 18 Fr Medtronic CoreValve System: the Rotterdam experience. EuroIntervention 2010;5:673–9.

26. Fraccaro C, Buja G, Tarantini G, et al. Incidence, predictors, and outcome of conduction disorders after transcatheter self-expandable aortic valve implantation. Am J Cardiol 2011;107:747–54.

27. van der Boon RM, Nuis RJ, Van Mieghem NM, et al. New conduction abnormalities after TAVI--frequency and causes. Nat Rev Cardiol 2012;9:454–63.

28. Sherif MA, Abdel-Wahab M, Stocker B, et al. Anatomic and procedural predictors of paravalvular aortic regurgitation after implantation of the Medtronic CoreValve bioprosthesis. J Am Coll Cardiol 2010;56:1623–9.

29. Nuis RJ, Van Mieghem NM, Schultz CJ, et al. Frequency and causes of stroke during or after transcatheter aortic valve implantation. Am J Cardiol 2012;109:1637–43.

30. Eggebrecht H, Schmermund A, Voigtlander T, Kahlert P, Erbel R, Mehta RH. Risk of stroke after transcatheter aortic valve implantation (TAVI): a meta-analysis of 10,037 published patients. EuroIntervention 2012;8:129–38.

31. Abdel-Wahab M, Mehilli J, Frerker C, et al. Comparison of balloon-expandable vs self-expandable valves in patients undergoing transcatheter aortic valve replacement: the CHOICE randomized clinical trial. JAMA 2014;311:1503–14.

32. Sinning JM, Hammerstingl C, Vasa-Nicotera M, et al. Aortic regurgitation index defines severity of peri-prosthetic regurgitation and predicts outcome in patients after transcatheter aortic valve implantation. J Am Coll Cardiol 2012;59:1134–41.

33. Athappan G, Patvardhan E, Tuzcu EM, et al. Incidence, predictors, and outcomes of aortic regurgitation after transcatheter aortic valve replacement: meta-analysis and systematic review of literature. J Am Coll Cardiol 2013;61:1585–95.

34. Wong DT, Bertaso AG, Liew GY, et al. Relationship of aortic annular eccentricity and paravalvular regurgitation post transcatheter aortic valve implantation with CoreValve. J Invasive Cardiol 2013;25:190–5.

35. Takagi K, Latib A, Al-Lamee R, et al. Predictors of moderate-to-severe paravalvular aortic regurgitation immediately after CoreValve implantation and the impact of postdilatation. Catheter Cardiovasc Interv 2011;78:432–43.

36. Detaint D, Lepage L, Himbert D, et al. Determinants of significant paravalvular regurgitation after transcatheter aortic valve: implantation impact of device and annulus discongruence. J Am Coll Cardiovasc Intv 2009;2:821–7.

37. Colli A, D'Amico R, Kempfert J, Borger MA, Mohr FW, Walther T. Transesophageal echocardiographic scoring for transcatheter aortic valve implantation: impact of aortic cusp calcification on postoperative aortic regurgitation. J Thorac Cardiovasc Surg 2011;142:1229–35.

38. Ewe SH, Ng AC, Schuijf JD, et al. Location and severity of aortic valve calcium and implications for aortic regurgitation after transcatheter aortic valve implantation. Am J Cardiol 2011;108:1470–7.

39. Staubach S, Franke J, Gerckens U, et al. Impact of aortic valve calcification on the outcome of transcatheter aortic valve implantation: results from the prospective multicenter German TAVI registry. Catheter Cardiovasc Interv 2013;81:348–55.

40. Dumonteil N. Need for permanent pacemaker following implantation of the repositionable second-generation LOTUS device for transcatheter aortic valve replacement: results from the pivotal REPRISE II trial. J Am Coll Cardiol 2013;62:B39.

KEY WORDS aortic stenosis, CoreValve, Lotus, transcatheter aortic valve replacement