JACC: CARDIOVASCULAR INTERVENTIONS
VOL. 9, NO. 4, 2016

ISSN 1936-8798/$36.00
PUBLISHED BY ELSEVIER
http://dx.doi.org/10.1016/j.jcin.2015.12.012

Transcatheter Aortic Valve Replacement Using the Repositionable LOTUS Valve

United Kingdom Experience

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ABSTRACT

OBJECTIVES This study sought to present the U.K. experience to date with the second-generation LOTUS bioprosthesis (Boston Scientific, Natick, Massachusetts).

BACKGROUND First-generation transcatheter aortic valves have limitations. Second-generation repositionable valves may improve on some of those limitations.

METHODS Prospectively collected data relating to procedural and in-hospital outcome was analyzed from 10 implantation centers in the United Kingdom.

RESULTS Implants in 228 patients age 81.4 ± 7.6 years were studied; 53.5% were male. Mean logistic EuroScore was 17.5 ± 12.4. One hundred eighty-seven (82.0%) were undertaken for aortic stenosis, 7 (3.1%) for aortic regurgitation, and 34 (14.9%) for mixed aortic valve disease. A total of 67.1% of cases were done under local anesthetic and/or sedation with transfemoral access in 94.7% and transaortic in 5.3%. Three device sizes were used: 23 mm (n = 66, 28.9%), 25 mm (n = 39, 17.1%), and 27 mm (n = 123, 53.9%). The valve was successfully deployed in 99.1% of procedures. After implantation, the mean aortic gradient was 11.4 ± 5.4 mm Hg and aortic valve area 1.6 ± 0.5 cm^2. In-hospital mortality was 1.8% (n = 4). Complications included cardiac tamponade (1.8%), conversion to sternotomy (1.3%), stroke (3.9%), vascular access-related (7.0%), and acute kidney injury (7.9%). The incidence of moderate/severe aortic regurgitation was 0.8% (n = 2). A total of 31.8% of patients required new permanent pacemaker implantation.

CONCLUSIONS This analysis represents the largest published series on use of the LOTUS valve. Outcomes using this valve are excellent. In-hospital mortality is very low. Complication rates are low, and the LOTUS valve improves on first-generation valves, particularly with regard to residual aortic regurgitation. (J Am Coll Cardiol Intv 2016;9:367–72)

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Manuscript received July 21, 2015; revised manuscript received November 24, 2015, accepted December 3, 2015.

ABBREVIATIONS AND ACRONYMS

AR = aortic regurgitation

LBBB = left bundle branch block

TAVR = transcatheter aortic valve replacement

Transcatheter aortic valve replacement (TAVR) has established itself as a superior alternative for patients with severe aortic stenosis who are not suitable for conventional aortic valve replacement (1). Results from randomized trials confirm a significant mortality benefit over conventional treatment, and indeed over surgery (2,3). This is reflected in the Class 1, Level of Evidence: A recommendation of TAVR in the recent European Society of Cardiology guidelines (4). However, the complications of this procedure have also become apparent over time and include stroke, renal impairment, vascular damage, aortic regurgitation, and the need for permanent pacemakers (5).

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Second-generation devices aim to improve on first-generation devices in some of these regards. The LOTUS bioprosthesis is a second-generation device that combines repositionability with an adaptive seal to reduce aortic regurgitation. We present our experience of implantation of the LOTUS device to this date in the United Kingdom.

METHODS

All centers in the United Kingdom collect and collate prospective data regarding all TAVR procedures to be sent to the National Institute for Cardiovascular Outcomes Research. Bespoke datasets conforming to these data fields were distributed to the 10 U.K. sites who undertook implantation of the LOTUS valve between March 2013 and March 2015. Anonymized data on a total of 228 patients were obtained and analyzed.

Information on patient characteristics, procedural details, complications, and in-hospital outcomes were collected. The definition of procedural complications conformed to Valve Academic Research Consortium 2 (VARC2) recommendations (5). Hemodynamic data on the aortic stenosis was obtained pre- and post-device insertion. These included rates of in-hospital stroke, pacemaker implantation, kidney injury, vascular complications, and mortality during the admission. We did not have data on periprocedural myocardial infarction.

The procedure itself was carried out as previously described (6). Briefly, after transarterial access was gained via the preferred access route, a Safari wire (Boston Scientific, Natick, Massachusetts) with a preformed curve was placed in the left ventricle. This was used to support the introduction of the Lotus delivery system. This houses a device made of a braided nitinol frame with a mounted trileaflet bioprosthetic valve made of bovine pericardium. The device also has a distal adaptive seal to mitigate against paravalvular aortic regurgitation. The device is repositionable and retrievable. The access route and perioperative imaging modalities were at the discretion of the operator.

STATISTICAL ANALYSIS. Statistical analysis was performed using IBM SPSS version 22 (IBM, Armonk, New York). Continuous variables are expressed as mean ± SD and were compared using the Student *t* test or a nonparametric test where a Shapiro-Wilk test suggested non-normal distributions. Categorical variables are expressed as percentages.

TABLE 1 Patient Demographics (N = 228)

Age, yrs	81.4 ± 7.6
Male	122 (53.5)
Body mass index	27.2 ± 5.6
Diabetes mellitus	66 (28.9)
Chronic pulmonary disease	69 (30.3)
Significant liver disease	5 (2.2)
Previous cerebrovascular disease	34 (14.9)
Previous cardiac surgery	48 (21.0)
Atrial fibrillation	53 (23.2)
Peripheral vascular disease	37 (16.2)
Critical pre-operative state	6 (2.6)
Pulmonary hypertension	69 (30.2)
Logistic EuroScore	17.5 ± 12.4
EuroScore II	5.5 ± 5.5
Left ventricular function	
≥50%	149 (65.4)
30%-50%	58 (25.4)
<30%	21 (9.2)
Coronary artery disease	
1-vessel	34 (14.9)
2-vessel	29 (12.7)
3-vessel	24 (10.5)
Not investigated	11 (4.8)
Aortic valve pathology	
Stenosis	187 (82.0)
Regurgitation	7 (3.1)
Mixed	34 (14.9)
Etiology	
Degenerative	218 (95.6)
Bioprosthetic	2 (0.9)
Bicuspid	4 (1.8)
Rheumatic	3 (1.3)
Other	1 (0.4)
Aortic valve calcification	
None	2 (0.9)
Mild	56 (24.6)
Moderate	77 (33.8)
Severe	56 (24.6)

Values are mean ± SD or n (%).

RESULTS

BASELINE CHARACTERISTICS. Table 1 summarizes the preprocedural characteristics of the cohort. The mean age was 81.4 ± 7.6 years, 53.5% were male, and the mean logistic EuroScore was 17.5 ± 12.4. A total of 21.0% of the cohort had previous cardiac surgery (n = 48), and 71.9% (n = 164) were in New York Heart Association functional class III or IV. Left ventricular function was poor in 9.2% of cases. A total of 15.8% of the cases were done on an urgent basis. A case was defined as urgent if it was performed during the same hospital episode as the emergency admission of the patient.

Although the main indication for device implantation was aortic stenosis (82.0%, n = 187), a small proportion of patients with predominant aortic regurgitation (3.1%, n = 7) were also treated, with the remainder 14.9% (n = 34) having mixed aortic valve disease. The degree of aortic valve calcification was assessed on angiography and graded at the discretion of the operator.

PROCEDURAL CHARACTERISTICS. The transfemoral access route was used in 94.7% of cases, with the remainder being undertaken via direct aortic access. 67.1% (n = 153) of the cases were done under local anesthetic and/or sedation (Table 2). Preimplantation balloon valvuloplasty was performed in 69.3% of cases. The 27-mm device was used in over one-half the cases (53.9%) followed by the 23-mm device in 29% of cases, and finally, the 25 mm in only 17% of cases, possibly reflecting the later commercial availability of the 25-mm valve. The device was successfully deployed in 99.1% (n = 226) of cases, with no report of device malposition or embolization. There was 1 case of failure to release the valve from the delivery system necessitating a surgical sternotomy and a surgical aortic valve replacement. Balloon post-dilation was performed in 3 cases (1.4%). The valve was implanted at a depth of 5.6 ± 3.1 mm below the annular plane.

Over three-quarters (75.8%) of patients did not have any aortic regurgitation post-implant, as assessed by angiography or echocardiography. There were only 2 cases of moderate-severe aortic regurgitation following the procedure.

Percutaneous vascular closure was successful in 90.9% of cases, whereas surgical closure was planned in 6.6% of cases.

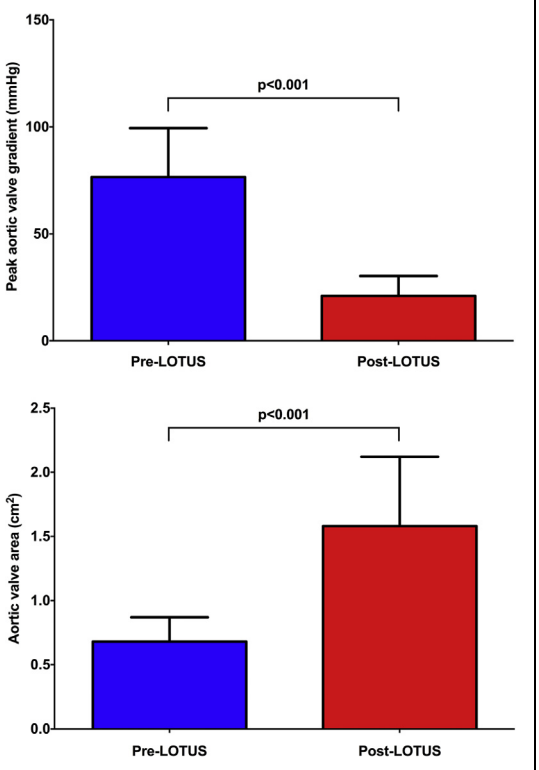
Excluding those patients with "pure" aortic regurgitation as the indication (n = 221), the preprocedural mean aortic gradient was 45.3 ± 16.4 mm Hg, and aortic valve area 0.7 ± 0.2 cm^2. After implantation, the mean aortic gradient was 11.8 ± 5.5 mm Hg, and aortic valve area 1.6 ± 0.5 cm^2 (Figure 1).

TABLE 2 Procedural Details (N = 228)

Proctored	66 (28.9)
Urgent case	36 (15.8)
General anesthetic	75 (32.9)
Transesophageal echo-guidance	76 (33.3)
Access route	
Transfemoral	216 (94.7)
Transaortic	12 (5.3)
Valve size	
23 mm	66 (28.9)
25 mm	39 (17.1)
27 mm	123 (53.9)
Pre-implant balloon valvuloplasty	158 (69.3)
Successful deployment of Lotus device	226 (99.1)
Balloon post-dilation	3 (1.3)
Access site closure	
Percutaneous	206 (90.4)
Planned surgical	15 (6.6)
Unplanned surgical	6 (2.6)

Values are n (%).

FIGURE 1 Changes in Peak Aortic Valve Gradient and Aortic Valve Area



Changes in peak aortic valve gradient and aortic valve area in patients with aortic stenosis and/or mixed aortic valve disease before and after implantation of a Lotus device.

TABLE 3 Complications (N = 228)

Bailout valve in valve	0 (0)
Valve malpositioning	0 (0)
Post-procedure aortic regurgitation	
None	173 (75.8)
Mild	52 (22.8)
Moderate	1 (0.4)
Severe	1 (0.4)
Cardiac tamponade	4 (1.8)
Conversion to sternotomy	3 (1.3)
Coronary occlusion or compromise to flow	0 (0)
In-hospital stroke	9 (3.9)
Acute kidney injury (stages I to III)	18 (7.9)
Vascular access site and access related complications	16 (7.0)
Bleeding (composite of life-threatening, major and minor bleeding)	24 (10.5)
Post-procedural permanent pacemaker	64 (31.8)
In-hospital mortality	4 (1.8)

Values are n (%).

COMPLICATIONS. Four patients died either as a direct or indirect result of the procedure: an inpatient mortality rate of 1.8% (Table 3). Two deaths occurred in the context of cardiac tamponade requiring emergency sternotomy. A third patient died from rupture of the left ventricular wall secondary to a myocardial infarction 2 days after the procedure. The fourth patient had a significant cerebrovascular accident after TAVR and was transferred for ongoing neurological rehabilitation, and died of pneumonia 19 days after TAVR.

Minor vascular access complications occurred in 5 patients: their etiology and management are outlined in Table 4. The percutaneous treatment of vessel perforation and dissection via either the contralateral femoral route or radial approach was used successfully in 5 cases. Two of the cases were due to issues in deploying the closure device, whereas the remaining 3 cases were due to ongoing bleeding despite appropriate deployment of the closure device.

The definition of acute kidney injury included stages 1 to 3. Of the 18 patients (7.9%) who developed an acute kidney injury, only 1 patient (0.4%) required renal replacement therapy.

TABLE 4 Vascular Complication Details (N = 16)

Vascular Complications	Outcome
Major	
Tamponade (n = 2)	Death (n = 2)
Minor	
Pseudoaneurysm (n = 3)	Thrombin injection (n = 1) Unspecified (n = 2)
Thrombosis (n = 1)	Unspecified
Dissection (n = 1)	Surgery
Closure device failure (n = 6)	Surgical closure (n = 6)
Unspecified (n = 3)	

The incidence of stroke during the inpatient admission was 3.9% (n = 9).

The baseline pacemaker rate pre-procedure was 11.8% (n = 27). The pacemaker implantation rate was 31.8% with a median time to insertion of 3.0 ± 3.4 days. The indications for pacing were listed as complete atrioventricular block in 71.9% of cases, combination of first-degree atrioventricular block and left bundle branch block (LBBB) in 17.2%, whereas the indication was not specified in 10.9% of cases. Over one-half of the cohort (55.2%) developed new LBBB post-procedure. There was no statistical difference in pacing rates between centers, and when included as a variable in the univariate analysis, it did not meet our criteria of $p < 0.20$ for inclusion in a multivariate model. We also included a "learning curve" variable defined as in the first 10 cases at a center that also did not meet inclusion criteria.

DISCUSSION

This is the largest published analysis of the use of the LOTUS bioprosthesis in an all-comers cohort. In-hospital mortality is lower than previous comparable reported series (7-9), and the rate of significant aortic regurgitation is strikingly low.

Our patient cohort had a lower mean Logistic EuroScore when compared to older registries (7-9). The inpatient mortality rate of 1.8% includes the learning curve in each center and therefore is suggestive of an excellent safety profile.

Transfemoral access is associated with vascular complications with reported rates of up to 20%. The strong association with increased morbidity and mortality is well documented (10). Although the first-generation devices required a large introducer sheath (22-F to 24-F), the LOTUS system uses an 18-F and a 20-F for the 23 and 25/27-mm devices, respectively. Our reported incidence of 7.0% complication rate is higher than that from the REPRISE II (REpositionable Percutaneous Replacement of Stenotic Aortic Valve Through Implantation of Lotus™ Valve System - Evaluation of Safety and Performance) trial (2.5%) and may be more reflective of "real world" practice (11).

Stroke remains a major risk in the TAVR population. Results from the PARTNER trials showed an almost 2-fold increase in stroke rate in the TAVR arm compared with surgery (4.6% vs. 2.4%) (2). Cerebral emboli correlate with increasing manipulation of the delivery system within the aorta (12). The lower profile of LOTUS aims to facilitate negotiation through the aorta. The design of the bioprosthesis and the ability to reposition the valve before final deployment obviates the need for balloon post-dilation and

bailout valve-in-valve reducing manipulation of the aortic root and arch. Nonetheless, in our series, the stroke rate was significant at 3.9%. Our observation is limited by the fact that we did not have any information regarding the severity of cerebrovascular accident. Therefore, we cannot infer the effect of stroke on long term disability and morbidity in our cohort.

The CHOICE (A Comparison of Transcatheter Heart Valves in High Risk Patients With Severe Aortic Stenosis) trial showed a higher incidence of post-procedural permanent pacemaker implantation with the self-expanding CoreValve device (CoreValve, Medtronic, Luxembourg, Luxembourg) compared with the balloon-expandable Edwards system (Edwards Lifesciences, Irvine, California) (13). Beyond the choice of bioprosthesis, other factors have been implicated in conduction problems including pre-procedural conduction disease, prolonged QRS duration, depth of implantation and overgenerous sizing of the device (14). Our reported pacing rate of 31.8% is similar to the REPRISE II trial (28.6%) and is consistent with registries of self-expanding valves (15). The rate of pacing may decrease with a wider choice of device size.

The incidence of LBBB post-implant is consistent with the rate for self-expanding devices as reported previously (14). The clinical implication of LBBB, however, in the absence of other conduction abnormalities, has been equivocal (16). Further studies are needed to evaluate this in particular in the context of pre procedural LV impairment.

Paravalvular aortic regurgitation is associated with higher in-hospital and mid-term mortality (17). The PARTNER (Placement of AoRtic TraNscathetER Valves) trials reported an incidence of significant AR around 12% at 30 days. There was a low incidence of aortic regurgitation in our analysis, with only 2 patients reported as having moderate/severe AR. The vast majority of patients (76.1%) did not have any residual regurgitation. This may be explained by 2 factors: the adaptive seal surrounding the ventricular portion of the prosthesis designed to reduce gaps between the device and native tissue, and the ability to reposition the device in cases of suboptimal deployment.

STUDY LIMITATIONS. The analysis has the limitations inherent to any retrospective data analysis. The responsibility for data collection rested with the physicians involved in their respective centers, and there was no independent verification of its accuracy. Thus, we cannot firmly rule out underreporting of adverse events. Though every effort was made to collect as complete a dataset as possible, data was missing in a few fields notably in baseline risk scores and aortic valve area post-procedure. The current focus of this analysis was on in-hospital outcomes, and thus, our results cannot be extrapolated to longer-term follow-up.

CONCLUSIONS

There has been a rapid expansion of commercially available transcatheter aortic bioprostheses on the market over the last 3 years with the primary aim of improving deliverability and reducing complication rates. Our analysis reflects the first real-world experience with the second-generation LOTUS bioprosthesis. Our results are comparable to the REPRISE 2 trial data. In particular, TAVR with the LOTUS device is associated with a low incidence of aortic regurgitation compared with first-generation devices. The need for a permanent pacemaker following the procedure is still significant and is similar to first-generation self-expanding prosthesis. In-hospital mortality was rare and supports the safety of this device.

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PERSPECTIVES

WHAT IS KNOWN? The first-generation TAVR bioprostheses are effective but are associated with significant complication rates including the need for permanent pacing and aortic regurgitation.

WHAT IS NEW? Our study shows that the second-generation LOTUS device has a good safety profile and in particular is associated with a very low incidence of aortic regurgitation.

WHAT IS NEXT? The long-term safety and performance of this device needs to be confirmed.

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KEY WORDS aortic stenosis, complication, LOTUS, outcome, transcatheter aortic valve