Cardiovascular Innovations and Applications

Vol. 6 No. 4 (2022) 233–239
ISSN 2009-8618
DOI 10.15212/CVIA.2022.0009

RESEARCH ARTICLE

Comparison of Post-Procedural and 30-day Post-Implantation Transcatheter Aortic Valve Replacement Gradients with and without pre-implantation Balloon Valvuloplasty: A Real-World Analysis of Early Results using a Novel Balloon Expandable Transcatheter Aortic Valve

Mahesh Chandrasekhar[1], David Zhao[2] and Karl Richardson[2]

[1]*Cone Heart and Vascular Institute, 1126 North Church Street, Suite #300, Greensboro, North Carolina USA, 27401*
[2]*Wake Forest Baptist Medical Center, 1 Medical Center Blvd, Winston-Salem, NC 27157, United States*

Received: 19 March 2022; Revised: 27 May 2022; Accepted: 10 June 2022

Abstract

Objectives: This study describes a real-world experience of implanting a novel balloon expandable transcatheter aortic valve replacement (TAVR) compared to devices commonly used in clinical practice. As a secondary objective, the effect of balloon angioplasty (BAV) before TAVR on the transvalvular gradient 1 and 30 days after implantation was evaluated.
Background: For most commercial TAVR valves, the 30-day average mean aortic valve gradients have been reported. Our experience with the Lotus Valve System had indicated higher immediate post-implant gradients than those in the literature. We sought to evaluate both these valves, comparing them to other valves.
Methods: We analyzed discharge and 30-day echocardiograms of Lotus valves from 7/5/2019 to 8/27/2020. In response to higher-than-expected post-implant gradients, patients from 11/4/19 to 8/27/20 underwent BAV before the valve implantation, whereas patients from 7/5/19 to 10/18/19 did not (no-BAV). We compared these samples to each other and to a random sampling of TAVR valves implanted by the same interventionalist.
Results: At discharge, 27 patients received Lotus valves. The average mean aortic valve gradient was 16.7 mmHg (SD = 5.5 mmHg) for the no-BAV and 14.7 mmHg (SD = 3.7 mmHg) for the BAV (P = 0.177) cohorts. No-BAV Lotus valve mean gradients were significantly higher (P < 0.001) than those of the Sapien valve (M = 12 mmHg, SD = 4.3) and CoreValve (M = 9.18 mmHg, SD = 3.96). At the 30-day assessment, the mean gradients in the no-BAV and BAV groups were similar to those in the literature (M = 11 mmHg SD 3.5; M = 12 mmHg, SD 4.1 (P = 0.287)) and those of other valves.
Conclusions: The Lotus valve demonstrated higher post-implantation gradients than other valves. This effect was not attenuated by BAV. These elevated gradients were not significant at the 30-day follow-up.

Keywords: Transcatheter aortic valve replacement; balloon angioplasty; Lotus valves; CoreValve

Correspondence: Mahesh Chandrasekhar, MD,
Cone Heart and Vascular Institute, 1126 North Church Street, Suite #300, Greensboro, North Carolina USA, 27401
E-mail: mahesh.chandrasekhar@conehealth.com

Introduction

The Lotus Edge Transcatheter Aortic Valve System (Boston Scientific) received FDA approval on April 23, 2019. This valve consisted of a bioprosthetic aortic

compuscript

valve (AV) pre-mounted on a pre-shaped delivery catheter along with a sealing skirt to decrease paravalvular leak. Deployment was directed via gradual mechanical expansion, and full retrievability and repositionability were possible. In REPRISE III, the largest trial of this valve before FDA approval, the mean AV gradient at 30 days post-implantation was 12.5 ± 5.2 mmHg [1, 2]. Immediate post-implant gradients were not reported.

Prior data have shown that Doppler-measured and invasive, directly measured gradients can significantly vary [3–6]. Pressure recovery phenomena and fluid hemodynamics have been implicated as explanations. Nonetheless, echocardiography remains the mainstay of monitoring post-valve replacement, and elevated prosthetic valve gradients can be a harbinger of valve dysfunction or thrombosis. Although balloon-expandable valves are known to have higher gradients than self-expanding valves, the discrepancy between non-invasively and invasively measured gradients in the two valve types is largely similar [5]. Little is known regarding the effect of pre-implantation balloon angioplasty (BAV) on non-invasively measured post-implantation gradients.

The Lotus valve had a voluntary recall of all unused inventory because of the complexities associated with the delivery system [7]. At our center, higher-than-expected post-implantation gradients had raised concerns, thus prompting an investigation of our initial data. Although the operators in the clinical trial used pre-implantation BAV, this procedure is not specifically recommended by the manufacturing company, and our initial patients received implantation without BAV. After analysis of these initial data, because of concerns that the lack of BAV might have been leading to higher post-implantation gradients, we subsequently deployed Lotus valves with BAV, thus generating an opportunity to study the effect of BAV on post-implantation transvalvular gradients. The following is an analysis of our single-center experience comparing post-implantation gradients in Lotus valve transcatheter aortic valve replacement (TAVR) compared with other TAVR valves.

Methods

This study is a post-market evaluation of prosthetic valve outcomes as a retrospective, single-center study from a large academic institution. The protocol was approved by a locally appointed institutional review board. Patients were selected for TAVR implantation on the basis of assessments by a multi-disciplinary team, and both an interventional cardiologist and cardiothoracic surgeon.

Patient inclusion criteria included the diagnosis of severe aortic stenosis with an aortic valve mean gradient of 40 mmHg and an aortic valve area of <1 cm^2, along with New York Heart Association class III symptoms. These patients were required to be at high risk of surgical aortic valve replacement, on the basis of a Society of Thoracic Surgeons score greater than 12, to receive multi-disciplinary team approval for consideration of TAVR. Device sizing was performed on the basis of cardiac CT assessment through conventional sizing protocols [8].

Patients with bicuspid aortic valves and prosthetic aortic valves were excluded from Lotus valve implantation by the multi-disciplinary team, as were patients with indications for aortic regurgitation, the subset of patients with low flow low gradient aortic stenosis and paradoxical low flow low gradient aortic stenosis, and patients with concomitant heart failure with reduced ejection fraction. Patients with concomitant severe mitral valve regurgitation, active infections or endocarditis, and patients with an estimated life expectancy <12 months because of non-cardiac conditions were also excluded from valve implantation.

Patients were evaluated after Lotus valve implantation through a transthoracic echocardiogram performed on the first day post-implantation for immediate post-implantation data and at the 30-day follow-up. The echocardiographic parameters evaluated included the AV mean gradient, AV peak velocity, AV acceleration time and AV dimensionless velocity index (DVI). The initial patients implanted with a Lotus valve ($n = 17$) were placed in the no-BAV group. Because of the particularly high post-implantation gradients, the subsequent patients ($n = 10$) were implanted with Lotus valves with BAV. Two patients were excluded from analysis: one patient had originally been planned to receive a Lotus valve but received another valve, and one patient had hemodynamic compromise before valve implantation, thus requiring open heart surgery (Figure 1). Two patients from the post-BAV cohort were lost to follow up before the 30 day echocardiogram.

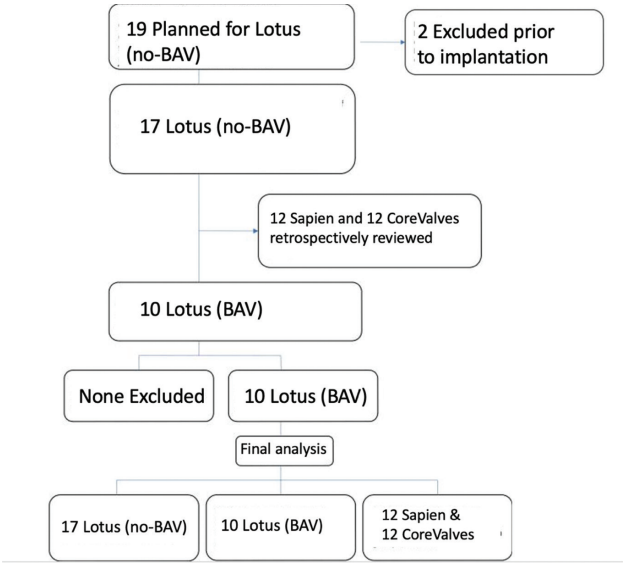

Figure 1 Study Flow Diagram.

Patients receiving comparison valves were selected through random sampling of the institution's TAVR database. TAVRs performed by the same implanting physician were selected to minimize procedural variations. Echocardiograms from patients 1 day after valve implantation were compared for the Lotus valve versus balloon expandable Edwards Sapien 3 and the self-expandable Medtronic CoreValve valves. Bicuspid valves and valve-in-valve procedures were excluded. All echocardiographic data were retrospectively reviewed by two members of the study team, and all Doppler envelopes were manually re-traced to confirm accuracy. The data obtained included the AV mean gradient (AV mean), AV peak velocity, the velocity time integral (VTI) of the peak AV spectral Doppler, the acceleration time of the AV velocity, and the DVI (an assessment of the VTI of the left ventricular outflow tract compared with the VTI of the prosthetic valve). All evaluated valves were implanted by the same operator.

Continuous variables were estimated as mean (SD) and compared with *t*-test or one-way ANOVA. Statistical analyses were performed in SAS software, version 9.2 or later (SAS Institute). Statistical significance was set at $P < 0.05$.

Results

We evaluated 27 patients who received Lotus valves between June 2019 and August 2020; 17 patients received implants with no BAV, and 10 received implants after BAV. Most baseline characteristics were similar (Table 1).

The post-implantation echocardiographic data did not significantly differ between the no-BAV and BAV Lotus valve cohorts. The average mean AV gradient was 16.7 mmHg (SD = 5.5 mmHg) for the no-BAV and 14.7 mmHg (SD = 3.7 mmHg) for the BAV ($P = 0.177$) cohorts, and the average AV peak velocity was 264 cm/s (SD = 43 cm/s) for the no-BAV and 243 cm/s (SD = 34 cm/s) for the BAV ($P = 0.097$) cohorts. No statistically significant changes were observed in acceleration time or DVI between the no-BAV and BAV groups (Table 2).

Patients in the no-BAV cohort had mean gradients that varied by valve size (Table 3). AV mean gradients and AV peak velocity were most elevated in the 23 mm valve subset, with an average mean gradient of 23 mmHg (SD = 4.7 mmHg) and a mean AV peak velocity of 315 cm/s (SD = 34 cm/s) (Table 3). This trend persisted in the BAV cohort; the 23 mm valve had the highest gradient, with an average AV mean gradient of 26 mmHg (SD = 0.97 mmHg) and a mean AV peak velocity of 291 cm/s (SD = 8.9 cm/s). DVI was also similar between the BAV and no-BAV cohorts.

Both the no-BAV and BAV Lotus valve patients had significantly higher day 1 post-implantation gradients and velocities than the patients receiving other TAVR valves (Table 4). Although power limited our ability to detect a statistically significant difference in no-BAV and BAV Lotus post-implantation gradients, the no-BAV to Sapien/Core valve comparison was the only comparison analysis with a significantly different DVI and acceleration time between valve types. This result confirmed a trend suggesting that pre-implantation BAV, compared with no-BAV, may decrease immediate post-implantation gradients.

Table 1 Limited Baseline Demographics Among Lotus Valve Patients.

	No BAV	SD	BAV	SD	P value
Age	77	8	79	9	0.27
Male (%)	47		70		
BMI	32	8	29	8	0.14

Abbreviations: BAV, balloon angioplasty; SD, mean.

Table 2 Comparison of Immediate Post-Implantation Echocardiographic Data between Lotus Valves with and without BAV.

	No BAV	SD	BAV	SD	P
AV mean (mmHg)	16.7	5.5	14.7	3.7	0.18
AV peak velocity (cm/s)	264	43	243	34	0.10
Peak AV VTI (cm)	50.8	10.0	47.8	9.8	0.25
DVI	0.47	0.10	0.49	0.11	0.27
Acceleration time (msec)	89	19	87	14	0.27

Abbreviations: AV, aortic valve; BAV, balloon angioplasty; DVI, dimensionless velocity index; SD, mean; VTI, velocity time integral.

Table 3 Comparison of Prosthetic Valve Measures Between the Same Lotus Valve Sizes with or without BAV.

No-BAV	Lotus 23	SD	P	Lotus 25	SD	P	Lotus 27	SD	P
AV mean (mmHg)	23.0	4.7	0.02	13.4	3.3	0.28	17.0	5.8	0.48
AV peak velocity (cm/s)	315	34	0.01	241	28	0.17	266	45	0.49
Peak AV VTI (cm)	58.0	1.7	0.42	46.0	3.9	0.43	54.0	15	0.35
DVI	0.41	0.07	0.17	0.48	0.10	0.25	0.50	0.15	0.001
Acceleration Time (msec)	90	29	0.43	96	14	0.13	75	13	0.23
BAV	**Lotus 23**	**SD**		**Lotus 25**	**SD**		**Lotus 27**	**SD**	
AV mean (mmHg)	26.0	1.0		12.0	1.4		17.0	4.6	
AV peak velocity (cm/s)	291	9		218	50		267	38	
Peak AV VTI (cm)	54.0	2.6		41.0	2.4		55.0	2.4	
DVI	0.47	0.01		0.54	0.01		0.45	0.01	
Acceleration Time (msec)	88	15		85	17		83	15	

Abbreviations: AV, aortic valve; BAV, balloon angioplasty; DVI, dimensionless velocity index; SD, mean; VTI, velocity time integral.

Table 4 Comparison of Immediate Post-Implantation Mean Prosthetic Valve Measures between the Lotus Valve with or without BAV and the SAPIEN 3 and CoreValve.

No BAV	Lotus	SD	Sapien	SD	CoreValve	SD	P
AV mean (mmHg)	16.7	5.5	11.0	4.1	9.0	3.8	0.0006
AV peak velocity (cm/s)	264	43	215	44	192	44	0.0004
Peak AV VTI (cm)	50.8	10.0	47.0	15.0	38.0	9.9	0.03
DVI	0.47	0.10	0.54	0.15	0.61	0.14	0.02
Acceleration time (msec)	89	19	90	13	76	12	0.045
BAV	**Lotus**	**SD**	**Sapien**	**SD**	**CoreValve**	**SD**	**P**
AV mean (mmHg)	14.7	3.7	11.0	4.1	9.0	3.8	0.01
AV peak velocity (cm/s)	243	34	215	44	192	44	0.03
Peak AV VTI (cm)	47.8	9.8	47.0	15.0	38.0	9.9	0.13
DVI	0.49	0.10	0.54	0.15	0.61	0.14	0.11
Acceleration time (msec)	87	14	90	13	76	12	0.04

Abbreviations: AV, aortic valve; BAV, balloon angioplasty; DVI, dimensionless velocity index; SD, mean; VTI, velocity time integral.

Table 5 Comparison of Prosthetic Valve Measures of Lotus Valves Post Implantation and at 30 days.

No BAV	No BAV	SD	No BAV 30-day	SD	P
AV mean (mmHg)	16.7	5.5	11.3	3.5	0.002
AV peak velocity (cm/s)	264	43	220	31	0.001
Peak AV VTI (cm)	50.8	10.0	49.6	11.0	0.39
DVI	0.47	0.10	0.46	0.01	0.40
Acceleration time (msec)	89.4	19	83	16	0.16
BAV	**BAV**	**SD**	**BAV 30-day**	**SD**	**P**
AV mean (mmHg)	14.7	3.7	12.2	4.1	0.09
AV peak velocity (cm/s)	243	34	230	42	0.24
Peak AV VTI (cm)	47.8	9.8	49.5	11.0	0.36
DVI	0.49	0.11	0.45	0.07	0.16
Acceleration time (msec)	87	14	85	11	0.5

Abbreviations: AV, aortic valve; BAV, balloon angioplasty; DVI, dimensionless velocity index; SD, mean; VTI, velocity time integral.

Interestingly, the elevations in prosthetic valve metrics did not persist at 30 days. The no-BAV cohort, but not the BAV cohort, showed a statistically significant difference between post-implantation and 30-day echo parameters, although similar trends were observed in both cohorts (Table 5). This statistical finding again suggested a possible subtle effect of pre-implantation BAV on immediate post-implantation AV gradients. Notably, we observed no statistical difference between BAV and no-BAV Lotus valves in the 30-day assessment of mean gradients (11.26 mmHg vs 12.2 mmHg, P = 0.29) and peak AV velocities (220 cm/s vs 230 cm/s, P = 0.25). These 30-day measurements for Lotus valves were also statistically similar to those of the other TAVR valves evaluated.

Discussion

The principal findings of this study are as follows: 1) immediately after implantation, non-invasively measured gradients in the Lotus valve were higher than those in other commercially available valves; 2) for the Lotus valve, pre-implantation BAV might have had a mild effect on immediate post-implantation gradients, as compared with no-pre-implantation BAV; and most importantly, 3) a marked normalization in non-invasively measured transvalvular gradients of this self-expanding prosthesis was observed from day 1 to day 30 post-implantation.

In a press release, Boston Scientific has noted that the voluntary recall of the Lotus EDGE was due to "the intricacies of the delivery system required to allow physicians to fully reposition and recapture the valve" [7]. The initial registry developed at our institution arose from concerns regarding problems with the delivery of the valve leading to higher post procedural gradients. Given the disconnect between the protocol for the REPRISE III trial and the open recommendations for BAV, we attempted balloon valvuloplasty before Lotus implantation to potentially improve post-implantation gradients. This intervention did not improve the ultimate post-implantation gradients yet did appear to have a subtle effect on immediate post-implantation gradients. The Lotus valve was designed with a polymeric outer adaptive seal specifically to decrease the paravalvular regurgitation. Elevated post-implantation gradients can be concerning regarding failed valve expansion, malpositioned or malfunctioning valves, and early valve thrombosis. Nonetheless, the post-implantation velocities and gradients appeared to "settle" at the 30-day mark, thus suggesting an absence of primary valve failure and that pre-implantation BAV may not be useful. The average mean AV gradients appeared to decrease by the 30-day mark to within the 12.5 ± 5.2 mmHg range reported by pivotal trial data, and approached those of other commercially available valves.

This experience is both encouraging and reassuring. The Lotus valve's novel seal, in contrast to

those of other woven nitinol bioprosthetic valves, might have accounted for the increase in valve gradients. Pressure recovery has been implicated in the discrepancy between invasive and non-invasively measured transvalvular gradients; it may also contribute to the gradient differential that we observed. The size of the valve, the size of the aorta and the turbulence generated by the valve are known to contribute to the severity of this phenomenon. Our findings might possibly represent a change in gradient from discharge to 30-day follow-up, caused by a change in the valve anatomy and adaptive seal post implantation. We considered that minor changes in the valve architecture that occurred as the valve settled into place after implantation might have decreased turbulence and therefore led to the observed discrepancy at the 30-day follow up.

Our data suggest that, in the absence of concerning clinical findings, conservative watchful waiting with re-imaging of the valve at 30 days may be an optimal approach to address this early finding of elevated gradients in this valve or other valves that reach the market. According to our real-world experience, BAV may not necessarily improve outcomes in routine implantation. This finding suggests hope, because the risk of annular rupture increases with BAV, and the current practice for implanting currently available valves does not use pre-dilation. We may examine patients with thick annular calcium or left ventricular outflow tract calcium for the specific use of BAV, although such an investigation is beyond the scope of our data.

Although no known plans currently exist to re-release the Lotus Edge Transcatheter System, our data provide reassurance that this fully retrievable and re-expandable system does not lead to significantly higher prosthetic gradients over time. Our data also suggest that pre-implantation BAV is not necessary to avoid unexpectedly high post-implantation gradients; however, this finding will need to be further assessed if the valve returns to the commercial market.

Limitations

The valves under study were implanted by one operator at a large single academic center. The small sample sizes precluded robust multivariate analysis and limited the study's statistical power. This was a real-world analysis of a single center experience with a novel valve, and thus the study design is less optimal that a randomized control-trial assessment. Although all patients had severe aortic stenosis of a tricuspid AV before implantation, this study was unable to adequately control for other baseline demographic changes, because few non-imaging data were available for review. If the Lotus valve returns to the market, more controlled cohort studies can and will be pursued.

Conclusions

Although the immediate post-implantation gradients for the Lotus valve were higher than expected, BAV had only a mild effect on immediate post-implantation gradients. Reassuringly, a normalization in transvalvular gradients was observed at 30-days post-implantation.

Funding Sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Reardon MJ, Feldman, TE, Meduri CU, Makkar RR, O'Hair D, Linke A, et al. Two-year outcomes after transcatheter aortic valve replacement with mechanical vs self-expanding valves: the REPRISE III randomized clinical trial. JAMA Cardiol 2019;4(3):223–9.
2. Boston Scientific (2019, August). Boston Scientific LOTUS Edge Valve System Master Brand Directions for Use [Manual].
3. Aalaei-Andabili SH, Park KE, Choi CY, Manning EW, Stinson WW, Van Woerkom R, et al. Relationship between invasive and echocardiographic transvalvular gradients after transcatheter aortic valve replacement. Cardiol Ther 2020;9(1):201–6.
4. Abbas AE, Mando R, Hanzel G, Gallagher M, Safian R, Hanson I, et al. Invasive versus echocardiographic evaluation of transvalvular gradients

immediately post-transcatheter aortic valve replacement demonstration of significant echocardiography-catheterization discordance. Circ Int 2019;12(7):e007973.
5. Mascherbauer J, Schima H, Maurer G, Baumgartner H. Doppler assessment of mechanical aortic valve prostheses: effect of valve design and size of the aorta. J Heart Valve Dis 2004;13(5):823–30.
6. Abbas AE, Mando R, Kadri A, Khalili H, Hanzel G, Shannon F, et al. Comparison of Transvalvular Aortic Mean Gradients Obtained by Intraprocedural Echocardiography and Invasive Measurement in Balloon and Self-Expanding Transcatheter Valves. JAHA 2021;10(19):e021014.
7. Backes T, Lisa S. Boston Scientific Announces LOTUS Edge™ Aortic Valve System Voluntary Recall and Product Discontinuation. Boston Scientific Press Releases 2020.
8. Otto C, Kumbhani D, Alexander K, Calhoon JH, Desai MY, Kaul S, et al. 2017 ACC expert consensus decision pathway for transcatheter aortic valve replacement in the management of adults with aortic stenosis. J Am Coll Cardiol 2017;69(10):1313–46.