Bioprosthetic valve fracture during valve-in-valve transcatheter aortic valve replacement

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ABSTRACT

Transcatheter aortic valve replacement (TAVR) valve-in-valve (VIV) therapy has been approved for select patients with surgically inoperable bioprosthetic valves that need replacement. Bioprosthetic valve fracturing (BVF) used in conjunction with VIV TAVR can reduce transvalvular gradients and increase the aortic valve area. Twelve patients who underwent BVF VIV TAVR at a single center were retrospectively analyzed. Measurements of hemodynamics and aortic valve area were performed at baseline, after VIV TAVR, after BVF, and at 30-day follow-up. The mean Society of Thoracic Surgeons Predicted Risk of Mortality score was $7.12 \pm 3.5\%$, with 75% of patients deemed high risk by the heart team. Mean gradients decreased from 44 mm Hg to 15 mm Hg following VIV TAVR, and to 7 mm Hg following BVF. The mean aortic valve area increased from 0.6 cm^2 to 1 cm^2 following VIV TAVR, and to 1.3 cm^2 following BVF. There were no postoperative permanent pacemaker implantations or vascular complications, and at 30 days, only one patient had died. While we report intraoperative mortality, BVF with VIV TAVR can be performed to reduce transvalvular gradients and increase effective aortic valve area in high-surgical-risk patients with failed bioprosthetic valves.

KEYWORDS Bioprosthetic valve fracturing; transcatheter aortic valve replacement; valve-in-valve

A large percentage of patients who received bioprosthetic valves are experiencing early valve degeneration and stenosis.¹ These events require intervention to restore proper hemodynamics and transvalvular gradients, yet surgical reoperation in high-risk patients is associated with elevated mortality and complications.² Valve-in-valve (VIV) transcatheter aortic valve replacement (TAVR) procedures are particularly useful in these high-risk patients. However, VIV TAVR within small bioprosthetic valves ($\leq 1 \text{ mm}$) results in higher transvalvular gradients from smaller aortic valve areas.^{3,4} Bioprosthetic valve fracturing (BVF) has been presented as an alternative treatment in these patients to increase aortic valve area and decrease transvalvular gradients.^{5,6} We present our single-center experience of 12 patients who underwent a BVF VIV TAVR.

METHODS

From November 2017 to June 2018, all VIV TAVR procedures in which BVF was planned ($n = 12$) were retrospectively reviewed at The Heart Hospital Baylor in Plano, Texas. Before the procedure, all patients were evaluated with a heart team approach in clinic and in a multidisciplinary conference using invasive and noninvasive imaging, Society of Thoracic Surgeons scores, New York Heart Association classification, and clinical presentation. Fracturing was planned in patients with small bioprosthetic valves to improve hemodynamics, reduce patient prosthesis mismatch, and prevent pinwheeling of valve leaflets, which may result in leaflet thrombosis and early valve degeneration.

Three patients received conscious sedation, while the remaining patients required general anesthesia. All procedures were performed such that VIV TAVR was followed by

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Table 1. Original surgical prosthesis and replacement prosthesis used in bioprosthetic valve fracture procedures

Surgical prosthesis		Replacement prosthesis			
		Self-expanding	Balloon-expandable		
			Sapien 3		Sapien XT
Type	mm	Evolut Pro 23 mm	20 mm	23 mm	23 mm
Magna	19		1		
	21		1	3	
	23			2	
Epic	21	1			
Mitroflow	21		2		
	25				1
Mosaic	21		1		

BVF, which was performed by placing the balloon across the sewing ring of the VIV during ventricular pacing. Pressure was increased until fracture, which was confirmed using fluoroscopy and pressure measurements. Postoperatively, patients were placed on antiplatelet regimens.⁷ They were evaluated perioperatively, postoperatively, and at 30 days using the primary endpoints of aortic valve gradients, aortic valve area, and mortality; additional endpoints included patient outcomes and comorbidities.

A wide variety of implanted bioprosthetic valves were fractured: 7 Magna valves (Edwards Lifesciences, Irving, CA), 3 Mitroflow (Sorin, Milan, Italy), 1 Epic (St. Jude Medical, Minneapolis, MN), and 1 Mosaic (Medtronic Inc., Minneapolis, MN). Replacement valves were as follows: 10 Sapien 3, 1 Sapien XT, and 1 CV Evolut (Edwards Lifesciences, Irving, CA). Bard True (Bard, Murray Hill, NJ) balloons of various sizes were used in all cases (*Table 1*).

Continuous data were reported as the mean $\pm$ standard deviation in normally distributed variables and median $\pm$ standard deviation in irregularly distributed variables. Categorical data were reported as a count with a percentage.

RESULTS

The mean age of our patients was 81 ± 11 years, and 6 were women. The mean Society of Thoracic Surgeons Predicted Risk of Mortality score was $7.12 \pm 3.5\%$, and the mean time from surgical implantation of the initial bioprosthesis was 11 ± 4 years. The mean ejection fraction for the cohort was $49 \pm 17\%$. Two patients were classified as extreme risk and six as high risk by clinicians. Six patients were New York Heart Association class III, six patients had atrial fibrillation, six had coronary artery disease, and six had chronic kidney disease (*Table 2*).

The mean preoperative aortic valve gradient was 44 mm Hg, and the mean preoperative aortic valve area was

Table 2. Baseline characteristics of 12 patients who underwent bioprosthetic valve fracturing during valve-in-valve transcatheter aortic valve replacement

Variable	Mean $\pm$ SD or n
Age (years)	81 ± 11
Women	6
Body mass index (kg/m ²)	24.1 ± 3.7
Intermediate risk	4
High risk	6
Extreme risk	2
Society of Thoracic Surgeons score	7.12 ± 3.5
New York Heart Association classification	
I	1
II	5
III	6
Ejection fraction (%)	48.9 ± 16.6
Atrial fibrillation	6
Coronary artery disease	6
Chronic kidney disease	6
Preoperation permanent pacemaker	2

0.59 cm^2 . The mean post-VIV TAVR aortic valve gradient was 14.9 mm Hg, and the mean post-VIV TAVR aortic valve area was 1.00 cm^2 . Post-BVF, the mean aortic valve gradient was 7.3 mm Hg, and the mean aortic valve area was 1.32 cm^2 . At 30-day follow-up ($n = 9$), the mean aortic valve gradient and the mean aortic valve area were 17.8 mm Hg and 1.05 cm^2 , respectively (*Table 3*, *Figure 1*). The mean postoperative ejection fraction also increased to $55\% \pm 15\%$. The mean length of stay in the hospital was 29 h. All gradients were obtained through Doppler echocardiogram.

One case of preoperative paravalvular leakage was resolved following BVF VIV TAVR. There were no operative cases of paravalvular leak, aortic root rupture, aortic insufficiency, stroke, or permanent pacemaker implantation. Successful fracturing occurred in 75% of BVF cases (*Table 4*). The three failed attempts involved the 22 mm Bard True balloon and the 21 mm Magna valve, with two balloons rupturing at 14 atm and one at 20 atm. Postoperatively, the failed attempts yielded hemodynamics and aortic valve area measurements that were similar to those of the successful attempts (*Table 3*). One case required reoperation to remove the VIV due to coronary obstruction. Emergent surgical exploration showed the left ostium to be obstructed by the initial bioprosthetic's leaflet.

There was one intraoperative death. The patient was a 90-year-old woman with a Society of Thoracic Surgeons

Table 3. Baseline, intraoperative, and 30-day follow-up data for 12 patients who underwent bioprosthetic valve fracturing during valve-in-valve transcatheter aortic valve replacement

Patient	Mean gradient (mm Hg)				Aortic valve area (cm ²)			
	Baseline	Post-VIV TAVR	Post-BVF	Follow-up	Baseline	Post-VIV TAVR	Post-BVF	Follow-up
1	19	X	4	9	0.8	X	1.6	0.9
2	22	2	No fracture	11	0.6	1.1	No fracture	1.1
3	29	19	11	7	0.8	1.1	1.6	0.9
4	31	22	5	11	0.7	1	1.14	1.2
5	40	16	10	19	0.8	1.06	1.2	0.9
6	42	X	8	Died	0.35	X	1	Died
7	62	X	4	29	0.55	X	1.2	1
8	45	7	No fracture	None	0.35	0.9	No fracture	None
9	96	20	6	15	0.4	0.96	1.3	1.4
10	31	20	10	21	0.7	0.96	1.3	1.2
11	44	9	No fracture	38	0.48	1.27	No fracture	0.8
12	69	19	8	None	0.5	0.73	1.5	None
Average	44.2	14.9	7.3	17.8	0.59	1	1.32	1.05

BVF indicates bioprosthetic valve fracturing; TAVR, transcatheter aortic valve replacement; VIV, valve-in-valve.

Predicted Risk of Mortality score of 7.1%, New York Heart Association class III, and a frailty score of 3 out of 4. Her other comorbidities included mitral regurgitation, tricuspid regurgitation, atrial fibrillation, left bundle branch block, chronic kidney disease stage III, peripheral vascular disease, hypertension, and hyperlipidemia. The preoperative aortic valve gradient and aortic valve area were 42 mm Hg and 0.35 cm², respectively. The patient underwent general anesthesia and, following successful BVF at 18 atm, the mean aortic valve gradient was 8 mm Hg. Following the BVF, the patient was administered protamine sulfate and subsequently entered a state of pulseless electrical activity. Cardiopulmonary bypass was performed, and cannulation of the coronary arteries was attempted. Angiography showed significant occlusions, and subsequent attempts at cannulation were again unsuccessful. Following the operation, coronary occlusion was the suspected cause of death. In addition to this one patient who died within 30 days of the operation, two patients were lost to follow-up.

DISCUSSION

Early bioprosthetic valves have limited durability and have been shown to undergo structural valve degeneration.^{1,8} A majority of these patients need a valve replacement. However, associated risk factors, including increased age and comorbidities, place these patients at prohibitively high risk for surgical reoperation.⁹ TAVR is a viable, less invasive alternative to surgical replacement, with similar survival benefits and a reduction in perioperative risks.^{2,3} VIV TAVR is

particularly indicated in cases with bioprosthetic valves that are stenotic.³ Although beneficial, the procedure can result in increased aortic valve gradients, reduced aortic valve area, and prosthetic-patient mismatch.^{10–14} With the use of high-pressure balloons to fracture the valvular ring while leaving the sewing cuff intact, BVF VIV TAVR facilitates the expansion of the new valve and improves hemodynamics by reducing the transvalvular gradient and increasing the aortic valve area.^{5,6}

In 2012, Dvir and colleagues presented 202 patients with degenerated bioprosthetic valves who underwent VIV TAVR.¹⁵ The most common mode of valve failure was stenosis (42%). While 93.1% of procedures were successful, procedural complications included device malposition (15.3%) and ostial coronary obstruction (3.5%). Mean postoperative aortic valve gradients were 15.9 ± 8.6 mm Hg. The 30-day all-cause mortality rate was 8.4%.¹⁵ This work was followed up in 2014 with an additional 459 patients. Again, stenosis was the most common mode of valve failure (39.4%). At 30 days, mortality was 7.6%. The overall 1-year Kaplan–Meier survival rate was 83.2%. Patients with small valves (≤21 mm) had worse 1-year survival when compared with those with both intermediate-sized valves (21–25 mm) and large valves (≥25 mm) ($P = 0.001$).⁴ These studies highlight the prevalence of stenosis in degenerated bioprosthetic valves, as well as the decreased survival in these patients and those with small-sized valves.

The work of Allen and colleagues showed the viability of BVF in bench testing.⁵ Notably, this study showed that

Figure 1. (a) Transaortic valve pressure gradients measurements and (b) aortic valve area measurements via transthoracic echocardiography. BVF indicates bioprosthetic valve fracturing; VIV TAVR, valve-in-valve transcatheter aortic valve replacement.

Table 4. Procedural and postprocedural data for 12 patients who underwent bioprosthetic valve fracturing during valve-in-valve transcatheter aortic valve replacement.

Variable	n (%)
General anesthesia	9 (75%)
Sedation	3 (25%)
Valve-in-valve fractured	9 (75%)
Postop permanent pacemaker	0
30-Day mortality	1/10 (10%)
Rehospitalization within 30 days	2/10 (20%)
New York Heart Association reduction	4 (33.3%)
Vascular complications	0

different valves require different fracturing pressures. Regardless of valve size, Epic valves were reported to fracture at 8 atm, Mosaic valves at 10 atm, Mitroflow valves at 12 atm, Magnaese valves at 18 atm, and Magna valves at 24 atm. In our case series, three failed fracturing attempts occurred with the 21 mm Magna valve and the 22 mm Bard True balloon, which failed to reach 24 atm, rupturing at 14 atm and again at 20 atm. While valves are often successfully fractured with balloons 1 mm larger than the labeled valve size, different balloons may be required depending on each valve's specific fracturing threshold.

Subsequent studies reported BVF in small numbers of VIV TAVR. Chhatriwalla et al presented 20 cases of BVF before or after VIV TAVR.⁶ BVF resulted in a reduction in

the mean aortic valve gradient from 20.5 ± 7.4 to 6.7 ± 3.7 mm Hg ($P < 0.001$) and an increase in aortic valve area from 1.0 ± 0.4 to 1.8 ± 0.6 cm² ($P < 0.001$), with no reports of procedural complications.⁶ Nielsen-Kudsk and colleagues presented 10 patients with failing 19 mm and 21 mm Mitroflow valves who underwent BVF VIV TAVR using Edwards SAPIEN 3 or XT valves (20 or 23 mm). The peak aortic valve gradient decreased from 66 ± 27 mm Hg to 29 ± 7 mm Hg ($P = 0.002$), and the aortic valve area increased from 0.7 ± 0.3 cm² to 1.1 ± 0.3 cm² ($P = 0.001$). One patient suffered a stroke with resolution of symptoms and another required permanent pacemaker implantation for atrio-ventricular block. Mortality at the end of follow-up was 0.⁹

In our case series, the mean preoperative aortic valve gradient was 44 mm Hg, which was reduced to 14.9 mm Hg following VIV TAVR, then to 7.3 mm Hg following BVF. However, at 30-day follow-up, the mean aortic valve gradient was 15.0 mm Hg, similar to the mean post-VIV TAVR gradient. This is likely because intraoperative gradients were obtained with Doppler echocardiogram while the patient was in supine position, which may yield different results compared to measurements taken when patients can be optimally positioned on their side. Also, intraoperative gradients may be lower after pacing and due to the effects of sedation. Furthermore, there were two cases of coronary occlusion in our case series, one that was the suspected cause of our only case of operative mortality and another that was successfully surgically repaired. Coronary obstruction is a clinically significant complication of VIV TAVR, with rates as high as 2.3%.¹⁶ It more commonly occurs in externally mounted leaflet or stentless bioprosthetic valves.¹⁶ Overall, available studies show that BVF VIV TAVR is a safe and feasible treatment method that yields clinical improvements in certain subsets of high-risk patients. However, in future studies, we recommend the use of a more uniform system of reporting valve gradients and areas to aid in the comparison of results.

In conclusion, in high-risk patients, BVF VIV TAVR is a viable alternative treatment method for replacing failed bioprosthetic valves. This method improves aortic valve gradients and valve area, particularly in patients with small bioprosthetic valves. Our results emphasize that the procedure is not without complications. Given the increasing use of bioprosthetic valves in patients and the early structural valve degeneration that has been observed in these valves, the expected number of patients needing the procedure will increase. BVF VIV TAVR can provide benefits to these patients.

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