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NEW RESEARCH PAPER

STRUCTURAL

Outcomes of Bioprosthetic Valve Fracture in Patients Undergoing Valve-in-Valve TAVR

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ABSTRACT

BACKGROUND Valve-in-valve (VIV) transcatheter aortic valve replacement (TAVR) is increasingly used to treat degenerated surgical bioprostheses. Bioprosthetic valve fracture (BVF) has been shown to improve hemodynamic status in VIV TAVR in case series. However, the safety and efficacy of BVF are unknown.

OBJECTIVES The primary objective of this study was to assess the safety and efficacy of VIV TAVR using SAPIEN 3 and SAPIEN 3 Ultra valves with or without BVF using data from the Society of Thoracic Surgeons/American College of Cardiology TVT (Transcatheter Valve Therapy) Registry.

METHODS The primary outcome was in-hospital mortality. Secondary outcomes included echocardiography-derived valve gradient and aortic valve area. Inverse probability of treatment weighting was used to adjust for baseline characteristics.

RESULTS A total of 2,975 patients underwent VIV TAVR from December 15, 2020, to March 31, 2022. BVF was attempted in 619 patients (21%). In adjusted analyses, attempted BVF was associated with higher in-hospital mortality (OR: 2.51; 95% CI: 1.30-4.84) and life-threatening bleeding (OR: 2.55; 95% CI: 1.44-4.50). At discharge, VIV TAVR with attempted BVF was associated with larger aortic valve area (1.6 cm^2 vs 1.4 cm^2; $P < 0.01$) and lower mean gradient (16.3 mm Hg vs 19.2 mm Hg; $P < 0.01$). When BVF was compared with no BVF according to timing (before vs after transcatheter heart valve implantation), BVF after transcatheter heart valve implantation was associated with improved hemodynamic status and similar mortality.

CONCLUSIONS BVF as an adjunct to VIV TAVR with the SAPIEN 3 and SAPIEN 3 Ultra valves is associated with a higher risk for in-hospital mortality and significant bleeding and modest improvements in echocardiography-derived hemodynamic status. The timing of BVF is an important determinant of safety and efficacy.
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Most surgical aortic valve replacement procedures in the United States are performed using bioprosthetic valves, a trend that has increased in recent years.[1,2] Although bioprosthetic valves avoid the bleeding risks of lifelong oral anticoagulation, structural valve deterioration remains an important limitation.[3]

Valve-in-valve (VIV) transcatheter aortic valve replacement (TAVR) has emerged as an important alternative to reoperation[4-6] for the treatment of bioprosthetic valve failure, which is associated with significant operative risks.[7] Despite the safety of VIV TAVR, patient-prosthesis mismatch (PPM) after VIV TAVR is a potential limitation and is associated with worse clinical outcomes, especially in patients with smaller surgical valves.[5,8]

Bioprosthetic valve fracture (BVF) is a technique that intentionally disrupts the stent frame of the surgical heart valve (SHV) to optimize expansion of the transcatheter heart valve (THV). BVF has been shown to reduce residual gradients and increase the effective orifice area after VIV TAVR.[9-11] Bench testing in commercially available SHVs has demonstrated that most SHVs can be fractured with a high-pressure balloon inflation,[9,10] which has resulted in clinical adoption in small observational studies.[9-18] However, important questions remain regarding the safety and efficacy of BVF in a large, unselected population of patients undergoing VIV TAVR.

The primary objective of this study was to analyze and compare the clinical characteristics, outcomes, and complications of patients undergoing VIV TAVR with or without BVF.

METHODS

PATIENTS. The Society of Thoracic Surgeons (STS) and American College of Cardiology (ACC) TVT (Transcatheter Valve Therapy) Registry is a collaborative clinical registry developed by the STS and the ACC in response to the Centers for Medicare and Medicaid Services national coverage determination requirement for national registry participation of all TAVR centers in the United States.

The STS/ACC TVT Registry uses standardized definitions and collects participant-reported data, which includes demographics, comorbidities, procedural details, and outcomes from consecutive patients undergoing TAVR using commercially approved devices.[19] The STS/ACC TVT Registry was granted a waiver of the requirement to obtain informed consent by Advarra.

Data on the use of BVF during VIV TAVR were not captured in the STS/ACC TVT Registry until January 2021. The registry contains 3 data elements that pertain to BVF: BVF attempted (yes or no), BVF timing (preimplantation or postimplantation), and valve observed to be fractured (yes or no). In this study, the STS/ACC TVT Registry was queried for patients undergoing VIV TAVR with the SAPIEN 3 or SAPIEN 3 Ultra device with or without attempted BVF.

STATISTICAL ANALYSIS. Continuous variables are reported as mean ± SD or median (IQR) and were compared using Student's *t*-test. Categorical variables are reported as number (percentage) and were compared using the chi-square test or Fisher exact test. In-hospital events are reported as incidence (percentage) and presented as ORs with 95% CIs. Mortality, stroke, and other safety outcomes at 30 days were calculated using adjusted Cox regression, and results are presented as HRs with 95% CIs.

ABBREVIATIONS AND ACRONYMS

ACC = American College of Cardiology

BVF = bioprosthetic valve fracture

ID = internal diameter

PPM = patient-prosthesis mismatch

SHV = surgical heart valve

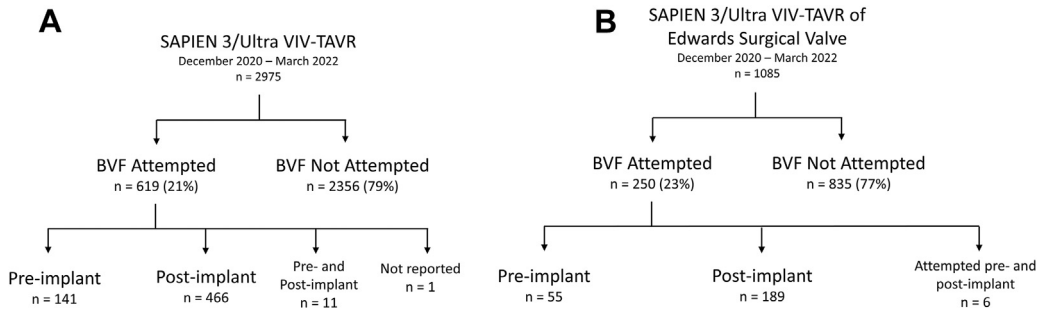
STS = Society of Thoracic Surgeons

TAVR = transcatheter aortic valve replacement

THV = transcatheter heart valve

VIV = valve-in-valve

FIGURE 1 Study Flow for the Evaluation of Safety and Hemodynamic Outcomes of VIV TAVR Procedures With and Without Attempted BVF



Study flow for safety **(A)** and hemodynamic **(B)** outcomes. Assessment of echocardiographic hemodynamic outcomes was restricted to patients in whom the true internal diameter (ID) of the surgical valve was known. BVF = bioprosthetic valve fracture; TAVR = transcatheter aortic valve replacement; VIV = valve-in-valve.

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TABLE 1 Unadjusted Patient Baseline Characteristics for Patients Who Underwent Valve-in-Valve Transcatheter Aortic Valve Replacement With and Without BVF

	BVF (n = 619)	No BVF (n = 2,356)	*P* Value
Age, y	73.7 ± 9.9 (618)	73.3 ± 11.1	0.45
Male	69.31 (429)	70.71 (1,666)	0.49
STS PROM	5.09 ± 4.14 (598)	5.61 ± 5.75 (2,261)	0.01
NYHA functional class III/IV	74.23 (455/613)	75.06 (1,740/2,318)	0.67
BMI, kg/m^2	29.55 ± 6.74 (617)	29.33 ± 10.08 (2,347)	0.54
Hypertension	89.98 (557)	87.73 (2,067)	0.12
Diabetes	34.41 (213)	30.77 (725)	0.08
Atrial fibrillation/flutter	40.39 (250)	46.18 (1,088)	0.01
Prior stroke	12.76 (79)	12.56 (296)	0.89
Prior CABG	38.13 (236)	30.98 (730)	<0.01
Prior PCI	24.23 (150)	21.05 (496)	0.09
Cardiogenic shock within 24 h	1.94 (12)	4.50 (106/2,354)	<0.01
Baseline pacemaker	12.92 (80)	16.72 (394)	0.02
Carotid stenosis	15.07 (93/617)	11.98 (282/2,354)	0.04
Heart failure within 2 wk	68.34 (382/559)	76.86 (1,657/2,156)	<0.01
Estimated GFR, mL/min/1.73 m^2	64.09 ± 25.08 (615)	61.76 ± 23.95 (2,342)	0.03

Values are mean ± SD (n) or % (n).

BMI = body mass index; BVF = bioprosthetic valve fracture; CABG = coronary artery bypass graft; GFR = glomerular filtration rate; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; STS PROM = Society of Thoracic Surgeons Predicted Risk of Mortality.

To characterize the safety of attempted BVF, in the primary analysis we compared patients undergoing VIV TAVR with (treated group) and without (untreated group) BVF. The primary safety outcome measure was in-hospital mortality. To adjust for confounding, inverse probability of treatment weighting for average treatment effect among the treated was used to achieve a balanced distribution of baseline confounders between the subgroups. Missing values were imputed using the Markov-chain Monte Carlo method prior to modeling. The underlying model covariates included age, race, sex (male), body mass index, access site, prior percutaneous coronary intervention, prior coronary artery bypass graft, prior stroke, carotid stenosis, peripheral arterial disease, hypertension, diabetes, chronic lung disease, immunocompromise, porcelain aorta, atrial fibrillation, creatinine, hemoglobin level, estimated glomerular filtration rate, aortic valve mean gradient, left ventricle ejection fraction, aortic regurgitation, mitral regurgitation, tricuspid regurgitation, New York Heart Association functional class III or IV, 5-m walk test, Kansas City Cardiomyopathy Questionnaire Score overall score, currently on dialysis, pacemaker, previous implantable cardioverter-defibrillator, cardiogenic shock within 24 hours, current or recent smoking, prior transient ischemic attack, prior surgical repair, endocarditis, and primary indication for VIV TAVR (ie, mode of surgical valve failure).

To further characterize the impact of BVF during VIV TAVR, valve hemodynamic status obtained prior to discharge was compared in patients undergoing VIV TAVR with or without attempted BVF. Given that BVF was preferentially used to treat smaller surgical bioprosthetic valves (true internal diameter [ID] ≤21 mm), a secondary analysis was performed to assess the hemodynamic impact of BVF on this cohort of VIV TAVR patients. As part of the data-sharing agreement, Edwards Lifesciences was provided information regarding surgical valve model and size only for patients with degenerated Edwards valves. Therefore, this analysis was restricted to Edwards Lifesciences surgical valves, and for the analysis of hemodynamic outcomes, the true ID of the prior valve was added as a covariate in the adjusted model. A 2-tailed *P* value of <0.05 was considered to indicate statistical significance. Statistical analyses were performed using SAS version 9.4 (SAS Institute).

RESULTS

From December 15, 2020, to March 31, 2022, 2,975 VIV TAVR procedures using SAPIEN 3 or SAPIEN 3 Ultra THVs were recorded in the STS/ACC TVT Registry. BVF was attempted in 619 (21%) of VIV TAVR cases. A Consolidated Standards of Reporting Trials flow diagram is presented in Figure 1A. True ID information was available for Edwards Lifesciences surgical valves (n = 1,085 [36% of the cohort]). Of these patients with known true ID information, 250 (23%) underwent VIV TAVR with attempted BVF (Figure 1B). During the study period, 658 sites performed VIV TAVR procedures. Of these sites, 419 (64%) did not perform any BVF during the study period. Of the 26 institutions that performed BVF in ≥50% of VIV TAVR procedures, the median number of VIV TAVR procedures was 2. Successful BVF (valve observed to be fractured) was site reported in 83% of attempted BVF procedures (512 of 619).

Patient baseline and echocardiographic characteristics are shown in Table 1. Patients in whom BVF was attempted had lower STS Predicted Risk of Mortality; were less likely to have histories of atrial fibrillation, pacemaker implantation, recent heart failure exacerbation, and cardiogenic shock within 24 hours; were more likely to have histories of coronary artery bypass surgery and carotid artery stenosis; and had higher glomerular filtration rates. Patients in whom

TABLE 2 Procedural Data for Patients Who Underwent Valve-in-Valve Transcatheter Aortic Valve Replacement With and Without BVF

	BVF (n = 619)	No BVF (n = 2,356)	Overall (n = 2,975)	*P* Value
Transfemoral access	95.80 (593)	95.45 (2,247/2,354)	95.53 (2,840/2,973)	0.71
Conscious sedation	51.62 (319/618)	49.64 (1,169/2,355)	50.05 (1,488/2,973)	0.38
Procedure time, min	78.49 ± 38.49	74.95 ± 58.79	75.69 ± 55.19	0.07
Contrast volume, mL	52.12 ± 49.95 (540)	56.31 ± 54.12 (2,050)	55.44 ± 53.29 (2,590)	0.09
Implantation success	98.71 (611)	98.98 (2,332)	98.92 (2,943)	0.56
Length of stay, d	2.21 ± 3.69	2.40 ± 4.40	2.36 ± 4.26	0.28
THV information				
SAPIEN 3 Ultra	90.63 (561)	82.72 (1,949)	84.37 (2,510)	<0.01
SAPIEN 3	9.37 (58)	17.28 (407)	15.63 (465)	<0.01

Values are % (N), % (n/N), mean ± SD, or mean ± SD (N).
BVF = bioprosthetic valve fracture; THV = transcatheter heart valve.

BVF was attempted were less likely to have moderate or greater aortic insufficiency and had higher left ventricular ejection fractions. After adjustment, the baseline characteristics between the BVF and no-BVF groups were similar (Supplemental Table 1). No significant differences in procedural sedation, procedure time, contrast volume, and device success were observed between groups (**Table 2**).

In adjusted analyses, in-hospital all-cause mortality (OR: 2.51; 95% CI: 1.30-4.84), cardiac death (OR: 2.47; 95% CI: 1.13-5.39), all-cause mortality or stroke (OR: 1.94; 95% CI: 1.13-3.33), and life-threatening bleeding (OR: 2.55; 95% CI: 1.44-4.50) were higher in patients in whom BVF was attempted (**Table 3**).

At 30 days, 9.04% of patients were lost to follow-up. Thirty-day all-cause mortality (HR: 1.84; 95% CI: 1.09-3.10), cardiac death (HR: 2.12; 95% CI: 1.09-4.16), all-cause mortality or stroke (HR: 1.63; 95% CI: 1.04-2.55), and life-threatening bleeding (HR: 2.35; 95% CI: 1.33-4.16) were higher in patients in whom BVF was attempted (**Table 4**). No significant differences in stroke, new dialysis requirement, aortic dissection or aortic annulus rupture were observed. Safety outcomes in patients with Edwards Lifesciences surgical valves are reported in Supplemental Table 2.

TIMING OF BVF AND SAFETY OUTCOMES. BVF was performed prior to THV implantation in 141 of 619 patients (23%) in whom BVF was attempted and after THV implantation in 466 of 619 patients (75%). BVF was attempted both before and after THV implantation in 11 of 619 patients (2%), and the timing of BVF was not reported for 1 patient. Successful BVF was site reported in 85% of patients (395 of 466) when performed after THV implantation and 77% (109 of 141) when performed prior to THV implantation ($P < 0.01$). Eighty-one of 239 sites performed at least 1 BVF case prior to THV implantation, and 42 of these sites (52%) exclusively performed BVF prior to THV implantation.

In-hospital all-cause mortality (OR: 2.9; 95% CI: 1.21-6.94), cardiac death (OR: 3.42; 95% CI: 1.25-9.37), all-cause mortality or stroke (OR: 2.02; 95% CI: 0.88-4.63), new onset of atrial fibrillation (OR: 3.84; 95% CI: 1.07-13.83), and major vascular complications (OR: 4.09; 95% CI: 1.37-12.20) were higher in patients in whom BVF was attempted prior to THV implantation compared with patients in whom BVF was not attempted. In contrast, in-hospital all-cause mortality (OR: 2.1; 95% CI: 0.8-5.1), cardiac death (OR: 1.91; 95% CI: 0.68-5.40), all-cause mortality or stroke (OR: 1.88; 95% CI: 0.98-3.60), new-onset atrial fibrillation (OR: 1.73; 95% CI: 0.55-5.39), and major vascular complications (OR: 1.29; 95% CI: 0.48-3.53) were not significantly higher in patients in whom BVF was attempted after THV implantation compared with patients in whom BVF was not attempted (**Figure 2**). Life-threatening bleeding was higher in the attempted BVF group irrespective of timing (prior to THV OR: 4.48 [95% CI: 2.07-9.72]; after THV OR: 2.0 [95% CI: 0.99-4.04]).

HEMODYNAMIC OUTCOMES. In analyses adjusted for covariates including the true ID of the surgical valve, echocardiography-derived aortic valve area was higher and transvalvular gradients were lower in patients in whom BVF was attempted vs not attempted (**Figure 3**). Although BVF was performed more often in patients with small surgical valves (true ID ≤21 mm [30% vs 15%; $P < 0.01$]), these differences were observed both in patients with small surgical valves and those with larger surgical valves (Supplemental Table 3). In patients in whom BVF was attempted prior to VIV TAVR, no significant differences in aortic valve area were observed compared with patients without attempted BVF. In patients in whom BVF was

TABLE 3 Adjusted Rates of In-Hospital Outcomes for Patients Who Underwent Valve-in-Valve Transcatheter Aortic Valve Replacement With and Without BVF

	BVF, %	No BVF, %	OR (95% CI)	*P* Value
All-cause mortality	2.26	0.91	2.51 (1.3-4.84)	<0.01
Cardiac death	1.62	0.66	2.47 (1.13-5.39)	0.02
Stroke	1.13	0.91	1.25 (0.52-2.98)	0.62
All-cause mortality or stroke	3.23	1.69	1.94 (1.13-3.33)	0.02
Life-threatening bleeding[a]	3.39	1.36	2.55 (1.44-4.5)	<0.01
Major vascular complication[a]	1.62	0.79	2.06 (0.95-4.44)	0.07
New requirement for dialysis	0.48	0.37	1.31 (0.35-4.9)	0.69
New pacemaker without baseline	2.78	1.99	1.41 (0.76-2.64)	0.28
New-onset atrial fibrillation	1.86	0.86	2.17 (0.87-5.43)	0.10
Annular rupture	0.16	0.05	3.15 (0.26-38.86)	0.37
Aortic dissection	0.16	0.05	3.4 (0.3-38.09)	0.32
Cardiac perforation	0.16	0.00	NA	NA
Coronary artery obstruction	0.65	0.45	1.44 (0.44-4.71)	0.55
Any readmission	0.32	0.29	1.1 (0.22-5.54)	0.91

[a]Definitions for life-threatening bleeding and major vascular complications are provided in Supplemental Table 4.
BVF = bioprosthetic valve fracture; NA = not applicable.

attempted prior to VIV TAVR valve, gradients were lower compared with patients without attempted BVF; however, the difference in valve gradient at 30-day follow-up did not reach statistical significance. Patients in whom BVF was performed after THV implantation had significantly larger aortic valve areas (1.6 cm^2 vs 1.4 cm^2; $P < 0.01$) and lower mean gradients at 30 days (18.3 mm Hg vs 22.6 mm Hg; $P < 0.01$) compared with patients without attempted BVF (Figure 4).

DISCUSSION

This study represents the largest cohort of patients to date who underwent BVF as an adjunct to VIV TAVR.

TABLE 4 Adjusted Kaplan-Meier Rates of 30-Day Outcomes for Patients Who Underwent Valve-in-Valve Transcatheter Aortic Valve Replacement With and Without BVF

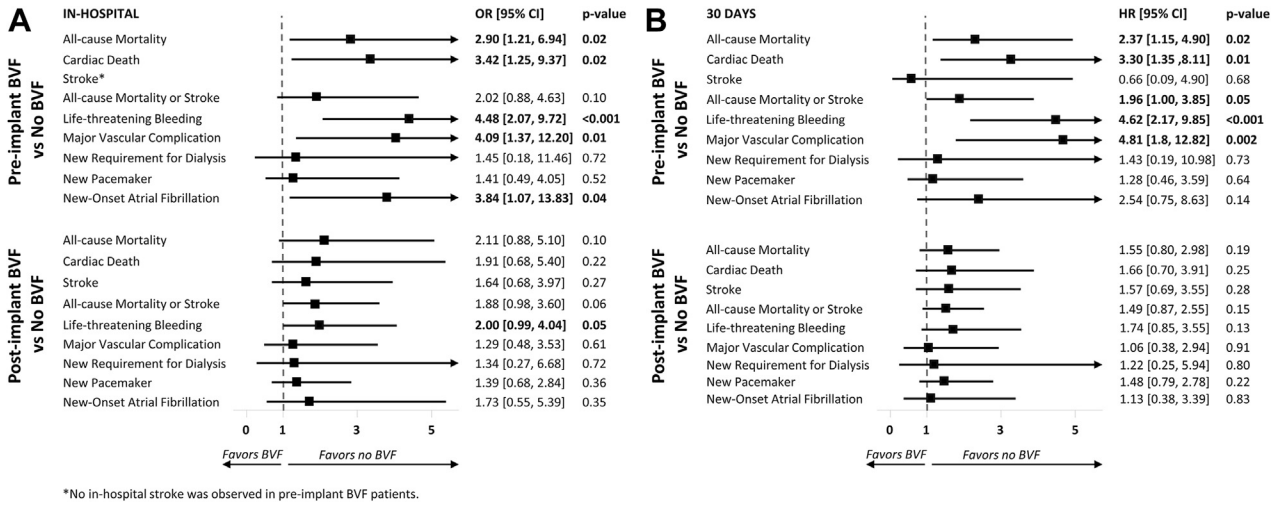
	BVF, %	No BVF, %	HR (95% CI)	*P* Value
All-cause mortality	3.56	1.98	1.84 (1.09-3.1)	0.02
Cardiac death	2.20	1.05	2.12 (1.09-4.16)	0.03
Stroke	1.50	1.13	1.33 (0.62-2.89)	0.47
All-cause mortality or stroke	4.70	2.95	1.63 (1.04-2.55)	0.03
Life-threatening bleeding	3.43	1.51	2.35 (1.33-4.16)	<0.01
Major vascular complication	1.80	0.94	1.93 (0.91-4.12)	0.09
New requirement for dialysis	0.51	0.42	1.23 (0.34-4.53)	0.75
New pacemaker without baseline	3.48	2.44	1.43 (0.82-2.52)	0.21
New-onset atrial fibrillation	1.91	1.37	1.43 (0.6-3.43)	0.42
Any readmission	5.51	6.00	0.92 (0.61-1.37)	0.67

BVF = bioprosthetic valve fracture.

There are several important findings (Central Illustration). First, BVF is commonly performed as an adjunct to VIV TAVR in the United States, particularly in patients with small surgical valves (30% frequency). Nevertheless, institutional volumes of attempted BVF are relatively low, with fewer than 35 hospitals performing 5 or more BVF procedures per year. Third, in adjusted analyses, in-hospital and 30-day mortality, cardiac death, all-cause death or stroke, and life-threatening bleeding were higher in patients who underwent VIV TAVR with attempted BVF compared with those who underwent VIV TAVR without BVF. However, these differences were numerically smaller and not statistically significant in patients who underwent BVF after THV implantation, compared with patients in whom BVF was not attempted, suggesting that procedural technique plays an important role in the safety of the procedure. Last, although significant differences in valve area and valve gradient were observed in patients who underwent BVF following THV implantation compared with patients in whom BVF was not attempted, no differences were seen in patients in whom BVF was attempted prior to THV implantation. This suggests that procedural technique plays an important role in the efficacy of BVF as well. Taken together, our observations suggest that when clinically indicated, BVF should be performed after, rather than before, THV implantation.

BVF in the setting of VIV TAVR optimizes THV expansion and can mitigate PPM, which is associated with higher mortality after VIV TAVR.[9] However, the longer-term effect of BVF on clinical outcomes remains unknown. BVF in conjunction with VIV TAVR increases the effective aortic valve area and reduces valve gradients. Despite these improvements, questions regarding the true clinical benefits of BVF remain, given the lack of longer-term prospective data and a control arm as a comparator. In this study, higher mortality was observed in patients undergoing attempted BVF, particularly in patients in whom BVF was performed prior to THV implantation. One concern with BVF performed prior to VIV TAVR is the potential for surgical valve leaflet injury causing acute severe valvular regurgitation and hemodynamic compromise for a period of time until a competent THV can be implanted. Other complications that could be directly linked to BVF, such as annular rupture, aortic dissection, and coronary occlusion, were rare (<1%). The higher risk for significant bleeding because of major vascular complications with attempted BVF is also a concern. This complication could be due to technical issues such as unplanned sheath exchanges (eg, balloon

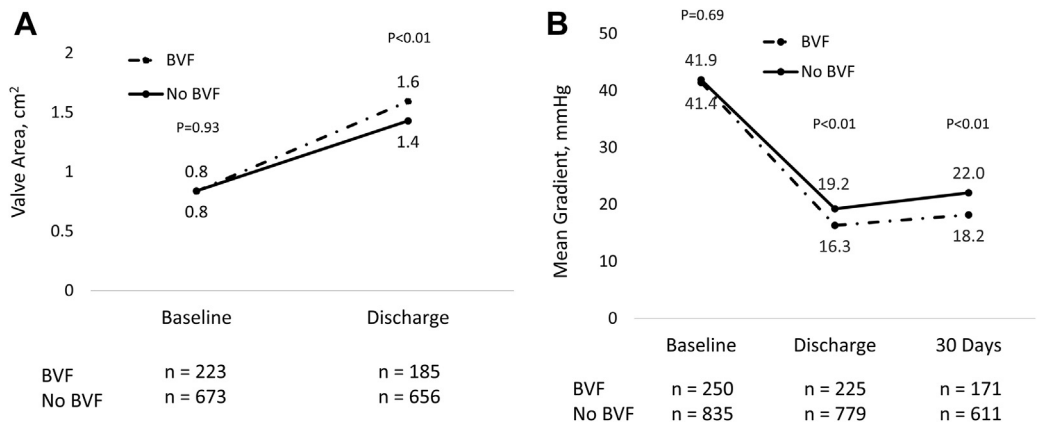
FIGURE 2 Safety Outcomes of Patients Undergoing BVF According to Timing of BVF



(A) In-hospital and **(B)** 30-day safety outcomes of patients who underwent attempted BVF before or after VIV TAVR compared with VIV TAVR without attempted BVF. Abbreviations as in Figure 1.

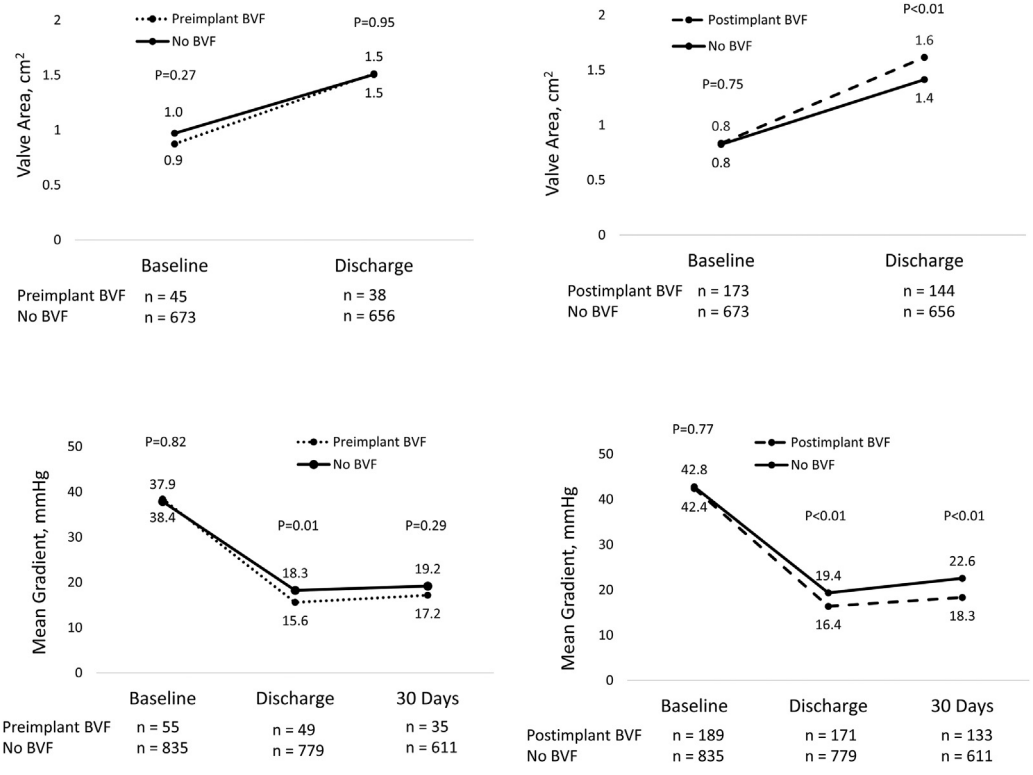
rupture with an inability to remove the balloon through the valve delivery sheath) or access-site complications caused by the need for emergent mechanical circulatory support in the setting of hemodynamic instability. Interestingly, despite the higher rate of observed complications in patients with attempted BVF, average procedure time was not higher. As such, presumably these complications were infrequent enough to not result in any statistically significant difference in the overall procedure time between groups. The STS/ACC TVT Registry dataset lacks granularity to assess the exact cause for the observed higher rates of mortality and other safety endpoints associated with attempted BVF in this analysis, which will require further study. Although it appears that BVF performed after THV implantation is the safer option, the question of whether the smaller hazard observed with this

FIGURE 3 Echocardiography-Derived Aortic Valve Area and Mean Gradient in Patients Who Underwent VIV TAVR With or Without Attempted BVF



(A) Echocardiography-derived aortic valve area. **(B)** Mean aortic valve gradient. Abbreviations as in Figure 1.

FIGURE 4 Echocardiography-Derived Aortic Valve Area and Mean Gradient in Patients Who Underwent Attempted BVF Before THV Implantation and Patients Who Underwent Attempted BVF After THV Implantation

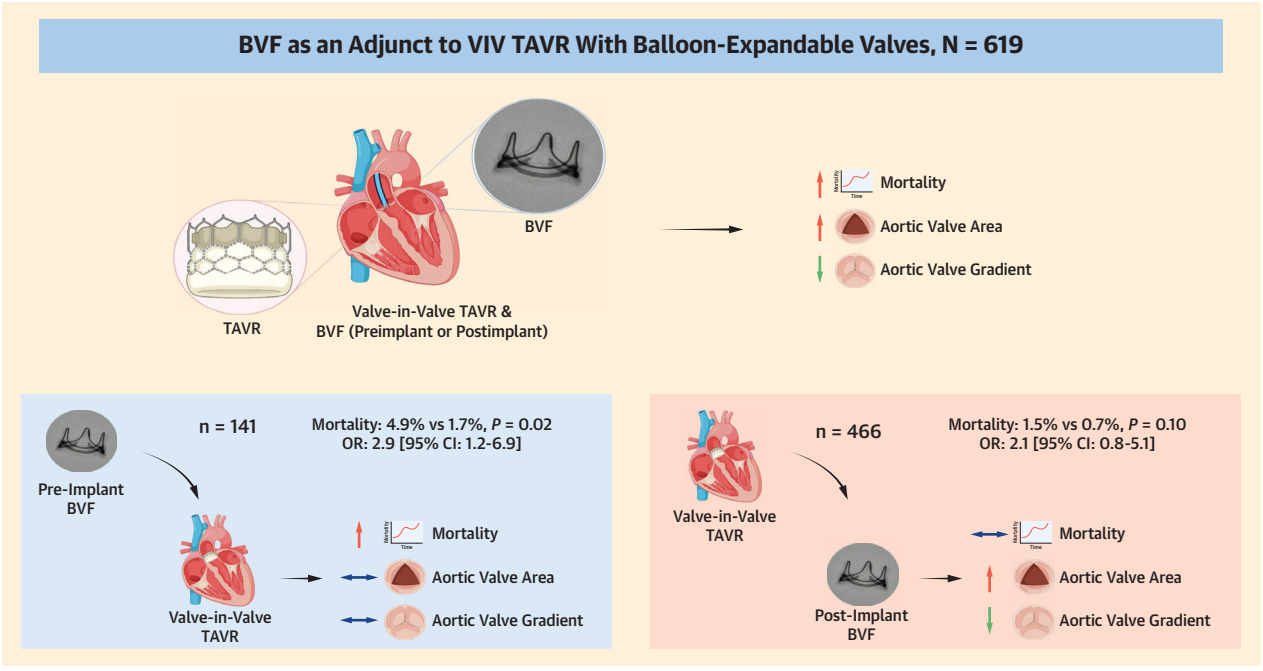


BVF = bioprosthetic valve fracture; THV = transcatheter heart valve.

technique could be offset by longer-term clinical benefits needs prospective confirmation.

The differences in aortic valve area and mean valve gradient observed in patients undergoing BVF in this study were smaller than those reported in prior case series. In a prior analysis of 66 patients who underwent VIV TAVR followed by BVF, the mean aortic valve area was 0.8 cm^2 at baseline, increased to 1.4 cm^2 following VIV TAVR, and increased further to 2.1 cm^2 following BVF ($P < 0.001$) as measured invasively. Similarly, the mean valve gradient in this cohort was 41 mm Hg at baseline, decreased to 19 mm Hg following VIV TAVR, and decreased further to 8 mm Hg following BVF ($P < 0.001$). However, in that series each patient served as his or her own control. In the TVT Registry, no data regarding interim gradients before BVF are available, and it is possible and perhaps even likely that the patients who underwent attempted BVF were those with more severe PPM and/or higher residual gradients following VIV TAVR. Furthermore, BVF was reported to be successful in all cases in the prior case series, whereas in the present study, BVF was not always observed to be successful. Prior bench testing has demonstrated that most, but not all, surgical valves can be fractured. However, surgical valves vary greatly in their composition, and the threshold at which a valve fractures is dependent on the composition of the valve, its ID, and the size of the balloon being used for BVF, and the balloon pressure required to fracture may exceed 20 atm in many cases. Moreover, successful BVF is not always visually apparent on fluoroscopy. Some valves have radiopaque elements, which can be visually observed to fracture, whereas others do not. As a result, the recommended technique to perform BVF involves a steady increase in the inflation pressure until the inflation pressure drops suddenly; at that point, either the valve has fractured or the balloon has ruptured. Even balloon rupture can be subtle, as in the case of a pinhole rupture, which complicates the assessment of successful BVF. Although the success of BVF in this self-reported real-world registry is difficult to surmise, the hemodynamic results of BVF observed in this study suggest

CENTRAL ILLUSTRATION **Bioprosthetic Valve Fractures (BVF) Outcomes**



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Attempted bioprosthetic valve fracture (BVF) is associated with increased risk for in-hospital mortality, modest gains in aortic valve area, and reduction in transvalvular gradients. The timing of BVF in relation to the valve-in-valve (VIV) transcatheter aortic valve replacement (TAVR) procedure is an important determinant of efficacy and safety outcomes. BVF attempted prior to VIV TAVR was associated with increased mortality and no changes in hemodynamic parameters, whereas BVF attempted after VIV TAVR was associated with similar mortality and improved hemodynamic status.

that BVF was not successfully achieved in a substantial proportion of cases. It should also be noted that the hemodynamic analysis was performed only in the subgroup of patients with surgical valves with known true ID and that previous studies compared gradients using the same individual as a control rather than aggregate data from large samples. Although most Edwards Lifesciences surgical valves are amenable to BVF and have a metallic stent frame that typically facilitates visualization of a successful fracture, they exhibit higher fracture thresholds relative to polymer stent frames.[20] The inability to reach these high-pressure thresholds during BVF may have contributed to the attenuated hemodynamic response. Additionally, the high-pressure threshold required to fracture Edwards surgical valves could explain the higher risk for new permanent pacemaker after BVF (Supplemental Table 2). Contemporary surgical valve designs, which include fluoroscopically visible markers and expandable stent frames, may facilitate VIV TAVR procedures and optimize hemodynamic status without the need to fracture the surgical sewing ring using high-pressure balloon inflations.[21]

BVF performed after VIV TAVR involves a high-pressure inflation with a noncompliant balloon within the deployed THV that may result in more optimal THV expansion, compared with BVF performed prior to VIV TAVR. This has been demonstrated through caliper measurements during bench testing but has not been evaluated in situ.[11] However, the findings of this study support the findings of a prior case series, which showed that valve hemodynamic parameters are most optimal when BVF is performed after VIV TAVR compared with BVF performed before THV implantation. One potential concern with BVF performed within the deployed THV has been the risk for THV leaflet injury, resulting in acute aortic insufficiency or early degeneration. However, the risk for acute THV injury with BVF appears to be very low and can be mitigated by careful attention to balloon sizing and position.[22] Moreover, a previous study involving implantation of THV

leaflets into an accelerated calcification animal model demonstrated no difference in leaflet calcification following BVF performed before or after VIV TAVR.[23]

STUDY LIMITATIONS. This was a retrospective, observational study, and despite adjustment for various demographic, clinical, and procedural factors, unmeasured variables can confound the results of this analysis. Data in the STS/ACC TVT Registry are site reported and not adjudicated; however, automatic system validation, reporting of data completeness, random auditing of participating centers, and education and training of data site managers is performed to promote quality assurance. Data fields pertaining to BVF were only added in January 2021, limiting the scope of the analysis. Data regarding surgical valve type and size were available only for the subgroup of patients with surgical valves manufactured by Edwards Lifesciences, which limited the applicability of the analysis of hemodynamic parameters in this study. Finally, the ability to determine success in achieving BVF was site reported and cannot be adjudicated.

CONCLUSIONS

The use of BVF as an adjunct to VIV TAVR with SAPIEN 3 and SAPIEN 3 Ultra valves is associated with a higher risk for in-hospital mortality, excess bleeding, modest reduction in echocardiographic valve gradient, and gain in valve area. The timing of BVF relative to THV implantation is important, and BVF performed after THV implantation is safer and more effective. Prospective controlled studies are needed to confirm these preliminary findings and to assess long-term risk vs clinical benefit of BVF.

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PERSPECTIVES

WHAT IS KNOWN? PPM following Valve in Valve TAVR (VIV-TAVR) is associated with increased morbidity and mortality and can be mitigated by performing BVF.

WHAT IS NEW? BVF following VIV-TAVR is associated with better hemodynamic results and no significant difference in procedural complications whereas BVF prior to VIV-TAVR is associated with no difference in hemodynamic results and higher in-hospital mortality and life-threatening bleeding

WHAT IS NEXT? Prospective studies are needed to further evaluate the safety and short- and long-term efficacy of BVF during VIV-TAVR.

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KEY WORDS bioprosthetic valve fracture, transcatheter aortic valve replacement, valve-in-valve

APPENDIX For supplemental tables and an interactive version of the Central Illustration, please see the online version of this paper.