

Outcomes of valve-in-valve transcatheter aortic valve implantation with and without bioprosthetic valve fracture

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KEYWORDS

- aortic stenosis
- degenerative valve
- TAVI
- valve-in-valve

Abstract

Background: Bioprosthetic valve fracture (BVF) is a technique to reduce gradients in valve-in-valve transcatheter aortic valve implantation (VIV-TAVI) procedures. The outcome of VIV-TAVI with BVF has not been compared with VIV-TAVI without BVF.

Aims: The aim of this study was to evaluate the outcome of VIV-TAVI with BVF compared to VIV-TAVI without BVF.

Methods: In total, 81 cases of BVF VIV-TAVI (BVF group) from 14 centres were compared to 79 cases of VIV-TAVI without BVF (control group).

Results: VARC-2-defined device success was 93% in the BVF group and 68.4% in the control group ($p < 0.001$). The mean transvalvular gradient decreased from 37 ± 13 mmHg to 10.8 ± 5.9 mmHg ($p < 0.001$) in the BVF group and from 35 ± 16 mmHg to 15.8 ± 6.8 mmHg ($p < 0.001$) in the control group with a significantly higher final gradient in the control group ($p < 0.001$). The transvalvular gradients did not change significantly over time. In-hospital major adverse events occurred in 3.7% in the BVF group and 7.6% in the control group ($p = 0.325$). A linear mixed model identified BVF, self-expanding transcatheter heart valves (THVs) and other surgical aortic valve (SAV) types other than Mitroflow as predictors of lower transvalvular gradients.

Conclusions: Compared to VIV-TAVI alone, VIV-TAVI with BVF resulted in a significantly lower transvalvular gradient acutely and at follow-up. Independent predictors of lower gradients were the use of self-expanding THVs and the treatment of SAVs other than Mitroflow, irrespective of BVF performance. BVF significantly reduced the gradient independently from transcatheter or surgical valve type.

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Abbreviations

BASILICA	bioprosthetic or native aortic scallop intentional laceration to prevent iatrogenic coronary artery obstruction
BVF	bioprosthetic valve fracture
ID	internal diameter
PPM	prosthesis-patient mismatch
SAV	surgical aortic valve
STJ	sinotubular junction
TAVI	transcatheter aortic valve implantation
THV	transcatheter heart valve
VIV-TAVI	valve-in-valve transcatheter aortic valve implantation
VTC	virtual transcatheter heart valve to coronary ostium distance
VTSTJ	virtual transcatheter heart valve to sinotubular junction distance

Introduction

Valve-in-valve transcatheter aortic valve implantation (VIV-TAVI) is a valuable therapeutic approach in patients with degenerated surgical aortic valve bioprostheses¹. After surgical aortic valve (SAV) replacement, up to 45% of patients have prosthesis-patient mismatch (PPM), which is particularly frequent in patients with small SAVs^{2,3}. In this cohort VIV-TAVI may result in high residual gradients, which impact on survival^{1,4-6}.

Bioprosthetic valve fracture (BVF) is a technique to reduce gradients in VIV-TAVI procedures by fracturing the sewing ring of the SAV with high-pressure non-compliant balloon inflation⁷⁻¹⁰. A comparison of acute as well as long-term outcome data between VIV-TAVI with BVF versus without BVF in patients with comparable baseline characteristics, including SAV type, is missing and defines the scope of the present study.

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Material and methods

Fourteen international centres provided data on BVF VIV-TAVI procedures in patients with degenerated SAVs with fracturable or dilatable sewing rings. Data were collected retrospectively and prospectively. Patients with VIV-TAVIs performed during the same time period in SAVs, which were suitable for but did not undergo BVF, served as a control group.

Deteriorated SAVs were categorised as stenotic, regurgitant or mixed (stenosis and regurgitation \geq moderate). Indexed effective orifice area (iEOA) and PPM were calculated after surgical valve replacement. PPM was defined as mild (iEOA \geq 0.85-1.0), moderate (iEOA 0.65-0.85) or severe (iEOA \leq 0.65). The technique of BVF has been described elsewhere⁹. Timing of BVF (before or after transcatheter heart valve [THV] implantation) and choice of balloon size were per the operator's discretion. BVF was performed with non-compliant balloons 1-6 mm larger than the SAV's true internal diameter (ID). THVs were categorised as adequately or oversized for the patient's SAV based on recommendations of the Valve in Valve app version 2.0 (UBQO Limited, London, United Kingdom). BVF was considered successful if the

inflation pressure dropped suddenly without balloon perforation and the THV was fully expanded (in case of SAVs, which cannot be fractured but remodelled). Device success was defined as a correctly implanted THV without the use of a second valve and with a final mean gradient $<$ 20 mmHg, no moderate/severe aortic regurgitation and the absence of procedural death.

A VARC-2-defined early safety composite, clinical efficacy after 30 days and periprocedural complications including aortic root rupture, ventricular septal perforation, balloon rupture leading to clinical consequences, cardiac tamponade, coronary obstruction, among others, as well as reinterventions at follow-up, was evaluated.

STATISTICAL ANALYSIS

Continuous data are summarised as means \pm standard deviations or as medians (25th and 75th percentiles) as appropriate. Categorical data are presented as N (%). A linear mixed model was applied to associate mean gradient at discharge and follow-up to the treatment groups (BVF vs control), THV type (self-expanding vs balloon-expandable) and SAV type (Mitroflow vs non-Mitroflow). Estimates were adjusted with baseline mean transvalvular gradient. The time of measurement was included in the model. The response variable was log transformed to fulfil model assumptions. Parameter estimates and 95% confidence intervals of the parameter estimates are presented. Wilcoxon and Pearson/Fisher's exact tests were conducted to compare variables between groups. All p-values were two-sided and a p-value $<$ 0.05 was considered significant. All calculations were performed with the statistical analysis software R (R Core Team, 2020; R Foundation for Statistical Computing, Vienna, Austria).

Results

BVF VIV-TAVI was performed in 81 patients in the time period between August 2015 and March 2020 and VIV-TAVI alone in 79 patients in the time period between July 2014 and March 2020. Baseline data are summarised in **Table 1**. Both groups were comparable, with the exception of more male patients (65 vs 42%, $p=0.004$), larger SAVs (24.1 \pm 2.4 vs 22.1 \pm 2.1, $p<0.001$) and true IDs (20.7 \pm 2.5 mm vs 19.1 \pm 1.8 mm, $p<0.001$) in the control group.

Ten types of surgical valve were treated, mainly Mosaic[®] (Medtronic, Minneapolis, MN, USA), Mitroflow (Sorin Group, Saluggia, Italy), PERIMOUNT (Edwards Lifesciences, Irvine, CA, USA) and Magna (Edwards Lifesciences). The most common mode of degeneration according to the standardised definition was stenosis and mixed (94% vs 78% in the control group, $p=0.036$). Mean interval to SAV failure in the BVF group was 10.9 \pm 3.4 vs 11.8 \pm 4.6 years ($p=0.08$). Moderate/severe PPM was present in the BVF group in 54%/9% vs 45%/3% ($p=0.072$). Baseline mean gradient in the BVF group was 37 \pm 13 mmHg vs 35 \pm 16 mmHg ($p=0.11$), and iEOA was 0.81 \pm 0.24 cm²/m² vs 0.85 \pm 0.32 cm²/m² ($p=0.73$). Moderate/severe aortic regurgitation was more frequent in the control group (66% vs 50%, $p=0.049$). The main access was transfemoral ($p=0.34$); cerebral protection was more often applied

Table 1. Baseline data.

	N	BVF (N=81)	Control (N=79)	p-value			
Age, years	160	76±8	75±11	0.91			
Female gender, %	160	58 (47)	35 (28)	0.004			
Height, cm	156	167.4±10.8	172.4±9.5	0.004			
Weight, kg	159	74±15	80±16	0.033			
Hypertension, %	160	80 (65)	76 (60)	0.51			
Diabetes, %	160	31 (25)	25 (20)	0.43			
Glomerular filtration rate, ml/min	146	58±20	61±24	0.37			
Coronary artery disease, %	147	41 (28)	54 (43)	0.11			
Myocardial infarction, %	108	17 (14)	26 (7)	0.33			
Prior cerebrovascular event, %	149	11 (8)	11 (9)	0.99			
Atrial fibrillation, %	149	27 (19)	37 (29)	0.21			
Bundle branch block, %	119	20 (16)	29 (11)	0.26			
Permanent pacemaker, %	149	9 (6)	15 (12)	0.22			
Log. EuroSCORE I, %	138	22±12	25±19	0.55			
NYHA Class III-IV, %	159	83 (67)	96 (75)	0.006			
Surgical valve type, %	160	CE standard (can be remodelled)	4 (3)	10 (8)	<0.001		
		Epic	5 (4)	0 (0)			
		Magna	20 (16)	1 (1)			
		Mitroflow	28 (23)	10 (8)			
		Mosaic	22 (18)	46 (36)			
		PERIMOUNT	20 (16)	15 (12)			
		Trifecta (can be remodelled)	1 (1)	4 (3)			
		Freedom SOLO	0 (0)	6 (5)			
		Freestyle	0 (0)	6 (5)			
		Sutureless Perceval	0 (0)	1 (1)			
		Surgical valve size, mm	160	22.1±2.1		24.1±2.4	<0.001
		True ID, mm	158	19.1±1.8		20.7±2.5	<0.001
Mean valve duration, years	155	10.9± 3.4	11.8±4.6	0.079			
Mode of deterioration	158	Stenosis	47 (38)	36 (28)	0.036		
		Regurgitation	6 (5)	19 (15)			
		Mixed	47 (38)	44 (34)			
iEOA, cm ² /m ²	141	0.81±0.14	0.83±0.12	0.19			
PPM moderate/severe, %	149	62 (50)	48 (33)	0.072			
Perimeter-derived diameter, mm	74	19.5±2.3	21.4±2.7	0.001			
Area, mm ²	67	295±72	355±95	0.002			
LVOT diameter	70	21.8±6.9	26.0±3.8	0.003			
LMCA height, mm	93	10.3±4.7	12.7±5.6	0.042			
RCA height, mm	90	13.0±5.6	18.1±5.3	<0.001			
AV max gradient, mmHg	129	64±20	60±25	0.096			
AV mean gradient, mmHg	148	37±13	35±16	0.11			
Aortic valve area, cm ²	94	0.81±0.24	0.85±0.32	0.73			
Aortic regurgitation: moderate/severe, %	152	50 (38)	0.66 (50)	0.049			
Mitral regurgitation: moderate/severe, %	133	27 (17)	0.28 (20)	0.92			
Ejection fraction, %	154	56±11	53±11	0.15			
Pulmonary pressure, mmHg	99	44±17	45±13	0.58			

in the BVF group (31% vs 9%, $p \leq 0.001$) (Table 2). Balloon-expandable SAPIEN (Edwards Lifesciences) THVs were utilised slightly more often in the control group (29% vs 22%). Among the self-expanding THVs in both groups, the most prevalent was Evolut™ (Medtronic).

For BVF the TRUE® Dilatation balloon (Bard Peripheral Vascular Inc., Tempe, AZ, USA) was used for valve fracturing in 88% and Atlas® GOLD (Bard Peripheral Vascular Inc.) in 12%. BVF was performed in 89% after THV implantation, and in 11% before. Balloons were 2.8±1.1 mm (range 1-6 mm) oversized in relation to the true ID of the SAV and inflated with a pressure of 15.8±3.6 atm. In 84% THV sizing was in accordance with the recommendation of the Valve in Valve app; in 16% the THVs were oversized. Procedure duration was longer in the BVF group (87±42 min vs 57±25 min, $p < 0.001$), as well as fluoroscopy time (26.2±18 min vs 16.6±11.9 min, $p < 0.001$).

Table 2. Procedural data.

	N	BVF (N=81)	Control (N=79)	p-value	
THV type, %	160	SAPIEN 3	22 (18)	29 (23)	0.004
		ALLEGRA	2 (2)	0 (0)	
		Evolut R/Pro	70 (57)	59 (47)	
		ACURATE neo	1 (1)	1 (1)	
		Portico	2 (2)	0 (0)	
		J-valve	1 (1)	0 (0)	
		DFM	0 (0)	1 (1)	
		Lotus	0 (0)	9 (7)	
		THV size, mm	160	23.7±1.7	
THV oversized in relation to SAV	160	13 (16)	0		
Contrast, ml	143	100±55	84±50	0.076	
Fluoroscopy time, min	139	26.2±18.0	16.6±11.9	<0.001	
Procedure duration, min	138	87±42	57±25	<0.001	
Cerebral protection	159	31 (25)	9 (7)	<0.001	
Access transfemoral	158	94 (75)	99 (77)	0.34	
Balloon type for BVF	81	True dilatation	88 (71)		
		Atlas	12 (10)		
Balloon oversizing in relation to true ID	79	2.8±1.1			
Balloon size, mm	79	21.8±1.8	21.1±2.0		
Max balloon pressure, atm	65	15.8±3.6			
Final mean transvalvular gradient, mmHg	145	10.8±5.9	15.8±6.8	<0.001	

IN-HOSPITAL OUTCOME

Device success was achieved in 93% in the BVF group and in 68.4% in the control group ($p < 0.001$). The main reason for procedure failure was a residual mean gradient ≥ 20 mmHg in both groups, which was found in 5 of 6 failures in the BVF group and in 22 of 25 failures in the control group (Table 3).

Failures due to high gradients were predominantly seen in Mitroflow valves (100% in the BVF group and 62.5% in the control group). Out of 5 failures in the BVF group, 3 patients received

Table 3. Complications in-hospital for VIV-TAVI with BVF versus without BVF.

	BVF (N=81)	Control (N=79)	p-value
Device success, %	93 (75)	68 (54)	<0.001
Prosthesis failure, %*	6 (5)	28 (22)	
2 nd valve required, %	0 (0)	4 (3)	
In-hospital mortality, % ⁺	1 (1)	3 (2)	
Ventricular septal rupture, %	3 (2)	(0)	
Aortic root rupture, %	0 (0)	(0)	
All stroke, %	0 (0)	3 (2)	
Coronary obstruction, %	0 (0)	3 (2)	
Balloon rupture, %	0 (0)	(0)	
Cardiac tamponade, %	0 (0)	(0)	
Permanent pacemaker, %	1 (1)	3 (2)	

*due to residual gradient ≥ 20 mmHg. ⁺BVF: retroperitoneal bleeding after balloon rupture in iliac artery. Control: one patient due to severe cardiomyopathy, one patient due to coronary obstruction at day 3.

a self-expanding and two a balloon-expandable THV. Out of 22 failures in the control group, 14 patients received a self-expanding and 8 a balloon-expandable THV. Only in the control group was a second valve required in 3 cases (in 2 patients Evolut THVs were malpositioned, 1 received a second Evolut and 1 a SAPIEN. A third patient received a second SAPIEN after embolisation of the first into the left ventricle, which was retrieved surgically) (Table 3).

The mean gradient decreased from 37 ± 13 mmHg to 10.8 ± 5.9 mmHg ($p < 0.001$) in the BVF group and from 35 ± 16 mmHg to 15.8 ± 6.8 mmHg ($p < 0.001$) in the control group (Figure 1). The difference in the final mean gradient between the BVF group and the control group was significant ($p < 0.001$). At discharge, moderate paravalvular aortic regurgitation was present in only one case in the control group.

Severe in-hospital complications occurred in 3.7% in the BVF group and 7.6% in the control group ($p = 0.325$). In the BVF group,

one patient died from an iliac artery perforation; in the control group, one died from severe cardiomyopathy and another from coronary obstruction at day 3. Other complications were two ventricular septal ruptures after BVF with balloons 4 mm larger than the true ID of the SAV, both without clinical consequences. In the control group, two strokes occurred and one coronary obstruction, which could be managed by percutaneous coronary intervention.

OUTCOME AT FOLLOW-UP

The clinical follow-up rate was 88.8% in the BVF group (9 patients lost to follow-up) with a mean follow-up time of 276 days (range 25-1,710 days) and 86% in the control group (11 patients lost to follow-up) with a mean follow-up time of 1,184 days (range 30-2,211 days).

In the BVF group one patient died of unknown cause, and one patient needed a second valve due to severe aortic regurgitation, which was not present at discharge but developed within 12 weeks. BVF during the index procedure was performed with a 2 mm oversized balloon.

Another patient was re-hospitalised due to heart failure and pneumonia. He had no THV dysfunction. In the control group 11 patients died; one death was valve related. Five patients required a surgical reintervention, 2 due to THV dysfunction, 3 due to endocarditis.

In the BVF group echocardiographic follow-up was obtainable in 59 of 71 patients (83.1%) with a mean follow-up time of 281 (range 25-709 days) in the BVF group and in 55 of 66 patients (83.3%) with a mean follow-up time of 831 (range 37-2,081 days) in the control group.

In both groups the mean gradient remained stable over time (BVF group: 10.8 ± 5.9 mmHg at discharge, 12.4 ± 6.3 mmHg at follow-up; control group: 15.8 ± 6.8 at discharge and 18.4 ± 9.4 mmHg at follow-up) (Figure 1).

LINEAR MIXED MODEL TO PREDICT MEAN TRANSVALVULAR GRADIENT FROM BASELINE DATA

The linear mixed model (Table 4) identified three predictors of a lower mean gradient: BVF compared to non-BVF (Figure 1), the use of self-expanding compared to balloon-expandable THVs (Figure 2), and other SAVs compared to the Mitroflow valve (Figure 3).

This interaction of THV and SAV type was observable in both the BVF group and the control group (Figure 2, Figure 3). The lowest gradients were achieved with BVF in non-Mitroflow SAVs and the use of self-expanding THVs (Figure 4, left upper panel). The highest gradients in VIV procedures were found if a Mitroflow SAV was treated with a balloon-expandable THV without performing BVF (Figure 4, lower panel right).

Discussion

The main findings of the present study are:

1. In patients with degenerated SAVs, BVF in VIV-TAVI resulted in a significant mean gradient reduction compared to VIV-TAVI alone.

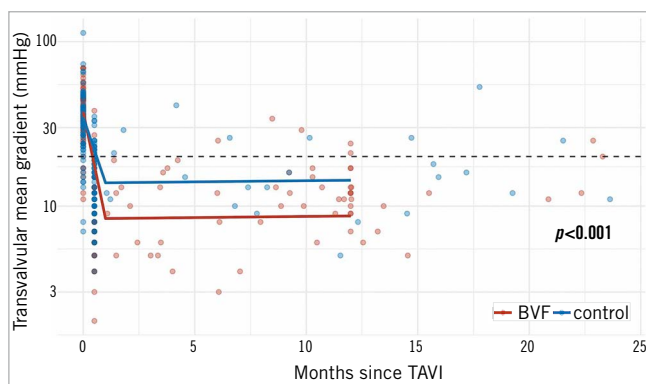


Figure 1. Reduction in mean transvalvular gradients by BVF (red line) versus non-BVF (blue line) in VIV-TAVI procedures acutely and over time.

Table 4. Model summary.

	Parameter estimate	Std error	Z-statistic	p-value	exp_est	ci_lower	ci_upper
Baseline log. AV gradient	0.329	0.078	4.224	< 0.001	1.390	1.193	1.619
Follow-up (months)	0.003	0.002	1.700	0.089	1.003	1.000	1.007
Control versus BVF group	0.501	0.086	5.820	<0.001	1.650	1.394	1.952
Self-expanding valve type (SAPIEN: others)	0.254	0.114	2.225	0.026	1.290	1.031	1.613
Surgical valve type (Mitroflow: others)	0.414	0.102	4.072	<0.001	1.513	1.240	1.847
Interaction surgical valve * Group	-0.137	0.179	-0.764	0.445	0.872	0.614	1.239
Interaction THV * Group	-0.024	0.152	-0.159	0.873	0.976	0.724	1.316

The predictors, parameter estimates, standard errors, test statistic and p-value. Re-transformation of the parameter estimates (exp_est) and confidence intervals (ci_lower, ci_upper).

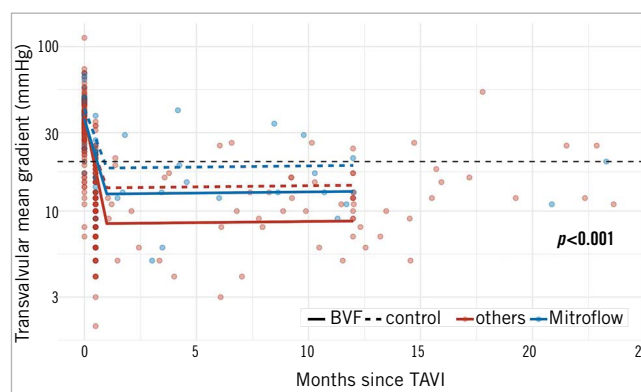
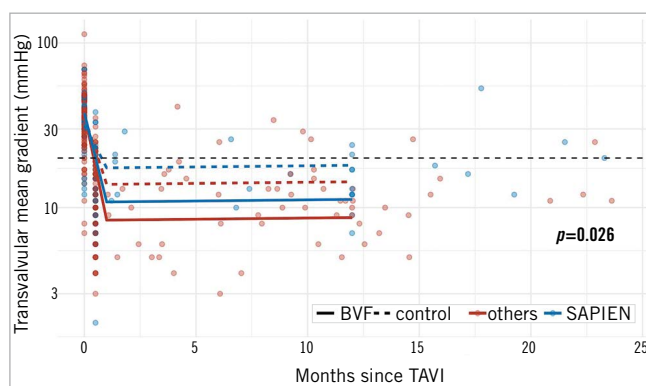


Figure 2. Mean gradients acutely and over time in VIV-TAVI after BVF (continuous line) or without BVF (dashed line) in SAPIEN THVs (blue) and in self-expanding THVs (red).

Figure 3. Mean gradients acutely and over time in VIV-TAVI after BVF (continuous line) or without BVF (dashed line) in Mitroflow SAVs (blue) and in non-Mitroflow SAVs (red).

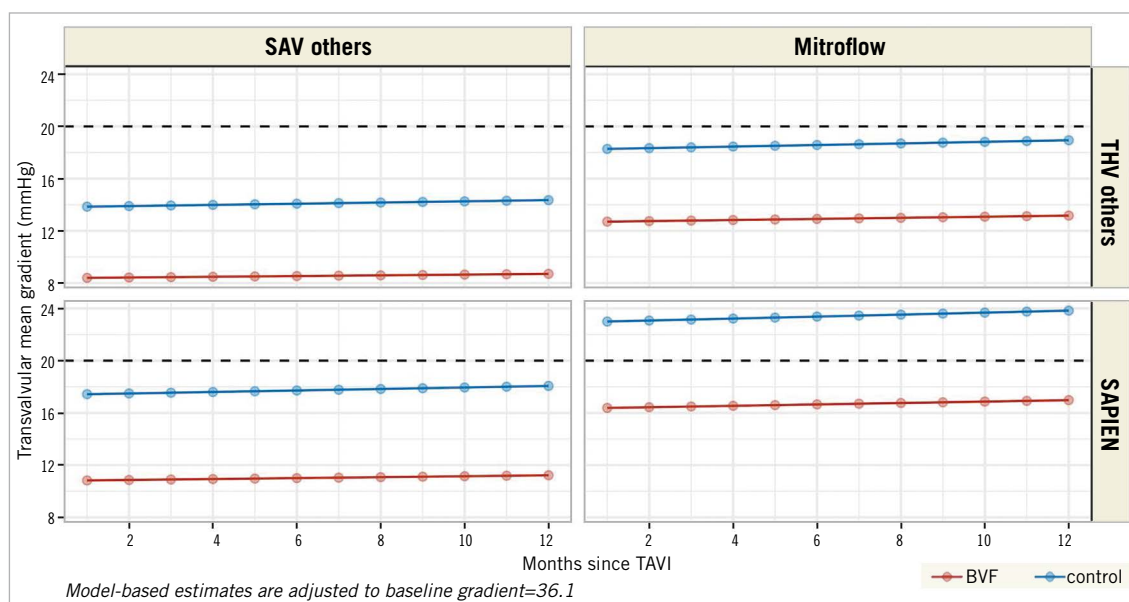


Figure 4. Model-based estimates of the mean transvalvular gradient over time after BVF (red lines) and without BVF (blue lines) for patients with self-expanding THVs in non-Mitroflow SAVs (left upper panel), for patients with non-Mitroflow SAVs and SAPIEN THVs (left lower panel), for patients with Mitroflow SAV and self-expanding THVs (right upper panel) and patients with Mitroflow SAVs and SAPIEN THVs (right lower panel). Model-based estimates are adjusted to the baseline gradient.

2. The difference in the mean gradient between the two groups remained stable over time.
3. Independent predictors of lower gradients were the use of self-expanding THVs and the treatment of SAVs other than the Mitroflow, irrespective of BVF performance.
4. Compared to VIV-TAVI alone, BVF significantly reduced the gradient independently from THV or SAV type.

Although VIV-TAVI is an attractive option to avoid reoperation in failed SAVs, it has some major shortcomings. In small SAVs it can result in high gradients which impact on mortality¹. Procedural results and long-term outcome of VIV-TAVI have been analysed in large registries^{1,4}. The post-procedure mean gradient after VIV-TAVI reported by Dvir et al was 15.8 ± 8.9 mmHg¹, which was replicated in the current control group (15.8 ± 6.8 mmHg). Also, the mean gradient at long-term follow-up of the control group (18.4 ± 9.4 mmHg) is consistent with prior findings after one year (16.9 mmHg and 17.6 mmHg)^{1,4}. As is evident from our data, but not emphasised in the registries mentioned, a mean gradient of such magnitude implies that a significant number of patients present with a mean gradient ≥ 20 mmHg, which per VARC definition is a device failure. In these patients in particular the risk of reintervention increases over time¹¹.

BVF integrated in a VIV-TAVI procedure has been shown to be feasible in reducing transvalvular gradients¹². The aim of the present study was to compare acute as well as long-term data of a VIV-TAVI group with a cohort of patients who underwent VIV-TAVI in conjunction with BVF. To the best of our knowledge, this analysis is the first to compare the clinical and haemodynamic outcome of VIV-TAVI with BVF versus VIV-TAVI alone. The control group comprised patients who were treated in a similar time period, who differed in baseline data only marginally and whose potentially crackable SAVs were not fractured.

In the control group, with significantly more male patients, the SAVs and true IDs were larger compared to the BVF group, which would attenuate the difference in the final mean transvalvular gradient between the groups. Despite the larger true IDs in the control group, however, the mean gradient after BVF was significantly lower, in fact in the same range as that shown by others¹². For that reason, there was a striking difference in the VARC-defined device failure rate, which was driven mainly by a final mean gradient ≥ 20 mmHg, in favour of BVF (6.2% vs 27.8%, $p < 0.001$). In consequence, these patients with higher gradients in our control group would have been candidates for BVF.

The gradient after VIV-TAVI remained stable at follow-up, which is in accordance with prior findings^{1,4}. Until now, however, it was unknown whether gradient stability is also seen after BVF. For the first time, the present study shows that there is no significant change in the gradient after BVF over time. Additionally, we were able to show that the achieved difference in the gradient between the BVF group and the control group (5 mmHg) stays stable over time (6 mmHg). Because higher gradients are a risk factor for mortality and reintervention, BVF may potentially improve long-term survival and reduce the reintervention rate by correcting a pre-existing PPM⁶.

A key question is whether the achievement of favourable gradients by BVF comes with an increased procedural risk, as the safety of BVF procedures so far has only been examined in small studies. In this context, a comparison with a non-BVF VIV-TAVI group is of interest. We found a 30-day mortality rate of 1.2% in the BVF group, which corresponds to the findings of Allen et al¹², and 2.5% in the control group, which corresponds to the data of the PARTNER 2 Valve-in-Valve Registry⁴. Of concern, however, are two ventricular septal perforations observed after BVF, both performed with 4 mm oversized balloons. Both patients had an uneventful clinical course without further treatment. Although we could not identify any unsuitable anatomy in these patients, based on this very limited experience, we would recommend not oversizing the balloon > 3 mm; precaution should be taken with aggressive BVF in the presence of severe annular or left ventricular outflow tract (LVOT) calcification or narrow anatomy.

Another complication was the development of severe valvular aortic regurgitation in one patient three months after BVF, which was performed with a 2 mm oversized balloon after THV implantation and possibly resulted in leaflet damage. Although in our cohort BVF was performed after THV implantation in 89% of cases, the best timing of BVF (prior to or after TAVI) is still open for discussion¹².

Coronary obstruction is an additional potential danger in VIV procedures. This complication is determined by virtual THV to coronary ostium distance (VTC), virtual THV to sinotubular junction distance (VTSTJ) and the leaflet in relationship to the coronary ostia and sinotubular junction (STJ). When cracking the valve, the VTC is even more narrowed, which increases the risk of coronary obstruction. In the BVF group, no such case occurred. In 3 patients, however, preventive measures were taken such as bio-prosthetic or naïve aortic scallop intentional laceration to prevent iatrogenic coronary artery obstruction (BASILICA) interventions (2 patients) and stent implantation using the chimney technique (1 patient). In contrast, we observed 2 coronary obstructions in the control group, which caused the death of one patient. Based on our limited experience, BVF does not increase the risk of coronary obstructions, but further investigations have to confirm this impression.

To look for independent predictors for lower final gradients, which could be helpful for future procedure planning and performance, a linear mixed model was applied. Three independent predictors were identified: the performance of BVF, the use of self-expanding THVs and the treatment of SAVs other than Mitroflow. Interestingly, these latter two predictors were valid for both the BVF group as well as the control group. The fact that balloon-expandable compared to self-expanding THVs in VIV-TAVI lead to higher gradients has already been shown¹¹. We were now able to demonstrate that this also applies for BVF in VIV-TAVI, which has not been described before.

The Mitroflow as a risk factor for higher gradients is a novel finding. Different to other SAVs treated in this cohort, this valve

has leaflets sutured outside the stent. Whether this particular valve design impacts on the gradient needs to be examined in larger series.

Eventually it would be desirable to develop an algorithm for how to treat degenerated SAVs and achieve an optimal result. Our findings may contribute to this proposal by providing the information that treatment of a Mitroflow SAV with a SAPIEN THV leads to the highest gradients, and treatment of a non-Mitroflow SAV with a self-expanding THV to the lowest (**Central illustration**). However, in any combination of SAVs with THVs, performance of BVF significantly reduces the gradient acutely and over time (**Figure 4**).

Limitations

This was an observational study with inherent limitations. There was no echocardiographic core lab, and data were not adjudicated by an independent committee. Timing of BVF and the degree of balloon oversizing were per the operator's discretion. The control cohort was not randomised and differed in some aspects that may have extenuated the difference in the gradients between the groups.

Conclusions

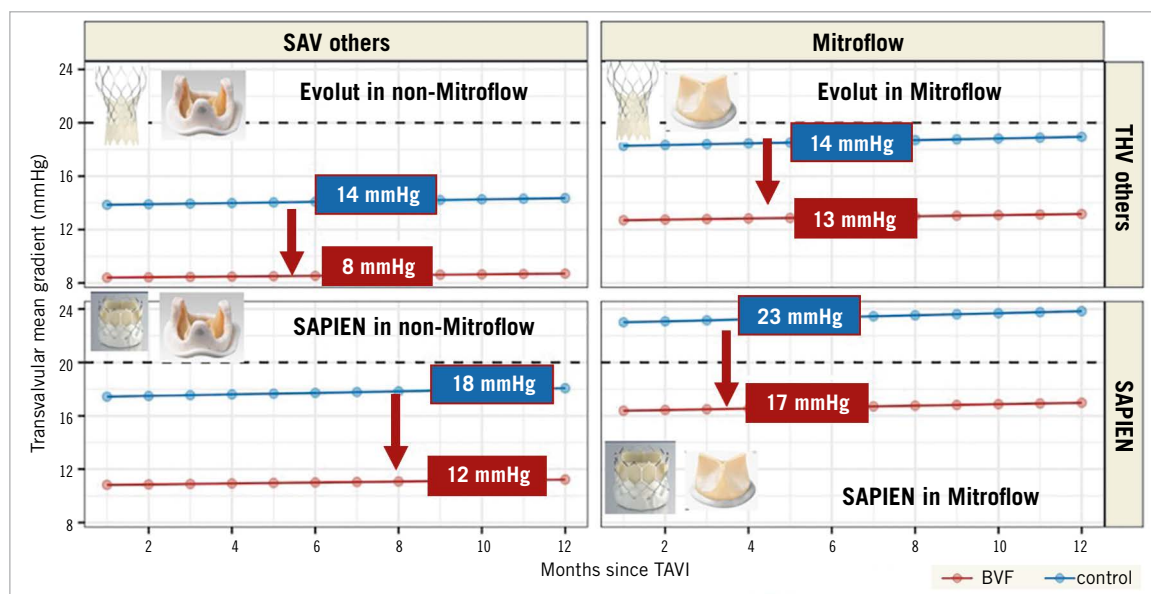
In patients with degenerated SAVs, VIV-TAVI in conjunction with BVF resulted in a significantly lower gradient compared to VIV-TAVI alone. The gradient as well as the difference in gradient between the groups remained stable over time. Independent predictors of lower final gradients were the performance of BVF, the use of self-expanding THVs and the treatment of SAVs other than Mitroflow. BVF significantly reduced the gradient independently from THV or SAV type.

Impact on daily practice

Regarding the final transvalvular gradient, the most unfavourable clinical scenario in VIV procedures would be the treatment of a Mitroflow SAV with a balloon-expandable THV without performing BVF. The lowest gradient can be achieved in SAVs other than Mitroflow treated with self-expanding THVs in conjunction with BVF.

Conflict of interest statement

M. Abdel-Wahab is a consultant to Medtronic and Boston Scientific. F. Bedogni is a consultant and proctor of Medtronic, Abbott, BSI, and Meril. L. Conradi is a consultant to Edwards, Medtronic, Boston and Abbott. D Hildick-Smith is a proctor/advisor for Abbott, Boston, Edwards, and Medtronic. A. Latib is a consultant for Medtronic, Abbott, Edwards Lifesciences, ICS and Keystone Heart. N.M. Van Mieghem has received research grant support from Abbott Vascular, Boston Scientific, Edwards Lifesciences, Abiomed, Medtronic, PulseCath BV, and Daiichi Sankyo and advisory fees from Abbott, Boston Scientific, Abiomed, Medtronic, PulseCath BV, and Daiichi Sankyo. T. Pilgrim has received research grants to the institution from Boston Scientific, Edwards Lifesciences and Biotronik; speaker fees from Boston Scientific and Biotronik, declares consultancy for HighLifeSAS (CEC), and proctoring for Medtronic. M. Taramasso is a consultant for Abbott, Boston Scientific, 4tech, and CoreMedic, and has received honoraria from Edwards Lifesciences, Mitraltech, and SwissVortex. L. Testa is a medical proctor for Boston Scientific, Meril, Concept Medical, Abbott, and Philips, and is an advisory board member and/or has received speaker fees and/or institutional research grants from BSCI, Philips, Abbott, Medtronic, Terumo, and



Central illustration. Summary of mean transvalvular gradients in VIV-TAVI with and without BVF. The highest transvalvular gradients are expected in patients with SAPIEN in Mitroflow without BVF, the lowest in patients with Evolut in non-Mitroflow valves with BVF. In any combination, BVF reduces by approximately 6 mmHg.

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