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Balloon Post-Dilation Following Implantation of a Self-Expanding Transcatheter Aortic Valve Bioprosthesis

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ABSTRACT

OBJECTIVES This study sought to explore the impact of balloon post-dilation (BPD) on outcomes in the CoreValve US Clinical Trials.

BACKGROUND BPD following transcatheter aortic valve replacement (TAVR) has been used in selected cases to optimize hemodynamic results.

METHODS Procedural details of 3,532 patients were examined to determine whether BPD was performed after self-expanding TAVR. "Best practice" guidelines recommended BPD for treatment of suboptimal intraprocedural valve function, primarily manifested by moderate or severe residual aortic regurgitation (AR).

RESULTS Procedural BPD was performed in 782 patients (22%) patients. The most common (58.1%) indication was greater than or equal to moderate AR following valve deployment. Greater baseline aortic valve gradients ($p < 0.001$), higher grades of baseline AR ($p < 0.001$), larger annular diameters ($p < 0.001$), and lower device to annular ratios ($p < 0.001$) were more common in patients who underwent BPD. BPD was performed less often with the 26-mm valve (17.9%) compared to the 31 mm (38.1%) ($p < 0.05$). BPD reduced moderate or severe AR by 75.6% from 58.1% to 14.2%. Thirty-day and 1-year clinical events were similar in the 2 groups, although acute kidney injury was more common in patients undergoing BPD ($p = 0.026$). In-hospital major adverse cardiovascular and cerebrovascular event rates were 9.3% in the BPD group versus 7.5% for others ($p =$ NS). There was no increase in neurological events.

CONCLUSIONS BPD of the self-expanding bioprosthesis was performed in 22% of patients in the CoreValve US Clinical Trials most commonly to reduce the degree of residual AR. BPD was effective in acutely improving valve performance without an associated increase in neurologic events. (Safety and Efficacy Study of the Medtronic CoreValve System in the Treatment of Symptomatic Severe Aortic Stenosis in High Risk and Very High Risk Subjects Who Need Aortic Valve Replacement; NCT01240902; Safety and Efficacy Continued Access Study of the Medtronic CoreValve System in the Treatment of Symptomatic Severe Aortic Stenosis in Very High Risk Subjects and High Risk Subjects Who Need Aortic Valve Replacement; NCT01531374) (J Am Coll Cardiol Intv 2017;10:168–75)

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The CoreValve bioprosthesis (Medtronic, Minneapolis, Minnesota) comprises a self-expanding nitinol frame that supports a tri-leaflet, supra-annular porcine pericardial tissue valve (1). Porcine pericardium is also sewn onto the lower 12 mm of the inflow circumference to provide annular tissue sealing at the time of deployment. In contrast to a balloon-expandable bioprothesis that "circularizes" the eccentric annulus at the time of deployment (2), the CoreValve bioprosthesis elliptically conforms to the annulus (3), and then remodels the annulus with progressive frame expansion over time (4).

The clinical benefit of self-expanding transcatheter aortic valve replacement (TAVR) over medical therapy has been demonstrated in patients deemed unsuitable for surgery (1), and over surgical aortic valve replacement in patients deemed at increased risk for surgery (5); these benefits are sustained at least 2 years after the procedure (6,7). To avoid the deleterious effects of residual aortic regurgitation (AR) (8–10), "best practice" used in the CoreValve US Clinical Trials recommended hemodynamic (11,12), echocardiographic (13), and angiographic assessment of valve performance after implantation (13). Bioprosthesis repositioning, balloon post-dilation (BPD), or both have been recommended in the event of suboptimal valve performance (13). The potential benefit of BPD on improved conformation of the CoreValve frame to the annulus (14,15) needs to be balanced against the potential risk of serious adverse events including neurologic events (16–19), worsened AR (20), and annular rupture (21,22). Malposition of the stent valve frame and injury to the porcine prosthetic valve leaflets after BPD are also considerations.

The purposes of this analysis were to identify the frequency of BPD after self-expanding TAVR, to understand its predisposing factors, and to assess the early hemodynamic and 30-day and 1-year clinical outcomes associated with BPD in the CoreValve US Clinical Trials.

METHODS

STUDY POPULATION. The CoreValve US Clinical Trials include 3,532 patients enrolled in the Extreme Risk Pivotal Trial (n = 634) and Continued Access Registry (n = 1,614) and the High Risk Pivotal Trial (n = 390) and Continued Access Registry (n = 1,027). Patients who received 2 or more bioprostheses were excluded from the analysis (n = 133).

Inclusion and exclusion criteria and regulatory compliance for these studies have been reported in detail elsewhere (1,5). In brief, extreme-risk patients were considered to have a surgical risk of death or major morbidity ≥50% at 30 days (1) and high-risk patients were considered to have a ≥15% surgical mortality rate at 30 days (5). Patients with New York Heart Association (NYHA) functional class II or greater symptoms were considered for inclusion. Severe aortic stenosis was defined as an aortic valve area ≤0.8 cm^2 or aortic valve area index ≤0.5 cm^2/m^2 and either a mean aortic valve gradient >40 mm Hg or a peak aortic valve velocity >4.0 m/s at rest or with dobutamine if the left ventricular ejection fraction was <50%. Anatomical exclusion criteria included an aortic annular diameter <18 mm or >29 mm. Patients were treated with a 23 mm, 26 mm, 29 mm, or 31 mm CoreValve device (Medtronic). The size nomenclature refers to the inflow diameter of the unconstrained stent valve frame.

Pre-procedural multidetector computer tomography (MDCT) was required in all patients and detailed analyses of these images were used for CoreValve size selection. Perimeter-based annular diameters between 18 and 20 mm were treated with a 23-mm CoreValve; annular diameters between 20 and 23 mm were treated with a 26-mm CoreValve; annular diameters between 23 and 27 mm were treated with a 29-mm CoreValve; and annular diameters between 26 and 29 mm were treated with a 31-mm CoreValve. Eccentricity ratio was defined as major axis annular diameter / minor axis annular diameter. A device annular sizing ratio was determined by the following: ([valve perimeter − annulus perimeter] / annular perimeter) × 100.

CoreValve IMPLANTATION PROCEDURE. Best practices for implantation of the self-expanding bioprosthesis were developed early in the CoreValve US Clinical Trials. Although individual operators used

ABBREVIATIONS AND ACRONYMS

AR = aortic regurgitation

BPD = balloon post-dilation

MDCT = multidetector computed tomography

NYHA = New York Heart Association

TAVR = transcatheter aortic valve replacement

VARC = Valve Academic Research Consortium

Edwards Lifesciences, Tendyne, Valtech, Neochord, and Abbott Vascular; served as a consultant to Abbott Vascular, Bracco Diagnostics, Tendyne, Neochord, and Valtech Cardio; and has served in the echo core lab for Neochord and Valtech Cardio. Dr. Hebeler serves as a proctor for Medtronic. Ms. Chang is an employee and shareholder of Medtronic. Dr. Popma has received institutional grant support from Medtronic, Boston Scientific, and Direct Flow Medical; has served on the medical advisory board for Boston Scientific; and has received consultant fees from and owns equity in Direct Flow Medical. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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TABLE 1 Baseline Demographics

	All Patients (N = 3,532)	No BPD (n = 2,750)	BPD (n = 782)
Age, yrs	83.3 ± 7.8	83.3 ± 7.7	83.6 ± 7.9
Female	1,469 (46.7)	1,356 (49.3)	293 (37.5)*
STS predicted risk of mortality, %	8.9 ± 4.7	9.0 ± 4.8	8.5 ± 4.6*
Logistic EuroSCORE, %	22.2 ± 15.9	22.2 ± 15.9	22.0 ± 15.8
NYHA functional class III or IV	3,090 (87.5)	2,416 (87.9)	674 (86.2)
Hypertension	3,276 (92.8)	2,558 (93.0)	718 (91.8)
Diabetes mellitus	1,335 (37.8)	1,052 (38.3)	283 (36.2)
Coronary artery disease	2,782 (78.8)	2,158 (78.5)	624 (79.8)
Peripheral vascular disease	1,605 (45.6)	1,257 (45.8)	348 (44.7)
Prior coronary bypass surgery	1,238 (35.1)	961 (34.9)	277 (35.4)
Creatinine >2.0 mg/dl	155 (4.4)	121 (4.4)	34 (4.3)
Atrial fibrillation	1,558 (44.2)	1,236 (45.0)	322 (41.4)

Values are mean ± SD or n (%). *p < 0.05 for balloon post-dilation vs. no balloon post-dilation.

BPD = balloon post-dilation; EuroSCORE = European System for Cardiac Operative Risk Evaluation; NYHA = New York Heart Association; STS = Society of Thoracic Surgeons.

their discretion for particular cases, it was recommended that patients undergo dilation of the stenotic native aortic valve before CoreValve deployment with a recommended balloon valve size to be less than or equal to the short-axis diameter of the native aortic valve annulus as determined by the preoperative MDCT. Following deployment and release from the delivery catheter, clinical operators were encouraged to perform transthoracic or transesophageal echocardiography to identify residual gradients or valvular regurgitation, hemodynamic assessment using transvalvular gradient measurements, and aortography to evaluate the position of the bioprosthesis and extent of AR. Best practices recommended that operators wait 10 min after valve deployment before valve performance was determined. BPD was performed at the discretion of the operators, reserved for residual gradients, incomplete frame expansion, or moderate or severe regurgitation. A maximal balloon diameter equal to the mean of the aortic annulus diameter was recommended.

PROCEDURAL ECHOCARDIOGRAPHIC ANALYSIS. This analysis included 3,532 patients who had clinical site echocardiographic evaluations available during the procedure. General recommendations were made to the clinical sites for adherence to the Valve Academic Research Consortium (VARC)-1 criteria (23). AR was graded by using multiple parameters including regurgitation color jet density and width, circumferential extent of turbulent regurgitation color jet around the aortic annulus for paravalvular regurgitation, descending and abdominal aorta diastolic flow reversal on pulsed wave Doppler, and pressure half-time of AR on continuous wave Doppler signal (23). Patients were classified as having none, mild, moderate, or severe residual AR. No designation for trace AR was included in the analysis consistent with the VARC-1 criteria (23).

CLINICAL OUTCOMES. Clinical events included all-cause death, myocardial infarction, all stroke, re-intervention to alter, adjust, or replace a previously implanted valve, and implantation of a permanent pacemaker. Symptom status was assessed using the NYHA classification system. Major and minor stroke were defined using VARC-1 criteria (23).

STATISTICAL ANALYSIS. Categorical variables were compared with the use of the chi-square test or Fisher exact text. Continuous variables were presented as mean ± SD and compared with the use of Student *t* test. Multivariate logistic regression model was performed to identify factors associated with post-dilation, and variables with p value <0.05 were included in the model. Stepwise model selection method was used and the significance level thresholds for entry and exit of independent variables were set at 0.10. All testing used a 2-sided alpha level of 0.05. All statistical analyses were performed with the use of SAS software, version 9.2 (SAS Institute, Cary, North Carolina).

RESULTS

BASELINE CLINICAL CHARACTERISTICS. BPD was performed in 782 (22%) patients treated in the CoreValve US Clinical Trials. Clinical demographics of patients are found in Table 1. Patients were elderly (83.3 ± 7.8 years of age) and frequently (87.5%) had NYHA functional class III or IV symptoms of dyspnea. Patients were high risk with a Society of Thoracic Surgeons predicted risk of mortality of 8.9 ± 4.7%; Society of Thoracic Surgeons predicted risk of mortality was lower in patients who underwent BPD (p = 0.016). BPD was performed in 293 (17.8%) of 1,649 women and in 489 (26.0%) of 1,883 men (p < 0.001). Other clinical demographics were similar in the 2 groups.

AORTIC VALVE ANATOMY AND HEMODYNAMIC FINDINGS. Baseline MDCT findings are found in Table 2. The aortic valve annulus defined by MDCT was larger in those who underwent post-dilation compared to those who did not (p < 0.001). The annular eccentricity ratio did not differ in the 2 groups. The device annular ratio was lower in patients treated with BPD (p < 0.001); BPD was performed in 30.9% of patients with a device annulus ratio ≤10% compared with 11.5% in patients with a device annulus ratio >20% (p < 0.001).

Baseline hemodynamic findings obtained at the time of valve implantation are found in Table 2. Patients who underwent BPD had higher baseline aortic

valve gradients ($p < 0.001$) and had more baseline moderate or greater aortic valve regurgitation ($p < 0.001$) than those who did not undergo BPD.

PROCEDURAL FINDINGS. Balloon pre-dilation was performed in the majority (84.3%) of patients before CoreValve implantation, (Table 3). BPD was performed in 21.6% of patients who underwent pre-dilation and in 25.2% of patients without pre-dilation (p = NS). The pre-dilation balloon to annular ratio was 1.0 ± 0.2 and was not different in the 2 groups. BPD was used more often in patients treated with a 31-mm CoreValve (30.3%) compared with the 23-mm CoreValve (25.9%), 26-mm CoreValve (15.6%), and 29-mm CoreValve (20.6%). The depth of implantation was similar in the 2 groups.

MULTIVARIATE ANALYSIS OF VARIABLES RELATED TO BPD. Larger aortic annular perimeter (defined by MDCT), greater baseline aortic valve mean gradient, baseline moderate or greater AR, and lesser degrees of device to aortic valve annulus oversizing were associated with BPD in the multivariate analysis (Table 4).

The most common indication for BPD was moderate or greater AR after CoreValve deployment. Moderate or greater AR was present in 58.1% in the BPD group (vs. 3.2% in the no-BPD group; $p < 0.001$). BPD resulted in a 75.6% reduction in the frequency of moderate or greater residual regurgitation (from 58.1% to 14.2% at the end of the procedure; $p < 0.001$). Numed balloons (B. Braun, Bethlehem, Pennsylvania) were used most commonly for CoreValve post-dilation (n = 597, 76.4%). The post-dilation balloon diameter to aortic annulus minor diameter was 1.2 ± 0.1. Details of balloon use are found in Table 5.

CLINICAL OUTCOMES. Clinical outcomes to 30 days are found in Table 6. The rates of in-hospital major adverse cardiovascular and cerebrovascular events were similar in those who did and did not undergo post-dilation. Procedural deaths in patients undergoing BPD are documented in Table 7.

There were no differences in all-cause mortality, any neurologic events or need for permanent pacemaker in the 2 groups. The incidences of acute kidney injury (p = 0.026), estimated contrast volume ($p < 0.001$) and life-threatening or disabling bleeding ($p < 0.001$) were higher in patients undergoing BPD. One-year clinical outcomes are found in Table 6.

DISCUSSION

We found that BPD was used in approximately 22% of patients undergoing self-expanding TAVR; primarily to optimize hemodynamic results detected with careful procedural monitoring for residual AR. BPD was associated with a 75.6% reduction in the frequency of moderate or severe residual AR. The need

TABLE 2 Baseline Aortic Valve Anatomy and Ventricular Hemodynamics

	All Patients	No BPD	BPD
Multidetector CT findings	(N = 1,695)	(n = 1,383)	(n = 312)
Annular maximum diameter, mm	27.2 ± 2.6	27.1 ± 2.5	27.9 ± 2.5*
Annular minimum diameter, mm	21.8 ± 2.3	21.6 ± 2.2	22.5 ± 2.3*
Annular mean diameter, mm	24.5 ± 2.2	24.4 ± 2.2	25.2 ± 2.2*
Annular perimeter, mm	77.3 ± 6.9	76.8 ± 6.8	79.5 ± 7.0*
Eccentricity ratio†	1.3 ± 0.1	1.3 ± 0.1	1.2 ± 0.1
Device annular sizing ratio, % oversizing‡	15.6 ± 5.4	16.0 ± 5.3	13.8 ± 5.2*
Device annular sizing ratio*			
≤10%	243 (14.4)	168 (12.2)	75 (24.0)
>10% to ≤15%	588 (34.8)	469 (34.0)	119 (38.1)
>15% to ≤20%	495 (29.3)	419 (30.4)	76 (24.4)
>20%	366 (21.6)	324 (23.5)	42 (13.5)
Hemodynamic findings	(N = 3,161)	(n = 2,461)	(n = 700)
Aortic mean gradient, mm Hg	42.1 ± 16.0	41.3 ± 15.7	44.8 ± 16.5*
Aortic regurgitation %*	(N = 3,350)	(n = 2,610)	(n = 740)
None	591 (17.6)	494 (18.9)	97 (13.1)
Mild	2,236 (66.7)	1,752 (67.1)	484 (65.4)
Moderate to severe	523 (15.6)	364 (13.9)	159 (21.5)
LV ejection fraction, %	53.9 ± 13.7	54.1 ± 13.7	53.5 ± 13.8
LV peak systolic pressure, mm Hg	160.7 ± 29.9	159.4 ± 29.5	165.5 ± 30.9*
LV end-diastolic pressure, mm Hg	17.6 ± 9.4	17.4 ± 9.6	18.3 ± 8.8*

Values are mean ± SD or n (%). *$p < 0.05$ for balloon post-dilation vs. no balloon post-dilation. †Eccentricity ratio = (annular maximum diameter/annular minimum diameter. ‡Device annular sizing ratio = ([CoreValve perimeter - annular perimeter] / annular perimeter) × 100.

BPD = balloon post-dilation; CT = computerized tomography; LV = left ventricular.

TABLE 3 Procedural Characteristics

	All (N = 3,532)	No BPD (n = 2,750)	BPD (n = 782)
Balloon pre-dilation performed	2,976 (84.3)	2,334 (84.9)	642 (82.1)
Pre-dilation balloon diameter, mm	21.0 ± 3.5	21.0 ± 3.6	21.1 ± 3.1
Estimated contrast volume, ml	155 ± 90	150 ± 87	173 ± 98*
CoreValve size*			
23 mm	58 (1.6)	43 (1.6)	15 (1.9)
26 mm	895 (25.3)	755 (27.5)	140 (17.9)
29 mm	1,594 (45.1)	1,265 (46.0)	329 (42.1)
31 mm	985 (27.9)	687 (24.9)	298 (38.1)
Depth of implant, mm	4.5 ± 2.7	4.5 ± 2.6	4.6 ± 2.7
Mean AV gradient post-deployment, mm Hg	4.8 ± 8.5	4.7 ± 8.7	5.4 ± 8.0*
Aortic regurgitation after CoreValve deployment*			
None	746 (21.9)	706 (26.7)	40 (5.3)
Mild	2,130 (62.6)	1,863 (70.1)	277 (36.6)
Moderate or greater	525 (15.4)	85 (3.2)	440 (58.1)
Aortic regurgitation after post-dilation			
None	NA	NA	76 (10.1)
Mild	NA	NA	569 (75.7)
Moderate or greater	NA	NA	107 (14.2)

Values are n (%) or mean ± SD. *$p < 0.05$ for balloon post-dilation vs. no balloon post-dilation.

AV = aortic valve; BPD = balloon post-dilation; NA = not applicable.

TABLE 4 Predictors of the Need for Post-TAVR Balloon Dilation

	Univariable Analysis		Multivariable	
	Odds Ratio (95% CI)	p Value*	Odds Ratio (95% CI)	p Value*
Female	0.62 (0.52–0.73)	<0.0001		
STS predicted risk of mortality, %	0.98 (0.96–1.00)	0.0165		
Annular perimeter, mm	1.06 (1.04–1.08)	<0.0001	1.04 (1.01–1.07)	0.0048
Baseline aortic mean gradient, mm Hg	1.01 (1.01–1.02)	<0.0001	1.01 (1.01–1.02)	0.0016
Baseline moderate or greater aortic regurgitation	1.69 (1.37–2.08)	<0.0001	1.42 (1.01–2.00)	0.0411
Left ventricular end diastolic pressure, mm Hg	1.01 (1.00–1.02)	0.0197		
Device annular sizing ratio, % oversizing	0.92 (0.90–0.94)	<0.0001	0.95 (0.91–0.98)	0.0038
31-mm valve	1.85 (1.56–2.19)	<0.0001		

*On the basis of logistic regression model. Stepwise method with thresholds for entry and exit = 0.10.
CI = confidence interval; STS = Society of Thoracic Surgeons.

for BPD was primarily related to undersizing of the bioprosthesis. Choosing the larger of 2 CoreValve sizes in patients whose annulus dimensions are between sizing cutoffs is expected to lead to less paravalvular regurgitation. However, this requires adequate sinus of Valsalva diameters and coronary ostial origins that allow the larger size to be used without compromising coronary artery flow. There was no increase in the occurrence of neurologic events in patients undergoing BPD. We conclude that BPD is an effective method to optimize procedural results with self-expanding TAVR.

IMPORTANCE OF MDCT SIZING. A number of studies have shown that the risk of residual paravalvular regurgitation can be reduced with the use 3-dimensional imaging before the procedure (24,25). We used MDCT for transcatheter valve selection throughout the CoreValve US Clinical Trials, and found that lower (≤10%) device to annular ratios were associated with a 30.9% need for BPD, whereas a device to annular ratio >20% had an 11.5% need for BPD. Newer iterations of self-expanding bioprostheses may enhance the conforming of the bioprothesis to the annulus, reducing residual regurgitation and potentially BPD.

IMPORTANCE OF RESIDUAL AR. We recommended that a careful assessment of residual AR be performed immediately after valve implantation, including transesophageal or transthoracic echocardiography (13), invasive hemodynamic assessments (12), and aortography to assess residual regurgitation and valve positioning (13). Incomplete frame expansion has been associated with a worsened clinical outcome (26). The CoreValve nitinol bioprosthesis is temperature sensitive, gaining radial strength as the nitinol warms. The valve is loaded in cold sterile saline to facilitate valve compression and loading within the delivery catheter. Accordingly, we also recommended that these assessments be performed 10 min after final deployment and release of the prosthesis before assessing AR. We have documented further frame expansion from 30 days to 1 year after valve implantation (4).

In patients with moderate or severe regurgitation after CoreValve implantation, we found that BPD reduced moderate or severe AR by 75.6%. Although depth of implantation may be an important determinant of residual AR after self-expanding TAVR (13), we did not find any difference in the depth of implantation between the 2 groups. This analysis excluded patients who received a second bioprosthesis placement during the procedure.

CLINICAL OUTCOMES IN PATIENTS UNDERGOING BALLOON POST-DILATION. Although early studies have suggested BPD after balloon-expandable TAVR results in a higher risk of neurological events (16–19), more recent analyses have not shown an increased risk for BPD (16,27). We did not find an increase in neurologic events in patients treated with BPD. We did note higher rates of contrast use and acute kidney injury in patients undergoing BPD. Acute kidney injury is associated with a worsened clinical outcome after TAVR (28). One patient in the BPD group experienced valve migration.

BALLOON SIZING FOR POST-DILATION. The inflow portion of the self-expanding nitinol frame conforms to the aortic annulus and is generally elliptical after implantation while allowing the leaflets to be supra-annular and circular (3). Post-deployment balloon valvuloplasty reduces the degree of residual AR after

TABLE 5 Post-Dilation Balloon Sizes Used on the Basis of Implanted Transcatheter Valve Size

Balloon Diameter (mm)	23 mm (n = 15)	26 mm (n = 140)	29 mm (n = 328)*	31 mm (n = 297)*
≤20	80.0 (12)	15.7 (22)	3.0 (10)	0.7 (2)
22	20.0 (15)	34.3 (48)	3.7 (12)	1.0 (3)
23	0	20.0 (28)	5.2 (17)	1.0 (3)
24	0	1.4 (2)	9.8 (32)	2.0 (6)
25	0	26.4 (37)	42.7 (140)	13.5 (40)
26	0	2.1 (3)	11.9 (39)	14.5 (43)
27	0	0	0	0
28	0	0	22.0 (72)	63.6 (189)
≥30	0	0	1.8 (6)	3.7 (11)

Values are % (n). *Balloon size information was not available for 1 patient treated with the 29 mm valve and 1 patient treated with the 31 mm valve.

TABLE 6 Clinical Outcomes

Clinical Event	30-Day Outcomes			1-Year Outcomes		
	All Patients (N = 3,532)	No BPD (n = 2,750)	BPD (n = 782)	All Patients (N = 3,532)	No BPD (n = 2,750)	BPD (n = 782)
In-hospital MACCE	280 (7.9)	207 (7.5)	73 (9.3)	NA	NA	NA
All-cause mortality	189 (5.4)	137 (5.0)	52 (6.7)	671 (22.2)	515 (21.8)	156 (23.5)
Any neurologic event	525 (15.0)	405 (14.9)	120 (15.6)	749 (23.6)	591 (23.9)	158 (22.3)
All stroke	163 (4.7)	125 (4.6)	38 (4.9)	256 (8.3)	203 (8.5)	53 (7.7)
Major stroke	94 (2.7)	70 (2.6)	24 (3.1)	147 (4.8)	115 (4.9)	32 (4.5)
Minor stroke	72 (2.1)	57 (2.1)	15 (2.0)	116 (3.8)	94 (3.9)	22 (3.3)
TIA	25 (0.7)	20 (0.7)	5 (0.7)	61 (2.1)	46 (2.0)	15 (2.6)
Encephalopathy	351 (10.1)	271 (10.0)	80 (10.5)	480 (15.1)	381 (15.4)	99 (13.7)
Permanent pacemaker	728 (20.9)	555 (20.4)	173 (22.5)	811 (24.1)	622 (23.7)	189 (25.4)
Myocardial infarction	32 (0.9)	24 (0.9)	8 (1.0)	63 (2.2)	50 (2.2)	13 (1.9)
Reintervention	18 (0.5)	11 (0.4)	7 (0.9)	35 (1.2)	21 (0.9)	14 (2.3)*
Acute kidney injury	369 (10.5)	271 (9.9)	98 (12.7)*	369 (10.5)	271 (9.9)	98 (12.7)*
Major vascular complication	242 (6.9)	183 (6.7)	59 (7.6)	252 (7.2)	191 (7.0)	61 (7.9)
Major bleeding	886 (25.2)	706 (25.8)	180 (23.1)	965 (28.4)	766 (28.8)	199 (26.7)
Life-threatening/disabling bleeding	412 (11.7)	288 (10.5)	124 (15.9)*	516 (15.6)	368 (14.3)	148 (20.1)*

Values are n (%). *$p < 0.05$ for balloon post-dilation vs. no balloon post-dilation.
MACCE = major adverse cardiovascular and cerebrovascular event(s); TIA = transient ischemic attack.

balloon-expandable (27,29,30) and self-expanding bioprotheses (31–33). One prior series showed a reduction in the need for BPD with MDCT-derived sizing (31). We also found that BPD reduced moderate or severe AR by 75.6% in our study, from 58.1% to 14.2%.

It is worth noting that balloon diameters for aortic valvuloplasty balloons do not achieve the diameter indicated in the manufacturers' instructions for use. These diameters are typically industry reported diameters at 5 atm pressure, a pressure only achieved with mechanical inflation devices. Hand inflation typical of balloon valvuloplasty and BPD typically achieves pressures ≤2 atm. Thus, diameters achieved with hand inflation, for example of the Numed Z-Med II balloon (B. Braun), typically achieve about

TABLE 7 Narratives of Procedural Deaths in Patients Undergoing Balloon Post-Dilation

Patient #	Annulus Size (mm)*	LVOT Size (mm)	Pre-BAV (mm)	CoreValve Size (mm)	Maximum BPD Size (mm)	No. of Inflations BPD	Predisposing Factors	Narrative
1	26.4	21.0	22	29	28	3	Radiation to chest, esophageal cancer	An 83-year-old man with significant amount of calcium with heavy calcification of 3 leaflets. Hourglass incomplete expansion with CoreValve implantation. Patient developed immediate hypotension and need for CPS. TEE demonstrated large tear from the mid anterior septum to the LV apex extending into the RV resulting in a VSD. The CEC adjudicated this as a valve-related cardiovascular death, VSD.
2	23.8	18.0	20	29	28	1		TTE showed a large pericardial effusion and the patient (83-year-old woman) developed severe hypotension requiring CPR. Thoracotomy showed a large laceration of the RV wall. During weaning of CPS, there was bright red bleeding from the aortic root. The CEC adjudicated this as a cardiovascular death; annular rupture which occurred on the day of the procedure.
3	29.0	20.0	23	31	28	1		An 87-year-old man underwent transfemoral access. Calcification noted within the valve and asymmetric within the LVOT and involving the septal and posterior portions of the LVOT. Placement of a 31-mm CoreValve was completed. Investigator noted hemodynamics suggestive of AR out of portion to the TEE. Aortography demonstrated incomplete expansion. BPD performed and immediate hypotension occurred and CPR was initiated. There was an enlarging pericardial effusion, and patient expired in the operating room. The CEC adjudicated this as prosthetic valve dysfunction cardiovascular death; cardiac perforation.

*Site-reported mean perimeter-derived diameter.
CEC = Clinical Events Committee; CPR = cardiopulmonary resuscitation; CPS = cardiopulmonary support; LVOT = left ventricular outflow tract; RV = right ventricle; TEE = transesophageal echocardiogram; TTE = transthoracic echocardiogram; VSD = ventricular septal defect.

1 mm less than the diameter indicated on the packaging. This is not the case for noncompliant balloons, of which the True Dilatation balloon (Bard Peripheral Vascular, Tempe, Arizona) is a good example. This balloon achieves the diameter specified on the packaging but provides very little radial force until the specified diameter is achieved.

Annular rupture does not occur after initial implantation of the self-expanding bioprosthesis, but may occur with oversizing of the post-dilation balloons. Importantly, there were 3 cases of fatal annular rupture that occurred with BPD likely due to balloon oversizing relative to the left ventricular outflow tract (**Table 7**). It is noteworthy that all 3 BPD annular rupture cases occurred with large-diameter (28 mm) balloons. Two of the 3 cases had BPD diameters greater than the CT angiographic mean annular diameter; the third case had severe annular and left ventricular outflow tract calcification. This rare but often fatal complication suggests that operators choose a conservative balloon diameter size for post-dilation, especially in patients with annular and left ventricular outflow tract calcification.

STUDY LIMITATIONS. BPD was not randomized in these studies, and was performed at the discretion of the operator for suboptimal acute procedural results. No pre-defined algorithm for the diameter of the BPD was specified in the protocol. We did not study the magnitude of aortic valve leaflet, or aortic annular or left ventricular outflow tract calcification on the occurrence of residual AR (34–36) or the need for BPD. We did not include patients who required a second valve in the analysis, limiting this analysis of BPD to procedures where an acceptable implant position was achieved. We acknowledge the worse clinical outcomes reported in patients treated with more than 1 valve (37,38). There were insufficient numbers of patients without pre-dilation to assess the effect of pre-dilation on the need for post-dilation (39).

CONCLUSIONS

We conclude that BPD is effective for the management of post-implantation AR, reducing moderate or severe residual regurgitation by 75.6% without an increase in neurologic events. Although BPD was not associated with an increase in neurologic events, a low incidence of valve migration, annular ruptures, and acute kidney injury were observed. Newer iterations of self-expanding transcatheter valves may improve annular conformability and reduce the need for BPD.

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PERSPECTIVES

WHAT IS KNOWN? BPD can be used in an attempt to acutely improve intraprocedural valve performance following self-expanding TAVR.

WHAT IS NEW? BPD was used in 22% of patients in the CoreValve US Clinical Trials. Balloon dilation was most commonly used for paravalvular AR and was successful in reducing AR in the overwhelming majority of such patients and was not associated with an increased incidence of ischemic neurologic events.

WHAT IS NEXT? Assess use and efficacy of BPD in procedures using the newest generation of self-expanding transcatheter valve prostheses.

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