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Impact of Balloon Post-Dilation on Clinical Outcomes After Transcatheter Aortic Valve Replacement With the Self-Expanding CoreValve Prosthesis

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ABSTRACT

OBJECTIVES The aim of this study was to assess the incidence and clinical impact of balloon post-dilation (BPD) after transcatheter aortic valve replacement (TAVR) with the CoreValve prosthesis (Medtronic Inc., Minneapolis, Minnesota).

BACKGROUND BPD is a widely adopted strategy to reduce the degree of paraprosthetic regurgitation in case of transcatheter heart valve underexpansion. However, controversies still remain regarding its real effectiveness and safety.

METHODS The ClinicalService (a nation-based data repository and medical care project) dataset was analyzed. All patients were dichotomized according to the need for BPD during the index procedure.

RESULTS Among 1,376 patients, BPD of the transcatheter heart valve was performed in 272 (19.8%). In 37% of cases, it was unsuccessful at reducing the paravalvular regurgitation to mild or less. No case of valve embolization, new intravalvular regurgitation, coronary occlusion, and aortic root injury occurred during BPD. There were no statistically significant differences between the 2 groups in the incidence of in-hospital all-cause and cardiovascular mortality, neurological events, myocardial infarction, bleeding, conversion to open-chest surgery, and the need for a permanent pacemaker. The need for BPD did not emerge as an independent risk factor for all-cause (adjusted hazard ratio [HR]: 1.33, 95% confidence interval [CI]: 0.81 to 2.19, $p = 0.264$) and cardiovascular (adjusted HR: 1.48, 95% CI: 0.74 to 2.97, $p = 0.265$) mortality at 1 year after the procedure. In addition, BPD did not predispose to higher odds of neurological events during 12 months after TAVR (HR: 0.92, 95% CI: 0.45 to 1.88, $p = 0.815$).

CONCLUSIONS This large study showed that BPD after TAVR was safe and not associated with increased rates of cerebrovascular events, mortality, myocardial infarction, and aortic root injury. (J Am Coll Cardiol Intv 2014;7:1014–21)

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Transcatheter aortic valve replacement (TAVR) has matured into a viable treatment alternative for patients with severe aortic stenosis at high-risk of conventional surgical aortic valve replacement (1,2). Although associated with excellent hemodynamic results, residual paravalvular regurgitation (PVR) occurs frequently with this procedure, having been reported in 80% to 96% of TAVR cases (3). Moderate or severe PVR occurs in ~10% to 15% of procedures, and this was observed to produce significantly worse outcomes (2,3).

Balloon post-dilation (BPD) has been shown to be a feasible and effective strategy to reduce significant PVR by enabling better expansion of the stent frame containing the biological valve and thus improved sealing (4). However, this technique is ineffective when PVR is caused by a "too high" or "too low" implantation, and some argue that post-dilation itself may potentially increase the risk of iatrogenic cerebrovascular events (5,6). However, these latter observations come from a few single-center studies with relatively small populations. The aim of this large multicenter analysis was to evaluate the prevalence of BPD after TAVR with a self-expanding prosthesis and its relative impact on clinical outcomes.

METHODS

PATIENT POPULATION. Starting in June 2007, all consecutive patients with severe aortic stenosis undergoing TAVR with the third-generation 18-French CoreValve device (Medtronic Inc., Minneapolis, Minnesota) at 7 Italian centers were prospectively included in the ClinicalService Project. This is a nation-based clinical data repository and medical care project aims to describe and improve the use of implantable devices in clinical practice in Italy. The project was approved by each site's institutional review board or medical director and conforms to the principles outlined in the Declaration of Helsinki. Each patient signed an informed consent for data collection and analysis. Clinical and echocardiographic follow-up were performed according to each center's clinical practice. Eligibility for TAVR was established at each center based on the consensus of a local multidisciplinary team, including clinical cardiologists, cardiac surgeons, and cardiac anesthesiologists. Sizing of the transcatheter heart valve (THV) was carried out by using multidetector computed tomography and an integration of echocardiography (transthoracic and/or transesophageal), angiography and simultaneous aortography during balloon valvuloplasty (7), according to each center's local practice. All the procedures were approved for compassionate use in patients considered at high risk of surgery. Clinical and echocardiographic follow-up were performed at 30 days and 1 year by clinical visits or telephone contacts. All events were site reported. Patients were dichotomized according to the need for BPD after release of the CoreValve prosthesis at the index procedure.

ABBREVIATIONS AND ACRONYMS

BPD = balloon post-dilation
CI = confidence interval
HR = hazard ratio
LBBB = left bundle branch block
PVR = paravalvular regurgitation
TAVR = transcatheter aortic valve replacement
THV = transcatheter heart valve
VASC = Valve Academic Research Consortium

PROCEDURE. Design features of the CoreValve prosthesis and technical details of the procedure were previously described (8–10). The CoreValve prosthesis, available in the 26-mm and 29-mm sizes and, starting September 2011 and August 2012, even in the 31-mm and 23-mm sizes, was implanted using the transfemoral, subclavian, and transaortic approaches with an 18-French delivery catheter, later improved by the use of the AccuTrak Stability Layer (Medtronic Inc.). All procedures were performed with patients under local anesthesia or general anesthesia and endotracheal intubation under fluoroscopic guidance. After prosthesis deployment, BPD was carried out under rapid pacing to reduce significant PVR or to optimize the frame expansion. Indications and technique of BPD were left to operators' practice. Intraprocedural quantification of PVR severity was carried out by using either echocardiography (Valve Academic Research Consortium criteria) or hemodynamic parameters according to the local institutional policies. The degree of PVR was further assessed by a transthoracic echocardiogram performed before discharge.

STATISTICAL ANALYSIS AND DEFINITIONS. Descriptive statistics are reported as mean ± SD for normally distributed continuous variables or as median and 25th to 75th percentile (interquartile range) otherwise. Normality of distribution was tested by means of the Kolmogorov-Smirnov test. Absolute and relative frequencies are reported for categorical variables. Continuous Gaussian variables were compared by means of a Student *t* test for independent samples, whereas skewed distributions

is on the Advisory Board of Medtronic and a consultant for Direct Flow Medical. Drs. Bedogni, Ettori, Bruschi, and Petronio are consultants for Medtronic. 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 Clinical and Echocardiographic Characteristics

	Overall	BPD Group	No-BPD Group	p Value
Clinical variables				
Age, yrs	81.6 ± 6.5	80.5 ± 7.9	81.9 ± 6.1	0.007
Female	52.5 (723/1,376)	38.2 (104/272)	56.1 (619/1,104)	<0.001
Hypertension	81.3 (1,117/1374)	80.8 (219/271)	81.4 (898/1103)	0.820
Diabetes mellitus	29.1 (398/1,370)	26.8 (72/269)	29.6 (326/1,101)	0.357
Atrial fibrillation	5.4 (74/1374)	5.9 (16/271)	5.3 (58/1103)	0.673
Previous myocardial infarction	17.6 (241/1,370)	18.1 (49/270)	17.5 (192/1100)	0.789
Previous stroke/TIA	11.3 (155/1376)	14.3 (39/272)	10.5 (116/1,104)	0.073
Previous CABG	14.8 (203/1,374)	18.1 (49/271)	14.0 (154/1,103)	0.087
Previous PCI	30.1 (412/1,368)	26.6 (72/271)	31.0 (340/1,097)	0.007
PVD	29.3 (403/1,374)	33.2 (90/271)	28.4 (313/1,103)	0.117
COPD	23.7 (325/1,374)	24.7 (67/271)	23.4 (258/1,103)	0.644
CRF*	25.9 (308/1,191)	23.9 (58/243)	26.4 (250/948)	0.427
Previous PPM	13.1 (174/1,326)	14.0 (37/264)	12.9 (137/1,062)	0.631
NYHA functional class III or IV	73.4 (1010/1,376)	80.9 (220/272)	71.6 (790/1,104)	0.002
Previous SAVR	2.4 (33/1,374)	4.1 (11/271)	2.0 (22/1,103)	0.047
STS score, %	7.1 (4–13)	7.5 (4–14)	6.9 (5–13)	0.711
Echocardiographic variables				
LVEF, %	50.7 ± 12.6	48.0 ± 13.7	51.4 ± 12.2	0.001
Mean aortic gradient, mm Hg	51.7 ± 15.5	51.8 ± 15.7	51.7 ± 15.4	0.430
AVA, cm^2	0.4 ± 0.2	0.4 ± 0.2	0.4 ± 0.2	0.610
Moderate or severe MR	44.9 (583/1,297)	53.8 (135/251)	42.8 (448/1,046)	0.002

Values are mean ± SD or n/N (%). *Defined as a glomerular filtration rate <30 ml/min.

AVA = aortic valve area; BPD = balloon post-dilation; CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; CRF = chronic renal failure; LVET = left ventricular ejection fraction; MR = mitral regurgitation; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; PPM = permanent pacemaker; PVD = peripheral vascular disease; SAVR = surgical aortic valve replacement; STS = Society of Thoracic Surgery; TIA = transient ischemic attack.

were compared using the Mann-Whitney nonparametric test. Differences in proportions were compared by applying a chi-square analysis. Time to long-term outcomes was described by means of the Kaplan-Meier curve and compared between groups by means of the log-rank test.

TABLE 2 Procedural Variables

	Overall	BPD Group	No-BPD Group	p Value
Access				0.996
Femoral	81.1 (1,116/1,376)	81.3 (221/272)	81.1 (895/1,104)	
Subclavian	14.4 (198/1,376)	14.3 (39/272)	14.4 (159/1,104)	
Aortic	4.5 (62/1,376)	4.4 (12/272)	4.5 (50/1,104)	
General anesthesia	26.7 (368/1,376)	22.1 (60/272)	27.9 (308/1,104)	0.051
Valve-in-valve	4.9 (68/1,374)	14.0 (38/271)	2.7 (30/1,103)	<0.001
Prosthesis size, mm				0.001
26	47.3 (650/1,374)	32.5 (88/271)	51.0 (562/1,103)	
29	45.6 (627/1,374)	54.6 (148/271)	43.4 (479/1,103)	
31	6.6 (90/1,374)	12.9 (35/271)	5.0 (55/1,103)	
Procedural time, min	100.0 (65-127)	120.0 (140-240)	98.0 (60-127)	<0.001

Values are % (n/N) or n (range).

BPD = balloon post-dilation.

After testing for proportional hazard assumptions, Cox models were fitted considering all variables from Tables 1 and 2, and hazard ratios (HRs) with 95% confidence intervals (95% CIs) were computed. A Cox multivariable analysis including all variables with probability value <0.15 in each Cox univariate analysis was used to determine independent predictors of the outcomes. All statistical analyses were performed using SAS version 9.3 for Windows (SAS Institute, Inc., Cary, North Carolina). All outcomes were reported according to VARC criteria (11).

RESULTS

PATIENT POPULATION. Of 1,376 patients, BPD was performed in 272 (19.8%). Clinical and echocardiographic characteristics of the overall population, as well as those of the BPD and no-BPD patients, are summarized in Table 1. Compared with no BPD patients, those in the BPD group were younger (80.5 ± 7.9 years vs. 81.9 ± 6.1 years; p = 0.007). Significant differences were also seen between the 2 groups in terms of the prevalence of male sex, New York Heart Association functional class III or IV, and degenerated surgical aortic bioprosthesis, which were more frequent in the BPD group (Table 1). Conversely, previous percutaneous coronary intervention was more frequent among no-BPD patients. Additionally, BPD patients had lower left ventricular ejection fraction and more frequently reported baseline moderate/severe mitral regurgitation and aortic regurgitation (Table 1). There were no differences between these 2 groups in terms of other preoperative variables.

PROCEDURAL AND IN-HOSPITAL OUTCOMES. Main procedural variables are presented in Table 2. The transfemoral approach was the most frequently used (81.1%), followed by the transsubclavian (14.4%) and transaortic (4.5%) approaches, with no differences between the 2 groups (p = 0.996). BPD was more frequently performed when the 29-mm (54.6% vs. 43.4%) and the 31-mm (12.9% vs. 5.0%) prostheses were implanted (p < 0.001) and when a second CoreValve was required as a bailout procedure for acute implant failure (14.0% vs. 2.7%; p < 0.001). The balloon sizes used for BPD for each THV size are listed in the Table 3. Neither valve embolization nor aortic root injury and coronary occlusion occurred during BPD. There were no statistically significant differences between the 2 groups in the incidence of in-hospital all-cause and cardiovascular mortality, neurological events, myocardial infarction, bleeding, and conversion to open-chest surgery. Of note, a trend toward a higher rate of high-degree conduction disturbances requiring permanent pacemaker

implantation was reported in the BPD group, whereas a statistically significant higher rate of left bundle branch block was reported in the no-BPD group (26.1% vs. 32.6%; p = 0.038) (Table 4). Conversion to surgery occurred in 6 patients: 3 had left ventricular perforation caused by the stiff guidewire, 1 patient had aortic dissection caused by delivery catheter trauma, 1 early patient had THV embolization in the ascending aorta and it was decided to convert the procedure to conventional open-chest valve replacement, and the last patient had annular rupture during valvuloplasty before THV implantation.

On echocardiography, no differences in terms of residual transprosthetic gradient were reported in the 2 groups, whereas residual PVR more than mild was still more frequently observed in the BPD group (37.9% vs. 17.1%; p < 0.001).

TABLE 3 Balloon Sizes Used for BPD

	CoreValve		
	26 mm	29 mm	31 mm
Balloons, mm			
20	3.6 (3/83)	0.0 (0/144)	0.0 (0/31)
22	13.3 (11/83)	0.7 (1/144)	0.0 (0/31)
23	14.5 (12/83)	3.5 (5/144)	0.0 (0/31)
24	1.2 (1/83)	1.4 (2/144)	0.0 (0/31)
25	56.6 (47/83)	24.3 (35/144)	16.1 (5/31)
26	3.6 (3/83)	6.9 (10/144)	0.0 (0/31)
27	0.0 (0/83)	0.7 (1/144)	0.0 (0/31)
28	7.2 (6/83)	58.4 (84/144)	71.0 (22/31)
29	0.0 (0/83)	2.1 (3/144)	0.0 (0/31)
30	0.0 (0/83)	2.1 (3/144)	12.9 (4/31)

Values are % (n/N). In 14 patients, balloon size for BPD was not available. No patients received 23-mm CoreValve (Medtronic, Minneapolis, Minnesota).
BPD = balloon post-dilation.

ONE-YEAR OUTCOMES. Kaplan-Meier curves depicting all-cause mortality, cardiovascular mortality, and neurological events for the BPD and no-BPD groups are reported in Figures 1 to 3. The need for BPD was associated with higher all-cause (hazard ratio [HR]: 1.43, 95% confidence interval [CI]: 1.03 to 1.98, p = 0.036) and cardiovascular (HR: 1.59, 95% CI: 1.01 to 2.51, p = 0.046) mortality, whereas this technique was not associated with an increased hazard of neurological events >1 year after TAVR (HR: 0.92, 95% CI: 0.45 to 1.88, p = 0.815). Other univariate predictors of all-cause and cardiovascular mortality are shown in Tables 5 and 6.

After adjustment for confounders by multivariable analysis, moderate or greater residual PVR (adjusted HR: 2.36, 95% CI: 1.56 to 3.56, p < 0.001), baseline atrial fibrillation (adjusted HR: 1.62, 95% CI: 1.04 to 2.52, p = 0.034), and severe renal insufficiency defined as a glomerular filtration rate <30 ml/min (adjusted HR: 1.79, 95% CI: 1.17 to 2.73, p = 0.004) were found to be independently associated with all-cause mortality. Independent predictors of cardiovascular mortality were age (adjusted HR: 0.96, 95% CI: 0.92 to 0.99, p = 0.014), and moderate or greater residual PVR (adjusted HR: 2.60, 95% CI: 1.54 to 4.67, p = 0.001). Of note, when forced into the model, BPD did not emerge as being independently associated with all-cause (adjusted HR: 1.33, 95% CI: 0.81 to 2.19, p = 0.264) and cardiovascular (adjusted HR: 1.48, 95% CI: 0.74 to 2.97, p = 0.265) mortality. In contrast, when moderate or greater residual PVR was excluded as a possible predictor from the multivariable analysis, BPD emerged as an independent predictor of both all-cause (adjusted HR: 1.48, 95% CI: 1.00 to 2.18, p = 0.048) and cardiovascular (adjusted HR: 1.73, 95% CI: 1.02 to 2.95, p = 0.043) mortality.

TABLE 4 In-Hospital and 30-Day Outcomes

	Overall	BPD group	No-BPD group	p Value
In-hospital				
All-cause mortality	4.1 (56/1,376)	4.4 (12/272)	4.0 (44/1,104)	0.750
Cardiovascular mortality	3.0 (41/1,376)	2.9 (8/272)	3.0 (33/1,104)	0.967
Stroke/TIA	2.2 (30/1,376)	2.2 (6/272)	2.2 (24/1,104)	0.974
Major stroke	1.3 (18/1,376)	2.2 (6/272)	1.1 (12/1,104)	0.146
Minor stroke	0.3 (4/1,376)	0.0 (0/272)	0.4 (4/1,104)	1.000
TIA	0.6 (8/1,376)	0.0 (0/272)	0.7 (8/1,104)	0.368
Life-threatening bleeding	4.7 (64/1,376)	3.7 (10/272)	4.9 (54/1,104)	0.394
Major bleeding	13.0 (179/1,376)	11.4 (31/272)	13.4 (148/1,104)	0.378
Myocardial infarction	1.2 (16/1,376)	1.5 (4/272)	1.1 (12/1,104)	0.597
Cardiac tamponade	2.0 (27/1,376)	2.6 (7/272)	1.8 (20/1,104)	0.417
New PPM	24.0 (330/1,376)	29.0 (79/272)	22.7 (251/1,104)	0.092
New LBBB	31.3 (431/1,376)	26.1 (71/272)	32.6 (360/1,104)	0.038
Conversion to surgery	0.4 (6/1,376)	0.4 (1/272)	0.5 (5/1,104)	0.848
Coronary occlusion	0.0 (0/1,376)	0.0 (0/272)	0.0 (0/1,104)	–
AKI stage				
1	15.6 (187/1,201)	16.5 (40/243)	15.3 (147/958)	
2	2.6 (31/1,201)	2.1 (5/243)	2.7 (26/958)	0.902
3	1.8 (22/1,201)	2.1 (5/243)	1.8 (17/958)	
PVR more than mild	20.0 (230/1,150)	37.9 (91/240)	17.1 (139/810)	<0.001
30-day				
All-cause mortality	5.9 (81/1,376)	6.6 (18/272)	5.7 (63/1,104)	0.567
Cardiovascular mortality	3.5 (48/1,376)	4.4 (12/272)	3.3 (36/1,104)	0.354
MI	1.3 (18/1,376)	1.5 (4/272)	1.3 (14/1,104)	0.792
Stroke/TIA	2.5 (35/1,376)	2.9 (8/272)	2.4 (27/1,104)	0.642
Major stroke	1.5 (21/1,376)	2.6 (7/272)	1.3 (14/1,104)	0.116
Minor stroke	0.5 (7/1,376)	0.0 (0/272)	0.6 (7/1,104)	0.188
TIA	0.7 (3/1,376)	0.4 (1/272)	0.7 (8/1,104)	0.513

Values are % (n/N).
AKI = acute kidney injury; LBBB = left bundle branch block; PVR = paravalvular regurgitation; other abbreviations as in Table 1.

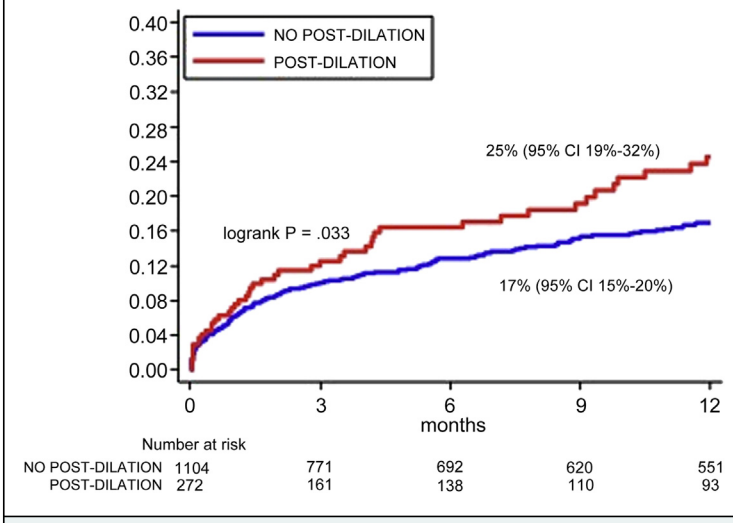

FIGURE 1 1-Year Incidence of All-Cause Mortality

Kaplan-Meier survival curves at 1-year follow-up depending on balloon post-dilation after transcatheter aortic valve replacement. CI = confidence interval.

DISCUSSION

Post-dilation of a THV is a widely adopted strategy to reduce the degree of paraprosthetic regurgitation in case of frame underexpansion or inadequate sealing (12). The feasibility and indications of this technique have already been described (4,12). However, controversies still remain regarding its real effectiveness and safety. In particular, although BPD does not seem to affect the valve performance, 2 single-center studies (encompassing about one-fourth of patients included in the present analysis) suggested that this comes at the price of a higher risk of cerebral embolization (5,6).

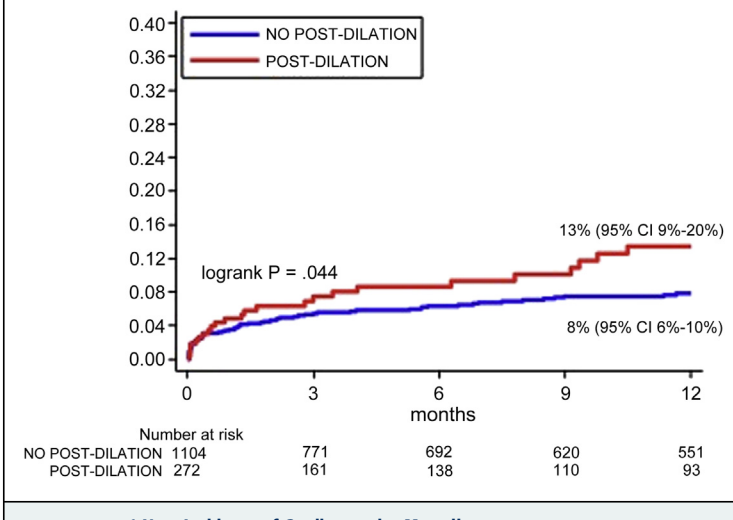

FIGURE 2 1-Year Incidence of Cardiovascular Mortality

Kaplan-Meier survival curves at 1-year follow-up depending on balloon post-dilation after transcatheter aortic valve replacement. CI = confidence interval.

The present large multicenter analysis adds meaningfully to the understanding of the impact of BPD during TAVR with the self-expanding CoreValve prosthesis with the following observations. First, balloon post-dilation was performed in almost 20% of cases, and it was more frequently done when the larger valves (29 and 31 mm) were implanted and after a second prosthesis was required to treat an acute implant failure. Second, in 37% of cases, BPD was unsuccessful at reducing PVR to mild or less. Third, BPD was not associated with higher rates of in-hospital and 30-day mortality and neurological events. Finally, after adjustment for confounders, BPD was not found to be an independent predictor of all-cause and cardiovascular mortality at 1 year.

The prevalence of post-dilation in this series was ~20%. In literature, the adoption rate of this bailout strategy varies widely (from 9% to 29%), reflecting different thresholds for BPD across TAVR centers (12). Consistent with previous observations with the balloon-expandable transcatheter prosthesis (5,6), we reported a higher frequency of BPD in patients receiving larger valve sizes, supporting the intuitive idea that the larger the diameter of the prosthesis, the lower the radial force expressed by the frame of the THV to the landing zone of the aortic annulus, thus requiring BPD to obtain greater expansion. Alternatively, 31-mm valves may have been placed in very large anatomy with suboptimal results, causing higher BPD rates.

We reported a success rate of balloon post-dilation of ~63%. These data are in line with those reported by previous studies with balloon-expandable valves (5,6,13). The possible explanations for these fairly disappointing results may be several. First, the calcium burden located in the aortic valve is very high. It has been reported that the degree of valve calcification contributes to nonoptimal success of BPD, precluding a complete sealing of the paravalvular space or favoring recoil phenomena of the prosthesis frame (5). Second, balloon post-dilation is performed inappropriately or with an undersized balloon; as matter of fact, when the cause of PVR is a "too low" or "too high" implant, as well as the deployment of an undersized THV, any attempt at further frame dilation is generally futile (12). In these cases, the best options to decrease the degree of PVR is to implant a second prosthesis in a Valve-in-Valve fashion (14) or, in the case of the CoreValve device,

to snare the first valve out from its anatomic position and deploy a second one (4). With these considerations in mind, we can argue that more aggressive pre-dilation and stricter indications for BPD in very selected cases (only overt frame underexpansion, avoiding it in the cases of evident low or high deployment) might be successful in improving the outcomes of this bailout technique.

In terms of clinical outcomes, the results of this study tend to support the safety of BPD immediately after valve implantation to reduce the incidence of PVR after TAVR with self-expanding valves. No cases of intraprosthetic regurgitation, coronary occlusion, aortic/annulus injury, and valve dislodgment were reported. In addition, we showed that BPD was not associated with higher mortality, myocardial infarction, or bleeding rates, although there was a tendency toward a higher rate of permanent pacemaker implantation in patients who had BPD likely caused by greater mechanical stress on the ventricular septum and potential damage to the conduction branches and the atrioventricular node. Interestingly, a statistically higher rate of left bundle branch block (LBBB) was reported in the no-BPD group. A possible explanation for this finding might be the higher incidence of high-degree atrioventricular block requiring permanent

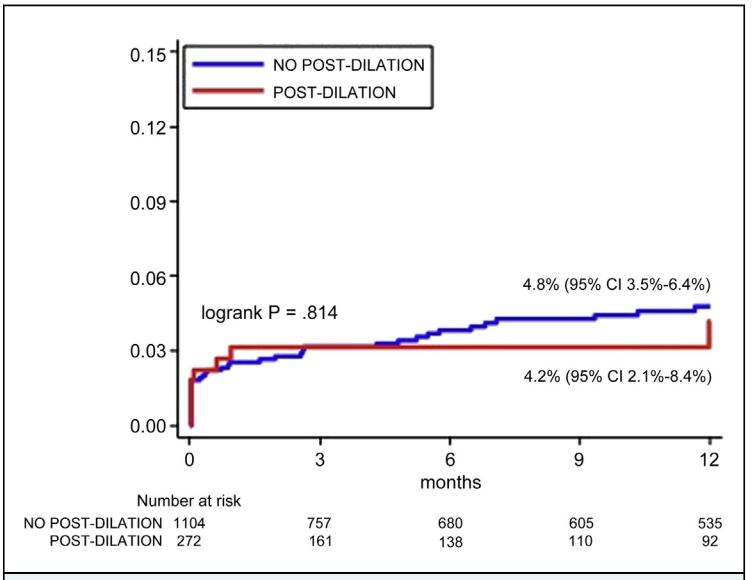

FIGURE 3 1-Year Incidence of Stroke

Kaplan-Meier survival curves at 1-year follow-up depending on balloon post-dilation after transcatheter aortic valve replacement. CI = confidence interval.

TABLE 5 Univariate and Multivariate Analysis for 1-Year All-Cause Mortality

	Univariate			Multivariate		
Variables	**Hazard Ratio**	**95% Confidence Interval**	**p Value**	**Hazard Ratio**	**95% Confidence Interval**	**p Value**
Balloon post-dilation	1.43	1.03–1.98	0.034	1.33	0.81–2.19	0.264
PVR moderate or severe	2.42	1.70–3.43	<0.001	2.36	1.56–3.56	<0.001
CRF*	2.18	1.59–2.99	<0.001	1.79	1.17–2.73	0.007
Chronic AF	1.46	1.07–1.99	0.016	1.62	1.04–2.52	0.034
NYHA functional class III–IV	1.84	1.27–2.67	0.001	1.41	0.84–2.38	0.196
Log-EuroSCORE	1.01	1.00–1.02	0.003	1.00	0.99–1.01	0.935
Baseline MR moderate or greater	1.45	1.09–1.94	0.011	1.25	0.83–1.89	0.284
Previous MI	1.28	0.91–1.79	0.148	1.31	0.81–2.12	0.268
Age	0.99	0.97–1.01	0.377			
Female	0.86	0.65–1.13	0.270			
Previous TIA/stroke	1.29	0.85–1.96	0.235			
LVEF <35%	1.12	0.76–1.67	0.557			
sPAP >60 mm Hg	1.33	0.86–2.06	0.194			
Baseline AR moderate or greater	1.22	0.91–1.64	0.181			
Previous PPM	1.02	0.68–1.55	0.905			
Hypertension	0.82	0.59–1.15	0.250			
Previous PCI	1.15	0.86–1.55	0.342			
Previous CABG	0.91	0.61–1.35	0.638			
Previous SAVR	0.44	0.11–1.77	0.249			
COPD	1.08	0.78–1.48	0.642			
PVD	1.15	0.85–1.54	0.364			
Valve-in-valve	0.99	0.50–1.94	0.979			

*Defined as a glomerular filtration rate <30 ml/h.

AF = atrial fibrillation; AR = aortic regurgitation; MI = myocardial infarction; sPAP = systolic pulmonary artery pressure; PCI = percutaneous coronary intervention; other abbreviations as in Tables 1 and 4.

TABLE 6 Univariate and Multivariate Analyses for 1-Year Cardiovascular Mortality

	Univariate Analysis			Multivariate Analysis		
Variables	**Hazard Ratio**	**95% Confidence Interval**	**p Value**	**Hazard Ratio**	**95% Confidence Interval**	**p Value**
Balloon post-dilation	1.59	1.01–2.51	0.046	1.48	0.74–2.97	0.265
PVR moderate or severe	2.62	1.61–4.25	<0.001	2.60	1.45–4.67	0.001
CRF*	1.90	1.19–3.02	0.007	1.74	0.93–3.23	0.081
Previous MI	1.83	1.17–2.86	0.008	1.48	0.77–2.87	0.240
Log-EuroSCORE	1.01	1.00–1.03	0.019	1.00	0.98–1.02	0.823
Age	0.97	0.95–100	0.059	0.96	0.92–0.99	0.014
Baseline MR moderate or greater	1.48	0.98–2.34	0.062	1.13	0.63–2.02	0.689
Chronic AF	1.23	0.78–1.96	0.376			
NYHA functional class III–IV	1.19	0.74–1.90	0469			
Female	0.86	0.57–1.28	0.448			
Previous TIA/stroke	0.97	0.46–1.80	0.779			
LVEF <35%	1.32	0.77–2.26	0.309			
sPAP >60 mm Hg	1.06	0.54–2.11	0.859			
Baseline AR moderate or greater	1.10	0.71–1.70	0.668			
Previous PPM	0.83	0.43–1.60	0.580			
Hypertension	0.91	0.55–1.51	0.722			
Previous PCI	1.00	0.65–1.55	0.993			
Previous CABG	1.21	0.72–2.04	0.479			
Previous SAVR	0.92	0.23–3.73	0.906			
COPD	1.11	0.71–1.76	0.642			
PVD	1.04	0.68–1.61	0.845			
Valve-in-valve	1.67	0.76–3.64	0.197			

*Defined as a glomerular filtration rate <30 ml/h.
Abbreviations as in Tables 1, 4, and 5.

pacemaker implantation in the BPD group. Because either the LBBB or the third-degree atrioventricular block belongs to the spectrum of the same pathology, it is possible that in patients who received BPD, a higher degree of conduction disturbance developed, thus determining lower frequency of an LBBB.

Recent data have suggested that post-dilation of a transcatheter heart valve was associated with higher rates of cerebrovascular events (5,6). These findings were not confirmed in this larger analysis, where cerebral embolic events were similar between groups both acutely and at mid-term follow-up. This difference might be explained by different techniques and balloons used to accomplish BPD or by characteristics of the self-expanding prosthesis itself. In fact, we might speculate that the longer stent of the CoreValve, as well as the fabric skirt that covers a larger part of the frame compared with the balloon-expandable SAPIEN valve (Edwards Lifesciences, Irvine, California) allows fewer calcific particle embolisms from the aortic valve during post-dilation. However, this explanation is hypothesis generating only and needs to be demonstrated by dedicated analyses. Another possible explanation for these discrepancies in terms of neurological events between previous studies and this analysis might be the lower baseline risk profile of the patient population enrolled in the present study.

STUDY LIMITATIONS. First, the transthoracic and transesophageal echocardiograms were read locally at the participating site. Grading of PVR may be heterogeneous across readers and sites. However, all local site readings were performed by level 3 echocardiographers with significant experience in TAVR and graded according to the standardized VARC definitions (11). Second, the indications and technique of BPD, as well as balloon choices, were left to the discretion of the physician of each site. Third, the exact mechanism of PVR (underexpansion, low implantation, high implantation) was not available. Finally, the dataset of the ClinicalService did not incorporate detailed computed tomography data, which may have provided information regarding aortic valve morphology, distribution of aortic valve calcification, and cover index, features that have demonstrated to significantly predict the need for BPD after TAVR (5). However, the main objective of this paper was to shed more light on the clinical impact of this bailout technique in a larger TAVR population than that previously reported in earlier studies.

CONCLUSIONS

This large multicenter analysis showed that BPD was ineffective at reducing PVR after TAVR with the self-expanding CoreValve in 37% of cases. This strategy was safe and was not associated with increased cerebrovascular events, mortality, myocardial infarction, and aortic root injury rates.

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