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ORIGINAL RESEARCH

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Balloon Predilation in Transcatheter Aortic Valve Replacement with Self-expanding Valves

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ABSTRACT

Introduction: The utility of routine balloon predilation in transcatheter aortic valve replacement (TAVR) with self-expanding valves is not established. Clinical outcomes at 30 days and 1 year post TAVR, deploying the "no balloon predilation" strategy have not been systematically described.

Methods: Between October 2011 and September 2016, all patients who underwent TAVR with self-expanding valves (CoreValve®, Medtronic, Inc., Minneapolis, MN, USA) were stratified into predilation and no predilation groups. Of the 564 patients in the study, predilation was performed in 410 (72.7%) patients.

Results: The need for postdilation was less when predilation was performed (30.2%), compared with no predilation (39.0%; adjusted odds ratio [aOR]:0.741, 95% confidence interval [CI]: 0.493–1.114). "Clinically significant" paravalvular leak (PVL) was similar in the predilation (5.9%) and no predilation (6.8%) groups (aOR: 0.886, 95% CI: 0.398–1.971). Permanent pacemaker implantation was higher following predilation (25.1%), compared with no predilation (15.6%; aOR:3.086, 95% CI:1.413–6.738). There were no differences in 30-day myocardial infarction, or 30-day and 1-year stroke and death. When patients undergoing predilation were further stratified into conservative predilation (predilation balloon size ≤ minimum annulus diameter) and aggressive predilation (predilation balloon size > minimum annulus) groups, need for postdilation was lowest with aggressive predilation. PVL, 30-day and 1-year stroke rates were similar in the aggressive, conservative and no predilation groups.

Conclusion: Balloon predilation in TAVR with a self-expanding prosthesis was associated with a significant decrease in the need for balloon postdilation, and a significant increase in the need for a permanent pacemaker. There was no difference in PVL, and 30-day and 1-year stroke and death rates between the two groups.

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KEYWORDS Transcatheter aortic valve replacement; predilation; postdilation; self-expanding valve; CoreValve

Introduction

Transcatheter aortic valve replacement (TAVR) is an effective treatment strategy for patients at high or intermediate risk for surgical aortic valve replacement (SAVR).[1,2] In 2015, more than 24,000 TAVRs were performed in the United States alone.[3]

Balloon aortic valvuloplasty or predilation has been performed as a "primer" prior to TAVR in the vast majority of cases during implantation of both balloon expandable and self-expanding valves. However, there has been a significant debate with regard to its routine use. While some have speculated a heightened risk of thromboembolic events and damage to the native leaflet resulting in hemodynamic instability following balloon predilation, others have advocated its use to increase leaflet flexibility and facilitate easier delivery and expansion of the prosthetic valve resulting from fracture of calcified nodules on the aortic valve leaflets. In addition, predilation may also decrease the need for balloon postdilation. Prior studies have focused on balloon expandable valves, and have been limited by small sample sizes.[4,5] Moreover, the optimal balloon sizing strategy for balloon predilation is not well established.

In this study, short- and long-term outcomes associated with balloon predilation prior to TAVR with self-expanding valves were evaluated. In addition, clinical outcomes in

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Supplementary material for this article can be accesssed here.

patients who underwent either conservative or aggressive predilation were compared with those who were not predilated.

Materials and methods

All patients who underwent TAVR at Houston Methodist Hospital between January 2011 and October 2016 were included in the study. Baseline demographic information (age, gender, body mass index [BMI], body surface area, ethnicity), past medical history, echocardiographic findings (pre- and post-TAVR), preoperative computed tomography (CT) data, intraoperative data (predilation, valve size, and postdilation), and clinical outcomes were collected retrospectively.

The following definitions were used in accordance with the Valve Academic Research Consortium (VARC)-2 TAVR consensus document: vascular complication, neurological events, periprocedural myocardial infarction, and acute kidney injury.[6] Paravalvular leak (PVL) was determined from post-procedure echocardiography performed prior to discharge. PVL was further classified as "clinically significant" PVL if the PVL was graded as at least moderate on the post TAVR echocardiogram. Post-procedure laboratory evaluation was conducted at the discretion of the treating physician. For baseline laboratory results, the last evaluation before the procedure was utilized. Aggressive predilation was defined as predilation balloon size 1 cm or greater than the minimum aortic annular diameter assessed by pre-procedural CT scan; conservative predilation was defined using predilation balloon size equal to or less than the minimum aortic annular diameter.

The study was approved by the Institutional Review Board. No extramural funding was used to support the study.

Statistical analysis

Treatment group differences for continuously-scaled baseline and outcome variables were analyzed using analysis of variance (ANOVA), with results presented in the form of group-wise mean and standard deviation (SD). Between-group homoscedasticity was assessed using Bartlett's test, and Welch ANOVA (W-test) was employed if there were significant differences in group-specific variance. Chi-squared contingency table testing with Fisher's exact test was employed for groupwise comparison of categorical count data. Firth logistic regression with a penalized likelihood function for complete and quasi-complete separation was employed for determining crude and adjusted odds ratios for binary (yes/no) outcomes.[7] There were two logistic models used for assessing crude odds ratios (ORs) and adjusted odds ratios (aOR) for each outcome. First, a 2-level treatment factor (0-no predilation, 1-predilation) was employed, which included gender (0-male, 1-female), height, pacemaker implantation (0-no, 1-yes), history of percutaneous coronary intervention (PCI) (y/n), chronic lung disease (y/n), and peripheral vascular disease (PVD) (y/n) when pre-dilation aOR was generated. The second type of model involved a 3-level treatment factor (0-no predilation, 1-conservative predilation, 2-aggressive predilation), for obtaining a pair of ORs or aORs, which incorporated gender, ever smoking (y/n), current smoker (y/n), height, weight, pacemaker implantation (y/n), PCI (y/n), and PVD (y/n) when each pair of aORs were generated. Two-sided tests were used for all analyses assuming a Type I error rate (α) of 0.05. All statistical analyses were performed using Stata V14 (College Station, TX).

Results

Between January 2011 and October 2016, a total of 830 patients underwent TAVR at our center. Of these, 564 patients who received the self-expanding CoreValve® (Medtronic, Inc., Minneapolis, MN, USA) (CoreValve® = 406; CoreValve® Evolut R = 158) were included in the study. Patients were stratified based on whether or not they underwent predilation prior to valve implantation (predilation group [n = 410]; no-predilation group [n = 154]). There were no differences in the mean age (80.8 ± 10.19 years in the predilation group vs. 81.8 ± 8.94 years in the no-predilation group, P = 0.405), and mean BMI (27.5 ± 19.11 kg/m^2 vs. 27.3 ± 6.29 kg/m^2, P = 0.051) between the two groups. However, the proportion of men (60.4% vs. 47.6%, P = 0.006) and average height (171.34 ± 13.24 cm vs. 167.01 ± 10.97, P < 0.001) were higher in the no-predilation group. The proportion of white patients was higher in the predilation group (76.8% Whites in predilation group vs. 62.3% in no-predilation group, P < 0.001). A greater proportion of patients in the predilation group had a history of prior PCI (19.8% vs. 8.4%, P = 0.001) and PVD (16.1% vs. 7.8%), compared with patients in the no-predilation group. All other baseline clinical characteristics (history of coronary artery disease [CAD], prior cardiac surgery, hypertension, diabetes mellitus, hyperlipidemia, smoking, malignancy, chronic lung disease, stroke, transient ischemic attack, atrial fibrillation and chronic kidney disease) were similar in both the groups (Table 1).

A greater proportion of patients in the predilation group (73.1%) had an ejection fraction more than 50% compared with the no-predilation group (58.9%). Similarly, a lower proportion of patients in the predilation group had an ejection fraction less than 30% (5.7% vs. 12.6%) (P = 0.002 for difference between ejection fraction categories) (Table 1). The two groups were similar with regard to aortic valve area (0.67 ± 0.20 cm^2 in the predilation group vs. 0.67 ± 0.21 cm^2 in no-predilation group). The mean aortic valve gradient (44.22 ± 14.46 mmHg in the predilation group vs. 39.40 ± 11.34 mmHg in the no-predilation group, P = 0.003), and peak velocity (4.2.49 ± 0.74 m/s vs. 3.96 ± 0.59 m/s, P = 0.009) were higher in the predilation group. The mean minimum aortic annular diameter (21.73 ± 2.45 mm in the predilation group vs. 21.93 ± 2.68 mm in the no-predilation group), maximum aortic annular diameter (26.69 ± 2.83 mm vs. 26.80 ± 3.81 mm), perimeter (77.92 ± 7.67 mm vs. 78.11 ± 11.62 mm), and sinotubular junction height (25.44 ± 4.40 mm vs. 26.14 ± 5.97 mm), as determined from pre-TAVR CT scans were not different between the two groups.

Table 1. Baseline characteristics of patients undergoing transcatheter aortic valve replacement with CoreValve® (Medtronic, Inc., Minneapolis, MN).

	No predilation (n = 154)	Predilation (n = 410)	*P*-value
Age, mean ± SD (years)	80.8 ± 10.19	81.83 ± 8.94	0.293
Men, n (%)	93 (60.4%)	195 (47.6%)	0.007
BMI, mean ± SD (kgm^2)	27.3 ± 6.29	27.5 ± 19.11	0.051
CAD, n (%)	83 (53.9%)	221 (53.9%)	0.999
Prior cardiac surgery, n (%)	35 (22.7%)	89 (21.7%)	0.794
Previous PCI, n (%)	13 (8.4%)	81 (19.8%)	0.001
OSA, n (%)	6 (3.9%)	28 (6.8%)	0.192
Hypertension, n (%)	124 (80.5%)	350 (85.4%)	0.161
Diabetes mellitus, n (%)	45 (29.2%)	151(36.8%)	0.091
Hyperlipidemia, n (%)	97 (63.0%)	253 (61.7%)	0.780
COPD, n (%)	25 (16.2%)	77 (18.8%)	0.469
Malignancy, n (%)	35 (22.7%)	77 (18.8%)	0.295
Liver cirrhosis, n (%)	2 (1.3%)	8 (2.0%)	0.601
Prior stroke, n (%)	14 (9.1%)	40 (9.8%)	0.811
TIA, n (%)	8 (5.2%)	22 (5.4%)	0.936
Peripheral vascular disease, n (%)	12 (7.8%)	66 (16.1%)	0.011
Atrial fibrillation, n (%)	46 (29.9%)	132 (32.2%)	0.597
GFR			0.550
Normal, n (%)	23 (14.9%)	64 (15.6%)	
Mild, n (%)	45 (29.2%)	140 (34.1%)	
Moderate, n (%)	71 (46.1%)	162 (39.5%)	
Severe, n (%)	6 (3.9%)	24 (5.9%)	
ESRD, n (%)	9 (5.8%)	20 (4.9%)	
Left ventricular ejection fraction			0.002
< 30%, n (%)	12 (12.6%)	15 (5.7%)	
30–39%, n (%)	20 (21.1%)	26 (9.8%)	
40–49%, n (%)	7 (7.4%)	30 (11.4%)	
≥ 50%, n (%)	56 (58.9%)	193 (73.1%)	
Valve type			< 0.001
CoreValve®	129 (83.8%)	277 (67.6%)	
CoreValve Evolut R®	25 (16.2%)	133 (32.4%)	
Race			< 0.001
White, n (%)	96 (62.3%)	315 (76.8%)	
African American, n (%)	4 (2.6%)	20 (5.0%)	
Hispanic, n (%)	4 (2.6%)	22 (5.4%)	
Others, n (%)	11 (7.1%)	22 (5.4%)	
Smoking status			0.410
Current, n (%)	22 (14.3%)	65 (15.9%)	
Former, n (%)	24 (15.6%)	81 (19.8%)	
Bicuspid aortic valve, n (%)	3 (2.3%)	13 (3.6%)	0.575
AVA mean ± SD (cm^2)	0.67 ± 0.21	0.67 ± 0.20	0.813
Mean gradient mean ± SD (mmHg)	39.40 ± 11.34	44.22 ± 14.46	0.003
Peak velocity mean ± SD (cms^{-1})	396.47 ± 58.58	416.49 ± 73.88	0.009
Minimum annular diameter mean ± SD (mm)	21.93 ± 2.68	21.73 ± 2.45	0.417
Maximum annular diameter mean ± SD (mm)	26.80 ± 3.81	26.69 ± 2.83	0.759
Perimeter mean ± SD (mm)	78.11 ± 11.62	77.92 ± 7.67	0.857
Aortic root mean ± SD (mm)	34.29 ± 4.69	33.50 ± 3.84	0.102
Sinotubular junction mean ± SD (mm)	26.14 ± 5.97	25.44 ± 4.40	0.362

Notes. BMI, body mass index; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; ESRD, end-stage renal disease; GFR, glomerular filtration rate; OSA, obstructive sleep apnea; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

A lesser proportion of patients undergoing predilation required balloon postdilation compared with those in the no-predilation group (39.0% vs. 30.2%; odds ratio [OR]: 0.679, 95% confidence interval [CI]: 0.462–0.998) (Supplemental Table 1). Perioperative myocardial infarction (MI) (5.6% vs. 1.3%; OR: 3.699, 95% CI: 0.991–13.810) in the predilation and no-predilation groups were not significantly different. A significantly greater proportion of patients underwent pacemaker implantation if they were predilated compared with those who were not (25.8% vs. 13.6%; OR: 2.133, 95% CI:

1.153–3.946). Prior to discharge, the proportion of patients with any PVL was higher in the predilation group compared with the no-predilation group (61.8% vs. 49.9%; OR: 1.668, 95% CI: 1.134–2.454), but similar between the two groups when "clinically significant" PVL was compared (5.9% vs. 6.8%; OR: 0.841, 95% CI: 0.396–1.787). After multivariate analysis, the difference in the incidence of balloon postdilation (adjusted OR [aOR]: 0.741; 95% CI: 0.493–1.114) and perioperative MI (aOR: 3.367; 95% CI: 0.886–12.803) remained insignificant (Table 2). There were no annular ruptures observed in either group.

At 30 days, death (2.4% in the predilation group vs. 1.9% in the no-predilation group; OR: 1.135, 95% CI: 0.334–3.860), cardiovascular death (2.4% vs. 1.3%; OR: 1.599, 95% CI: 0.398–6.433), stroke (2.4% vs. 1.3%; OR: 1.599, 95% CI: 0.399–6.433), and major vascular complication (4.1% vs. 3.9%; OR: 1.016, 95% CI: 0.405–2.549) were not significantly different. At 1 year, death (5.4% vs. 4.5%; OR: 1.139, 95% CI: 0.488–2.659) and stroke (3.4% vs. 1.9%; OR: 1.583, 95% CI: 0.485–5.163) were also not significantly different. After multivariate analysis, rates of death (aOR: 1.131, 95% CI: 0.316–4.049), cardiovascular death (aOR: 1.599, 95% CI: 0.398–6.433), major vascular complication (aOR: 1.016, 95% CI: 0.405–2.549) and sepsis (aOR: 0.373, 95% CI: 0.640–2.176) at 30 days were not different. Similarly, death (aOR: 1.139, 95% CI: 0.488–2.659) and stroke at 1 year (aOR: 1.583, 95% CI: 0.485–5.163) were not different after adjusting for covariates.

Table 2. Clinical outcomes with adjusted odds ratios in patients after transcatheter aortic valve replacement with CoreValve® (Medtronic, Inc., Minneapolis, MN, USA) at 30 days and 1 year.

	No predilation (n = 154)	Predilation (n = 410)	Adjusted Odds Ratio (95% CI)	*P*-value
Post-dilation, n (%)	60 (39.0%)	124 (30.2%)	0.741 (0.493–1.114)	0.150
30 days				
Death, n (%)	3 (1.9%)	10 (2.4%)	1.131 (0.316–4.049)	0.850
Cardiovascular death, n (%)	2 (1.3%)	10 (2.4%)	1.551 (0.365–6.596)	0.552
Stroke, n (%)	2 (1.3%)	10 (2.4%)	1.029 (0.246–4.307)	0.969
Major vascular complication, n (%)	6 (3.9%)	17 (4.1%)	0.870 (0.339–2.236)	0.773
Sepsis, n (%)	2 (1.3%)	2 (0.5%)	0.303 (0.463–1.981)	0.213
Pacemaker implantation, n (%)	24 (15.6%)	103 (25.1%)	3.086 (1.413–6.738)	0.005
Perioperative MI, n (%)	2 (1.3%)	23 (5.6%)	3.367 (0.886–12.803)	0.075
"Clinically significant" paravalvular leak, n (%)	10 (6.5%)	23 (5.6%)	0.886 (0.398–1.971)	0.767
1 year				
Death, n (%)	7 (4.5%)	22 (5.4%)	1.090 (0.452–2.627)	0.848
Stroke, n (%)	3 (1.9%)	14 (3.4%)	1.259 (0.377–4.207)	0.708

Notes. CI, confidence interval; MI, myocardial infarction.

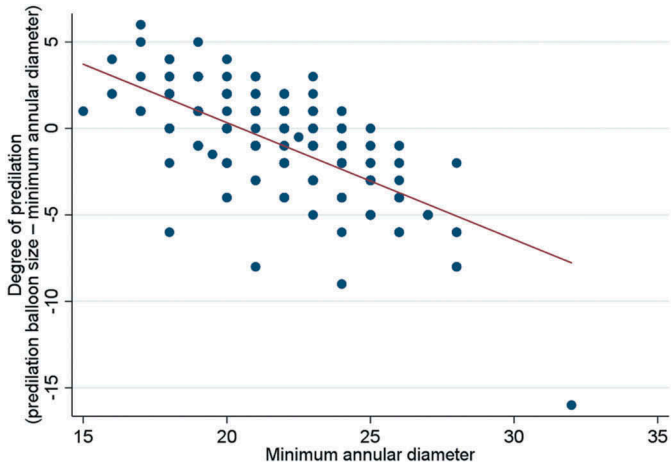

Figure 1. A scatter plot showing the degree of predilation with increasing minimum annular diameter.

In a subgroup analysis of patients who underwent predilation (conservative [n = 301] and aggressive [n = 109]), we observed that patients with lower minimum annular diameter tended to undergo more aggressive predilation ($P < 0.001$ for trend) (Figure 1). The need for balloon postdilation was lower in the aggressive (22.9%) and conservative (32.9%) predilation groups compared with no-predilation group (39.0%) (OR for aggressive predilation vs. no predilation: 0.471, 95% CI: 0.273–0.815) (Supplemental Table 3, Figure 2). After adjusting for confounders, balloon postdilation (aOR for aggressive predilation vs. no-predilation: 0.520, 95% CI: 0.288–0.941) remained lower in the aggressive predilation group (Table 5).

Pacemaker implantation was highest with conservative predilation (27.9%) compared with aggressive predilation (17.4%) and no predilation (15.6%). While the difference in pacemaker implantation was significantly higher for conservative predilation compared with no predilation (OR for conservative predilation vs. no-predilation: 2.571, 95% CI: 1.375– 4.810), the difference was not statistically significant for aggressive predilation compared with no predilation (OR for aggressive predilation vs. no-predilation: 1.106, 95% CI: 0.475–4.810). After multivariate analysis, the proportion of patients receiving pacemaker implantation remained significantly higher in the conservative predilation group (aOR for conservative predilation vs. no predilation: 3.504, 95% CI: 1.543–7.957) and was not different in

Table 3. Paravalvular leak (all categories) after transcatheter aortic valve replacement with CoreValve® (Medtronic, Inc., Minneapolis, MN, USA) prior to discharge.

	No predilation, n (%)	Predilation, n (%)	Adjusted Odds Ratio (95% CI)
None	93 (61.8%)	196 (50.1%)	1.51 (1.04–2.18)
Trace	14 (9.5%)	53 (13.6%)	
Mild	31 (20.9%)	119 (30.4%)	
Mild-Moderate	7 (4.7%)	20 (5.1%)	
Moderate	3 (2.0%)	3 (0.8%)	

Note. CI, confidence interval.

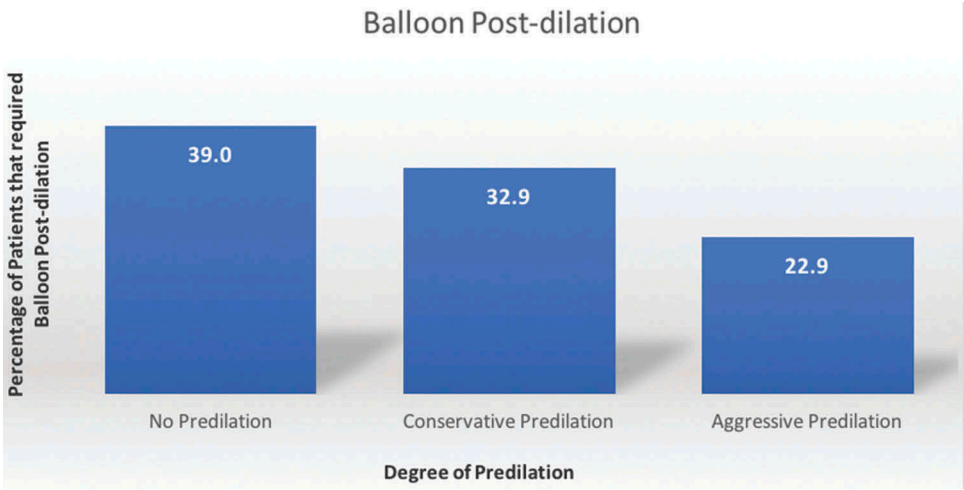

Figure 2. A bar graph showing the percentage of patients that required balloon post-dilation with varying degrees of predilation.

Table 4. "Clinically significant" paravalvular leak after transcatheter aortic valve replacement with CoreValve® (Medtronic, Inc., Minneapolis, MN, USA) prior to discharge.

	No predilation, n (%)	Predilation, n (%)	Adjusted Odds Ratio (95% CI)
Non-significant	138 (93.2%)	368 (94.1%)	0.886 (0.398–1.971)
Significant	10 (6.8%)	23 (5.9%)	

Note. CI, confidence interval.

the no-predilation group (aOR for aggressive predilation vs. no predilation: 2.940, 95% CI: 0.986–8.759).

PVL was higher in the conservative predilation group compared with no-predilation group (51.7% vs. 68.2%; aOR: 1.800; 95% CI: 1.201–2.697), while the difference was not significant when aggressive predilation was compared with the no-predilation group (46.8% vs. 68.2%; aOR: 1.359; 95% CI: 0.820–2.253). Similar to the two-group analysis, when clinically significant PVL was compared, there was no difference between the aggressive (6.7%) and conservative predilation groups (5.6%) with the no-predilation group (6.8%; aOR for aggressive predilation vs. no predilation: aOR: 1.11; 95% CI: 0.388–3.175) (Tables 3 and 4).

Rates of stroke at 30 days in the aggressive (3.7%), conservative (2.0%), and no-predilation groups (1.3%) were not different (OR for aggressive predilation vs. no-predilation: 2.602, 95% CI: 0.544–12.454). After adjusting for covariates, stroke at 30 days remained not different (aOR for aggressive predilation vs. no-predilation: 1.256, 95% CI: 0.234–6.749). At 1 year, stroke rates in the aggressive predilation group (4.6%) were comparable with those in conservative predilation (3.0%) and no-predilation groups (1.3%; OR for aggressive predilation vs. no-predilation: 2.278, 95% CI: 0.583–8.904). Multivariate analysis showed no difference in the incidence

Table 5. Clinical outcomes with adjusted odds ratios in patients after transcatheter aortic valve replacement with CoreValve® (Medtronic, Inc., Minneapolis, MN, USA) at 30 days and 1 year.

	No predilation (n = 154), n (%)	Conservative predilation (n = 301), n (%)	Conservative vs. no predilation, Adjusted Odds Ratio (95% CI)	*P*-value	Aggressive predilation (n = 109), n (%)	Aggressive vs. no predilation, Adjusted Odds Ratio (95% CI)	*P*-value
Post-dilation, n (%)	60 (39.0%)	99 (32.9%)	0.748 (0.490–1.14)	0.180	25 (22.9%)	0.520 (0.288–0.941)	
30 days							
Death, n (%)	3 (1.9%)	9 (3.0%)	1.229 (0.341–4.435)	0.752	1 (0.9%)	0.592 (0.795–4.404)	0.608
Cardiovascular death, n (%)	2 (1.3%)	9 (3.0%)	1.640 (0.380–7.089)	0.508	1 (0.9%)	0.750 (0.874–6.428)	0.793
Stroke, n (%)	2 (1.3%)	6 (2.0%)	0.860 (0.188–3.929)	0.845	4 (3.7%)	1.256 (0.234–6.749)	0.790
Major vascular complication, n (%)	6 (3.9%)	11 (3.7%)	0.749 (0.274–2.048)	0.574	6 (5.5%)	1.264 (0.390–4.094)	0.696
Sepsis, n (%)	2 (1.3%)	2 (0.7%)	0.452 (0.075–2.720)	0.386	0 (0.0%)	0.275 (0.126–6.010)	0.412
New pacemaker implantation, n (%)	24 (15.6%)	84 (27.9%)	3.504 (1.543–7.957)	0.003	19 (17.4%)	2.940 (0.986–8.759)	0.053
Perioperative MI, n (%)	2 (1.3%)	17 (4.5%)	3.078 (0.788–12.030)	0.106	6 (5.5%)	3.872 (0.839–17.874)	0.083
"Clinically significant" paravalvular leak, n (%)	10 (6.5%)	16 (5.3%)	0.847 (0.365–1.961)	0.002	7 (6.4%)	0.388 (3.175)	0.846
1 year							
Death, n (%)	7 (4.5%)	17 (5.6%)	1.062 (0.427–2.644)	0.897	5 (4.6%)	1.138 (0.344–3.762)	0.832
Stroke, n (%)	3 (1.9%)	9 (3.0%)	1.127 (0.318–3.993)	0.853	5 (4.6%)	1.579 (0.371–6.706)	0.536

Notes. CI, confidence interval; MI, myocardial infarction.

of stroke (aOR for aggressive predilation vs. no-predilation: 1.579, 95% CI: 0.371–6.706) between the two groups at 1 year.

Discussion

This study evaluated the effect on clinical outcomes of predilation prior to TAVR with self-expanding valves. The most important finding was a significant decrease in the need for postdilation when patients were predilated aggressively (22.9% in aggressive, 32.9% in conservative, and 39.0% in no-predilation groups, respectively). There was also no difference in stroke rates between patients in the predilation (2.4%) and no-predilation (1.3%; aOR 1.029, 95% CI: 0.246–4.307) groups. However, more patients required permanent pacemaker implantation (25.1% with predilation vs. 15.6% without predilation; aOR: 3.086, 95% CI: 1.413– 6.738). It is also important to note that when predilation was performed aggressively, there was no increase in peri-TAVR stroke (3.7% in the aggressive predilation group vs. 1.3% in the no-predilation group; aOR for aggressive predilation vs. no-predilation: 1.235, 95% CI: 0.234–6.749).

The finding of comparable stroke rates at 30 days in patients who underwent predilation and those who did not is consistent with prior studies in patients with self-expanding valves.[8–12] Stroke rate from these prior studies were highly variable, due in part to the small sample size in these studies. Two studies that did have large sample sizes did have stroke rates similar to our study.[11,12] One other study found a higher rate of stroke in patients who did not undergo predilation (11.9% vs. 5%).[13] However, that study did not adjust for covariates. Previous studies have not reported stroke rates at 1 year associated with predilation.

Lower balloon postdilation rates (22.9% in aggressive, 32.9% in conservative, and 39.0% in the no-predilation groups, respectively) were expected. "Best practice" guidelines recommend balloon postdilation for intraoperative suboptimal valve function. Prior studies have shown the need for balloon postdilation to be as high as 22%.[14] A recent systematic review including 889 patients showed that the incidence of stroke was greater in patients with postdilation (OR, 1.71; 95% CI, 1.10–2.66).[15] In addition, intraoperative balloon postdilation might conceivably predispose valve prostheses to leaflet damage, compromising long-term valve durability. As TAVR is expanded to lower risk populations with increased post procedure life expectancies, valve durability is likely to become an increasingly important issue. Our study found a 25% relative reduction in the need for balloon postdilation following predilation, with no difference in the peri-procedural stroke risk. This was also seen in the study by Fink et al.[11] where balloon postdilation was lower in the predilation group (9%) compared to the no-predilation group (26%; $P < 0.001$) without increasing stroke risk.

A higher incidence of pacemaker implantation is expected with self-expanding valves due to a difference in structure of the prosthesis compared with balloon expandable valves.[16] Similarly, larger valvuloplasty balloon sizes are associated with higher pacemaker rates.[17] Our findings of higher pacemaker implantation rates in the predilation group, and lowest pacemaker implantation rates in the no-predilation group are thus expected. However, pacemaker rates being higher in conservative predilation group compared with aggressive predilation group is likely due to chance alone. It is also worth noting that pacemaker rates differ with valve types due to structural differences. CoreValve® has higher pacemaker rates compared with CoreValve Evolut R®. In our study, 17.2% patients receiving CoreValve® underwent new pacemaker implantation, while only 7.6% patients who received CoreValve Evolut R® underwent new pacemaker implantation ($P < 0.01$) (Supplemental Table 5). With regard to postdilation, one study compared outcomes with and without predilation, and concluded that while outcomes were not affected by predilation, there was a lesser need to postdilate in patients who had predilation (21.5% in predilation group vs. 35.6% in the no-predilation group, $P < 0.001$).[4] Of the 517 patients, only 246 patients received self-expanding valves, and a subgroup analysis for these patients was not provided.

With regard to PVL, there are limited data available. One of the challenges is the high degree of subjectivity in quantifying PVL. Fiorina et al.[9] assessed severe PVL as their clinical outcome, while Giustino et al[10] and Fink et al[11] reported on the occurrence of moderate PVL. Neither study reported any differences in PVL with balloon predilation. In our study, we reported the different grades of PVL and stratified them into "clinically significant" and "non-significant" categories as well, and similar to other studies, did not find any significant differences.

The trend of more aggressive predilation in patients with a lower minimum annular diameter is interesting to note (Figure 1). While a multitude of factors (ejection fraction, annular size, operator preference, etc.) are considered before making a decision to predilate, this would suggest that operators tend to feel the need to predilate more aggressively with lower minimum annular diameters. This may be driven by the belief that this would allow valves to expand more fully, and hence reduce PVL if the aortic annulus is expanded to approximate the valve size prior to valve implantation.

Limitations

The major limitation of this study is its retrospective design. Decision on whether or not to predilate prior to TAVR is made by the operator taking into consideration a variety of factors such as depressed systolic function and calcification of aortic valve leaflets/cusps, which introduces a selection bias. There are also no standard guidelines to define aggressive and conservative predilation. This study attempts to propose one such criterion by taking into consideration the minimum aortic annular diameter and predilation balloon size. We also report higher pacemaker rates with aggressive predilation, but identification of factors that contributed to these higher pacemaker rates is beyond the scope of our study.

Conclusion

Balloon predilation in TAVR with a self-expanding prosthesis was associated with a decrease in the need for balloon postdilation, albeit with an increase in the odds of requiring a permanent pacemaker post-TAVR. There were no differences in stroke and death rates at 30 days and 1 year between no-predilation and predilation groups (with either conservative or aggressive predilation).

Disclosure statements

Dr Deepak L. Bhatt discloses the following relationships – Advisory Board: Cardax, Elsevier Practice Update Cardiology, Medscape Cardiology, Regado Biosciences; Board of Directors: Boston VA Research Institute, Society of Cardiovascular Patient Care; Chair: American Heart Association Quality Oversight Committee; Data Monitoring Committees: Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute), Cleveland Clinic, Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine, Population Health Research Institute; Honoraria: American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org; Vice-Chair, ACC Accreditation Committee), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute; clinical trial steering committee), Belvoir Publications (Editor in Chief, Harvard Heart Letter), Duke Clinical Research Institute (clinical trial steering committees), HMP Communications (Editor in Chief, Journal of Invasive Cardiology), *Journal of the American College of Cardiology* (Guest Editor; Associate Editor), Population Health Research Institute (clinical trial steering committee), Slack Publications (Chief Medical Editor, Cardiology Today's Intervention), Society of Cardiovascular Patient Care (Secretary/Treasurer), WebMD (CME steering committees); Other: Clinical Cardiology (Deputy Editor), NCDR-ACTION Registry Steering Committee (Chair), VA CART Research and Publications Committee (Chair); Research Funding: Abbott, Amarin, Amgen, AstraZeneca, Bristol-Myers Squibb, Chiesi, Eisai, Ethicon, Forest Laboratories, Ironwood, Ischemix, Lilly, Medtronic, PhaseBio, Pfizer, Regeneron, Roche, Sanofi Aventis, The Medicines Company; Royalties: Elsevier (Editor, Cardiovascular Intervention: A Companion to Braunwald's Heart Disease); Site Co-Investigator: Biotronik, Boston Scientific, St. Jude Medical (now Abbott), Svelte; Trustee: American College of Cardiology; Unfunded Research: FlowCo, Merck, PLx Pharma, Takeda. Dr Kalra is a consultant to Medtronic, Inc. The other authors report no conflicts of interest.

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