Original Article

Clinical utility of a predictive model for paravalvular aortic regurgitation after transcatheter aortic valve implantation with a self-expandable prosthesis ☆

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A B S T R A C T

Background: A predictive model for Paravalvular aortic regurgitation (PAR) integrating the left ventricular outflow tract-to-ascending aorta angle (LVOT-AO) and depth to the non-coronary cusp (NCC) after TAVI with CoreValve prosthesis (MCP) was retrospectively identified ($2 \times \angle$LVOT-AO + [depth to NCC-10]2; cutoff = 50). However, the validity and clinical utility of this model remain unknown.
Methods: A total of 100 patients (79.6 ± 7 years, mean EuroScore 24.9 ± 16.3%, 41 males) constituted a validation cohort for the predictive model. Both angle (LVOT-AO) and depth to NCC were considered during patient selection and device implantation.
Results: Significant AR occurred in 16% (group A) vs. 84% (group B). Angle $\angle$LVOT-AO and depth to NCC were larger in group A compared to group B (16.4 ± 7.2 vs. 11.8 ± 4.1, $p < 0.001$, and 9.1 ± 4.8 mm vs. 6.6 ± 2.7 mm, $p = 0.004$). The model showed a sensitivity of 68.7% and a specificity of 88.1% in prediction of PAR. Comparing the derivation cohort (initial experience, $n = 50$) and validation cohort (later experience, $n = 100$) it is showed that the $\angle$LVOT-AO, valve depth and PAR were significantly lower (12.5 ± 4.9 and 6.9 ± 3.2 mm vs. 19.7 ± 7.9 and 10.4 ± 3.7 mm, 40% vs. 16% respectively, all $p < 0.001$) in the validation cohort.
Conclusion: The predictive model for significant PAR after TAVI using MCP is valid with a reassuring specificity and an acceptable sensitivity. A strategy incorporating these anatomical and procedural variables improves PAR after TAVI.

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1. Introduction

Transcatheter aortic valve implantation (TAVI) is becoming a mature technique with a growing impact on the treatment of patients with severe aortic stenosis. Accumulating data have indicated promising results concerning procedural success, quality of life improvement, short- and more recently long-term outcomes,[1] but the clinically relevant limitations of TAVI are the occurrence of aortic regurgitation (AR) after valve implantation, which is mainly of paravalvular origin.[2,3] Data from various registries randomized TAVI trials have linked the occurrence of post-TAVI paravalvular AR (PAR) with increased in-hospital and long-term mortality,[2–6] which highlights the importance of prediction, prevention and treatment of PAR after TAVI.

We have recently identified anatomical and procedural variables strongly linked to the occurrence of PAR after implantation of the self-expandable Medtronic CoreValve prosthesis (MCP, Medtronic, Inc., Minneapolis, MN, USA), and a predictive model integrating the left ventricular outflow tract-to-ascending aorta angle ($\angle$LVOT-AO) and device depth in relation to the non-coronary cusp (NCC) was retrospectively identified ($2 \times \angle$LVOT-AO + [depth to NCC-10]2; cutoff = 50).[7] The purpose of the current study was to prospectively validate the previously derived model, and to investigate the clinical impact of adopting a strategy incorporating these measurable anatomical and procedural variables on the occurrence of PAR after TAVI using MCP.

2. Methods

2.1. Patient population

The previously published predictive model was retrospectively derived from a cohort of 50 consecutive patients treated with TAVI

using MCP.[7] The model is as follows: $2 \times \angle\text{LVOT-AO} + [\text{depth to NCC-10}]^2$; with a calculated cutoff of 50. The test is positive if it has a value of ≥ 50, and the predicted sensitivity was 85% and the specificity 86.7% for detection of significant ($\geq 2/4$) PAR after TAVI.[7]

In the period of 2 years, 108 consecutive patients were further treated with transfemoral TAVI using MCP at our institution. All patients had severe symptomatic aortic stenosis with an aortic valve area (AVA) <1.0 cm^2 or a body surface area-indexed AVA (iAVA) <0.6 cm^2/m^2. The baseline operative risk of the patients was calculated by the logistic European System for Cardiac Operative Risk Evaluation score (EuroSCORE).[8] The decision to perform TAVI was made by a multi-disciplinary team consisting of an interventional cardiologist, a conservative cardiologist, a cardiac surgeon and an anaesthesiologist, as suggested by current recommendations.[9] Eight patients were excluded from analysis (4 patients due to failure of valve implantation and 4 patients with previous bioprosthetic aortic valve replacement [valve-in-valve]), and thus the final study population consisted of 100 patients, which constituted a validation cohort where the suggested predictive model was prospectively evaluated. Data collection was approved by the institutional review board, and all patients provided a written informed consent for analysis of their anonymized data.

2.2. Pre-interventional assessment

Pre-interventional patient screening included transthoracic (TTE) and transesophageal echocardiography (TEE) to confirm diagnosis, assess aortic and aortic valve dimensions and morphology, and determine the grade and distribution of calcification. Invasive cardiac evaluation with coronary angiography, left ventriculography (in 30° right anterior oblique [RAO] and 50° left anterior oblique [LAO] projections), right heart catheterization and peripheral arteriography was performed in all patients. Multislice computed tomography (CT) was not routinely performed.

2.3. Device description and procedure

The MCP consists of a trileaflet bioprosthetic porcine pericardial tissue valve, which is mounted and sutured in a self-expanding nitinol stent. Details of the device have been described previously.[9] Clinical and anatomic selection criteria and device size selection were in line with the published investigational study for the third-generation (18 F) CoreValve device.[9] Selection of the prosthetic valve size (26 mm inflow device for 20–23 mm annulus, 29 mm inflow device for 23–27 mm annulus and 31 mm inflow device for 26–29 mm annulus) was based on the measurements of the diameter of the aortic valve annulus obtained by TEE. Vascular access was obtained percutaneously through the common femoral artery, and the procedure was performed with local anesthesia in combination with a mild systemic sedative/analgesic treatment. Details of the implantation procedure have been described elsewhere.[9]

2.4. Angle, depth and AR assessment

The angle of the LVOT to ascending aorta was considered as the angle between the axis of the first 4 cm of the ascending aorta representing the contact surface with the upper part of the prosthesis, and the LVOT axis representing the landing zone of the prosthesis and represented by a line perpendicular to the plane of the aortic valve annulus.[7] This angle was measured using left ventriculography in RAO 30° during the pre-intervention innovise assessment as previously described by our group (Fig. 1A).

Depth of final device position in the LVOT was measured using a final aortogram of the deployed bioprosthesis in RAO projection, displaying the aortic valve in optimal alignment with all 3 leaflets visible in the same plane.[7] The depth of delivery was defined as the distance from the native aortic annular margin on the side of the NCC to the most proximal edge on the corresponding side (deepest in the left ventricle) of the deployed stent-frame (Fig. 1B). The depth of delivery from the annular margin of the left coronary cusp (LCC) to the corresponding side was also measured. Both the $\angle\text{LVOT-AO}$ and the valve depth were measured using commercially available software (Jivex Dicom Viewer, version 4.0.2, VISUS Technology Transfer GmbH, Bochum, Germany) by 2 independent blinded observers to evaluate the reproducibility of measurements and to assess both intra- and inter-observer variability.

The endpoint of the study was the early occurrence of significant PAR, evaluated at the end of the procedure after valve implantation and corrective measures (including post-dilatation) if needed. Significant AR was defined as $\geq$ grade 2. Estimation of residual AR grade was done using qualitative angiography with visual estimation of the concentration of contrast medium in the left ventricle after pump injection of 35 cc of contrast in the aortic root.[10] Mild (grade 1) AR was diagnosed when a small amount of contrast entered the left ventricle during diastole and cleared with each systole. Moderate (grade 2) AR was diagnosed when more contrast entered with each diastole and faint opacification of the entire left ventricular chamber occurred, while a moderately severe (grade 3) AR was diagnosed when the left ventricular chamber was well opacified with an equal density compared with the ascending aorta. Severe (grade 4) AR was defined as complete, dense opacification of the ventricular chamber on the first beat, with the left ventricle more densely opacified than the ascending aorta.[10]

2.5. Statistical analysis

Statistical analysis was done using Minitab software (Minitab, Release 13.1, State College, Pennsylvania, USA). Data are expressed as mean ± SD, numbers and percent or as median and interquartile range. Comparisons of baseline and procedure-related characteristics of patients according to AR $\geq$ 2 or <2 as well as comparisons of derivation and validation cohorts were performed using the t test or chi-square test as appropriate. Sensitivity and specificity of the predictive model when prospectively applied were calculated. Intra- and inter-observer variability were evaluated using intra- and inter-observer variance and correlation coefficients for angles and depth and the whole predictive model. A p-value <0.05 was considered significant.

3. Results

3.1. Baseline characteristics

Overall, 100 consecutive patients treated with transfemoral TAVI using the MCP were included. Mean age was 79.6 ± 7.0 years and 41 patients were males. More than 70% of patients had concomitant coronary artery disease and 98% of patients were severely symptomatic at baseline with New York Heart Association functional class (NYHA) III or IV. After TAVI, 16 patients had significant post-procedural PAR ($\geq$grade 2), while 84 patients had no, trace or grade 1 PAR after MCP implantation. Table 1 illustrates the baseline clinical characteristics of the whole cohort and a comparison of patients with (group A) and without significant PAR (group B). Patients in group A were more commonly males (75.0% vs. 34.5%, p = 0.003), while other clinical characteristics were comparable.
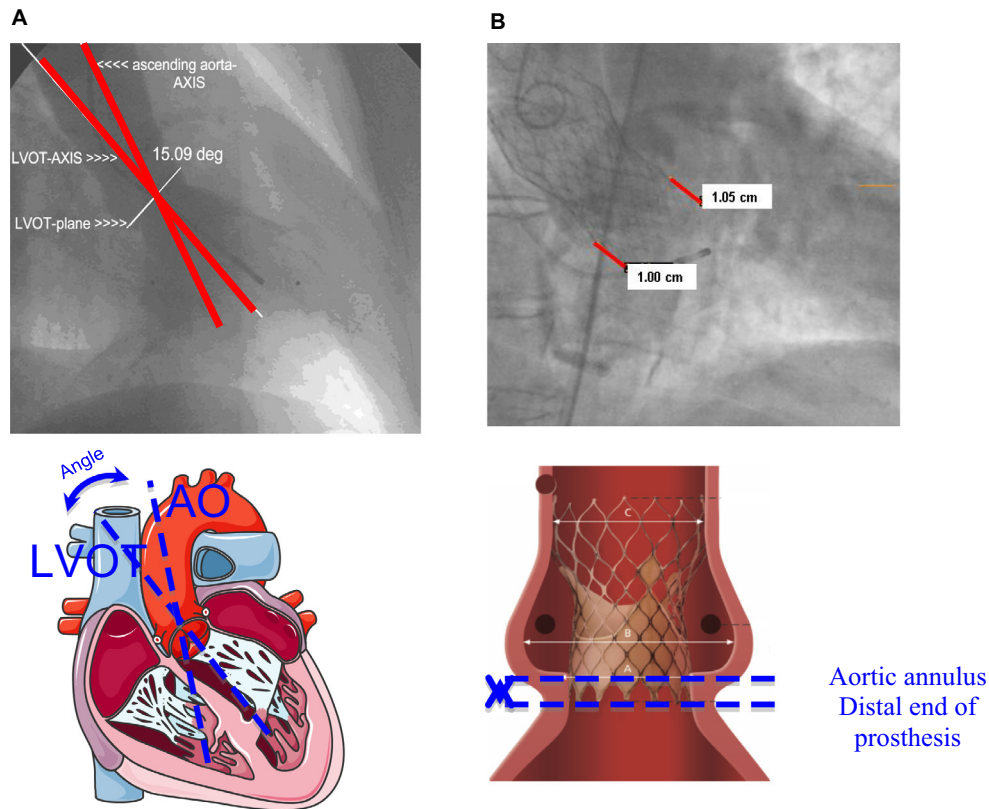
Figure 1. (A) Illustration of angle measurements between the LVOT and the ascending aorta, (B) Illustration of implantation depth measurements after MCP implantation.

Table 1
Baseline clinical characteristics.

	Total population (n = 100)	PAR ($\geq$2) (n = 16)	PAR < 2 (n = 84)	P-value[*]
Age, years	79.6 ± 7.0	81.6 ± 3.7	79.2 ± 7.4	0.19
Male	41 (41%)	12 (75%)	29 (34.5%)	0.003
BMI, kg/m^2	27.3 ± 5.9	26.9 ± 3.9	27.4 ± 6.2	0.80
Diabetes	24 (24%)	5 (31.3%)	19 (22.6%)	0.46
Hypertension	77 (77%)	14 (87.5%)	63 (75%)	0.28
Atrial fibrillation	30 (30%)	8 (50%)	22 (26.2%)	0.15
Dyslipidemia	56 (56%)	8 (50%)	48 (57.1%)	0.07
CAD	72 (72%)	10 (62.5%)	62 (73.8%)	0.36
Previous PCI	37 (37%)	5 (31.3%)	32 (38.1%)	0.60
Previous CABG	19 (19%)	0 (0%)	19 (22.6%)	0.09
PAD	14 (14%)	0 (0%)	14 (16.7%)	0.08
Carotid disease	15 (15%)	3 (18.8%)	12 (14.3%)	0.65
Previous stroke	9 (9%)	1 (6.3%)	8 (9.5%)	0.68
Logistic EuroSCORE	24.9 ± 16.3	21.9 ± 13.5	25.5 ± 16.8	0.34
NYHA class				0.64
II	2 (2%)	0 (0%)	2 (2.4%)	
III	85 (85%)	13 (81.3%)	72 (85.7%)	
IV	13 (13%)	3 (18.8%)	10 (11.9%)	
NT-pro-BNP, pg/ml	2804 (1434–7657)	2526 (1494–15635)	2812 (1417–7254)	0.62
S. creatinine, mg/dl	1.06 (0.8–1.4)	1.13 (0.9–1.5)	1.02 (0.8–1.4)	0.21

Values are illustrated as number (percentage), mean ± standard deviation or median (inter-quartile range).
BMI: body mass index, CAD: coronary artery disease, PCI: percutaneous coronary intervention, CABG: coronary artery bypass graft, PAD: peripheral arterial disease, NYHA: New York Heart Association, BNP: brain natriuretic peptide.
[*] p-values are calculated for the comparison between patients with PAR $\geq$ 2 and PAR < 2.

The mean AVA was 0.74 ± 0.27 cm^2 and the mean EF was 46.9 ± 16.1%. TTE and TEE data including a comparison between group A and group B are summarized in Table 2. The peak transvalvular pressure gradient before TAVI was significantly higher in group A compared to group B (86.3 ± 26.3 vs. 70.2 ± 23.9 mmHg, p-value = 0.02). Although the aortic annular size was larger in group A patients when compared to group B patients (24.8 ± 2.1 vs. 23.9 ± 2.6), however this was not statisti-

cally significant (p = 0.003). Other echocardiographic variables showed no significant differences between both groups.

3.2. Angiographic and procedural data

Angiographic and procedural data are summarized in Table 3 and Fig. 2. The mean annular diameter measured angiographically was larger in group A compared to group B (25.02 ± 2.3 vs. 23.9 ± 2

Table 2
Baseline transthoracic and transesophageal echocardiographic data.

	Patients (n = 100)	PAR (≥2) (n = 16)	PAR < 2 (n = 84)	P-Value*
AVA (continuity equation), cm/m²	0.74 ± 0.27	0.68 ± 0.2	0.76 ± 0.3	0.26
Degree of AR				0.74
0	27 (27%)	3 (18.8%)	24 (28.6%)	
1	55 (55%)	10 (62.5%)	45 (53.6%)	
2	9 (9%)	2 (12.5%)	7 (8.3%)	
3	4 (4%)	0 (0%)	4 (4.8%)	
4	2 (2%)	0 (0%)	2 (2.4%)	
Peak PG, mmHg	72.3 ± 25.2	86.3 ± 26.3	70.2 ± 23.9	0.02
Mean PG, mmHg	49.3 ± 16.2	54 ± 18.9	48.4 ± 15.5	0.23
MR				0.77
0	8 (8%)	1 (6.3%)	7 (8.3%)	
1	56 (56%)	8 (50%)	48 (57.1%)	
2	28 (28%)	6 (37.5%)	22 (26.2%)	
3	4 (4%)	0 (0%)	4 (4.8%)	
PAP, mmHg	45.3 ± 15.3	48.7 ± 13.4	44.6 ± 15.7	0.35
LVEDD, mm	48.9 ± 11.6	47.9 ± 9.6	49.2 ± 12.2	0.79
EF, %	46.9 ± 16.1	44.3 ± 17.3	47.4 ± 15.9	0.50
Posterior wall thickness, mm	14.7 ± 3.4	15.7 ± 1.8	14.5 ± 3.6	0.35
Septal wall thickness, mm	15.1 ± 3.2	16.5 ± 2.5	14.7 ± 3.2	0.1
AVA planimetry, cm²	0.7 ± 0.3	0.66 ± 0.16	0.73 ± 0.27	0.32
Aortic annulus, mm	24 ± 2.5	24.8 ± 2.1	23.9 ± 2.6	0.26
Sinotubular junction, mm	27.2 ± 3.1	26.6 ± 3.4	27.3 ± 3	0.59
Ascending aorta, mm	30 ± 3.9	31.2 ± 3.8	30 ± 3.9	0.28
Severe leaflet calcification	70 (70%)	13 (81.3%)	57 (67.9%)	0.28

Values are illustrated as number (percentage) or mean ± standard deviation.
AVA: aortic valve area, AR: aortic regurgitation, PG: pressure gradient, MR: mitral regurgitation, PAP: pulmonary artery pressure, LVEDD: left ventricular end-diastolic diameter, EF: ejection fraction.
* p-values are calculated for the comparison between patients with PAR ≥ 2 and PAR < 2.

Table 3
Angiographic and procedural data.

	Patients (n = 100)	PAR (≥2) (n = 16)	PAR < 2 (n = 84)	P-Value*
AVA (Gorlin's), cm²	0.6 ± 0.2	0.59 ± 0.23	0.6 ± 0.3	0.62
EF, %	47.6 ± 16.6	49 ± 19.7	47.3 ± 16.1	0.7
Peak-to-peak PG, mmHg	50.6 ± 19.3	55.6 ± 19.6	49.3 ± 19.6	0.26
AR pre				0.51
0	28 (28%)	3 (18.8%)	25 (29.8%)	
1	55 (55%)	10 (62.5%)	45 (53.6%)	
2	5 (5%)	2 (12.5%)	3 (3.6%)	
3	5 (5%)	1 (6.3%)	4 (4.8%)	
4	2 (2%)	0 (0%)	2 (2.4%)	
Annulus diameter, mm	24.1 ± 2.1	25.02 ± 2.3	23.9 ± 2.0	0.06
Valve size				0.73
26-mm inflow device	23 (23%)	3 (18.8%)	20 (23.8%)	
29-mm inflow device	74 (75%)	13 (81.3%)	62 (73.8%)	
31-mm inflow device	2 (2%)	0 (0.0%)	2 (2.4%)	
Balloon/annulus ratio	0.99 ± 0.08	0.99 ± 0.05	0.99 ± 0.9	0.73
Post-delivery inflation	35 (35%)	13 (81.3%)	22 (26.2%)	<0.001
AR post				<0.001
0	25 (25%)	0 (0%)	25 (29.8%)	
1	59 (59%)	0 (0%)	59 (70.2%)	
2	13 (13%)	13 (81.3%)	0 (0%)	
3	1 (1%)	1 (6.3%)	0 (0%)	
4	2 (2%)	2 (12.5%)	0 (0%)	
Procedural time, min	76.9 ± 20.4	88.1 ± 25.2	74.6 ± 18.9	0.09
LVOT-AO angle	12.5 ± 5	16.4 ± 7.2	11.8 ± 4.1	<0.001
Depth-NCC, mm	7 ± 3.2	9.1 ± 4.8	6.6 ± 2.7	0.004
Depth LCC, mm	7.8 ± 3.6	9.7 ± 5.4	7.4 ± 3.1	0.01

Values are illustrated in number (percentage) or mean ± standard deviation.
AVA: aortic valve area, EF: ejection fraction, PG: pressure gradient, AR: aortic regurgitation, LVOT: left ventricular outflow tract, AO: aorta, NCC: non-coronary cusp, LCC: left coronary cusp.
* p-values are calculated for the comparison between patients with PAR ≥ 2 and PAR < 2.

mm, p = 0.06). Post-delivery inflation was more commonly performed in group A patients (81.3% vs. 26.2%, p < 0.001). The ∠LVOT-AO was significantly larger in group A compared to group B (16.4 ± 7.2 vs. 11.8 ± 4.1, p < 0.001). Implantation depth of MCP to NCC was larger in group A (9.1 ± 4.8 vs. 6.6 ± 2.7 mm, p = 0.004), as was the implantation depth to LCC (9.7 ± 5.4 vs. 7.4 ± 3.1 mm, p = 0.018).

3.3. Model calculation, sensitivity and specificity for prediction of PAR after TAVI

Prospective application of the model was done in all patients. The mean calculated value in the whole cohort was 44.5 ± 22.2. Mean calculated values for group A and B were 54.8 ± 24.6 vs. 42.3 ± 21.3, respectively (p = 0.04). Applying our model in this
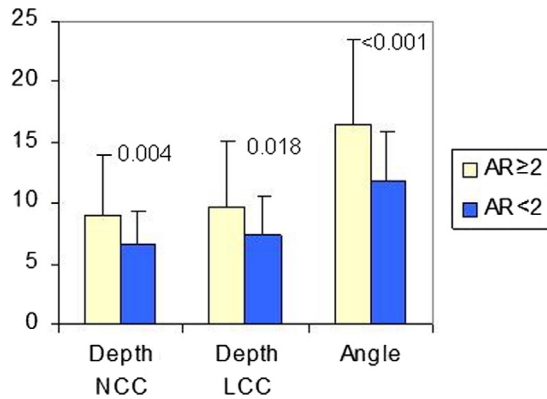
Figure 2. Clustered column chart comparing the mean and standard deviation values for depth and angle in the study population.

Table 4
Comparison of procedural data and outcomes for both derivation and validation cohorts.

	Derivation cohort ($n = 50$)	Validation cohort ($n = 100$)	P-Value
EuroSCORE, %	22.6 ± 11.5	25.0 ± 16.3	0.29
Annulus-TEE, mm	23.26 ± 1.4	24.03 ± 2.5	0.02
26 mm inflow device, n (%)	30 (60%)	23 (23%)	<0.001
Cover index	14.3 ± 5.5	15.6 ± 6.2	0.47
Post-delivery inflation, n (%)	4 (8%)	33 (33%)	0.001
Angle	19.7 ± 7.9	12.5 ± 4.9	<0.001
Depth NCC, mm	10.4 ± 3.7	6.9 ± 3.2	<0.001
Depth LCC, mm	11.35 ± 3.7	7.8 ± 3.6	<0.001
Post-procedural (≥2) PAR, n (%)	20 (40%)	16 (16%)	0.001

Values are illustrated as number (percentage) or mean ± standard deviation.
TEE: transesophageal echocardiography, NCC: non-coronary cusp, LCC: left coronary cusp.

cohort of patients had a sensitivity of 68.7% (the model was positive in 11/16 patients with significant PAR) and a specificity of 88.1% (the model was negative in 74/84 patients without significant PAR) for prediction of significant PAR after TAVI.

3.4. Reproducibility of angle and depth measurements

Intra-observer variability for angle measurements was 2.01 while inter-observer variability was 8.58. Intra-observer variability for depth measurements was 0.50 and the inter-observer variability was 1.23. Intra- and inter-observer variability for the whole predictive score were 23.22 and 62.87, respectively. Although the inter-observer variability for both the angle and the predictive score measurements was relatively high, there was little evidence that the second observer systematically recorded measurements either higher or lower than the first observer.

The intra-observer correlation coefficient for angle, depth and predictive score was 0.91, 0.96 and 0.95, respectively. The inter-observer correlation coefficient for angle, depth and the whole predictive score was 0.66, 0.87 and 0.85, respectively.

3.5. Comparison of procedural data and outcome of derivation vs. validation cohort

To evaluate the effect of integrating the described model on the incidence of PAR after TAVI, we compared procedural data and outcomes of the 50 patients from which the model was derived (initial experience = derivation cohort) and the following 100 patients (later experience = validation cohort) (Table 4). The prospective application of the model was reflected on patient selection and technical aspects of valve implantation. Patients of the validation cohort had significantly smaller angles when compared with those of the derivation cohort (12.5 ± 4.9 vs. 19.7 ± 7.9, $p < 0.001$) reflecting better patient selection. Similarly, depth of valve implantation was significantly less in the validation cohort when compared to the derivation cohort (6.9 ± 3.2 vs. 10.4 ± 3.7 mm for the NCC, $p < 0.001$, and 7.8 ± 3.6 vs. 11.3 ± 3.7 mm for the LCC, $p < 0.001$) (Figs. 3 and 4).

The cover index (100 × [prosthesis diameter − transesophageal echocardiography annulus diameter]/prosthesis diameter), which is used to evaluate the congruence between the annular size and selected device size, was not significantly different between the validation and derivation cohorts. Nevertheless, 60% of patients of the derivation cohort received the smaller 26-mm inflow device compared to only 23% of patients of the validation cohort. The incidence of significant AR decreased from 40% in the derivation cohort to 16% in the validation cohort ($p = 0.001$).

4. Discussion

The most important findings of the current study are as follows: first, PAR after TAVI using the MCP is common and can be related to identifiable anatomical and procedural factors; second, a predictive model for significant AR after MCP integrating two important factors (∠LVOT-AO and device depth) appears to be valid with an acceptable sensitivity and reassuring specificity and is reasonably reproducible; and third, a strategy incorporating these measurable anatomical and procedural variables can improve the results of MCP implantation with reduction in PAR.

As in-stent restenosis has long been the Achilles heel after percutaneous coronary intervention, AR seems to be the Achilles heel after TAVI. Minor paravalvular regurgitation is common with current valves, with an incidence ranging from 40% to 67%,[11–13] while the incidence of more than mild paravalvular regurgitation varies between 7% and 20%.[11–13] More than mild AR after TAVI is no longer considered benign, and patients with moderate or severe AR have higher in-hospital[2] and long-term mortality.[1,4,5] Therefore, anticipation and prevention of paravalvular leaks after TAVI remains an important target.

The occurrence of PAR might be related to the aortic root anatomy and its relation to the implanted prosthesis including the shape and size of the annulus, degree of annular and leaflets calcifications,[14] landing zone calcification,[15] LVOT anatomy and the prosthesis/annulus discongruence.[7,16] In addition to the inherent limitations of the interventional approach for valve therapy that lead to the higher incidence of AR when compared to surgical aortic valve replacement, specific device-related factors may also have an impact.

MCP, being a long device, is influenced by a variety of anatomical and procedural variables. Some of these variables are non-modifiable, such as the angle between the LVOT and aorta, which might influence the radial force of the prosthesis and its ability to completely seal the paravalvular space, while others can be modified such as the depth of prosthesis implantation in relation to the native aortic annulus. This was supported by the previous analysis of the derivation cohort patients ($n = 50$) that represent our initial experience with TAVI implantation. Both ∠LVOT-AO and depth of the implanted valve from the NCC were identified as independent predictors of AR after MCP implantation.[7] Similar to the analysis obtained from the initial derivation cohort, the ∠LVOT-AO and the final device depth were significantly larger in patients who developed post-procedural significant PAR in the population of the current study. This supports the notion that patients with large angles are less suitable for the MCP, and that
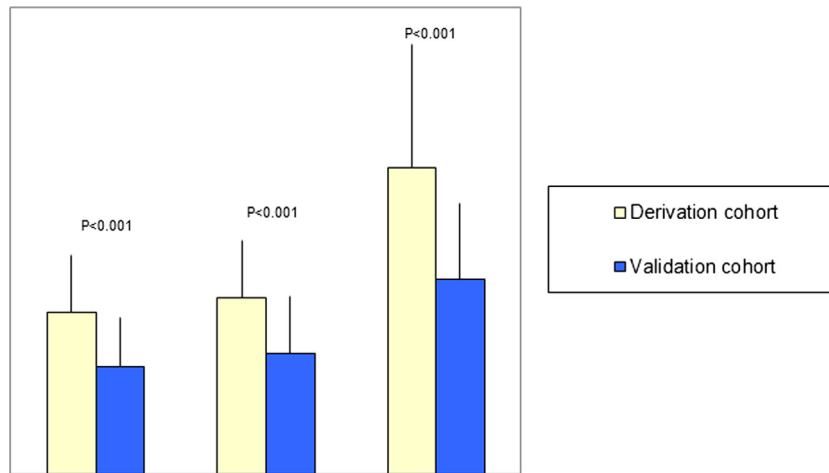
Figure 3. Clustered column chart representing mean and standard deviation values for depth and angle in both the derivation and validation cohorts.
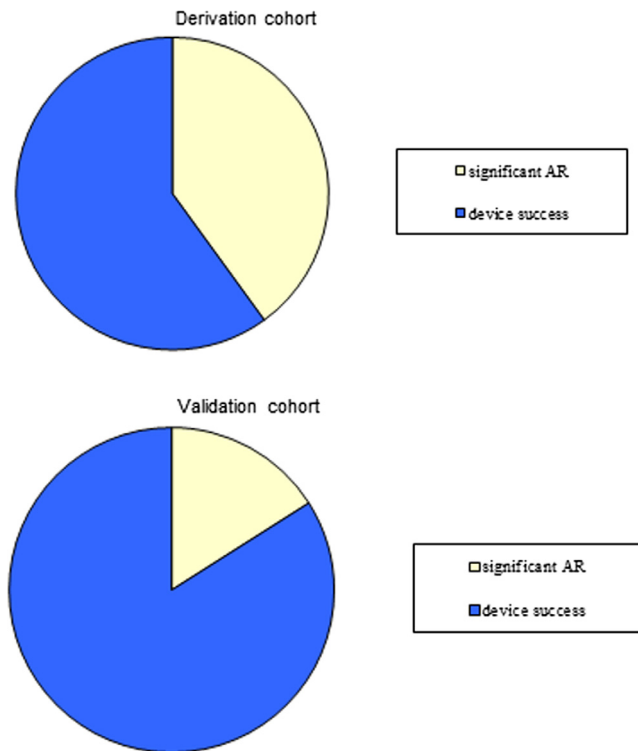

Figure 4. Pie diagram illustrating incidence of significant AR and device success rates in derivation (above) and validation cohorts (below).

deep implantation should be avoided to prevent post-procedural AR. Both factors are integrated in the described predictive model, which had the weakness of being retrospectively derived from a rather small patient population. This validation study was thus performed prospectively on a relatively larger patient population. Although the specificity has held-up well but the sensitivity, although not disastrous, is relatively low. We should put into consideration that only 16 patients in the validation cohort developed post-procedural significant AR making the estimation of the sensitivity relatively imprecise. The high specificity and acceptable sensitivity of the model in this prospective evaluation add to its robustness and underscore its validity.

As mentioned before, two independent blinded observers did the measurements that showed to be reasonably reproducible and the properties of the test seem to be robust against repeated observations and different observers. In addition, measurements for angle, depth and the whole predictive model can be easily performed in routine clinical practice.

Considering these 2 factors (∠LVOT-AO and implantation depth) together with integrating the predictive model into clinical practice resulted in better patient selection and significant improvement of the device success rate in our later experience when compared to our initial published experience. In our later experience, patients with extreme angulations (>25°) were not treated with the MCP. Higher attention was given to the depth of prosthesis implantation from the NCC, and deep device implantation was largely avoided (mean depth of MCP to NCC in validation vs. derivation cohorts was 6.9 ± 3.2 vs. 10.4 ± 3.7 mm, $p < 0.001$).

Another important point based on improved experience was the better echocardiographic assessment of the aortic annulus. Sizing of the aortic valve prosthesis is usually achieved in a multifactorial process that is based on ≥ 1 imaging modality and does not rely on a single echocardiographic measurement alone.[17] Growing evidence suggests that computed tomography (CT) offers valuable information about prosthesis sizing in TAVI and that incorporating CT-derived dimensions of the aortic annulus may improve outcome of the procedure[17] and this is one of the limitations of our work where CT analysis was not part of the routine preprocedural assessment at the time of the study performance. Although there was no significant difference between the cover index measurements (used to evaluate the congruence between the annular size and selected device size) in both validation and derivation cohorts, 60% of patients of the derivation cohort received the smaller 26-mm inflow device compared to only 23% of patients of the validation cohort. This might point to a possible underestimation of aortic annular measurements in the patients included in the derivation cohort leading to implantation of smaller valve sizes in underestimated larger annular sizes, which might be an additional cause for the higher incidence of post procedural AR in the derivation cohort. Similarly, post-delivery dilatation was more commonly performed in the validation cohort, aiming at reducing residual AR to the least possible degree.

Although several studies pointed out the importance of valvular and landing zone calcification in the occurrence or post-implantation paravalvular AR,[12,14] this was not evident in our study similar to the data of the prospective multicenter German TAVI registry.[18] This might be partly explained by the non-detailed description and evaluation of the calcium amount and

distribution in the current analysis, and the lack of systematic assessment with multislice CT.

4.1. Study limitations

Our data are only valid for the MCP and are not valid for other devices available for TAVI. Although the specificity of the model in the validation cohort is reassuringly high, the sensitivity is comparably low. This could be partially explained by the overall low incidence of AR in the validation cohort making the estimated sensitivity very imprecise. A larger sample size with higher incidence of AR would be needed for better assessment of sensitivity and applying that predictive model with newer valve generation sounds to be interesting as well. Detailed description of the calcification degree and distribution (especially the landing zone calcification) is missing in this analysis as multislice CT was not part of the pre-procedural patient evaluation during the study period.

5. Conclusion

This study confirms the validity of a previously derived predictive model for the occurrence of significant paravalvular AR after TAVI using the Medtronic CoreValve prosthesis, with a reassuring specificity and an acceptable sensitivity. Both ∠LVOT-AO and device depth measurements are reasonably reproducible. A strategy incorporating these measurable anatomical and procedural variables can reduce the incidence of paravalvular AR after TAVI and positively influence the procedural success rates.

Conflict of interest

We have no conflict of interest to declare.

References

1. Toggweiler S, Humphries KH, Lee M, Binder RK, Moss RR, Freeman M, et al.. 5-year outcome after transcatheter aortic valve implantation. *J Am Coll Cardiol.* 2013;61:413–419.
2. Abdel-Wahab M, Zahn R, Horack M, Gerckens U, Schuler G, Sievert H, et al.. Aortic regurgitation after transcatheter aortic valve implantation: incidence and early outcome. Results from the German transcatheter aortic valve interventions registry. *Heart.* 2011;97:899–906.
3. Vasa-Nicotera M, Sinning JM, Chin D, Lim TK, Spyt T, Jilaihawi H, et al.. Impact of paravalvular leakage on outcome in patients after transcatheter aortic valve implantation. *JACC Cardiovasc Interv.* 2012;5:858–865.
4. Moat NE, Ludman P, de Belder MA, Bridgewater B, Cunningham AD, Young CP, et al.. Long-term outcomes after transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis: The U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) Registry. *J Am Coll Cardiol.* 2011;58:2130–2138.
5. Tamburino C, Capodanno D, Ramondo A, Petronio AS, Ettori F, Santoro G, et al.. Incidence and predictors of early and late mortality after transcatheter aortic valve implantation in 663 patients with severe aortic stenosis. *Circulation.* 2011;123:299–308.
6. Kodali SK, Williams MR, Smith CR, Svensson LG, Webb JG, Makkar RR, et al.. PARTNER Trial Investigators. Two-year outcomes after transcatheter or surgical aortic-valve replacement. *N Engl J Med.* 2012;366:1686–1695.
7. Sherif MA, Abdel-Wahab M, Stöcker B, Geist V, Richardt D, Tölg R, et al.. Anatomic and procedural predictors of paravalvular aortic regurgitation after implantation of the Medtronic CoreValve bioprosthesis. *J Am Coll Cardiol.* 2010;56:1623–1629.
8. Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). *Eur J Cardiothorac Surg.* 1999;16:9–13.
9. Grube E, Schuler G, Buellesfeld L. Percutaneous aortic valve replacement for severe aortic stenosis in high-risk patientsusing the second- and current third-generation self-expanding CoreValve prosthesis: device success and 30-day clinical outcome. *J Am Coll Cardiol.* 2007;50:69–76.
10. Sellers RD, Levy MJ, Amplatz K, Lillehei CW. Left retrograde cardioangiography in acquired cardiac disease: technic, indications and Interpretations in 700 cases. *Am J Cardiol.* 1964;14:437–447.
11. Webb JG, Pasupati S, Humphries K, Thompson C, Altwegg L, Moss R, et al.. Percutaneous transarterial aortic valve replacement in selected high-risk patients with aortic stenosis. *Circulation.* 2007;116:755–763.
12. De Jaegere PP, Piazza N, Galema TW, Otten A, Soliman OI, Van Dalen BM, et al.. Early echocardiographic evaluation following percutaneous implantation with the self-expanding CoreValve Revalving System aortic valve bioprosthesis. *EuroIntervention.* 2008;4:351–357.
13. Walther T, Simon P, Dewey T, Wimmer-Greinecker G, Falk V, Kasimir MT, et al.. Transapical minimally invasive aortic valve implantation: multicenter experience. *Circulation.* 2007;116:I240–I245.
14. Haensig M, Lehmkuhl L, Rastan AJ, Kempfert J, Mukherjee C, Gutberlet M, et al.. Aortic valve calcium scoring is a predictor of significant paravalvular aortic insufficiency in transapical-aortic valve implantation. *Eur J Cardiothorac Surg.* 2012;41:1234–1240.
15. John D, Buellesfeld L, Yuecel S, Mueller R, Latsios G, Beucher H, et al.. Correlation of Device landing zone calcification and acute procedural success in patients undergoing transcatheter aortic valve implantations with the self-expanding CoreValve prosthesis. *JACC Cardiovasc Interv.* 2010;3:233–243.
16. Détaint D, Lepage L, Himbert D, Brochet E, Messika-Zeitoun D, Iung B, et al.. Determinants of significant paravalvular regurgitation after transcatheter aortic valve: implantation impact of device and annulus discongruence. *JACC Cardiovasc Interv.* 2009;2:821–827.
17. Achenbach S, Delgado V, Hausleiter J, Schoenhagen P, Min JK, Leipsic JA. SCCT expert consensus document on computed tomography imaging before transcatheter aortic valve implantation (TAVI)/transcatheter aortic valve replacement (TAVR). *J Cardiovasc Comput Tomogr.* 2012;6:366–380.
18. Staubach S, Franke J, Gerckens U, Schuler G, Zahn R, Eggebrecht Hon behalf of the German Transcatheter Aortic Valve Implantation-Registry Investigators. Impact of aortic valve calcification on the outcome of transcatheter aortic valve implantation: results from the prospective multicenter German TAVI registry. *Catheter Cardiovasc Interv.* 2013;81:348–355.