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BRIEF COMMUNICATION

# Predictors of permanent pacemaker implantation after ACURATE *neo* transcatheter heart valve implantation

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## Abstract

**Background:** Rates of permanent pacemaker implantation (PPI) have been low using the self-expanding ACURATE *neo* device, but data regarding risk factors of PPI for this specific device are scarce.

**Methods:** The study cohort consisted of patients ($n = 1000$) with severe aortic stenosis undergoing transfemoral transcatheter aortic valve implantation (TAVI) using the ACURATE *neo* prosthesis in our center between May 2012 and December 2019. For the present analysis, we excluded patients with previous permanent pacemaker ($n = 110$), high-grade AV block prior to TAVI ($n = 3$), and patients requiring conversion to surgical valve replacement ($n = 4$) or the implantation of a second prosthesis as valve-in-valve ($n = 15$). Preexisting conduction abnormalities were determined, and the implantation depth of the prosthesis was measured on final angiography. Differences across quartiles based on the original consecutive cohort were analyzed with respect to implantation depth and PPI rate. Predictors of PPI were identified using logistic regression.

**Results:** The PPI rate was 10%. Preexisting AV block I°, right bundle branch block (RBBB), and the implantation depth were independent predictors of PPI. Across quartiles, the implantation depth differed significantly with lowest values in the last quartile, whereas differences of PPI rates across quartiles were not statistically significant, but showed a notable decrease in the last quartile.

**Conclusion:** Preexisting RBBB, AV block I°, and low implantation depth were independent predictors of PPI following TAVI using the ACURATE *neo* device. Instead of deliberately aiming at a high position, avoidance of a low implantation depth may represent a reasonable compromise to reduce the rate of PPI without increasing the risk of malpositioning.

KEYWORDS
aortic stenosis, pacemaker implantation, self-expanding, TAVI, THV

**Abbreviations:** LCC, left coronary cusp; NCC, non coronary cusp; PPI, permanent pacemaker implantation; RBBB, right bundle branch block

## 1 | INTRODUCTION

Permanent pacemaker implantation (PPI) is a common complication after transcatheter aortic valve implantation (TAVI) that might adversely impact long-term outcome.[1] Reported frequencies of PPI vary and may be affected by diverse variables.[2] Among procedure-related factors, a lower implantation depth of the prosthesis has been found to increase the risk of PPI due to the anatomical proximity of the conduction system to the aortic annulus.[2] For the self-expanding ACURATE *neo* (Boston Scientific, Marlborough, MA, USA), PPI rates are among the lowest,[3] but a relationship with implantation depth was not observed in a recent study.[4] Limitations may have been a relatively small sample size and presumably an inadequate method of measuring the implantation depth. Hence, there is uncertainty regarding the optimal implantation depth for this specific device, as in the mid-term experience of using the ACURATE *neo*, a lower positioning was recommended to obtain best results in terms of paravalvular leakage[5] and to avoid aortic device embolization.[6]

The present study assessed the risk of PPI after TAVI with the ACURATE *neo* in a large cohort using a revised method of implantation depth measurement.

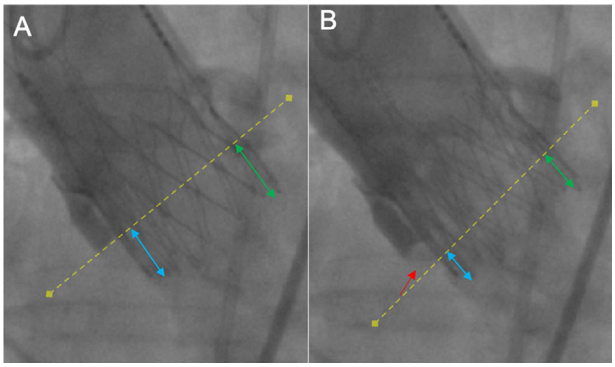


**FIGURE 1** Measurement of implantation depth. Implantation depth of the prosthesis at the non- (NCC; blue double arrows) and left coronary cusps (LCC; green double arrows). Panel A illustrates an erroneous measurement where only the contrasted area at the noncoronary cusp was considered, whereas Panel B depicts a proper measurement taking into account the noncontrasted areas of the sinus (red arrow). Lower implantation depth corresponds to a larger LCC or NCC depth (i.e., the distance between LCC or NCC and the lower valve frame), while higher implantation depth corresponds to smaller LCC or NCC depth [Color figure can be viewed at wileyonlinelibrary.com]

## 2 | METHODS

The data for the present analysis were derived from a previous registry of consecutive patients ($n = 1000$) with severe aortic stenosis undergoing transfemoral TAVI using the ACURATE *neo* prosthesis between May 2012 and December 2019.[7] For this specific analysis, we excluded patients with previous permanent pacemaker ($n = 110$), high-grade AV block prior to TAVI ($n = 3$), and those who required conversion to surgical valve replacement ($n = 4$) or the implantation of a second THV as valve-in-valve ($n = 15$). Preexisting conduction abnormalities (right [RBBB] and left bundle branch block; AV block I°) and the duration of the PQ interval and QRS complex were determined from a 12-channel ECG. The cover index was derived from computed tomography measurements in relation to the annular perimeter and left ventricular outflow tract (LVOT) diameter. The implantation depth of the prosthesis was defined as the distance in mm between the lower portion of the valve frame and the aortic annulus at the left and non coronary cusps (NCC) in the angiographic view chosen for valve deployment; this was accomplished by extrapolating the nadir of the sinus by taking into account the noncontrasted areas of the sinus due to displaced native leaflets instead of only measuring the contrasted areas (Figure 1).

The study was conducted in accordance to the Declaration of Helsinki and was approved by the ethics committee of the Justus-Liebig University of Giessen.

Continuous variables are presented as median and interquartile range [IQR] and were compared with the Mann–Whitney *U* test or Kruskal–Wallis rank test. Categorical data are presented as numbers and percentages and were compared using the two-sided Fisher's exact or the chi-square test. Patients were categorized according to quartiles of the original consecutive cohort ($n = 1000$) to preserve the different stages of the learning curve with the aim to compare the implantation depth in relation to the rates of PPI and ≥ moderate paravalvular leakage across quartiles. In the initial experience, the positioning strategy was indetermined, but was modified from a low positioning in quartile 2 to a higher positioning in quartile 4. Predictors of PPI were identified using multivariable binary logistic regression including all variables with *p*-values < .1 in the univariate analysis. The Hosmer–Lemeshow test based on 10 groups was applied to determine goodness-of-fit for the regression model. A two-sided *p*-value < .05 was considered significant. For all statistical analyses, STATA IC version 16.0 (StataCorp LCC, College Station, TX, USA) was used.

## 3 | RESULTS

Baseline characteristics and procedural results are summarized in Table 1. The final study cohort comprised 868 PPI-naïve patients. The PPI rate was 10% for all indications and 8.8% for high-degree AV block. The median time from TAVI to PPI was 4 days [IQR 1-7], and was nonsignificantly shorter for PPI due to high-degree AV block than for other indications (3 days [1-7] vs. 7 days [3.5-9.5]; $p = .051$). Preexisting RBBB, AV block I°, and the implantation depth at NCC (per each mm of depth increase: odds ratio 1.26 [95% CI 1.07-1.49]; $p = .005$) were independent predictors of PPI for high-degree AV block (Table 2). Across quartiles, the implantation depth at NCC differed significantly with lowest values in the last quartile ($p = .044$), whereas differences of PPI rates across quartiles were not statistically significant ($p = .52$), but compared to quartiles 1-3 markedly decreased in the last quartile (10.9% vs. 7.4%; $p = .14$; Figure 2).

**TABLE 1** Baseline characteristics and procedural data

| Variable | Total cohort ($n = 868$) |
|---|---|
| Age (years) | 81.9 [78.5-84.9] |
| Female sex | 582 (67.1%) |
| Body mass index (kg/m$^2$) | 26.8 [24.1-30.5] |
| EuroSCORE II (%) | 4.0 [2.5-6.8] |
| STS PROM | 3.9 [2.8-5.8]; $n = 733$ |
| eGFR (mL/min/1.73 m$^2$) | 66.5 [48.0-85.0] |
| Atrial fibrillation | 309 (35.6%) |
| Ejection fraction (%) | 65.0 [60.0-65.0] |
| Aortic mean pressure gradient (mmHg) | 42.0 [32.0-51.0] |
| Aortic valve area (cm$^2$) | 0.7 [0.6-0.8] |
| Annulus perimeter (mm) | 23.7 [22.7-24.9] |
| Cover index annulus (%) | 5.2 [3.2-7.4] |
| Cover index LVOT (%) | 10.4 [6.3-14.8] |
| Aortic valve calcium score (AU) | 2094 [1492-2873] |
| Baseline AV block 1° | 181/683 (26.2%) |
| Baseline RBBB | 81 (9.3%) |
| Baseline LBBB | 100 (11.5%) |
| PQ duration (ms) | 178 [160-200] |
| QRS width (ms) | 100 [92-114] |
| Prosthesis size | |
| S | 224 (25.8%) |
| M | 378 (43.6%) |
| L | 266 (30.7%) |
| Procedural duration (min) | 35.0 [29.0-44.0] |
| Fluoroscopy time (min) | 8.8 [6.6-11.9] |
| Contrast agent (mL) | 85.0 [65.0-110.0] |
| Predilatation | 589 (67.9%) |
| Postdilatation | 336 (38.7%) |
| Implantation depth | |
| Non coronary cusp (mm) | 5.0 [4.0-6.0] |
| Left coronary cusp (mm) | 6.0 [4.0-6.0] |
| Pacemaker implantation | 87 (10.0%) |
| For AV block 2° or 3° | 76 (8.8%) |
| Other indications[a] | 11 (1.2%) |
| Time from TAVI to pacemaker implantation (days) | 4 [1-7] |
| For AV block 2° or 3° (days) | 3 [1-7] |
| Other indications[a] (days) | 7 [3.5-9.5] |
| 30-day mortality | 16/862 (1.9%) |

Data are displayed as median [interquartile range] and *n* (%).

Abbreviations: eGFR, estimated glomerular filtration rate; LBBB, left bundle branch block; RBBB, right bundle branch block.

[a]Indications for permanent pacemaker indication other than high-degree AV block included sick sinus syndrome ($n = 9$), bifascicular block and new onset AV block I° ($n = 1$), and implantation of an internal cardiac defibrillator due to ventricular tachycardia ($n = 1$).

**TABLE 2** Binary logistic regression for predictors of permanent pacemaker implantation

| | Univariate analysis | | Multivariable analysis[a] | |
|---|---|---|---|---|
| | Odds ratio [95% CI] | *p*-Value | Adjusted odds ratio [95% CI] | *p*-Value |
| Preexisting RBBB | 5.06 [2.88-8.88] | <.001 | 5.34 [1.27-22.47] | .022 |
| Preexisting LBBB | 1.85 [0.99-3.45] | .052 | 1.20 [0.31-4.71] | .789 |
| Preexisting AV block 1° | 2.21 [1.27-3.85] | .005 | 2.46 [1.29-4.71] | .016 |
| Preexisting RBBB and AV block 1° | 8.62 [3.15-23.63] | <.001 | 0.71 [0.17-2.87] | .626 |
| Preexisting LBBB and AV block 1° | 1.97 [0.74-5.33] | .177 | | |
| QRS width (ms) | 1.03 [1.02-1.03] | <.001 | 1.01 [0.99-1.03] | .362 |
| Depth NCC (mm) | 1.19 [1.06-1.34] | .004 | 1.26 [1.07-1.49] | .005 |
| Cover index annulus (%) | 1.05 [0.96-1.13] | .274 | | |
| Cover index annulus ≥ 10% | 1.46 [0.34-6.22] | .611 | | |
| Cover index LVOT (%) | 1.00 [0.98-1.02] | .775 | | |
| Aortic valve calcium score (AU) | 0.99 [0.99-1.00] | .631 | | |
| Predilatation | 1.42 [0.88-2.30] | .154 | | |
| Postdilatation | 1.03 [0.63-1.66] | .918 | | |
| Pre- and postdilatation | 1.22 [0.71-2.07] | .469 | | |

Abbreviations: CI, confidence interval; LVOT, left ventricular outflow tract; LBBB, left bundle branch block; NCC, noncoronary cusp, RBBB, right bundle branch block.
[a]Hosmer–Lemeshow chi$^2$ (10 groups): 11.17; $p = .192$.

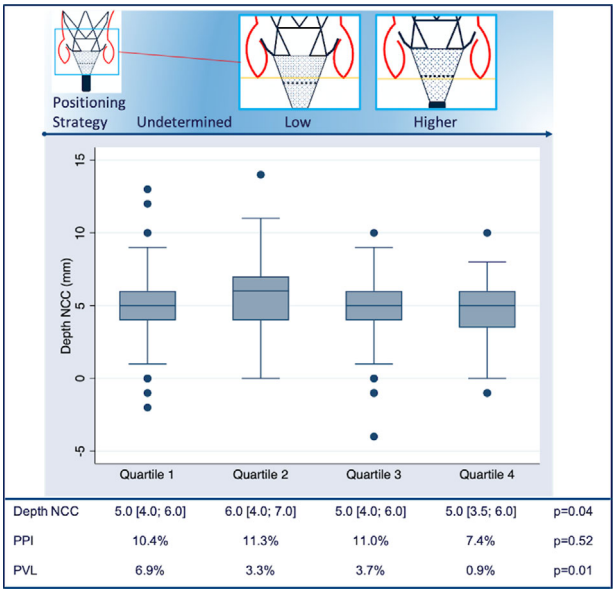


**FIGURE 2** Impact of implantation depth on the rate of permanent pacemaker implantation across quartiles. Association between implantation depth at the NCC and rates of PPI and PVL ≥ moderate across the quartiles of our consecutive experience using the ACURATE *neo* prosthesis. We maintained the categorization of the original cohort ($n = 1000$) to preserve the different stages of the learning curve. In the initial experience, the positioning strategy was indetermined, but was modified from a low positioning in quartile 2 to a higher positioning in quartile 4, which resulted in a significant difference of the implantation depth at the NCC ($p$-values are derived from Kruskal–Wallis test). Even though differences regarding PPI rates were not significant across the quartiles, the drop of the PPI rate in quartile 4 is notable (quartile 1-3: 10.9% vs. quartile 4: 7.4%; $p = .14$) and most likely is related to the higher implantation depth. The decrease of the ≥ moderate PVL rate is rather related to the improved selection and sizing strategy over time and was not affected by implantation depth. Abbreviations: NCC, noncoronary cusp; PPI, permanent pacemaker implantation; PVL, paravalvular leakage ≥ moderate. [Color figure can be viewed at wileyonlinelibrary.com]

## 4 | DISCUSSION

Our finding that preexisting conduction disturbances—in particular RBBB—independently predicted PPI is consistent with existing literature.[8] Conversely, the association of a lower implantation depth with PPI as observed in the present analysis contradicts previous data.[4] This may be related to the considerably larger sample size and the revised methodology of implantation depth measurement (Figure 1). Recently, it was shown that contrary to previous assumptions[5] the implantation depth of the ACURATE *neo* does not impact paravalvular leakage.[7] Hence, a higher position appears to reduce the burden of PPI without compromising the incidence of paravalvular leakage. Figure 2 illustrates that the positioning strategy was modified from a low positioning in quartile 2 to a somewhat higher positioning (rather normal positioning approach) in quartile 4, which resulted in a significant difference of the implantation depth at the NCC. Even though PPI rates were not significantly different across the quartiles, the drop of the PPI rate in quartile 4 is notable and most likely is related to the higher device position and not to adjusted selection or procedural strategies as shown in the multivariable analysis (Table 2). By contrast, the decrease of the PVL ≥ moderate rate was rather related to the improved selection and sizing strategy over time and was not affected by implantation depth.[7] It should be emphasized that a deliberately too high positioning may not be advisable due to the increasing risk of prosthesis migration, albeit an intentionally deep implantation should be avoided. Of note, an impact of annular oversizing, LVOT size, and pre- or postdilatation on PPI, as previously presumed,[3] was not observed in the present study. In particular, the finding that oversizing had no effect on the PPI rate contradicts previous studies with other devices,[9,10] but may be ascribed to the lesser degree of oversizing using the ACURATE *neo* valve with a median cover index of 5.2% in this cohort, and the specific distribution of radial force that has its maximum in the mid stent-body and decreases markedly in the inflow part.[11]

Apart from its retrospective nature, the main limitation of this study is the use of fluoroscopy images to measure the implantation depth, which may not represent the "true" extent of the prosthesis position. However, the uniform approach we used for implantation depth measurement may be sufficient for a comparative analysis to detect interindividual differences. Strengths of this manuscript are the large and homogeneous study cohort and the comprehensive analysis of predictors that included ECG, computed tomography, and procedural data.

## 5 | CONCLUSIONS

In this large cohort of patients treated with the ACURATE *neo* prosthesis, preexisting RBBB, AV block I°, and low implantation depth were independent predictors of PPI. Instead of deliberately aiming at a high position, avoiding a low implantation depth may represent a reasonable compromise to reduce the rate of PPI without increasing the risk of malpositioning.

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### AUTHOR CONTRIBUTIONS

*Concept and design, data collection and analysis, and drafting of the manuscript*: Won-Keun Kim. *Drafting, critical revision, and approval of the manuscript*: Helge Möllmann, Thomas Walther, and Christian W. Hamm.

### CONFLICT OF INTEREST

Won-Keun Kim: Proctor fees and/or speaker honoraria from Abbott, Boston Scientific, Edwards Lifesciences, and Medtronic; Helge Möllmann: Proctor fees and/or speaker honoraria from Abbott, Boston Scientific, Biotronik, and Edwards Lifesciences; Christian W. Hamm: Advisory board Medtronic. All other authors declare that they have no conflict of interest.

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