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Risk of conduction disturbances following different transcatheter aortic valve prostheses: the role of aortic valve calcifications

Francesco Pollari[1,✉], Ferdinand Vogt[1], Irena Großmann[1], Jill Marianowicz[1], Marie Claes[1], Steffen Pfeiffer[1], Johannes Schwab[2,3], Theodor Fischlein[1]

1. Cardiac Surgery, Cardiovascular Center, Klinikum Nürnberg, Paracelsus Medical University, Nuremberg, Germany;
2. Cardiology, Cardiovascular Center, Klinikum Nürnberg, Paracelsus Medical University, Nuremberg, Germany;
3. Radiology, Klinikum Nürnberg, Paracelsus Medical University, Nuremberg, Germany

✉ Correspondence to: francesco.pollari@klinikum-nuernberg.de
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ABSTRACT

OBJECTIVES To assess the impact of prosthesis choice and aortic valve calcifications on the occurrence of conduction disturbances after transcatheter aortic valve implantation (TAVI).

METHODS We retrospectively analyzed the preoperative clinical characteristics, electrocardiograms, contrast-enhanced multidetector computed tomography scans and procedural strategies of patients who underwent TAVI in our center between January 2012 and June 2017. Quantification of calcium volume was performed for each aortic cusp above (aortic valve) and below (left ventricular outflow tract, LVOT) the basal plane. Multivariate analysis was performed to evaluate risk factors for the onset of new bundle branch block (BBB), transient and permanent atrioventricular block (tAVB, pAVB).

RESULTS A total of 569 patients were included in the study. Six different prostheses were implanted (Edwards Sapien XT, n = 162; Edwards Sapien 3, n = 240; Medtronic CoreValve, n = 27; Medtronic CoreValve Evolut R, n = 21; Symetis Acurate, n = 56; Symetis Acurate neo, n = 63). The logistic regression analysis for BBB showed association with baseline left anterior hemiblock. The logistic regression for tAVB, found the prior valvuloplasty and the balloon post-dilatation associated with the outcome. Baseline left and right BBB, degree of oversizing, and LVOT calcification beneath the non-coronary cusp were associated with pAVB. Neither the prosthesis model, nor the use of a self-expandable prosthesis showed statistical significance with the above-mentioned outcomes on univariate analysis.

CONCLUSIONS LVOT calcification beneath the non-coronary cusp, baseline left anterior hemiblock, right BBB, balloon post-dilatation, prior valvuloplasty and oversizing are independently associated with postprocedural conduction disturbances after TAVI. Use of a self-expandable prosthesis may show a lower incidence of AVB, if applied in lower calcified aortic valves.

Transcatheter aortic valve implantation (TAVI) has emerged as a valid alternative to surgical aortic valve replacement (SAVR) for severe aortic valve stenosis but concerns about the high incidence of some complications are yet limiting its wider application in low-risk and young patients.[1] Conduction disturbances, such as a high degree atrioventricular block (AVB) or postprocedural bundle branch block (BBB), are relevant complications and are associated with increased risk of all-cause death and heart failure hospitalization during follow-up.[2,3] We previously investigated the factors associated with AVB in a cohort receiving a balloon-expandable prosthesis, finding aortic valve calcification as a novel risk factor, together with other patient-related as well as procedural variables.[4] However, scarce evidence is available regarding the interaction of different prosthesis models in different settings of valve calcification.

The aim of this study was to assess the risk of the different prostheses on the onset of the conduction disturbances following TAVI considering the grade and distribution of valve calcification.

METHODS

Study Population and Outcomes

We enrolled retrospectively all consecutive patients that underwent TAVI in our institution between January 2012 and June 2017. Exclusion criteria were: bicuspid aortic valve, baseline pure aortic valve regurgitation and aborted procedures because of annulus diameter of > 30 mm. Overall, 713 patients were treated in this period of time. After exclusion of the valve-in-valve procedures (n = 42) and/or of those patients who had a previous pacemaker implantation (n = 75), and implantation of prostheses in the pre-market phase (n = 5), all patients who underwent TAVI for symptomatic severe stenosis of the native aortic valve were included in the study. Severe aortic valve stenosis was defined in accordance with international guidelines.[5] Overall, 592 patients were eligible for the study. However, four patients had no preoperative contrast-enhanced multidetector computed tomography (MDCT) scans because of severe renal impairment; and in 19 patients preoperative electrocardiograms (ECGs) were not retrievable. Thus, a total of 569 patients were evaluable (Figure 1). Baseline ECGs were retrospectively evaluated by one investigator unaware of the clinical data for the presence of conduction abnormalities as defined by the American Heart Association/American College of Cardiology recommendations for ECG standardization and interpretation.[6] Clinical and operative data were prospectively collected in our institutional database for internal quality control. According to the Valve Academic Research Consortium (VARC)-2 recommendations, the following intraoperative and in-hospital outcomes were recorded: postoperative transient/reversible (tAVB, defined as any third-degree AVB or Mobitz type II second-degree AVB lasting less than 7 days or not requiring a permanent pacemaker implantation, "permanent pacemaker implantation (PPI)", before hospital discharge), permanent/non-reversible (pAVB) high-degree AVB (defined as third-degree AVB or Mobitz type II second-degree AVB lasting at least 7 days following the procedure or needing a PPI before hospital discharge), and a new-onset or worsening intraventricular conduction delay (BBB, including

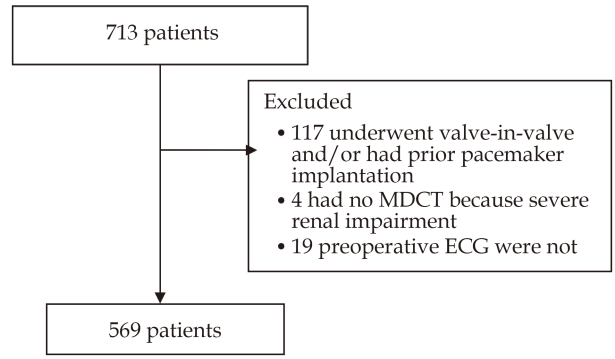

Figure 1 Flowchart of the selection process of the study population. MDCT: multidetector computed tomography.

incomplete or complete left BBB or left anterior hemiblock [LAHB]).[7] Other procedural complications were also recorded: unplanned cardiopulmonary bypass, conversion to surgery, coronary obstruction, valve prosthesis malpositioning, second prosthesis implantation and intraoperative percutaneous coronary intervention, immediate procedural mortality, in-hospital mortality, 30-day mortality. All patients provided written informed consent for the use of their data anonymously, and the study was approved by our institutional review board (IRB-2017-006). The study protocol conforms to the ethical guidelines of the Declaration of Helsinki.

Computed Tomography Angiography and Calcium Quantification

Patients underwent contrast-enhanced ECG-gated MDCT (330 ms rotation, helical mode, 60%-70% gating, 0.6 × 64 mm collimation, 50-100 mL of i.v. contrast agent (Solutrast 370, Bracco Imaging Deutschland GmbH, Konstanz, Germany) at 4 mL/s) for assessment of aortic root anatomy (suitability for TAVI) and femoral and pelvic vessel calcification and tortuosity (suitability for transfemoral (TF) approach). All MDCT studies were performed with a 64-slice SOMATOM Definition AS (Siemens Healthcare GmbH, Erlangen, Germany). MDCT data were analyzed by the implanting team, using 3mensio Structural Heart software (v. 7.0 SP1, Medical Imaging BV, Bilthoven, the Netherlands) in order to plan the procedure, as previously described.[4,8] Three-dimensional analysis of MDCT scans allowed assessment of the basal plane (aortic annulus), defined as the virtual plane crossing the nadir of each aortic cusp in diastole. The following data were prospect-

ively collected: virtual basal annular dimensions (maximum and minimum diameter), area, circumference, left and right coronary ostium distance from the basal plane. Calcium volume in the aortic valve was retrospectively measured using 3mensio Structural Heart in three different regions of interest: (1) in the aortic valve from the basal plane to the origin of the lowest coronary ostium; (2) from the basal plane to 10 mm into the left ventricular outflow tract (LVOT)—these two regions of interest were considered either as a whole or for each cusp separately; (3) in the device landing zone (DLZ), defined as the sum of the first two (Figure 2). After manual adjustment, the software automatically performed separation of the three aortic valve cusps (left = LCC; right = RCC and non-coronary = NCC). The threshold for calcium detection was set to two different cut-off values depending on the average Hounsfield units (HU) of blood in the ascending aorta. For values between 130 and 300 HU, a threshold of 500 HU was chosen, in line with previous studies.[9–11] In contrast, for values between 300 and 600 HU (55 patients), an empiric threshold of 800 HU was chosen. Measurements of calcium volume were performed by two investigators experienced in TAVI procedures and trained for the use of 3mensio (F.P. and F.V.). Interobserver variability was tested for the first 30 cases by a third cardiac surgeon (S.P.).

The degree of over- or undersizing was calculated as the prosthesis valve area (provided by the manufacturer)/MDCT annular area ratio. Prosthesis valve area was derived according to the geometrical rule: $A = \pi(d/2)^2$, where d is the labeled prosthesis size. The aortic annulus eccentricity index was calculated on the basis of MDCT annulus measurements as 1 – (shortest diameter/longest diameter).

Heart Team, TAVI Procedure and Management of Postoperative Conduction Disturbances

Our institutional Heart Team and TAVI procedure were extensively described in previous articles.[4,8] Briefly, the indication for TAVI is discussed within a Heart Team, composed of at least one cardiologist and one cardiac surgeon evaluating patients according to international guidelines.[4,5] TF-TAVI was preferred as first choice in all patients with suitable anatomy; alternatively, the transapical (TA-TAVI) access was used. All procedures were conducted in a hybrid operating room under fluoroscopic control (Artis Zeego System, Siemens AG, Erlangen, Germany), general anesthesia, periprocedural transesophageal echocardiography, and a cardiac perfusionist with ready-to-use cardiopul-

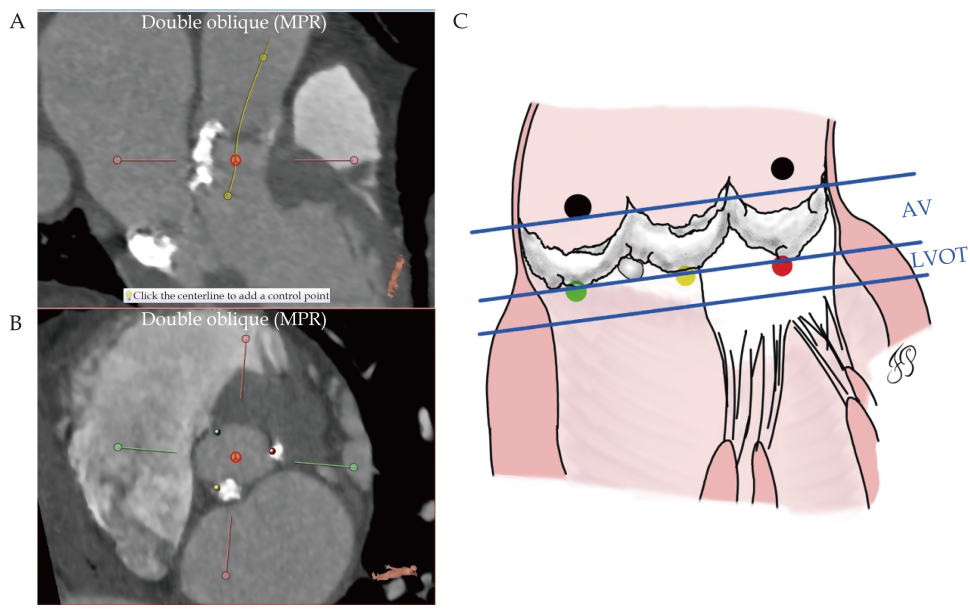

Figure 2 Aortic calcium volume quantification on MDCT. (A): Stretched vessel view of the aortic valve and ascending aorta; (B): transverse view of the native aortic valve with the three points identifying the basal plane (yellow = nadir of right coronary cusp; cyan = nadir of left coronary cusp; magenta = nadir of non-coronary cusp); and (C): draw highlighting of the region of interest of calcium scoring. AV: aortic valve; LVOT: left ventricular outflow tract; MDCT: multidetector computed tomography.

monary bypass on site. All implantations were performed by a multidisciplinary team composed of at least one cardiologist and a cardiac surgeon. Six different transcatheter heart valve prostheses were implanted in our center during the study period: Sapien XT/Sapien 3 (Edwards Lifesciences Inc., Irvine, CA), CoreValve/Evolut R (Medtronic, Minneapolis, MN), and Acurate/Acurate Neo (Symetis SA, Ecublens, Switzerland). Selection of the prosthesis type was preoperatively agreed with the cardiologist and the cardiac surgeon on the basis of several parameters: annular dimensions (based upon the perimeter-derived area of the aortic annulus), annular eccentricity, probability of needing future coronary catheterization, and distance of coronary arteries from the annulus.

Patients were extubated at the end of the procedure in the hybrid room and transferred to an intermediate care unit (IMCU) for at least 24-h monitoring (3-lead ECG and invasive blood measurement). 12-lead ECGs were obtained at admission to IMCU and at discharge. In case of bradycardia or AVB, monitoring was prolonged, and an electrophysiologist was consulted. PPI was performed in case of symptomatic bradycardia or high-degree AVB (Mobitz type II or III second-degree AVB) during up to 7 days, according to international guidelines.[12] In case of transient AVB, an observation time of 7 days was applied, whenever clinically possible, starting from the interruption of any beta blockers.

Statistical Analysis

Categorical variables are expressed as frequencies (percentages) and continuous variables as mean ± SD or median (interquartile range). Differences between groups were determined by ANOVA testing with Bonferroni correction and Kruskal-Wallis test. Predictors of BBB and high-degree AVB were evaluated using stepwise multivariate logistic regression, with probability of entry into the model set at 0.1. Clinical, procedural, ECG, echocardiographic, and preoperative MDCT variables were entered into univariate analysis. Statistical significance was assumed at a *P*-value of < 0.05. Statistical analysis was performed using SPSS software (IBM SPSS Statistics, Release 20.0.0, SPSS Inc., Chicago, IL, USA).

RESULTS

The study population consisted of 569 consecutive patients, of whom 397 were treated through a TF approach: 240 received a Sapien 3 (of whom 184 TF), 162 a Sapien XT (of whom 59 TF), 63 an Acurate neo (all TF), 56 an Acurate (all TA), 21 an Evolut R (all TF) and 27 a CoreValve (all TF).

Baseline characteristics of study groups are shown in Table 1. Supplementary table 1 shows the baseline characteristics according to the deployment-type (ie, ballon-expandable and self-expandable). In terms of clinical and demographic characteristics, the only significant difference between groups was the incidence of prior valvuloplasty, which was absent in the Acurate neo and CoreValve groups and interested only one patient in the Sapien 3 group. Also, the preoperative ECG findings showed no significant differences but the presence of negative T waves which were more frequent in the Acurate,

Table 1 Baseline characteristics of the study population.

	Acurate (*n* = 56)	Acurate neo (*n* = 63)	CoreValve (*n* = 27)	Evolut R (*n* = 21)	Sapien XT (*n* = 162)	Sapien 3 (*n* = 240)	*P*-value
Demographic characteristics							
Age, yrs	81.1 ± 5.7	82.7 ± 5.3	79.7 ± 8.9	81.3 ± 5.6	81.8 ± 6.4	81.6 ± 5.6	0.373
Female gender	29 (51.8%)	37 (58.7%)	10 (37%)	12 (57.1%)	88 (54.3%)	122 (50.8%)	0.518
BMI, kg/m^2	27.4 ± 5.4	27.8 ± 5	26.4 ± 5.1	27.3 ± 5.4	27 ± 4.9	27 ± 5.1	0.864
Creatinine, mg/dL	1.7 ± 1.4	1.3 ± 0.6	1.2 ± 0.6	1.2 ± 0.4	1.4 ± 0.9	1.5 ± 1	0.147
Extracardiac arteriopathy	25 (44.6%)	12 (19%)	6 (22.2%)	5 (23.8%)	47 (29%)	70 (29.2%)	0.06
Redo	14 (25%)	7 (11.1%)	5 (18.5%)	3 (14.3%)	38 (23.5%)	40 (16.7%)	0.211
Prior CABG	13 (23.2%)	7 (11.1%)	5 (18.5%)	3 (14.3%)	29 (17.9%)	34 (14.2%)	0.482
Prior valvuloplasty	2 (3.6%)	0 (0%)	0 (0%)	1 (4.8%)	7 (4.3%)	1 (0.4%)	0.046
COPD	11 (19.6%)	8 (12.7%)	7 (25.9%)	2 (9.5%)	32 (19.8%)	47 (19.6%)	0.576

Continued

	Acurate (*n* = 56)	Acurate neo (*n* = 63)	CoreValve (*n* = 27)	Evolut R (*n* = 21)	Sapien XT (*n* = 162)	Sapien 3 (*n* = 240)	*P*-value
IDDM	2 (3.6%)	3 (4.8%)	0 (0%)	0 (0%)	3 (1.9%)	7 (2.9%)	0.693
NIDDM	22 (39.3%)	18 (28.6%)	7 (25.9%)	7 (33.3%)	50 (30.9%)	75 (31.3%)	0.811
Recent myocardial infarction	3 (5.4%)	2 (3.2%)	0 (0%)	0 (0%)	9 (5.6%)	4 (1.7%)	0.205
EF (%)	51.9 ± 11.8	55.8 ± 12.2	49 ± 12.9	54.3 ± 9.5	53.3 ± 13.3	52.2 ± 12.5	0.18
Severe PHT	12 (21.4%)	18 (28.6%)	8 (29.6%)	6 (28.6%)	56 (34.6%)	82 (34.2%)	0.495
Prior PCI	17 (30.4%)	21 (33.3%)	9 (33.3%)	6 (28.6%)	57 (35.2%)	74 (30.8%)	0.952
ECG findings							
Heart rate	75.7 ± 17.2	74.8 ± 15.1	81 ± 13.3	78.2 ± 13	76.9 ± 15.4	77.1 ± 16.9	0.66
Sinus rhythm	33 (58.9%)	44 (69.8%)	16 (59.3%)	17 (81%)	116 (71.6%)	157 (65.4%)	0.28
Atrial fibrillation	23 (41.1%)	19 (30.2%)	11 (40.7%)	4 (19%)	46 (28.4%)	83 (34.6%)	0.28
LAHB	2 (3.6%)	1 (1.6%)	10 (37%)	0 (0%)	5 (3.1%)	9 (3.8%)	0.75
LBBB	4 (7.1%)	6 (9.5%)	3 (11.1%)	3 (14.3%)	21 (13%)	20 (8.3%)	0.66
RBBB	7 (12.5%)	6 (9.5%)	6 (22.2%)	3 (14.3%)	16 (9.9%)	23 (9.6%)	0.45
PR interval, ms	183.2 ± 39.5	182.1 ± .48	175.5 ± 40.1	165.4 ± 38.6	172.1 ± 38.4	179.8 ± 96.9	0.88
QRS duration, ms	102.3 ± 23.2	100.1 ± 25.7	105.4 ± 26.2	106.1 ± 31	103.5 ± 25.8	100.5 ± 24.2	0.73
Q waves	26 (46.4%)	41 (22%)	11 (40.7%)	5 (23.8%)	66 (40.7%)	106 (44.2%)	0.36
Negative T waves	44 (78.6%)	33 (52.4%)	21 (77.8%)	13 (61.9%)	128 (79%)	162 (67.5%)	0.001
Multidetector computed tomography characteristics and calcium volume							
Eccentricity index	0.19 ± 0.07	0.19 ± 0.07	0.18 ± 0.06	0.17 ± 0.06	0.18 ± 0.07	0.19 ± 0.07	0.63
Annulus area, cm^2	4.4 ± 0.8	4.3 ± 0.6	5.6 ± 1.2	4.6 ± 0.9	4.5 ± 0.8	4.7 ± 0.9	< 0.001
Annulus perimeter, mm	76 ± 7.3	74.9 ± 6	85 ± 9.8	77.4 ± 7.8	76.4 ± 6.9	78.4 ± 7.8	< 0.001
Distance annulus-RCA, mm	14.3 ± 4.5	14.8 ± 3.5	14.8 ± 3.5	14.6 ± 2.9	16.8 ± 3.6	15.3 ± 3.8	< 0.001
Distance annulus-LCA, mm	13.1 ± 2.8	12.4 ± 2.3	13.1 ± 3.3	13.1 ± 2.6	13.6 ± 3	13.6 ± 3.1	0.055
DLZ calcium, mm^3	611 [370-1 088]	763 [443-968]	1 124 [565-1 539]	835 [527-1 341]	748 [417.5-1 153]	769 [478-1 172]	0.041
Total calcium AV, mm^3	603 [308-1 053]	699 [386-941]	982 [554-982]	802 [445-1 339]	650 [405-1 018]	705 [436-1 096]	0.07
LCC calcium AV, mm^3	176 [91-334]	192 [113-276]	270 [160-436]	195 [79-303]	165 [82-306]	188 [95-340]	0.203
RCC calcium AV, mm^3	131 [72-255]	162 [60-274]	311 [130-429]	180 [68-368]	179 [83-315]	191 [115-313]	0.185
NCC calcium AV, mm^3	268 [140-384]	286 [170-433]	395 [176-544]	363 [184-549]	271 [169-425]	305 [176-474]	0.085
Total calcium LVOT, mm^3	32 [0.7-114]	13 [2-76]	65 [7-228]	22 [2-106]	11 [0-72]	20 [2-87]	0.026
LCC calcium LVOT, mm^3	11 [0-83]	5.7 [0.2-29]	8 [0-127]	0.9 [0-57]	0 [0-20]	2.2 [0-36]	0.134
RCC calcium LVOT, mm^3	0 [0-1.4]	0 [0-2.2]	0.1 [0-10]	0.1 [0-1.4]	0 [0-0]	0.1 [0-3.3]	0.133
NCC calcium LVOT, mm^3	3.2 [0-29]	0.7 [0-15.2]	16.7 [1.5-153]	8.3 [0-25.4]	1.2 [0-20]	2.1 [0-24.6]	0.016
Procedural characteristics							
Prosthesis size, mm	25 ± 1.9	24.9 ± 1.5	29.9 ± 1.8	28.6 ± 2	25.5 ± 2.2	25.2 ± 2.1	< 0.001
Oversizing, %	12.1 ± 11	14.8 ± 10	29.9 ± 18	41.7 ± 15	16.1 ± 15	7.3 ± 12	< 0.001
Valvuloplasty pre-implant	56 (100%)	62 (98.4%)	26 (96.3%)	21 (100%)	159 (98.1%)	229 (95.4%)	0.312
Balloon post-dilation	15 (26.8%)	60 (60.3%)	8 (29.6%)	8 (38.1%)	69 (42.6%)	54 (22.5%)	< 0.001

Values are presented as mean ± SD, *n* (%), or median [interquartile range]. Bold values are all the values < 0.05. AV: aortic valve; AVB: atrioventricular block; BMI: body mass index; CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; CPB: cardiopulmonary bypass; DLZ: device landing zone; ECG: electrocardiogram; EF: ejection fraction; IDDM: insulin-dependent diabetes mellitus; LAHB: left anterior hemiblock; LBBB: left bundle branch block; LCA: left coronary artery; LCC: left coronary cusp; LVOT: left ventricular outflow tract; NCC: non-coronary cusp; NIDDM: non-insulin-dependent diabetes mellitus; PCI: percutaneous coronary intervention; PHT: pulmonary hypertension; RBBB: right bundle branch block; RCA: right coronary artery; RCC: right coronary cusp.

CoreValve and Sapien XT groups (78.6%, 77.8% and 79%, respectively). Many differences between groups were observed in MDCT variables. In the CoreValve group, patients showed a larger annulus, in terms of area (5.6 ± 1.2 cm^2) and perimeter (85 ± 9.8 mm). Always the CoreValve group showed a significantly higher amount of calcium, especially in the DLZ (median 1123.7 mm^3), in the LVOT (65.2 mm^3) and in the LVOT beneath the NCC (16.7 mm^3). Supplementary Figure 1 shows the distribution of calcifications in different groups in form of box-plots. In terms of procedural variables, all the registered characteristics but the valvuloplasty pre-implantation showed significant differences between groups. The CoreValve and Evolut R groups showed a significant bigger mean prosthesis size (29.9 ± 1.8 and 28.6 ± 2 mm, respectively) in comparison with other groups, as well as a higher grade of oversizing (29.9% ± 18% and 41.7% ± 15%, respectively). The Acurate neo group had the highest incidence of balloon post-dilatation (60.3%).

Figure 3 shows the incidence of study outcomes. Overall incidence of new BBB (18%) was not significantly different between prostheses (P = 0.75); on the other hand, tAVB and pAVB were observed in 3.8% and 8% of the whole study population, respectively, with significantly higher incidence in the Evolut R (Tavb = 19%) and CoreValve (pAVB = 29%) groups. The lowest incidence of conduction disturbances was observed in the Acurate neo group (BBB = 11%, tAVB = 2%, pAVB = 5%). A multivariate binary logistic regression for the three study outcomes was performed (Table 2). Baseline LAHB was found to be independently associated with new onset or worsening of BBB. Prior valvuloplasty (intended as previously separated procedure), balloon post-dilatation and insulin-dependent diabetes mellitus were associated with tAVB. Finally, baseline right BBB, the oversizing degree, and the amount of LVOT calcification beneath the NCC were associated with pAVB (requiring PPI).

The rate of others major complications is shown in Supplementary Table 2: the newer prostheses generations showed a lower incidence of in-hospital mortality in comparison to their predecessors.

DISCUSSION

The main finding of our study was that patient-related characteristics (such as LVOT calcification beneath the NCC, together with baseline abnormal-

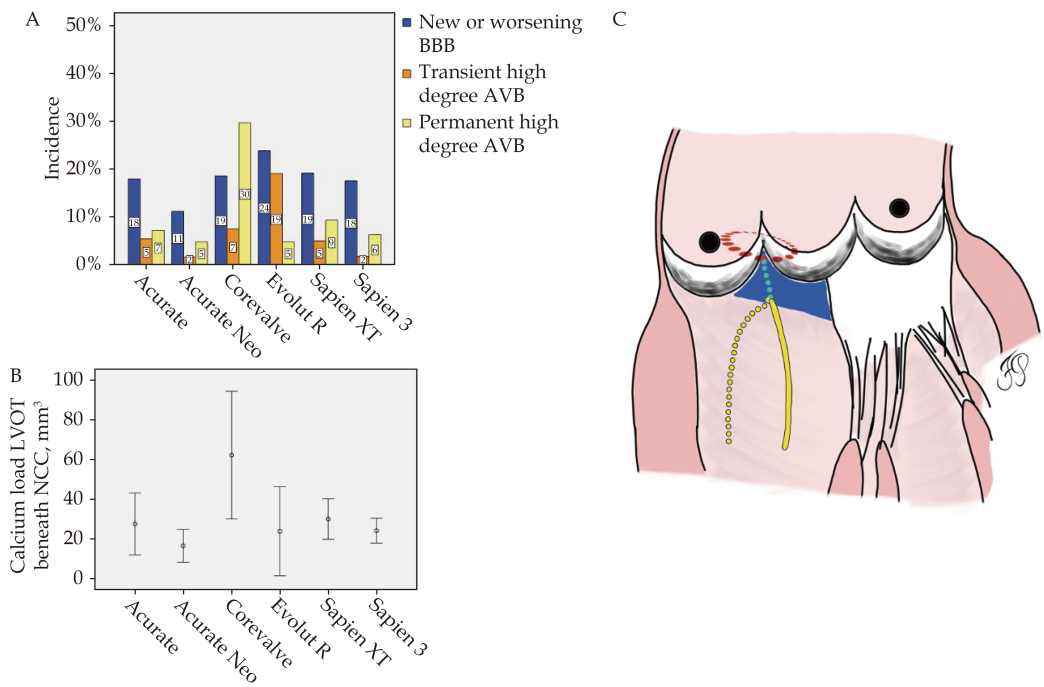

Figure 3 The incidence of study outcomes. (A): incidence of conduction disturbances according to prosthesis type; (B): mean and 95% CI of calcium load beneath the non-coronary cusp; (C): draw showing anatomy of conduction system and its spatial relationship with LVOT. AVB: atrioventricular block; BBB: bundle branch block. LVOT: left ventricular outflow tract.

Table 2 Univariate and multivariate logistic analysis.

	Univariate			Multivariate		
	Odds ratio	95% CI	*P*-value	Odds ratio	95% CI	P-value
New onset or worsening bundle branch block						
Baseline LAHB	3.19	1.2–8.6	0.02	3.33	1.2–9.1	0.02
NIDDM	1.5	0.96–2.3	0.07			
LVEF, %	0.98	0.97–1	0.08			
*NCC calcium LVOT, mm^3	1.3	1–1.6	0.08			
Access	1.5	0.96–2.35	0.07			
Transient reversible) high-degree AV block						
Prior valvuloplasty	5.97	1.2–29	0.01	9.99	1.79–55	< 0.01
COPD	0.2	0.03–1.49	0.08			
IDDM	4.1	0.86–19	0.05	8.7	1.6–48	0.01
Use of a self-expandable prosthesis	2	0.88–4.89	0.09			
Balloon post-dilatation	3.6	1.49–8.8	< 0.01	3.99	1.59–10	< 0.01
Permanent non-reversible) high-degree AV block						
Baseline RBBB	7.1	3.6–14	< 0.01	7.16	3.5–14	< 0.01
QTc interval, ms	1.01	1–1.02	< 0.01			
Q waves	2.1	1.14–3.8	0.01			
Oversizing, %	10.6	1.77–63	< 0.01	9.63	1.39–66	0.02
Eccentricity index, %	116	1.18–11420	0.04			
*NCC calcium LVOT, mm^3	1.5	1.1–1.9	0.02	1.6	1.2–2.1	< 0.01
Prosthesis size	1.16	1.02–1.31	0.02			

*Odds ratio rescaled to 100 mm^3. AV: atrioventricular; CI: confidence interval; COPD: chronic obstructive pulmonary disease; IDDM: insulin-dependent diabetes mellitus; LAHB: left anterior hemiblock; LVEF: left ventricular ejection fraction; LVOT: left ventricular outflow tract; NCC: non-coronary cusp; RBBB: right bundle branch block.

ities on ECGs) and procedural variables correlate with conduction disturbances after TAVI, independently of the prosthesis type.

TAVI showed an optimal short and mid-term outcome in patients of all risk categories. As aortic valve stenosis is a disease mainly predominant in the elderly and fragile population, TAVI has rapidly become a very attractive alternative to SAVR for the treatment of severe aortic valve stenosis, and the most frequent choice in German heart teams: an underestimated analysis from the German Heart Surgery Report accounted TAVI for 57.5% of isolated procedures on native aortic valve in 2018.[13] In this context, the extension of indication to a younger population is limited only by the long-term outcomes, such as prosthesis durability, quality of life and survival. The incidence of perioperative conduction disturbances remains higher than SAVR,[14] showing a reduced survival at follow-up in those patients experiencing BBB or PPI.[2,3] Left BBB and right ventricular pacing induce electrical and mechanical dyssynchrony that may lead to left ventricular systolic dysfunction. The risk of a PPI is particularly important in the elderly population, which represents the category of patients most widely exposed to TAVI. Elderly patients undergoing PPI are particularly exposed to PPI-related complications, such as cardiac perforation, showing a 2% of 30 days all-cause mortality in prior studies [15]. Moreover, the longer ICU length of stay is associated with higher 1-year mortality also in non-ventilated elderly patients [16]. These issues demands for a better understanding of risk factors in order to reduce the burden of this complication. Given that TAVI has been undergoing a standardization process with limited adaptability to patient characteristics, prosthesis selection is paramount for the heart team.

A number of studies from the literature have shown remarkable differences in the occurrence of conduction disturbances post-TAVI according to the type

of prosthesis used.[3] Among the various contributing factors, differences in the anchoring systems were found to play a role; in particular, the CoreValve is implanted significantly deeper into the LVOT compared with balloon-expandable prostheses, increasing the risk of damaging the His bundle and the left branching portion (Figure 3C). In an initial analysis mostly based on clinical and procedural variables, the use of first-generation CoreValve was associated with an increased risk of new-onset BBB and PPI. In the CHOICE randomized clinical trial,[17] the need for PPI was higher in the CoreValve group than in the Sapien XT group (37.6% *vs.* 17.3%). However, no study so far has evaluated the differences between the prosthesis models by quantifying aortic valve calcium, which is usually assessed qualitatively or semi-quantitatively. In CHOICE, aortic valve calcification was scored semi-quantitatively into four grades. More recently, in the multicenter randomized SOLVE-TAVI trial,[18] no significant difference in PPI was observed between patients implanted with the Evolut R or Sapien 3 valve (23% *vs.* 19.2%), though no calcium quantification was reported, nor if any degree of aortic valve calcification was established among the exclusion criteria. It is worth noting, however, that different generations of prostheses were used in the two aforementioned studies, which also greatly differed by sample size (n = 241 in CHOICE and n = 447 in SOLVE-TAVI). In contrast to our study results, the lack of calcium volume measurement may have affected the association between prosthesis model and the need for PPI.

Three transcatheter heart valve prostheses of two generations for each model were evaluated in our study. On multivariate analysis, the association of LVOT calcification beneath the NCC with oversizing degree and the need for PPI suggests that aortic valve calcification could act as a confounding factor that was not considered up to now. In high-volume centers like ours where different prosthesis types are used, the heart team will be more likely to agree on using a self-expandable transcatheter heart valve in patients with severe calcifications in order to minimize the risk of life-threatening complications (e.g., annular rupture). As our analysis was retrospective in nature, prosthesis selection was not based on quantitative measurement of the degree of calcification, as evidenced by the different calcium load in the CoreValve and Evolut R groups. In addition, a higher degree of device oversizing is usually recommended for the CoreValve and Evolut R self-expanding systems compared to other valves.[19]

Obviously, a calcification that is pushed by the prosthesis towards the conduction bundle will result in a higher risk of injury of the conduction system depending on the degree of oversizing. Both these variables (i.e., presence of calcifications and higher device oversizing) tend to be more common in patients receiving a CoreValve. This may generate a bias that accounts for the different results of our logistic regression analysis compared with previous observational studies. Furthermore, the lower rate of PPI reported with older generations of the CoreValve and Evolut R devices [20] should be interpreted in the light of a better patient selection rather than substantial differences in the structure of the two prostheses.

Our group demonstrated previously the role that LVOT calcification plays-together with other factors in causing the onset of new conduction disturbances following TAVI. Our previous study was focused only on one prosthesis model and, to the best of our knowledge, the present study is the largest to date investigating the role and distribution of aortic valve calcification in predicting conduction disturbances after TAVI in older and newer prosthesis generation. The results of the present investigation are consistent with our previous findings, showing that the amount of LVOT calcification beneath the NCC is associated with pAVB but not with tAVB, independently of the type of prosthesis used. This would suggest that a greater awareness of the anatomic interactions between the native architecture and the prosthetic device may better guide prosthesis selection and encourage the development of new valve models.

Interestingly, tAVB was found to be associated with diabetes, as also previously reported.[21] This observation, if confirmed in a larger number of studies, may be helpful in identifying higher risk patients that require more intensive follow-up.

Although risk factors for AVB and PPI have been widely addressed,[3] no study so far has investigated the variables associated with the risk of developing new-onset or worsening BBB. Limited data

exist on the incidence of new-onset or worsening BBB as its relevance has been underestimated for a long time until it was demonstrated an association with worse survival. In a recent systematic review and meta-analysis, the rate of new-onset LBBB at discharge ranged from 10.5% to 52.3%,[2] though most studies included only two valve systems (Sapien and CoreValve). The few data on the use of both prostheses show that implantation of the CoreValve is associated with higher rates of LBBB when compared to Sapien (Houthuizen et al. 53.8% vs 21.7%; Franzoni et al. 50% vs 13.5%; Schymik et al. 47.5% vs 27.1%).[22–24]

Our study is the first to report the incidence of BBB after TAVI with the self-expandable Acurate neo, which was lower than with the other types of prostheses, though without reaching statistical significance. Preoperative LAHB was also found to be associated with new-onset BBB following TAVI, which may suggest the presence of an impaired function of the conduction system prior to the procedure. This may also account for the increased relative risk of PPI at 1-year follow-up in these patients.[2]

Study Limitations

Our study has some limitations. The assessment of calcifications using a contrast-enhanced MDCT remains strongly dependent on the selected HU threshold. Indeed, the choice of testing the HU of blood in the ascending aorta was intended to avoid relevant mistakes deriving from the indiscriminate use of the same threshold for the whole study population. The threshold of 500 HU, and of 800 HU in some cases, is arbitrary and, though previously used in similar patient populations,[8–10] it should be validated in further studies. Some groups of our sample are underrepresented. Moreover, the retrospective nature and the analysis of in-hospital outcomes. Multicentric and prospective studies are needed to confirm our findings.

CONCLUSIONS

A high degree of oversizing and the presence of diffuse LVOT calcifications are associated with postprocedural conduction disturbances after TAVI, independently of the prosthesis type. Use of a self-expandable prosthesis, in contrast to the evidence available so far, may associate with a lower incidence of AVB, if applied in less calcified aortic valves with reduced oversizing grade.

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REFERENCES

[1] Siontis GCM, Overtchouk P, Cahill TJ, *et al*. Transcatheter aortic valve implantation *vs*. surgical aortic valve replacement for treatment of symptomatic severe aortic stenosis:an updated meta-analysis. *Eur Heart J* 2019; 40: 3143–3153.

[2] Faroux L, Chen S, Muntané-Carol G, *et al*. Clinical impact of conduction disturbances in transcatheter aortic valve replacement recipients: a systematic review and meta-analysis. *Eur Heart J* 2020; 41: 2771–2781.

[3] van Rosendael PJ, Delgado V, Bax JJ. Pacemaker implantation rate after transcatheter aortic valve implantation with early and new-generation devices: a systematic review. *Eur Heart J* 2018; 39: 2003–2013.

[4] Pollari F, Großmann I, Vogt F, *et al*. Risk factors for atrioventricular block after transcatheter aortic valve implantation: a single-centre analysis including assessment of aortic calcifications and follow-up. *Europace* 2019; 21: 787–795.

[5] Baumgartner H, Falk V, Bax JJ, *et al*. 2017 ESC/EACTS Guidelines for the management of valvular heart disease: the task force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2017; 38: 2739–2791.

[6] Surawicz B, Childers R, Deal BJ, *et al*. AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram: part III: intraventricular conduction disturbances: a scientific statement from the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society for Computerized Electrocardiology. *J Am Coll Cardiol* 2009; 53: 976–981.

[7] Kappetein AP, Head SJ, Généreux P, *et al*. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. *Eur Heart J* 2012; 33: 2403–2418.

[8] Pollari F, Dell'Aquila AM, Söhn C, *et al*. Risk factors for paravalvular leak after transcatheter aortic valve replacement. *J Thorac Cardiovasc Surg* 2019; 157: 1406–1415.e3.

[9] Jilaihawi H, Makkar RR, Kashif M, *et al*. A revised methodology for aortic-valvar complex calcium quantification for transcatheter aortic valve implantation. *Eur Heart J Cardiovasc Imaging* 2014; 15: 1324–1332.

[10] Seiffert M, Fujita B, Avanesov M, *et al*. Device landing

zone calcification and its impact on residual regurgitation after transcatheter aortic valve implantation with different devices. *Eur Heart J Cardiovasc Imaging* 2016; 17: 576–584.

[11] Khalique OK, Hahn RT, Gada H, *et al*. Quantity and location of aortic valve complex calcification predicts severity and location of paravalvular regurgitation and frequency of post-dilation after balloon-expandable transcatheter aortic valve replacement. *JACC Cardiovasc Interv* 2014; 7: 885–894.

[12] Brignole M, Auricchio A, Baron-Esquivias G, *et al*. 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: the Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). *Eur Heart J* 2013; 34: 2281–2329.

[13] Beckmann A, Meyer R, Lewandowski J, *et al*. German Heart Surgery Report 2018: The Annual Updated Registry of the German Society for Thoracic and Cardiovascular Surgery. *Thorac Cardiovasc Surg* 2019; 67: 331–344.

[14] Gleason TG, Reardon MJ, Popma JJ, *et al*. CoreValve U. S. Pivotal High Risk Trial Clinical Investigators. 5-Year Outcomes of Self-Expanding Transcatheter Versus Surgical Aortic Valve Replacement in High-Risk Patients. *J Am Coll Cardiol* 2018; 72: 2687–2696.

[15] Stevenson RT, Lugg D, Gray R, *et al*. Pacemaker implantation in the extreme elderly. *J Interv Card Electrophysiol* 2012; 33: 51–58.

[16] Moitra VK, Guerra C, Linde-Zwirble WT, Wunsch H. Relationship between ICU length of stay and long-term mortality for elderly ICU survivors. *Crit Care Med* 2016; 44: 655–662.

[17] Abdel-Wahab M, Mehilli J, Frerker C, *et al*. CHOICE Investigators. Comparison of balloon-expandable vs self-expandable valves in patients undergoing transcatheter aortic valve replacement:the CHOICE randomized clinical trial. *JAMA* 2014; 311: 1503–1514.

[18] Thiele H, Kurz T, Feistritzer HJ, *et al*. Comparison of newer generation self-expandable vs. balloon-expandable valves in transcatheter aortic valve implantation:the randomized SOLVE-TAVI trial. *Eur Heart J* 2020; 41: 1890–1899.

[19] Kasel AM, Cassese S, Bleiziffer S, *et al*. Standardized imaging for aortic annular sizing: implications for transcatheter valve selection. *JACC Cardiovasc Imaging* 2013; 6: 249–262.

[20] Sorajja P, Kodali S, Reardon MJ, *et al*. Outcomes for the commercial use of self-expanding prostheses in transcatheter aortic valve replacement: a report from the STS/ACC TVT Registry. *JACC Cardiovasc Interv* 2017; 10: 2090–2098.

[21] Movahed MR, Hashemzadeh M, Jamal MM. Increased prevalence of third-degree atrioventricular block in patients with type II diabetes mellitus. *Chest* 2005; 128: 2611–2614.

[22] Houthuizen P, van der Boon RM, Urena M, *et al*. Occurrence, fate and consequences of ventricular conduction abnormalities after transcatheter aortic valve implantation. *EuroIntervention* 2014; 9: 1142–1150.

[23] Franzoni I, Latib A, Maisano F, *et al*. Comparison of incidence and predictors of left bundle branch block after transcatheter aortic valve implantation using the CoreValve versus the Edwards valve. *Am J Cardiol* 2013; 112: 554–559.

[24] Schymik G, Tzamalis P, Bramlage P, *et al*. Clinical impact of a new left bundle branch block following TAVI implantation: 1-year results of the TAVIK cohort. *Clin Res Cardiol* 2015; 104: 351–362.

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