ESC European Society of Cardiology
Europace (2019) **00**, 1–9
doi:10.1093/europace/euy316

CLINICAL RESEARCH

Risk factors for atrioventricular block after transcatheter aortic valve implantation: a single-centre analysis including assessment of aortic calcifications and follow-up

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Received 28 June 2018; editorial decision 13 December 2018; accepted 13 December 2018

Aims To assess the contribution of aortic valve calcification to the occurrence of transient or permanent atrioventricular block (AVB) and the need for permanent pacemaker implantation (PPI) after transcatheter aortic valve implantation (TAVI) in a large single-centre cohort.

Methods and results We retrospectively analysed pre-operative contrast-enhanced multidetector computed tomography scans of patients who underwent TAVI in our centre between 2012 and 2016. Calcium volume was calculated for each aortic cusp above (aortic valve), and below [left ventricular outflow tract (LVOT)] the basal plane. Clinical and procedural data as well as pre-operative electrocardiograms were evaluated. Multivariate analysis was performed to evaluate risk factors for transient and permanent AVB. A total of 342 patients receiving a balloon-expandable prosthesis were included in the study. Overall incidence of transient and permanent AVB was 4% ($n = 14$) and 7.6% ($n = 26$), respectively. On logistic regression analysis, baseline right bundle branch block [odds ratio (OR) 7.36, 95% confidence interval (CI) 2.6–20.6; $P < 0.01$], degree of oversizing (OR 1.04, 95% CI 1.01–1.07 $P = 0.02$), prior percutaneous coronary intervention (OR 2.8, 95% CI 1.1–7.3), and LVOT calcification beneath the non-coronary cusp (OR for an increase of 10 $mm^3 = 1.06$, 95% CI 1–1.1; $P = 0.03$) were found to be independently associated with permanent AVB and PPI, whereas calcification of LVOT beneath the right coronary cusp (OR for an increase of 10 $mm^3 = 1.16$, 95% CI 1.02–1.3; $P = 0.02$) and balloon post-dilation (OR 3.8, 95% CI 1.2–11.8; $P = 0.02$) were associated with reversible AVB.

Conclusion Left ventricular outflow tract calcifications are associated with transient and non-reversible AVB after TAVI, and its evaluation could help in predicting onset and reversibility of AVB.

Keywords Aortic calcification • Calcium volume • Transcatheter aortic valve implantation • Conduction disturbance • Atrioventricular block • Pacemaker

Introduction

Transcatheter aortic valve implantation (TAVI) has emerged as an alternative to surgical aortic valve replacement (SAVR) for severe aortic valve stenosis in intermediate and high surgical risk or inoperable patients.[1] The occurrence of conduction disturbances requiring permanent pacemaker implantation (PPI) after the procedure is not uncommon and represents a clinically important event. Despite the

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What's new?

- Calcifications of aortic valve are a possible Achille's heel of transcatheter aortic valve implantations.
- Our study highlights the role of calcifications in left ventricular outflow tract in causing atrioventricular block and need of permanent pacemaker implantation.

increasing number of TAVI procedures and the reduction of such a complication over time, the incidence of PPI remains higher than that after SAVR.[2] Previously published studies have investigated the preoperative risk factors predicting the need for PPI.[3] The presence of aortic valve calcifications was found to be associated with atrioventricular block (AVB) and the need for PPI after TAVI as a result of mechanical trauma to the His bundle.[3,4]

The aim of this study was to assess risk factors for high-degree AVB after TAVI in a large single-centre cohort using a multiparameter approach taking into account aortic valve calcification, using a reproducible approach based on contrast-enhanced multidetector computed tomography (MDCT) measures.

Methods

Study population

We retrospectively analysed our single-centre experience with TAVI procedures between July 2009 and October 2016. Severe aortic stenosis was defined in accordance with international guidelines,[1] and the indication for TAVI discussed within our institutional Heart Team. Exclusion criteria were bicuspid aortic valve, pure aortic regurgitation, and annulus diameter of >30 mm. In this period of time, 707 patients underwent TAVI in our institution. After exclusion of the valve-in-valve procedures and of those patients who had a previous pacemaker implantation, 585 patients were eligible for the study. However, 94 patients did not have a MDCT scan (which was not applied as a standard pre-operative workup in 2009 and early 2010) or MDCT images retrievable from our 'picture archiving and communication system' for technical reasons; four patients had no pre-operative contrast-enhanced MDCT because of severe renal impairment; two patients did not have electrocardiogram (ECG)-triggered MDCT scans and were unsuitable for analysis; and 15 patients had irretrievable pre-operative ECGs. Thus, a total of 470 patients were eligible for the evaluation. In these patients, implantation was performed between January 2012 and October 2016. The majority of patients received a balloon-expandable prosthesis: Edwards SapienXT, *n* = 157 (Edwards Lifesciences Inc., Irvine, CA, USA); Edwards Sapien3, *n* = 185; Medtronic CoreValve, *n* = 27 (Medtronic, Minneapolis, MN, USA); Medtronic CoreValve EvolutR, *n* = 12; Medtronic Engager, *n* = 5; Symetis Acurate, *n* = 84 (Symetis SA, Ecublens, Switzerland). To avoid bias due to different learning curves and expertise, as well as to different interaction of prosthesis models with calcifications, we performed the analysis only on balloon-expandable prostheses (SAPIEN XT and SAPIEN 3, *n* = 342; *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.[5] Clinical data and operative outcomes, according to the Valve Academic Research Consortium (VARC)-2 recommendations,[6] were prospectively collected in our institutional database for internal quality control. The following intraoperative and in-hospital outcomes were recorded: post-operative transient or permanent high-degree AVB (defined as 3rd degree AVB or Mobitz Type II 2nd degree AVB), need for PPI, new-onset, or worsening intraventricular conduction delay [including incomplete or complete right bundle branch block (RBBB), left bundle branch block, and left anterior hemiblock]. 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.

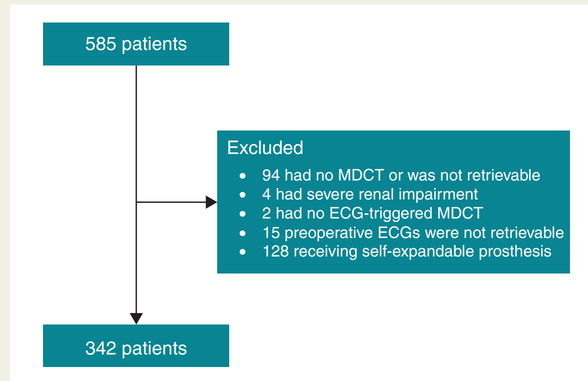


Figure 1 A flowchart showing selection process of the study population. ECG, electrocardiogram; MDCT, multidetector computed tomography.

Computed tomography angiography and calcium quantification

Patients underwent contrast-enhanced ECG-gated MDCT [330 ms rotation, helical mode, 60–70% gating, 0.6 mm × 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 approach). In our centre, all MDCT studies were performed with a 64-slice SOMATOM Definition AS (Siemens Healthcare GmbH, Erlangen, Germany). Multidetector computed tomography data were analysed 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. 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 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: (i) in the aortic valve from the basal plane to the origin of the lowest coronary ostium; (ii) 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; (iii) in the device landing zone, defined as the sum of the first two (*Figure 2*). The separation of the three aortic valve cusps (lef, LCC; right, RCC and non-coronary, NCC) was performed from the software automatically with occasionally manual adjustment, if necessary. As the His bundle is located between the RCC and NCC, calcium load in this region was evaluated also as a separate variable resulting from the sum of the two cusps. The threshold for calcium detection was set to two different cut-off values depending on the average

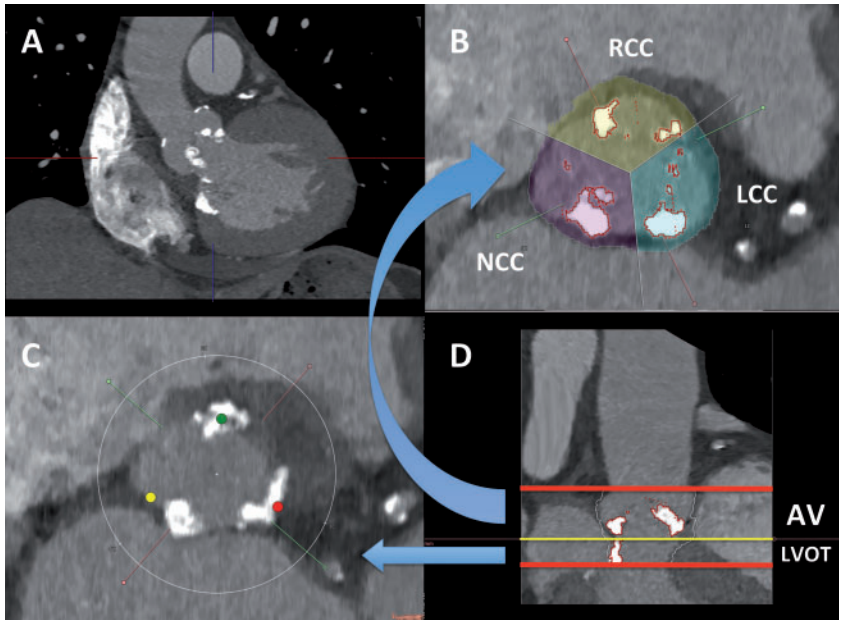


Figure 2 Aortic calcium volume quantification on 3mensio Structural Heart. (*A*) Coronal plane natural view of calcification in LVOT, aortic valve, and ascending aorta. (*B*) Transverse view of the native aortic valve with the three cusps (yellow, right coronary cusp; cyan, left coronary cusp; and magenta, non-coronary cusp). (*C*) Transverse view of calcifications in LVOT. (*D*) Stretched vessel view of the aortic valve and ascending aorta with highlighting of the region of interest. The yellow line identifies the basal plane (aortic annulus). AV, aortic valve; LCC, left coronary cusp; LVOT, left ventricular outflow tract; NCC, non-coronary cusp; RCC, right coronary cusp.

Hounsfield units (HU) of blood in the ascending aorta. For values between 130 HU and 300 HU, a threshold of 500 HU was chosen, in line with previous studies.[7–9] In contrast, for values between 300 HU and 600 HU (32 patients), an empiric threshold of 800 HU was chosen. Measurements of calcium volume were performed by a cardiac surgeon experienced in TAVI procedures and trained for the use of 3mensio (F.P.). Interobserver variability was tested for the first 20 cases by a second cardiac surgeon (S.P.) and was 4.7%.

The degree of over- or undersizing was calculated as prosthesis valve area (provided by the manufacturer)/MDCT annular area. Prosthesis valve area was derived according to the geometrical rule: $A = \pi(d/2)^2$, where d is the labelled prosthesis size. The aortic annulus eccentricity index was calculated on the basis of MDCT annulus measurements as 1 − (shortest diameter/longest diameter).[10]

Transcatheter aortic valve implantation procedure and management of post-operative conduction disturbances

Transfemoral-TAVI was preferred as first choice in all patients with suitable anatomy, alternatively, the transapical-TAVI access was used. All procedures were conducted in a hybrid operating room under fluoroscopic control (Artis Zeego System, Siemens AG, Erlangen, Germany), general anaesthesia, periprocedural transoesophageal echocardiography (TOE), and a cardiac perfusionist with ready-to-use cardiopulmonary bypass on site. All implantations were performed by a multidisciplinary team composed of at least a cardiologist and a cardiac surgeon. Selection of the prosthesis size was based upon the perimeter-derived area of the aortic annulus on MDCT as per vendor recommendations and re-evaluated by TOE and angiographic parameters (e.g. contrast reflux during valvuloplasty, balloon sizing) during the procedure. Immediately after the procedure, all patients were extubated in the hybrid room and transferred to an intermediate care unit (IMCU) for at least 24-h monitoring (three-lead ECG and invasive blood measurement). Twelve-lead ECGs were performed at admission to IMCU and at discharge. In case of bradycardia or conduction disturbance, monitoring was prolonged, and an electrophysiologist was consulted. Permanent pacemaker implantation was performed in case of symptomatic bradycardia or high-degree AVB (defined as 3rd degree AVB or Mobitz Type II 2nd degree AVB) during up to 7 days, according to international guidelines.[11] A telephone follow-up was performed to assess long-term survival. All pacemaker interrogations were performed in our institution or by the attending cardiologist.

Statistical analysis

Data consistency was checked and data were screened for outliers and normality. Continuous variables were tested for normality by using the Kolmogorov–Smirnov test. Categorical variables are expressed as frequencies (%) and continuous variables as mean (±standard deviation) or median [interquartile range (IQR)]. Continuous variables were compared by two-tailed paired *t*-test and categorical variables by the χ^2 test. Non-normally distributed data were tested using the Mann–Whitney test. Patients were divided in three groups according to onset of the AVB (any, transient/reversible, or permanent/non-reversible AVB). Baseline characteristics were analysed: clinical, procedural, electrocardiographic, echocardiographic, and pre-operative MDCT variables were entered into univariate analysis. On multivariate analysis, predictors of high-degree AVB and PPI were evaluated using stepwise binominal logistic regression. Probability of entry into the model was set at 0.05. Odds ratios with corresponding 95% confidence intervals (CIs) were computed in each model. Cumulative survival curves were computed according to the Kaplan–Meier method. The log-rank test was used to compare survival. Statistical significance was assumed at a *P*-value of <0.05. Statistical

Table 1 Baseline characteristics of the study population

	No high-degree AVB ($n = 302$)	Transient high-degree AVB ($n = 14$)	P-value[a]	Permanent high-degree AVB ($n = 26$)	P-value[b]
Demographic characteristics					
Age (years)	81.6 (±6)	83.5 (±6.7)	0.25	81.2 (±4.6)	0.72
Female gender	161 (53)	6 (43)	0.45	12 (46)	0.49
BMI (kg/m^2)	27.1 (±4.9)	25.1 (±3.5)	0.13	27 (±5.1)	0.92
Creatinine (mg/dL)	1.5 (±0.9)	1.3 (±0.4)	0.5	1.4 (±0.8)	0.77
Previous cardiac surgery	59 (20)	3 (21)	0.86	5 (19)	0.97
Prior CABG	47 (16)	2 (14)	0.9	5 (19)	0.62
COPD	59 (20)	0 (0)	**<0.01**	4 (15)	0.61
Recent myocardial infarction	11 (4)	0 (0)	0.47	2 (8)	0.31
EF (%)	52.4 (±13.2)	52.2 (±9.2)	0.97	56.6 (±12.7)	0.11
Severe PHT	104 (35)	3 (21)	0.28	9 (35)	0.99
Prior PCI	88 (33)	5 (38)	0.67	14 (61)	**0.01**
Logistic EuroSCORE (%)	24 (±16)	19.5 (±15)	0.31	21.4 (±13)	0.42
EuroSCORE II (%)	9.3 (±8.5)	7.9 (±5.8)	0.56	9.2 (±8.3)	0.96
ECG findings					
Heart rate (b.p.m.)	77.2 (±16.6)	72.2 (±12.6)	0.27	73.2 (±11.2)	0.23
Sinus rhythm	203 (67)	11 (79)	0.35	20 (77)	0.28
Atrial fibrillation	98 (33)	3 (21)	0.35	6 (23)	0.28
LAHB	5 (2)	0 (0)	0.63	0 (0)	0.51
LBBB	30 (10)	2 (14)	0.6	4 (15)	0.39
RBBB	20 (7)	1 (7)	0.95	9 (35)	**0.01**
PR interval (ms)	176.9 (±86.7)	160.4 (±48.4)	0.53	176 (±38.1)	0.96
QRS duration (ms)	100.4 (±24.3)	108.3 (±31.2)	0.25	118.2 (±32.7)	**0.01**
Q waves	143 (48)	6 (43)	0.71	19 (73)	**0.01**
Negative T waves	233 (78)	10 (71)	0.58	23 (88)	0.13
Multidetector computed tomography characteristics and calcium volume					
Eccentricity index	0.19 (0.14–0.23)	0.18 (0.15–0.21)	0.89	0.22 (0.14–0.25)	0.25
Annulus area (cm^2)	4.58 (3.93–5.3)	4.48 (3.94–5.35)	0.8	4.72 (3.6–5.2)	0.6
Annulus perimeter (mm)	77.6 (72.7–83.6)	75.1 (71.3–81.8)	0.55	79.4 (70.2–81.7)	0.63
Distance annulus-RCA (mm)	15.4 (13–18)	14.7 (13–18)	0.99	16.8 (13.7–18)	0.42
Distance annulus-LCA (mm)	13.8 (11.6–15.3)	13.1 (12.5–15)	0.99	14 (12–15.3)	0.2
LCC calcium AV (mm^3)	189.2 (92–331)	163.7 (55–292)	0.57	192.1 (99–417)	0.7
RCC calcium AV (mm^3)	189 (112–314)	149.7 (55–359)	0.75	205.7 (96–339)	0.84
NCC calcium AV (mm^3)	287.5 (176–428)	324.7 (205–547)	0.35	336.7 (213–552)	0.11
LCC calcium LVOT (mm^3)	0.95 (0–27)	0.1 (0–6.1)	0.64	0.1 (0–34.8)	0.85
RCC calcium LVOT (mm^3)	0 (0–0.5)	0 (0–4.1)	0.32	0 (0–1.2)	0.47
NCC calcium LVOT (mm^3)	1.95 (0–21.7)	0.2 (0–9.2)	0.46	2.65 (0–82.9)	0.11
Procedural characteristics					
Transfemoral access	210 (70)	7 (50)	0.12	19 (73)	0.73
Sapien3	166 (55)	6 (43)	0.38	13 (50)	0.63
Prosthesis size (mm)					
23	115 (38)	6 (43)	0.7	7 (27)	0.25
26	136 (45)	6 (43)	0.87	14 (54)	0.39
29	51 (17)	2 (14)	0.78	5 (19)	0.8
Oversizing (%)	10.6 (±14)	9.4 (±14.4)	0.68	17.6 (±19)	0.08
Valvuloplasty pre-implant	294 (98)	14 (100)	0.77	25 (96)	0.63
Balloon post-dilation	95 (32)	9 (64)	**0.01**	12 (46)	0.14
Aortic regurgitation ≥moderate	3 (1)	2 (14)	0.2	0 (0)	0.61
Conversion to surgery	5 (2)	1 (7)	0.46	0 (0)	0.51

Continued

Table 1 *Continued*

	No high-degree AVB (*n* = 302)	Transient high-degree AVB (*n* = 14)	*P*-value[a]	Permanent high-degree AVB (*n* = 26)	*P*-value[b]
Unplanned CPB	6 (2)	2 (14)	0.23	0 (0)	0.47
Coronary obstruction	2 (0.6)	0 (0)	0.76	0 (0)	0.68
Valve malpositioning	3 (1)	0 (0)	0.71	0 (0)	0.61

Values are presented as mean (± standard deviation), *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; ECG, electrocardiogram; EF, ejection fraction; 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; PCI, percutaneous coronary intervention; PHT, pulmonary hypertension; RBBB, right bundle branch block; RCA, right coronary artery; RCC, right coronary cusp.
[a]*P*-value refers to comparison between transient vs. no high-degree AVB.
[b]*P*-value refers to comparison between permanent vs. no high-degree AVB.

analysis was performed using SPSS software (IBM SPSS Statistics, Release 20.0.0, SPSS Inc., Chicago, IL, USA).

Results

The study population consisted of 342 consecutive patients. Of those, 14 (4%) experienced a transient (reversible), whereas 26 (7.6%) a permanent (non-reversible) AVB. Patient clinical and procedural characteristics, as well as baseline ECG findings and MDCT measurements for the three groups are shown in *Table 1*. In comparison to those who did not experienced AVB, the patients with transient AVB showed a higher incidence of balloon post-dilation, whereas those with permanent AVB showed a higher incidence of prior percutaneous coronary intervention (PCI), RBBB, and Q waves at baseline. No further significant differences were found between the groups. The anatomical distribution of calcifications is shown in *Figure 3* and Supplementary material online, *Table S1*. In the overall study population, as well as in each group, the cusp with the highest amount of calcium was the NCC, above (median 291.2 mm^3, IQR 180–445) as well as below the basal plane (median 1.7 mm^3, IQR 0–22.3). Of note, the permanent AVB group showed more NCC calcium load in the LVOT in comparison with other groups (*Figure 3B*), but the difference was not statistically significant (*Table 1* and Supplementary material online, *Table S1*).

Univariate and multivariate analyses (*Table 2*) based on all variables listed in *Table 1* and Supplementary material online, *Table S1*, identified factors independently associated with transient/reversible and permanent/non-reversible high-degree AVB. Right bundle branch block at baseline, LVOT calcium volume beneath the NCC, prior PCI, and degree of oversizing were found to be significantly associated with permanent/non-reversible AVB. On the other hand, RCC calcium volume beneath the RCC and post-implantation balloon dilation were significantly associated with transient/reversible high-degree AVB.

Other intraoperative complications and outcome

Outcomes and in-hospital complications according to VARC-2 criteria for the three groups are listed in *Table 3*. With exception of IMCU and hospital stay, no further differences were observed between the groups in terms of 30-day mortality, early safety, or other major complications.

Follow-up

Mean follow-up was 21.2 ± 18 months (median 18 months; IQR 5.6–32.9). The transient atrioventricular (AV) group showed a tendency to a lower survival in the first year after the index procedure (*Figure 4*), with a 42% (*n* = 6) of deadly events. Anyway the difference was not significant (log rank *P* = 0.1) probably due to the small sample size in the transient AVB group. The cause of death was known for four of these six patients and it is shown in the Supplementary material online, *Table S2*. In one case it was clearly related to an AVB III (occurring on the 4th post-operative day, 1 day before the planned discharge). No difference in survival was observed between the non-reversible AVB group and patients without conduction disturbances (log rank *P* = 0.53). A pacemaker interrogation after 12 months was possible in 14 of the 26 patients who had undergone PPI. Of these, 7 (50%) showed a ventricular pacing percentage of >95%, which is considered as absolute pacemaker dependency, whereas the remaining seven showed a ventricular pacing percentage <1%.

Discussion

The main findings of our study were (i) calcifications in the LVOT beneath the NCC correlate with permanent/non-reversible AVB and the need for PPI; (ii) in addition to the latter, other specific factors could discriminate reversible from non-reversible AVB; and (iii) post-operative reversible AVB showed a tendency to higher mortality at follow-up.

Permanent pacemaker implantation after TAVI is a relevant problem affecting this procedure since its introduction into clinical practice as an alternative treatment option for high-risk patients with severe aortic stenosis.[3] Many studies have been conducted to understand the underlying pathophysiological mechanisms.[12–14] Although the need for PPI has decreased over time, it still remains high. Gaede *et al.*[2] reported in 2016 an incidence of 11.4% in a large population from the German aortic valve registry, which was significantly lower than in 2015. Notwithstanding that, this complication remains high if

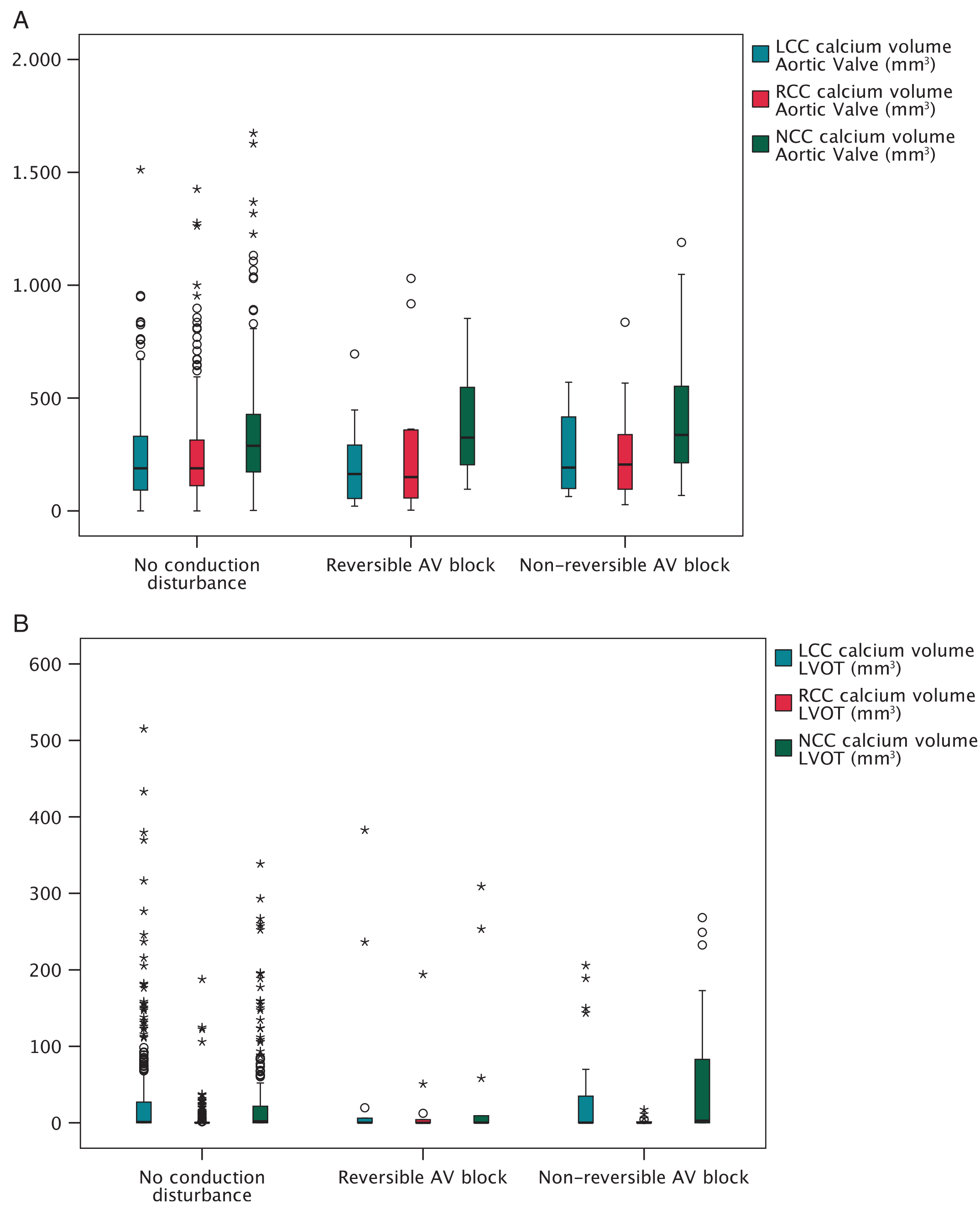


Figure 3 Side-by-side boxplots showing the anatomical distribution of calcium volume in the three study groups. (*A*) Distribution of calcification in the tree cusps above the basal plane. (*B*) Distribution of calcium volume in the three cusps below the basal plane. AV, atrioventricular; LCC, left coronary cusp; LVOT, left ventricular outflow tract; NCC, non-coronary cusp; RCC, right coronary cusp.

compared with that of patients undergoing isolated SAVR, which was reported to be 4.1% in the same registry, though including an unmatched patient cohort.[15]

Many authors have assessed pre-operative risk factors predicting PPI after TAVI, demonstrating a role of implantation depth,[12] membranous septal length,[13] baseline ECG abnormalities (e.g. RBBB),[3,14] and prosthesis type (e.g. CoreValve).[11] Although some authors[12,13] could not find a correlation with pre-existing RBBB, likely because of the small sample size or the retrospective nature of their studies, it is well recognized that mechanical stress to the conduction system may cause AVB after TAVI. The presence of aortic calcification may be an additional factor, exposing these structures to increased stress as previously postulated by Bagur *et al.*[3] To the best of our knowledge, our study is the largest to date, investigating the role of the amount and distribution of aortic valve calcification in predicting high-degree AVB and the need for PPI after TAVI. Only Fujita *et al.*[4] investigated

Table 2 Univariate and multivariate logistic analyses on study population

	Univariate				Multivariate			
	Odds ratio	95% CI		*P*-value	Odds ratio	95% CI		*P*-value
Outcome transient (reversible) high-degree AV block								
Balloon post-dilation	3.6	1.2	11.2	0.01	3.8	1.2	11.8	0.02
RCC calcium LVOT (mm^3)[a]	1.15	1.02	1.29	<0.01	1.16	1.02	1.3	0.02
Outcome permanent (non-reversible) high-degree AV block								
RBBB	7.38	2.94	18.6	<0.01	7.36	2.6	20.6	<0.01
Q waves	2.97	1.2	7.26	0.01				
Prior PCI	3.15	1.3	7.5	<0.01	2.8	1.1	7.3	0.03
Oversizing (%)	1.03	1.01	1.06	0.02	1.04	1.01	1.07	0.02
NCC calcium LVOT (mm^3)[a]	1.06	1.01	1.1	0.02	1.06	1	1.1	0.03

AV, atrioventricular; CI, confidence interval; LVOT, left ventricular outflow tract; NCC, non-coronary cusp; PCI, percutaneous coronary intervention; RBBB, right bundle branch block; RCC, right-coronary cusp.
[a]Odds ratio is rescaled to 10 mm^3.

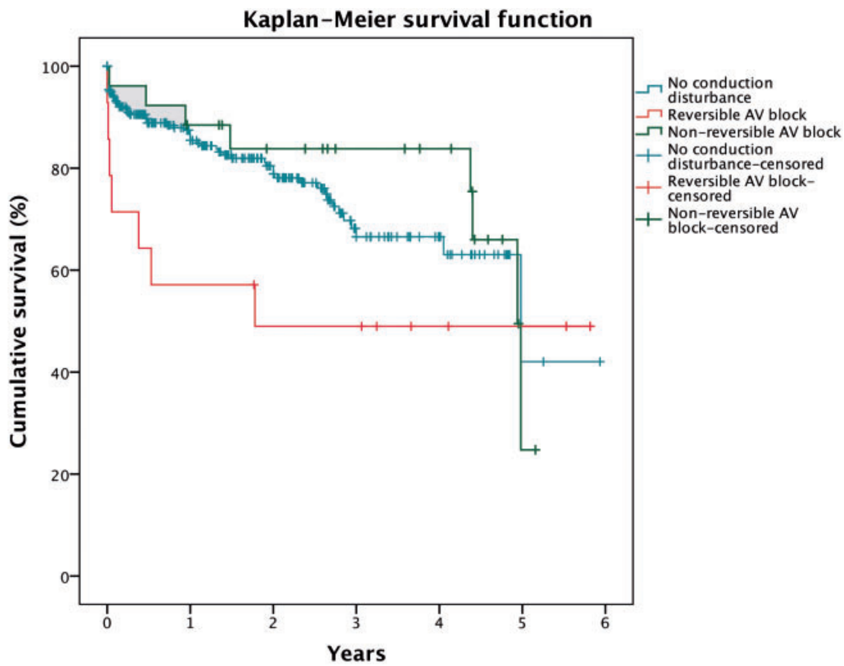
Table 3 Outcomes and in-hospital complications according to VARC-2 criteria

	No high-degree AVB (*n* = 302)	Transient high-degree AVB (*n* = 14)	*P*-value[a]	Permanent high-degree AVB (*n* = 26)	*P*-value[b]
IMCU stay (days)	2.1 (±3.4)	3.3 (±4.1)	0.19	4.7 (±4.6)	**<0.01**
Hospital stay (days)	11.4 (±9.4)	11 (±6.8)	0.88	15.5 (±5.5)	**<0.01**
Periprocedural MI	1 (<1)	1 (7)	0.36	0 (0)	0.77
Stroke	3 (1)	3 (21)	0.41	0 (0)	0.61
Life-threatening bleeding	8 (3)	2 (14)	0.25	1 (4)	0.72
Major vascular complications	10 (3)	2 (14)	0.28	1 (4)	0.89
New dialysis post-operative	27 (9)	8 (57)	0.24	5 (19)	0.39
30-day mortality	12 (5)	4 (33)	0.07	1 (4)	0.87
Device success	295 (98)	13 (93)	0.49	26 (100)	0.47
Early safety (at 30 days)	276 (92)	10 (71)	0.13	21 (87)	0.48

Values are presented as mean (± standard deviation) or *n* (%).
Bold values are all the values <0.05.
AVB, atrioventricular block; IMCU, intermediate care unit; MI, myocardial infarction; VARC, Valve Academic Research Consortium.
[a]*P*-value refers to comparison between transient vs. no high-degree AVB.
[b]*P*-value refers to comparison between permanent vs. no high-degree AVB.

the role of aortic calcification in patients undergoing TAVI, using a specific software (3mensio) to quantify calcium load. Our results are in agreement with their finding of pre-existing RBBB as a risk factor, but differ in terms of localization of aortic calcification. This is likely due to the fewer patients included in the Fujita's study (*n* = 162), which was also conducted in a different period (2012–13), or to the use of different valve prostheses (patients were treated with SapienXT and CoreValve). Additionally, and maybe more important, in our study the LVOT was evaluated not only as a whole, as Fujita *et al.*[4] did, but also for each valve cusp separately. Indeed, this is an important point to underline as the localization of the His bundle and membranous septum (localized between RCC/NCC in the LVOT) is central to the onset of AVB. Our results support the hypothesis that deployment of a transcatheter heart valve (THV) during the procedure could seriously injure the conduction system, in particular the left bundle branch fibres (probably the posterior, being more important than anterior[16]) that are located beneath the non-coronary aortic cusp.[17,18] In the presence of a RBBB at baseline, the patient develops a total conduction block between atria and ventricles, since all conduction ways are thereby interrupted. According to our results the more calcium being concentrated beneath the NCC, the more is the risk to develop an injury of the left bundle branch. Moreover, the risk further increases when the prosthesis is implanted with a higher percentage of oversizing, suggesting that not only the calcification per se is dangerous, but also its compression due to expansion of the THV.

Prior PCI was also found to be an independent predictor of permanent AVB. A possible explanation for this finding could be a certain degree of ischaemia with subsequent impaired distal and capillary perfusion of the conduction system, which could predispose these



						Number at risk
302	176	46	41	255	22	No conduction disturbance
14	8	6	6	3	2	Reversable AV block
26	22	17	13	11	1	Non-reversable AV block

Figure 4 Kaplan–Meier survival curves for patients with transient AVB (green), permanent AVB requiring permanent pacemaker implantation (red), and patients who did not suffered any AVB (blue). AVB, atrioventricular block.

patients to develop AVB. In such circumstances, prior PCI may be interpreted as a marker of subclinical myocardial ischaemia.

Current guidelines recommend a waiting time of about 7 days before performing PPI in patients treated with SAVR/TAVI, in order to assess possible restoration of sinus rhythm.[11] Consistent with a recent study of Gaede *et al.*,[14] our analysis showed different risk factors for reversible and non-reversible AVB. Of note, in multivariate analysis calcifications in the LVOT beneath the RCC (in correspondence of the muscular septum) are risk factors for reversible AVB, strengthening the concept that calcium load is fundamental for the onset of conduction disturbances. Moreover its localization in the LVOT could predict the reversibility of the damage. Thus, in the absence of baseline RBBB, and of large amount of calcium volume under the NCC, monitoring and waiting time may be prolonged since recovery is theoretically possible also later than 1 week after the index procedure. The observed recovery of AV conduction at follow-up in our study (50% of pacemaker interrogations) is in line with a recent publication of Marzahn *et al.*[19] In every case, it is worth noting that no significant differences were observed in in-hospital and follow-up complication rates between the groups, suggesting that PPI, though an undesirable complication, is a safe procedure, as confirmed also in previously studies from the literature.[20]

Patients with post-operative transient AVB (i.e. not requiring PPI) showed a tendency towards higher mortality rate at 1-year follow-up as compared with the rest of the population. We suspect that this could represent only the tip of the iceberg. Without a continuous monitoring, we could not determine the exact incidence of recurrent AVB, which indeed could be higher. Future prospective studies should investigate the potential risk of late recurrence of AVB in TAVI patients who are discharged in normal sinus rhythm, evaluating the need for longer close monitoring in this particular patient population.

Limitations

Our study has some limitations. First, the method used for assessing aortic calcification. The results of contrast-enhanced MDCT remain 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,[7–9] it should be validated in further studies. Second, the retrospective nature of our analysis.

Conclusions

Pre-operative assessment of aortic valve calcification could help in predicting the mechanical stress to the His bundle and the risk for the need of PPI. Aortic calcification of the LVOT beneath the NCC is associated with irreversible but not with reversible AVB, carrying the potential of AVB reversibility prediction. Finally, patients with reversible AVB may deserve closer monitoring during follow-up.

Supplementary material

Supplementary material is available at *Europace* online.

Acknowledgements

The authors thank Claudius Söhn, Jill Marianowicz, Pia Wiehofsky, and Martina Exner for their outstanding work in follow-up and database management of the patients involved in this study. Moreover, they want to thank PD Wolfgang Hitzl for his valuable contributions to the statistical analysis.

Conflict of interest: T.F. is consultant for LivaNova. S.P. is proctor for LivaNova. All remaining authors have declared no conflicts of interest.

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