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Chapter 10:

Left bundle branch block after sutureless, transcatheter, and stented biological aortic valve replacement for aortic stenosis

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Abstract

Background: Conventional aortic valve replacement (AVR), sutureless AVR (su-AVR) or transcatheter AVR (TAVI) for severe aortic stenosis (AS) are associated with conduction abnormalities. The aim of the present study was to assess the incidence of left bundle branch block (LBBB) after su-AVR and TAVI, in comparison to conventional AVR.

Methods: A total of 501 patients (mean age 74±8 years, 53% men) without preoperative cardiac conduction disturbances who underwent AVR or TAVI were included.

Results: Su-AVR patients and TAVI patients had a higher incidence of new-onset LBBB at hospital discharge (23% and 16%, respectively) compared to patients treated with conventional AVR (4%; p<0.001). On multivariate logistic regression analyses, type of surgery was independently associated with complete LBBB, taking age, preoperative QRS duration and heart rate into account (su-AVR and TAVI relative to the reference category conventional AVR: odds ratio, 8.5; 95% confidence interval, 3.7-19.5; p<0.001 and odds ratio, 5.8; 95% confidence interval, 2.4 – 14.1; p<0.001, respectively).

Conclusion: Su-AVR and TAVI were associated with higher risk of developing postoperative LBBB compared to conventional AVR, after adjusting for age, preoperative heart rate and QRS duration.
Introduction
Severe aortic stenosis (AS) is the most prevalent valvular heart disease among elderly populations. Selection of type of aortic valve replacement (AVR, surgical versus transcatheter) and type of prosthesis (biological versus mechanical) depends on clinical characteristics and operative risks of the patients. Particularly in the subgroup of elderly patients with symptomatic severe AS, a bioprosthesis is preferred over a mechanical prosthesis in order to minimize the risks of bleeding associated with life-long anticoagulation treatment. The advent of transcatheter aortic valve implantation (TAVI) and the development of sutureless biological prostheses have expanded the therapeutic alternatives in elderly patients with symptomatic severe AS. In high surgical risk patients, several studies have shown comparable mid-term outcomes of transcatheter bioprostheses, sutureless bioprostheses and stented bioprostheses. One of the complications that may occur after TAVI and surgical aortic valve replacement (AVR) is new-onset left bundle branch block (LBBB). However, there is a wide range in reported incidences of new-onset LBBB which may be explained by the presence of pre-existing conduction disturbances, position of the prosthesis into the left ventricular (LV) outflow tract and type of prosthesis. The aim of the present study was to assess the incidence and factors associated with the development of LBBB after su-AVR and TAVI, in comparison to conventional surgical AVR.

Methods

Patients
Of 682 patients who underwent AVR from 2008 to 2014 at the Leiden University Medical Center (The Netherlands), 501 were considered eligible based on analyzable pre- and postoperative electrocardiograms (ECG) and preoperative transthoracic echocardiography. Patients were divided into three groups, based on the treatment: su-AVR, TAVI or conventional AVR (Figure 1). Clinical characteristics were prospectively collected in the departmental Cardiology Information System (EPD-Vision®, Leiden University Medical Center, Leiden, The Netherlands) and retrospectively analyzed. The institutional review board approved this retrospective analysis of clinically acquired data and waived the need for patient written informed consent.

Electrocardiography
Standard 12-lead ECG were obtained before and after surgery at the day of hospital discharge. Heart rate, rhythm, heart axis, QRS duration and presence of bundle branch block were assessed. Right bundle branch block (RBBB) was defined as a QRS duration >120 ms in the presence of typical RBBB-morphology (rR’ in V1). Left bundle branch block (LBBB) was defined
Figure 1. Flowchart of patient inclusion.
AVR: aortic valve replacement; BBB, bundle branch block; ICD, implantable cardioverter defibrillator; LBBB, left bundle branch block; RBBB, right bundle branch block; su-AVR, sutureless aortic valve replacement; TAVI, transcatheter aortic valve implantation.

as QRS duration >120 ms and QRS complex negative in V1 with a small R or no R. Strict criteria were applied to define complete LBBB (QRS >140 ms in male and >130 ms in female with slurring or notching visible in at least 2 of the following leads: V1, V2, V5, V6, I and aVL).\textsuperscript{11}

Two-dimensional transthoracic echocardiography
Preoperative transthoracic echocardiography was performed using commercially available ultrasound systems (System Five, Vivid 7, and E9, General Electric Healthcare, Vingmed, Horten, Norway) equipped with 3.5-MHz or M5S transducers. Parasternal, apical, subcostal and supra-sternal views were obtained according to current recommendations.\textsuperscript{12} The echocardiographic data were digitally stored in cine-loop format and data were retrospectively analyzed using commercially available software (EchoPac 112.0.1, GE Medical Systems, Horten, Norway). Left ventricular (LV) dimensions and ejection fraction (LVEF) were assessed as recommended.\textsuperscript{12,13} Preoperative aortic valve function was evaluated using colour Doppler, continuous and pulsed wave Doppler according to current recommendations.\textsuperscript{14,15}
Aortic valve replacement and transcatheter aortic valve implantation

Treatment of aortic stenosis (surgical versus transcatheter) was decided based upon heart team discussions. Among patients who underwent surgical AVR, only patients who received a stented bioprostheses were selected in order to minimize heterogeneity and to ensure comparable groups in terms of number of patients. Su-AVR was performed as previously described with Sorin Perceval S valve (Sorin Biomedica Cardio Srl, Sallugia, Italy) or Medtronic 3f Enable valve (Medtronic Inc, Minneapolis, Minnesota). TAVI was performed according to current recommendations. Only patients who underwent TAVI via the transfemoral approach were included to minimize heterogeneity. Balloon valvuloplasty was performed under rapid right ventricular pacing prior to transfemoral implantation of a balloon-expandable prosthesis (Edwards SAPIEN valve, Edwards Lifesciences Corp, Irvine, California) or self-expandable prosthesis (Medtronic CoreValve, Medtronic Inc, Minneapolis, Minnesota). Figure 2 shows schematically the position of the different implanted prostheses in relation to the conduction system, in particular the left bundle branch.

Figure 2. Schematic overview of prosthesis implantation.
A: a 3-chamber view with the bundle branches. The su-AVR prosthesis (B) and TAVI prosthesis (C) were placed intra-annular. The conventional stented AVR prosthesis (D) was placed supra-annular. Ao, aorta; LA, left atrium; LBB, left bundle branch; LV, left ventricle; RBB, right bundle branch

Statistical analyses

All data analyses were performed using the SPSS software (Version 20.0. Armonk, NY: IBM Corp). Continuous variables were reported as mean ± standard deviation or median and interquartile range, as appropriate. Categorical variables were reported as counts and percentages. Differences were analysed using ANOVA or Kruskal Wallis tests and chi-square test. Linear mixed model analysis was performed to compare changes in heart rate and QRS...
duration over time between the three groups. Type of surgery and time of ECG were incorporated in the model as fixed variables. An unstructured covariance matrix was applied. The estimated marginal means ± standard error of the mean were presented.

Logistic regression analysis was performed to assess baseline factors associated with postoperative complete LBBB. All variables with p-value <0.1 on univariate logistic regression analysis were included in the multivariate model. The odds ratio and 95% confidence interval were calculated. All statistical tests were two-sided. A p-value <0.05 was considered statistically significant.

**Results**

A total of 501 patients (mean age 74±8 years, 53% men) were included in the present analysis. Patients who underwent conventional AVR were significantly younger and more often male compared to su-AVR and TAVI groups. Preoperative characteristics are shown in Table 1.

![Table 1: Baseline characteristics](image)

**Continuous variables were reported as mean ± standard deviation. Categorical variables were reported as counts and percentages. AVR: aortic valve replacement; LV: left ventricular; su-AVR: sutureless aortic valve replacement; TAVI: transcatheter aortic valve implantation.**

**Surgical characteristics**

Su-AVR was performed with the Medtronic 3f Enable valve in 68 patients (82%) and with the Perceval S valve in 15 patients (18%). TAVI was performed in 86 patients (79%) with Edwards SAPIEN valve and in 23 patients (21%) with Medtronic CoreValve. Conventional AVR was performed with stented bioprostheses: Carpentier-Edwards Perimount Magna valve (Edwards Lifesciences, Irvine, California) in 111 patients (36%), the Hancock valve (Medtronic Inc, Mineapolis, Minnesota) in 182 patients (59%) and the St Jude Medical Trifecta valve (St Jude Medical, St Paul, Minnesota) in the remaining 16 patients (5%). The size of the prosthesis was
significantly different between the three surgical techniques, the mean size in su-AVR patients was 23.5±2.0, in TAVI patients 25.9±2.2 and in patients undergoing conventional AVR 24.5±1.8 (p<0.001).

**ECG changes after AVR**

Table 2 shows the ECG parameters pre- and postoperatively at hospital discharge. Postoperative ECG was performed 3 (interquartile range: 2-4) days after TAVI compared to 6 (interquartile range: 5-8) days after su-AVR and 6 (interquartile range: 5-8) days after conventional AVR (p<0.001). The heart rate increased significantly after intervention in all three groups. The majority of the patients were in sinus rhythm (85%) before surgery. After surgery, the percentage of patients with atrial fibrillation increased to 17%, 17 patients showed atrial arrhythmia or junctional rhythm and 11 patients showed paced rhythm. The QRS duration increased significantly in all three groups after AVR. In addition, at hospital discharge, the QRS duration differed significantly between groups. Postoperatively, complete LBBB was observed significantly more often after su-AVR (23%) and TAVI (16%) compared to conventional AVR (4%; p<0.001). In addition, there were in total 12 patients (2%) with a RBBB and 19 patients (4%) with incomplete LBBB.

**Factors associated with complete LBBB**

Type of AVR was significantly associated with complete LBBB on univariate logistic regression analysis. Su-AVR (odds ratio: 8.5; 95% confidence interval: 3.7-19.5; p<0.001) and TAVI (odds ratio: 5.8; 95% confidence interval: 2.4 – 14.1; p<0.001) were independently associated with complete LBBB, after adjusting for age, preoperative rhythm and preoperative QRS duration.

**Discussion**

The main findings of the present study can be summarized as follows: the incidence of LBBB was 23% at discharge after su-AVR and 16% in TAVI patients, compared to 4% in patients undergoing conventional AVR. Su-AVR patients and TAVI patients more often new-onset complete LBBB, in comparison to patients treated with conventional AVR.

**Incidence of LBBB after AVR**

The incidence of new-onset LBBB after AVR ranged between 4 and 51% in previous studies. Differences in incidence of LBBB can be explained by differences in type of procedure, valve type and follow-up duration. In conventional AVR with a stented bioprosthesis, the incidence of LBBB at hospital discharge was low (4-6%). In contrast, studies reporting the incidence of LBBB after su-AVR or TAVI have shown considerably higher incidences compared with conventional AVR (39% and about 21%, respectively). In TAVI, the type of valve was an
Table 2: Electrocardiographic parameters preoperative and postoperative.

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>Postoperative</th>
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<tbody>
<tr>
<td></td>
<td>su-AVR (n=83)</td>
<td>TAVI (n=109)</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>70±1</td>
<td>74±1</td>
</tr>
<tr>
<td>Rhythm</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Sinus rhythm</td>
<td>72 (87%)</td>
<td>85 (78%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>11 (13%)</td>
<td>20 (18%)</td>
</tr>
<tr>
<td>Other atrial rhythm</td>
<td>0 (0%)</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>QRS axis</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>74 (89%)</td>
<td>99 (91%)</td>
</tr>
<tr>
<td>Right</td>
<td>9 (11%)</td>
<td>10 (9%)</td>
</tr>
<tr>
<td>QRS-duration (ms)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Bundle branch block</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
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</table>

Continuous variables were analysed using linear mixed models and were reported as mean ± standard error of the mean. Categorical variables were reported as counts and percentages. Other atrial rhythm includes atrial rhythm, atrial flutter and atrial tachycardia. AVR: aortic valve replacement; cLBBB: complete left bundle branch block; iLBBB: incomplete left bundle branch block; RBBB: right bundle branch block; su-AVR: sutureless aortic valve replacement; TAVI: transcatheter aortic valve implantation.

important determinant of new-onset LBBB: Medtronic CoreValve was associated with a higher incidence of LBBB (48-51%) compared with Edwards SAPIEN valve (12-27%). The present study showed higher incidence of LBBB in TAVI with Medtronic CoreValve (22%) compared to the SAPIEN valve (14%), although not statistically significant (p=0.555). Studies with longer follow-up duration demonstrated that new-onset LBBB present at hospital discharge was transient in some cases and resolved after months of follow-up. Persistent LBBB was present in only 9% of TAVI patients and 2% of patients treated with conventional AVR. Local inflammation, oedema and ischemia of the surrounding tissue following aortic valve implantation may explain the transient nature of acute postoperative LBBB.
**Mechanism underlying AVR-induced LBBB**

New-onset LBBB after AVR can be related to compression by the prosthesis on the conduction system. The bundle branch initiates at the base of the interleaflet triangle between the non-coronary and right-coronary cusps, located at the aortic annulus. Stented biological prostheses are placed supra-annular whereas the su-AVR and TAVI prostheses are placed intra-annular, close to the bundle branch which may lead to increased risk of damage of the conduction system. Previous studies in TAVI patients showed that a lower implantation depth was associated with new-onset LBBB.

Besides the position of the valve, the size of the implanted prosthesis relative to the annulus size is important in the pathophysiology of conduction abnormalities. In su-AVR and TAVI, slight oversizing is necessary to prevent severe paravalvular leakage. However, excessive oversizing can result in increased compression of the conduction system and aortic annulus rupture.

Another factor responsible for the occurrence of LBBB after AVR might be related to the expandable property of the su-AVR and TAVI prostheses. The stented biological prostheses are sutured to the annulus and afterwards, the prosthesis does not generate a radial force that compresses the conduction system. In contrast, the su-AVR and TAVI prostheses are anchored into the aortic root and generate a radial force expansion that may compress the conduction system and lead to conduction abnormalities. Previous studies hypothesized that the nitinol frame of the Medtronic CoreValve, with the unique property of shape memory, is responsible for increased ongoing compression on the conduction system, resulting in more frequent LBBB in comparison to the SAPIEN valve. This may additionally explain the higher incidence of LBBB in su-AVR prostheses mounted in a nitinol frame. However, in a direct comparison between Medtronic CoreValve (with nitinol frame) and SAPIEN XT (with cobalt chromium frame), there was no significant difference in the force posed on the annulus.

**Clinical implications**

The present study showed a significantly higher incidence of new-onset LBBB after su-AVR and TAVI in comparison to conventional AVR. The present results may impact on the selection of the type of surgery, especially in patients with an intermediate surgical risk. Furthermore, attention should be paid to the sizing and positioning of the prostheses in su-AVR and TAVI to improve outcomes with lower incidences of LBBB. Further technical development of both TAVI valves and sutureless valves and careful implantation of the valve (not too deep into the LVOT) may help to reduce the incidence of LBBB. Additionally, further clinical research should elucidate whether the occurrence of LBBB is transient or persistent and whether it impacts on the postoperative LV systolic function. In particular in older patients with preoperative reduced systolic function, this could be of importance when selecting the type of surgery. It
might influence the need for cardiac resynchronization therapy in patients with an impaired LV function who developed LBBB after AVR. Future studies should analyse which patients are more at risk in developing persistent LBBB and what actions can prevent new-onset LBBB.

Study limitations
The present study was retrospective, with all the inherent limitations of such a study design. The ECG parameters were assessed preoperatively and at discharge, with the strict criteria for complete LBBB. However, ECG follow-up was not systematically performed and, therefore, information on whether LBBB was persistent during long-term follow-up was lacking. The LBBB directly postoperative might have been transient and its clinical implications remain unclear. Because patients were discharged earlier after TAVI, the duration between surgery and postoperative ECG at discharge was shortest in this group compared to su-AVR and conventional AVR, which may resulted in an increased number of transient LBBB among TAVI patients. In addition, both Medtronic Corevalve and Edwards Sapien TAVI were used in the TAVI cohort. The Medtronic Corevalve tended to result in more complete LBBB than the Edwards Sapien valve, however this difference was not statistically significant and therefore both types of valves were included in the present analysis. Results cannot be extrapolated to stentless biological and mechanical prostheses and non-transfemoral TAVI. Furthermore, the present study described the first series of su-AVR patients; therefore the learning curve could be a contributing factor to the relatively high incidence of LBBB. The depth of implant of the three types of prostheses was not evaluated and therefore analyses whether depth of implant influenced the prevalence of new-onset LBBB could not be performed.

Conclusion
In conclusion, su-AVR and TAVI patients developed more frequently postoperative LBBB at discharge, in comparison to patients treated with conventional stented AVR bioprostheses. Su-AVR and TAVI were associated with higher risk on developing postoperative LBBB compared to conventional AVR, respectively, after adjusting for age, preoperative heart rate and QRS duration.

References


