Aortic valve implantation-induced conduction block as a framework towards a uniform electrocardiographic definition of left bundle branch block

S. Calle · M. Coeman · A. Demolder · T. Philipsen · P. Kayaert · M. De Buyzere · F. Timmermans · J. De Pooter

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Abstract

Introduction  New-onset left bundle branch block (LBBB) following transcatheter or surgical aortic valve replacement (LBBBAVI) implies a proximal pathogenesis of LBBB. This study compares electrocardiographic characteristics and concordance with LBBB definitions between LBBBAVI and non-procedure-induced LBBB controls (LBBBcontrol).

Methods  All LBBBAVI patients at Ghent University Hospital between 2013 and 2019 were enrolled in the study. LBBBAVI patients were matched for age, sex, ischaemic heart disease and ejection fraction to LBBBcontrol patients in a 1:2 ratio. For inclusion, a non-strict LBBB definition was used (QRS duration ≥120ms, QS or rS in V1, absence of Q waves in V5-6). Electrocardiograms were digitally analysed and classified according to three LBBB definitions: European Society of Cardiology (ESC), Strauss and American Heart Association (AHA).

Results  A total of 177 patients (59 LBBBAVI and 118 LBBBcontrol) were enrolled in the study. LBBBAVI patients had more lateral QRS notching/slurring (100% vs 85%, p=0.001), included a higher percentage with a QRS duration ≥130ms (98% vs 86%, p=0.007) and had a less leftward oriented QRS axis (−15° vs −30°, p=0.013) compared to the LBBBcontrol group. ESC and Strauss criteria were fulfilled in 100% and 95% of LBBBAVI patients, respectively, but only 18% met the AHA criteria. In LBBBcontrol patients, concordance with LBBB definitions was lower than in the LBBBAVI group: ESC 85% (p=0.001), Strauss 68% (p<0.001) and AHA 7% (p=0.035). No differences in electrocardiographic characterisation or concordance with LBBB definitions were observed between LBBBAVI and LBBBcontrol patients with lateral QRS notching/slurring.

Conclusion  Non-uniformity exists among current LBBB definitions concerning the detection of proximal LBBB. LBBBAVI may provide a framework for uniform criteria for true proximal LBBB.

Keywords  Left bundle branch block · Transcatheter aortic valve replacement · Surgical aortic valve replacement · QRS notching

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What’s new?

- Lateral QRS notching/slurring is an essential criterion for diagnosing proximal left bundle branch block (LBBB).
- The use of different LBBB definitions results in discordance when scoring LBBB.
- Aortic valve implantation (AVI)-induced LBBB showed the highest concordance with the 2013 European Society of Cardiology and Strauss definitions.
- AVI-induced LBBB provides a framework for uniform criteria for true proximal LBBB.
**Table 1** Clinical, echo- and electrocardiographic characteristics of aortic valve implantation (AVI)-induced left bundle branch block (LBBB\textsubscript{AVI}) and matched control LBBB (LBBB\textsubscript{control}) patients

| Clinical characteristics               | LBBB\textsubscript{AVI} (n = 59) | LBBB\textsubscript{control} (n = 118) | p-value |
|----------------------------------------|----------------------------------|--------------------------------------|---------|
| Median age (years)                     | 82 (75;85)                       | 81 (75;84)                           | Matched |
| Male                                   | 25 (42)                          | 50 (42)                              | Matched |
| BMI (kg/m\textsuperscript{2})          | 26 ± 4.5                         | 26 ± 4.1                             | 0.592   |
| BSA (m\textsuperscript{2})             | 1.80 ± 0.207                     | 1.80 ± 0.207                        | 0.920   |
| Coronary artery disease                | 23 (39)                          | 46 (39)                              | Matched |
| Acute coronary syndrome                | 6 (10)                           | 12 (10)                              | Matched |
| Echocardiographic measurements         |                                  |                                      |         |
| End-diastolic diameter (mm)            | 47 ± 6.0                         | 48 ± 7.7                             | 0.506   |
| Left ventricular mass/BSA (g/m\textsuperscript{2}) | 102 ± 28.9                      | 103 ± 36.4                           | 0.562   |
| Left ventricular systolic function     | Matched                          |                                      |         |
| Normal (≥ 55%)                         | 41 (70)                          | 82 (70)                              |         |
| Mildly reduced (45–54%)                | 9 (15)                           | 18 (15)                              |         |
| Moderately reduced (30–44%)           | 7 (12)                           | 14 (12)                              |         |
| Severely reduced (< 30%)               | 2 (3)                            | 4 (3)                                |         |
| ECG measurements                       |                                  |                                      |         |
| PR interval (ms)                       | 191 (168;208)                    | 174 (158;204)                        | 0.072   |
| QRS duration (ms)                      | 148 (140;160)                    | 145 (136;154)                        | 0.074   |
| Frontal QRS axis (°)                   | −15 (−37;11)                     | −30 (−45;−3)                         | 0.013   |
| R wave peak time (lead I) (µV)         | 58 (50;70)                       | 62 (56;72)                           | 0.065   |
| Notching/slurring lateral leads        | 59 (100)                         | 100 (85)                             | 0.001   |
| Notching/slurring inferior leads       | 49 (83)                          | 83 (70)                              | 0.067   |
| Notching/slurring V1-2                 | 12 (20)                          | 6 (5)                                | 0.002   |

Values are mean ± standard deviation, median (first quartile; third quartile) or number (%). BMI, body mass index; BSA, body surface area.

**Introduction**

Left bundle branch block (LBBB) in humans was first recorded electrocardiographically in 1914 [1]. Multiple criteria for LBBB have been proposed since, based on experimental canine studies [1, 2], human case studies [3], electrophysiological data [4] and observations in cardiac resynchronisation therapy (CRT) responders [1, 5–7]. However, the electrocardiographic pattern of LBBB has not been fully clarified and various LBBB definitions are currently used [1, 8–10], resulting in significant discordance when scoring LBBB in clinical practice [7, 11].

Although conduction block may theoretically occur at any level in the His-Purkinje network, growing evidence suggests that only proximal left bundle branch (LBB) lesions cause ‘true’ LBBB [12] and that only ‘true’ LBBB is considered a strong predictor of CRT response in heart failure patients [6, 13]. Notching or slurring of the QRS complex during LBBB has been linked to a proximal origin of the LBB conduction block and might be considered a key feature of proximal LBBB [14, 15]. A limitation of current LBBB definitions is that they are not exclusively based on electrocardiographic observations in patients with proximal LBBB, which may contribute to the heterogeneity in LBBB definitions.

New-onset LBBB after transcatheter (TAVR) or surgical aortic valve replacement (SAVR) implies a proximal pathogenesis of LBBB and may provide a ‘framework’ towards uniform criteria for proximal LBBB. In this study, we compare the electrocardiographic characteristics and LBBB definitions in aortic valve implantation (AVI)-induced LBBB to a non-procedure-induced LBBB control group.

**Methods**

**Study populations**

Enrolled in the study were all patients with AVI-induced LBBB (LBBB\textsubscript{AVI}), including both patients with TAVR- and SAVR-induced LBBB, at Ghent University Hospital between January 2013 and June 2019. All patients with a primary TAVR and SAVR procedure and without pre-existing LBBB were screened. Exclusion criteria were pre-procedural ventricular pacing and peri-procedural permanent pacemaker implant. Presence of acute LBBB was scored within 24 h following TAVR/SAVR.

A control group of LBBB patients (LBBB\textsubscript{control}) consisted of randomly selected LBBB patients at Ghent University Hospital. LBBB\textsubscript{control} Patients were matched for age, sex, left ventricular ejection fraction (LVEF),
history of coronary artery disease (CAD) and acute coronary syndrome to the LBBB <sub>AVI</sub> group in a 2:1 ratio. In both the AVI and control groups, LBBB was defined according to broad conventional criteria (QRS duration ≥ 120 ms, QS or rS in lead V1 and absence of Q waves in V5-V6) [9], Absence of Q waves in V5-V6-I-aVL and no R wave peak time criterion [10] (see Electronic Supplementary Material, Fig. S1). Continuous electrocardiographic characteristics (QRS, QRS axis, R wave peak time (RWPT)) were digitally analysed by the Marquette 12SL algorithm (GE Healthcare) [17]. RWPT was defined according to the Minnesota Code [18].

### Validation of proposed criteria for proximal LBBB

Based on our observations in LBBB<sub>AVI</sub>, we adapted currently used LBBB criteria and propose a revised definition of LBBB. The revised definition was validated in consecutive LBBB patients (broad criteria) who underwent implantation of a CRT device at Ghent University Hospital according to current guidelines (LVEF ≤ 35%) [9] and who were categorised as CRT super-responders (LBBB<sub>AVI</sub>) based on improvement in LVEF to >45% after at least 6 months of CRT therapy at a prospective echocardiographic examination between October 2018 and August 2020. All pre-implant ECGs were reviewed by an investigator blinded to the revised LBBB criteria.

### Statistical analysis

Categorical variables are expressed as absolute number (percentage). Continuous variables are expressed as mean (± standard deviation) in the case of Gaussian distribution or median (1st quartile; 3rd quartile) if data are non-Gaussian distributed. Normality was tested using the Shapiro-Wilk test. To compare means/medians of two variables, Student’s t-test and the Mann-Whitney U test were used. Comparison of categorical variables among groups was performed by

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### Table 2 Agreement with various left bundle branch block (LBBB) definitions among aortic valve implantation (AVI)-induced LBBB (LBBB<sub>AVI</sub>) and matched control LBBB patients (LBBB<sub>control</sub>)

| LBBB definition features | LBBB<sub>AVI</sub> (n=59) | LBBB<sub>control</sub> (n=118) | p-value |
|---------------------------|--------------------------|-------------------------------|---------|
| QRS duration ≥ 120 ms     | 59 (100)                 | 118 (100)                     | NP      |
| QRS duration ≥ 130 ms     | 58 (98)                  | 101 (86)                      | 0.007   |
| QRS duration ≥ 130 ms in females and ≥ 140 ms in males | 56 (95) | 95 (81) | 0.012 |
| QS or rS in V1            | 59 (100)                 | 118 (100)                     | NP      |
| Absence of Q waves in V5-6| 59 (100)                 | 118 (100)                     | NP      |
| Absence of Q waves in V5-6 and I | 57 (97) | 111 (94) | 0.720 |
| Absence of Q waves in V5-6, I and aVL | 50 (85) | 92 (78) | 0.286 |
| Presence of Q waves in aVL | 9 (15)                   | 26 (22)                       | 0.286   |
| R wave peak time > 60 ms in V5-6 | 16 (27) | 20 (17) | 0.113 |
| R wave peak time > 60 ms in V6 only | 30 (51) | 60 (51) | 1.000 |
| Notching/slurring in V5-6, I or aVL | 59 (100) | 100 (85) | 0.001 |
| Notching/slurring in V5-6, I and aVL | 32 (54) | 37 (31) | 0.003 |
| Notching/slurring in ≥ 2 leads (I, aVL, V1-2, V5-6) | 59 (100) | 93 (79) | <0.001 |

**LBBB definitions**

- ESC 2013 definition
- Strauss definition
- AHA 2009 definition

**AHA 2009 definition variations**

- Absence of Q waves in V5-V6-I and R wave peak time > 60 ms in V5-V6
- Absence of Q waves in V5-V6-I-aVL and R wave peak time > 60 ms in V5-V6
- Absence of Q waves in V5-V6-I and no R wave peak time criterion
- Absence of Q waves in V5-V6-I-aVL and no R wave peak time criterion

Values are number (%)

AHA American Heart Association, ESC European Society of Cardiology, NP not possible
**Original Article**

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**Fig. 1**  

- **a** Electrocardiogram of an 85-year-old control patient with non-procedure-induced left bundle branch block (LBBBcontrol) fulfilling none of the European Society of Cardiology (ESC) 2013, Strauss and American Heart Association (AHA) 2009 definitions.

- **b** Electrocardiogram of a 72-year-old patient with left bundle branch block following aortic valve implantation (LBBBAVI) fulfilling the ESC 2013 and Strauss definitions.

- **c** Electrocardiogram of an 86-year-old LBBBAVI patient fulfilling the ESC 2013, Strauss and AHA 2009 definitions.

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**Table:**

| LBBBcontrol fulfilling none of the ESC 2013, Strauss and AHA 2009 definitions | QRS duration: 130 ms |
| --- | --- |
| Frontal QRS axis = -42° |
| QS in V1 |
| Absent Q waves in V5-6 |
| R wave peak time <60 ms in V5-6 and normal in V1 |
| No QRS notching/ slurring in I, aVL, V5 and V6 |

| LBBBAVI fulfilling ESC 2013 and Strauss definition | QRS duration: 136 ms |
| --- | --- |
| Frontal QRS axis = 29° |
| rS in V1 |
| Absent Q waves in V5-6 |
| R wave peak time <60 ms in V5-6 and normal in V1 |
| QRS notching in aVL and V6 |
| QRS slurring in I |

| LBBBAVI fulfilling ESC 2013, Strauss and AHA 2009 definition | QRS duration: 154 ms |
| --- | --- |
| Frontal QRS axis = -9° |
| rS in V1 |
| Absent Q waves in V5-6 |
| R wave peak time >60 ms in V5-6 and normal in V1 |
| QRS notching in I, aVL, V5 and V6 |

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**A framework towards a uniform definition of left bundle branch block**
Results

Characteristics of patients with new-onset LBBB\textsubscript{AVI}

A total of 59 LBBB\textsubscript{AVI} patients (34 TAVR and 25 SAVR patients, median age 82 years, 42% male) were enrolled in the study. The characteristics of the TAVR and SAVR patients are shown in the Electronic Supplementary Material (Table S1). All patients had severe aortic valve stenosis with an aortic valve area < 1.0 cm\(^2\) as the indication for TAVR/SAVR. Pre-procedural conduction disease (left anterior/posterior hemiblock or intraventricular conduction delay) was observed in 8 (15%) patients. All patients developed LBBB immediately during implantation or within 24 h post-procedure. Except for age, no significant differences were observed between TAVR and SAVR patients.

With the occurrence of LBBB\textsubscript{AVI}, QRS increased from 94 (86;100) ms to 148 (140;160) ms (\(p<0.001\)) (Tab. 1). An LBBB QRS of \(\geq 130\) ms was observed in 98% of patients and, with regard to the Strauss definition, 95% of patients met the sex-specific QRS cut-off (Tab. 2). Notably, 100% of females had a QRS \(\geq 130\) ms and 88% of males had a QRS \(\geq 140\) ms. QRS in LBBB\textsubscript{AVI} males was longer than in females (154 [145;162] ms vs 145 [138;153] ms, \(p=0.006\)). No other electrocardiographic differences were observed between the sexes. In a multivariate linear regression model including age, height, weight, sex, CAD and end-diastolic diameter, only male sex was independently associated with increased QRSD (\(\beta=11.49; p=0.039\)). The baseline frontal QRS axis shifted from 9 (-15;45)° to -15 (-37;11)° post-AVI (\(p=0.001\)). In 72% of LBBB\textsubscript{AVI} patients with a normal QRS axis (90%), a leftward shift was observed.

Electrocardiographic analysis of LBBB\textsubscript{AVI} and LBBB\textsubscript{control}

The 59 LBBB\textsubscript{AVI} patients were matched to 118 LBBB\textsubscript{control} patients. The characteristics of LBBB\textsubscript{AVI} and LBBB\textsubscript{control} patients are shown in Tab. 1. Representative ECGs are shown in Fig. 1. No clinical or echocardiographic differences were observed between the two groups.

All LBBB\textsubscript{AVI} patients presented with QRS notchingslurring in the lateral leads (I, aVL, V5 or V6), whereas this was present in only 85% (100) of the LBBB\textsubscript{control} group (\(p=0.001\)). Inferior (lead II), lateral (lead V1 or V2), QRS notchingslurring was also more prevalent in the LBBB\textsubscript{AVI} group (83% vs 70%, \(p=0.007\) and 20% vs 5%, \(p=0.002\), respectively).

Overall, QRSD was not significantly different between the two groups, neither was RWPT. However, patients with LBBB QRSD \(\geq 130\) ms (98% vs 86%, \(p=0.007\)) and patients meeting the Strauss sex-specific QRS cut-off (95% vs 81%, \(p=0.012\)) were more frequently observed in the LBBB\textsubscript{AVI} group.

Classification according to current LBBB definitions

Of all LBBB\textsubscript{AVI} patients, 100% met the ESC 2013 and 95% the Strauss LBBB definition, whereas only 17% of patients met the AHA 2009 definition (Tab. 2, Fig. 2). Low concordance with the AHA definition is explained by the low prevalence of QRS notchingslurring combined in all four lateral leads (54%, Tab. 2). Interestingly, except for one patient, all LBBB\textsubscript{AVI} patients had QRS notchingslurring in at least two lateral leads (I, aVL, V5 or V6). Furthermore, only 27% of patients had an RWPT >60 ms in both leads V5 and V6, contributing to the low agreement with the AHA 2009 definition. When the analysis was restricted to the first three AHA 2009 criteria only, 48–53% of LBBB\textsubscript{AVI} patients fulfilled the AHA 2009 definition. The presence of a Q wave in lead aVL minimally reduced adherence to the AHA 2009 definition (Tab. 2).

In the LBBB\textsubscript{control} group, concordance with the different definitions was significantly lower than in the LBBB\textsubscript{AVI} group: ESC 2013 85% (\(p=0.001\)) and Strauss 68% (\(p<0.001\)) (Tab. 2, Fig. 2). The lower agreement with the different LBBB definitions is explained by: (1) lower prevalence of lateral notchingslurring (85% vs 100%, \(p=0.001\)) and (2) the higher number of patients with a shorter QRS (QRSD \(\geq 130\) ms, 86% vs 98%, \(p=0.007\) in the LBBB\textsubscript{control} group. Only 7% of patients fulfilled the AHA 2009 definition (\(p=0.035\), compared to LBBB\textsubscript{AVI}). As in the LBBB\textsubscript{AVI} group, low concordance with the AHA 2009 criteria is caused by a low combined prevalence of QRS notchingslurring in all four lateral leads (31%) and most patients not meeting the RWPT criterion (83%).
Table 3  Baseline clinical, echo- and electrocardiographic characteristics of cardiac resynchronisation therapy (CRT) super-responders with left bundle branch block (LBBB) before CRT implantation

| Clinical characteristics                      | LBBB_CRT (n=33) | p-value compared to LBBB_AVI |
|-----------------------------------------------|-----------------|-------------------------------|
| Median age (years)                            | 61 (48;71)      |                               |
| Male                                          | 17 (52)         |                               |
| Coronary artery disease                       | 6 (18)          |                               |
| Acute coronary syndrome                       | 1 (3)           |                               |
| Echocardiographic measurements                |                 |                               |
| End-diastolic diameter (mm)                   | 61 ± 7.7        |                               |
| End-systolic diameter (mm)                    | 52 ± 9.1        |                               |
| End-diastolic volume (ml)                     | 185 ± 48.0      |                               |
| End-systolic volume (ml)                      | 135 ± 37.0      |                               |
| Left ventricular ejection fraction (%)        | 27 ± 5.9        |                               |
| ECG measurements                              |                 |                               |
| PR interval (ms)                              | 180 (156;194)   | 0.103                         |
| QRS duration (ms)                             | 160 (155;173)   | <0.001                        |
| Frontal QRS axis (°)                          | −12 (~38.6)     | 0.937                         |
| LBBB definition features                     |                 |                               |
| QRS duration ≥ 120 ms                         | 33 (100)        | NP                            |
| QRS duration ≥ 130 ms                         | 32 (97)         | 0.149                         |
| QRS duration ≥ 130 ms in females and ≥ 140 ms in males | 31 (94) | 0.369                         |
| QS or rS in V1                                | 33 (100)        | NP                            |
| Absence of Q waves in V5-6                   | 33 (100)        | NP                            |
| Notching/slurring in V5-6, I or aVL           | 33 (100)        | NP                            |
| Notching/slurring in V5-6, I and aVL          | 25 (76)         | 0.047                         |
| Notching/slurring ≥ 2 leads (I, aVL, V1-2, V5-6) | 32 (97) | 0.359                         |
| LBBB definitions                              |                 |                               |
| ESC 2013 definition                           | 33 (100)        | NP                            |
| Strauss definition                            | 32 (97)         | 1.000                         |
| AHA 2009 definition                           | 11 (33)         | 0.119                         |
| AHA 2009 definition without R wave peak time criterion | 23 (70) | 0.127                         |

Values are mean ± standard deviation, median (first quartile; third quartile) or number (%)

| AHA American Heart Association, ESC European Society of Cardiology, NP not possible |

Subanalysis of LBBB_AVI versus LBBB_control with presence of lateral QRS notching

Comparison of LBBB_AVI patients and LBBB_control patients with lateral QRS notching/slurring is shown in the Electronic Supplementary Material (Table S2).

No differences in frontal QRS axis, nor in QRS duration and number of patients with QRS duration ≥ 130 ms were observed between the LBBB_AVI group and the LBBB_control group with lateral notching. Furthermore, concordance with the different LBBB definitions was comparable between LBBB_AVI patients and LBBB_control patients with lateral notching, but not when comparing LBBB_AVI versus LBBB_control without lateral notching.

Extrapolation of LBBB_AVI features to LBBB_CRT

Clinical, echo- and electrocardiographic characteristics of the 33 CRT responders (median age 61 (48;71) years, 52% male) are summarised in Tab. 3. During a median follow-up of 53 (20;77) months, as per definition, LVEF increased from 27± 5.9% to 54± 7.5% (p<0.001). Except for an increased QRS duration (160 [155;173] ms vs 148 [140;160] ms, p<0.001) and a higher prevalence of QRS notching/slurring in all four lateral leads (76% vs 54%, p=0.047) in the LBBB_CRT group, no differences in electrocardiographic features or agreement with the LBBB definitions were observed between LBBB_AVI and LBBB_CRT.

Discussion

Main findings

This study assesses and reviews electrocardiographic features of LBBB in a population with proximal LBBB, i.e. patients with AVI-induced LBBB. As all LBBB_AVI patients had lateral QRS notching/slurring, QRS notching/slurring in the lateral leads is fundamental in the diagnosis of proximal LBBB. The LBBB_AVI group
Proposed criteria for proximal left bundle branch block showed high concordance with ESC 2013 and Strauss definitions, but low agreement with the AHA 2009 definition. Our observations in LBBB AVI were compared to matched LBBB patients from a general population, showing a higher number of patients with QRSD ≥ 130 ms, a higher prevalence of lateral QRS notching/slurring and a higher concordance with LBBB definitions in the LBBB AVI group.

Obstacles in defining LBBB

Current controversy in defining LBBB is primarily related to the difficulty in identifying patients with ‘true’ electrocardiographic LBBB. As studies over the past century have included patients with various types of conduction delay (proximal vs distal, focal vs diffuse), this obviously resulted in heterogeneous LBBB electrocardiographic patterns and criteria. Furthermore, most current LBBB definitions are derived from the same 1985 consensus criteria [19], but with different adaptations and interpretations (Electronic Supplementary Material, Fig. S1).

True LBBB and proximal LBBB: two of a kind?

Although the importance of QRS notching/slurring was acknowledged even in early LBBB definitions [1, 20, 21], CRT was fundamental to the understanding of the relationship between electro-mechanical dyssynchrony in LBBB and a subset of LBBB electrocardiographic patterns with lateral QRS notching/slurring (‘true’ LBBB) [1, 13]. Patients without ‘true’ LBBB morphology were shown to demonstrate less electromechanical dyssynchrony [22], and absence of QRS notching/slurring resulted in less clinical and echocardiographic improvement than in true LBBB patients [6]. Experimental animal studies [14], His bundle pacing [23] and recent mapping studies [15] were able to link these ‘true’ LBBB electrocardiographic patterns with QRS notching to a proximal block in the LBB.

In our procedure-induced LBBB population, QRS notching/slurring was the most distinctive electrocardiographic characteristic of proximal LBBB. Our findings are in line with observational TAVR studies [24, 25] and a recent mapping study by Upadhyay et al., showing that QRS notching had the highest sensitivity and best negative predictive value to diagnose proximal LBBB [15]. Moreover, most proximal LBBBs were correctable by His bundle pacing in their study, indicating that in these patients no distal conduction disease was present. In contrast, LBBB patients without lateral notching demonstrated an intact proximal left conduction system and their LBBB was not correctable by His bundle pacing [15]. These findings suggest that an LBBB pattern without notching/slurring most likely reflects ‘distal block’ [1].
The question remains whether the presence of lateral QRS notching/slurring in a non-AVI-induced LBBB population also corresponds to proximal conduction disease of the left bundle. However, as uniformity was observed among LBBB$_{AVI}$ patients and LBBB$_{control}$ patients with lateral notching, these findings suggest pathophysiological similarities between the two groups and corroborate the evidence of a proximal block in all LBBB patients when notching/slurring is present.

**Proposed criteria for proximal LBBB**

AVI-induced LBBB implies an unequivocal proximal block and is therefore well suited for defining proximal LBBB. Based on our findings in LBBB$_{AVI}$, we selected and adapted currently used criteria (Fig. 3).

QRS duration ≥120 ms

A minority of LBBB$_{AVI}$ patients might present with a QRS duration <130 ms. Of interest is that female LBBB$_{AVI}$ patients had a shorter QRSD than male LBBB$_{AVI}$ patients. This is in line with the findings of previous work by our group, showing that female patients show proximal LBBB morphology at shorter QRSD [26].

QS or rS in lead V1 and absent Q waves in leads V5–6

At inclusion, all our patients had a QS or rS in lead V1 and absent Q waves in leads V5–6. We observed a small Q wave in leads I and aVL in 15% of proximal LBBB patients and therefore recommend against an ‘absent Q wave’ criterion in leads I and aVL.

QRS notching or slurring in ≥2 lateral leads

Patients with proximal LBBB always presented QRS notching/slurring in at least two lateral leads. Only half of the LBBB$_{AVI}$ patients had QRS notching/slurring in all four lateral leads, indicating that AHA 2009 requirements may lead to significant underdiagnosis of LBBB [7, 11, 27]. Whether the variable degree of QRS notching/slurring relates to suboptimal detection and/or differences in underlying electro-anatomical myocardial substrate remains unclear [28].

Leftward and superior oriented frontal QRS axis

Our observations in LBBB$_{AVI}$ support those of previous studies [25, 29], which showed that the onset of LBBB causes a variable degree of QRS axis shift in a leftward and superior direction in most patients. A more leftward oriented QRS axis may support the diagnosis of proximal LBBB, but we recommend against absolute cut-off values because of the large range.

**Advantages of the revised LBBB definition**

The ESC 2013 and Strauss definitions identify most LBBB$_{AVI}$ patients. However, 5–14% of our proximal LBBB patients did not reach the computer-simulation-based Strauss QRSD thresholds of 130 and 140 ms for females and males, respectively. As such, QRS prolongation with a lower limit of 120 ms is preferable to define proximal LBBB. Although the ESC 2013 definition provides excellent sensitivity (100% of LBBB$_{AVI}$ patients fulfilling the definition), the specificity might still be improved by adding the requirement of QRS notching/slurring in at least two lateral leads and the ancillary criterion of a leftward and superior oriented frontal QRS axis: 98% of LBBB$_{AVI}$ patients had QRS notching/slurring in at least two lateral leads and 85% of patients had a QRS axis ≤30°. As AVI-induced LBBB patients and CRT super-responders both represent a ‘true’ LBBB electromechanical substrate within the large spectrum of left ventricular dysfunction, excellent compliance (97%) with the proposed criteria among CRT super-responders corroborates our revised LBBB definition.

**Limitations**

A potential drawback in LBBB$_{AVI}$ patients for studying the characteristics and definition of LBBB may relate to the age and co-morbidity in this particular population. Studying LBBB in a population with an unaffected myocardial substrate could overcome these issues. However, the almost identical observations in LBBB$_{AVI}$ matched LBBB$_{control}$ with lateral notching and LBBB$_{CRT}$ patients argue against important myocardial substrate differences between these populations. In acute LBBB, as in LBBB$_{AVI}$, electrical remodelling might affect electrocardiographic characteristics and alter LBBB features over time. However, this mainly involves changes in repolarisation features rather than changes in QRS features [30].

**Conclusion**

In patients with proximal procedure-induced LBBB, the presence of QRS notching/slurring in the lateral leads seems a sine qua non for proximal LBBB. Non-uniformity exists among current recommendations for the diagnosis of proximal LBBB, with the ESC 2013 and Strauss definitions providing a higher sensitivity than the AHA 2009 definition. The LBBB$_{AVI}$ population may therefore provide a framework for uniform criteria for assessing proximal LBBB.

**Conflict of interest**

S. Calle, M. Coeman, A. Demolder, T. Philipsen, P. Kayaert, M. De Buyzere, F. Timmermans and J. De Pooter declare that they have no competing interests.

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