This is the accepted manuscript of the article, which has been published

in Annals of noninvasive electrocardiology, 2019, 24(4), e12644.

https://doi.org/10.1111/anec.12644

Re-evaluating the electro-vectorcardiographic criteria for left bundle branch block

Andrés Ricardo Pérez-Riera^a, MD PhD; Raimundo Barbosa-Barros^b, MD; Rodrigo

Daminello-Raimundo^a, PhD; Luiz Carlos de Abreu^a, PhD; Marcos Célio de Almeida^c,

MD PhD; Jani Rankinen^e, BM; Fabio Baeub Soler^d, MD; Kjell Nikus^e, MD PhD

^aLaboratorio de Metodologia de Pesquisa e Escrita Científica, Faculdade de Medicina do

ABC, Santo André, São Paulo, Brazil.

^bCoronary Center of the Hospital de Messejana Dr. Carlos Alberto Studart Gomes,

Fortaleza, Ceará, Brazil.

^cInstituto de Biologia-Genética e Morfologia, Universidade de Brasília, Campus

Universitário Darcy Ribeiro, Brasília, DF, Brazil

^dClinica Soler, São Paulo, SP, Brazil

^eHeart Center, Tampere University Hospital and Faculty of Medicine and Life Sciences,

University of Tampere, Finland.

Corresponding author

Andrés Ricardo Pérez-Riera

Rua Sebastião Afonso, 885 Zip code: 04417-100 Jardim Miriam, São Paulo-SP, Brazil

Phone/Fax: (55) 11 5621-2390 / e-mail: riera@uol.com.br

1

Abstract

The criteria for left bundle branch block have gained growing interest in the last few

years. In this overview, we discuss diagnostic and prognostic aspects of different criteria.

It was already shown that stricter criteria, including longer QRS duration and

slurring/notching of the QRS, better identify responders to cardiac resynchronization

therapy. We also include aspects of ST/T concordance and discordance and

vectorcardiography, which could further improve in the finetuning of the left bundle

branch criteria.

Keywords: Left bundle branch block; QRS duration; Cardiac resynchronization therapy;

Concordant and appropriate discordance; QRS notched/slurred R waves in lateral leads.

2

Introduction

In recent years, cardiac resynchronization therapy (CRT) has emerged as an attractive intervention to improve left ventricular (LV) mechanical function by changing the sequence of electrical activation, and it is considered an effective mode of treatment in addition to standard pharmacologic therapy for patients, who have moderate to severe systolic heart failure (NYHA class III-IV) with evidence of cardiac dyssynchrony. The analysis of the electrocardiographic aspects of complete left bundle branch block (CLBBB) has gained growing interest and generated a lot of debate, especially since works by Strauss et al., who questioned the classic criteria for this dromotropic disturbance not only in terms of QRS duration (QRSd) but also in reference to details of the shape and morphology of the QRS complexes. Additionally, the ventricular repolarization polarity related to the correspondent QRS complex has recently been highlighted as a prognostic factor. In discordant LBBB (dLBBB) or "appropriate discordance" the ST segments and T waves have a polarity opposite to the main vector of the QRS complex, while the opposite is true for concordant LBBB (cLBBB).

It is the purpose of this review to perform an update of the electrocardiographic criteria of CLBBB.

Electrocardiographic LBBB criteria analysis

- Supraventricular command: if the rhythm is sinus, the PR interval duration must always be ≥120 ms in adults.
- QRSd: this point is polemic. There are two main points of view related the cut-off value for QRSd:
 - a) Conventional ECG criteria: QRSd ≥120 ms in adults ≥18 years of age, ≥100 ms between 4 to 17 years of age, and ≥90 ms in children less than 4 years of age.

These conventional ECG criteria were included in the American Heart Association/American College of Cardiology Foundation/Heart Rhythm Society (AHA/ACCF/HRS) recommendations for the standardization and interpretation of the electrocardiogram: part III: intraventricular conduction disturbances (Surawicz et al., 2009). These values were also applied in The European Society of Cardiology (ESC) Class 1 Recommendation for CRT (Brignole et al., 2013), the Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION) trial, Cardiac Resynchronization in Heart Failure (CARE-HF) (Bristow et al., 2004), and Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT) (Tang et al., 2010). The conventional ECG criteria may include false-positive cases.

b) New strict criteria: QRSd ≥130 ms (women) or ≥140 ms (men) >18 years of age (Strauss et al., 2009). The new strict LBBB criteria increase the specificity of CLBBB diagnosis in the presence of left ventricular hypertrophy/dilatation and incomplete LBBB, which is critical for selecting CRT patients. The LBBB pattern is currently the most robust ECG criterion in predicting improvement in symptoms and mortality reduction for CRT. However, recent studies using three-dimensional mapping and cardiovascular magnetic resonance imaging (CMRI) have demonstrated heterogeneous LV activation patterns in patients with LBBB. This has led to intense debate on the activation pattern of "true LBBB" and resulted in the proposal of stricter criteria for defining LBBB. Unfortunately, there are patients with a wide QRS who have minimal mechanical dyssynchrony, while there are those with a narrow QRS with significant mechanical dyssynchrony. Reevaluation of the data of CRT trials and electrophysiologic findings in LBBB provided evidence that "true" LBBB requires a QRS width of ≥130 ms in women

and ≥140 ms in men. In "true" LBBB, after 40 ms of the QRS, notched/slurred R waves are characteristic in at least two contiguous leads of I, aVL, V₁, V₂, and V₅- V_6 leads in addition to a \geq 40 ms increase of the QRS complex as compared to the non-LBBB QRS complex. In contrast, slowly and continuously widened "LBBB like" QRS patterns mostly occur in left ventricular hypertrophy (LVH) or in metabolic/infiltrative diseases (Preda, 2013). Unfortunately, ≈30% of patients receiving a CRT do not benefit (non-responders) but are subjected to device complications and costs. Thus, there is a clear need for better selection criteria. Three key studies have suggested that \(^{1}\structure_{3}\) of patients diagnosed with LBBB by conventional ECG criteria may not have true LBBB, but likely have a combination of LVH and left anterior fascicular block (LAFB). Conventional criteria for CRT eligibility include a QRSd ≥120 ms. However, studies have suggested that only patients with LBBB, not those with right bundle branch block (RBBB) or nonspecific intraventricular conduction delay, benefit from CRT, and. Strauss et al reviewed the pathophysiologic and clinical evidence supporting why only patients with CLBBB benefit for CRT. Additionally, they pointed out that the threshold of 120 ms to define LBBB was derived subjectively at a time when criteria for LBBB and RBBB were mistakenly reversed. These authors proposed stricter criteria for CLBBB that include a QRS duration ≥140 ms for men and \geq 130 ms for women, along with mid-QRS notching or slurring in \geq 2 contiguous leads. Further studies are needed to reinvestigate the ECG criteria for CLBBB and the implications of these criteria for selecting patients for CRT. New strict LBBB criteria increase the specificity of CLBBB diagnosis in the presence of LVH/dilatation and incomplete LBBB, which is critical for selecting CRT patients (Galeotti, van Dam, Loring, Chan, & Strauss, 2013). In patients with guidelinedefined LBBB, the absence of ECG markers of residual left bundle conduction delay was predictive of a greater improvement in LV function with CRT. An r wave ≥ 1 mm in lead V_1 and/or a q wave ≥ 1 mm in lead aVL (q-aVL) are used to identify patients with residual left bundle branch conduction (Perrin et al., 2012). In patients with conventional wider LBBB morphology, the presence of mid-QRS notching or slurring is a strong predictor of better response to CRT (Tian et al., 2013). The typical surface ECG feature of LBBB is a prolongation of QRS above 110 ms in combination with a delay of the ventricular activation time (intrinsicoid deflection or "R-wave peak time") in the left leads V5 and V6 ≥60 ms and no septal q waves in leads I, V5-V6 due to the abnormal septal activation from right to left. LBBB may induce abnormalities in LV performance due to abnormal asynchronous contraction patterns, which can be compensated by biventricular pacing (resynchronization therapy). Asynchronous electrical activation of the ventricles causes regional differences in workload which may lead to asymmetric hypertrophy and LV dilatation, especially due to increased wall mass in lateactivated regions. This may aggravate preexisting LV systolic dysfunction or even induce it. Of special interest are patients with LBBB and normal LV dimensions and normal LV ejection fraction (LVEF) at rest but who may have an abnormal increase in pulmonary artery pressure during exercise, production of lactate during high-rate pacing, signs of ischemia (not caused by coronary artery narrowing) on myocardial scintigrams and abnormal ultrastructural findings on myocardial biopsy. For this entity, the term latent cardiomyopathy had been suggested (Breithardt & Breithardt, 2012). Figure 1 shows a typical example of "false" LBBB in a non-responder to CRT. In this case notching/slurring of the R after the initial 40 ms of the QRS in at least two contiguous leads of I, aVL, V1, V2, and

V5-V6 required for strict LBBB criteria ("true" LBBB) are missing. In the case of false LBBB, the QRS loop in the three planes does not have middle-final conduction delay manifested by nearer dashes, one additional vectorcardiographic criteria of slowed conduction, which is the hallmark of the truly LBBB. Narrow QRS and nonspecific intraventricular conduction delay patients have distinct mechanisms of LV activation, which may predict poor response to CRT (Derval et al., 2017). Strauss' stricter criteria remain controversial, so recent research shows that stricter definition of LBBB did not improve response to CRT in comparison to the current AHA definition (Bertaglia et al., 2017). On the other hand, patients with true LBBB, either Strauss or Predict criteria, had better echocardiographic response (Mascioli et al., 2012) and lower incidence of heart failure hospitalization than non-true LBBB with CRT (Garcia-Seara et al., 2018). Studies have identified sub-populations of non-LBBB patients that respond to resynchronization, such as those with prolonged PR intervals (≥ 230 ms) (Lin, Buhr, & Kipp, 2017), with RBBB and concomitant left-sided delay and those with significant burden of right ventricular pacing (Belkin & Upadhyay, 2017). Females show true LBBB pattern at shorter QRSd and have more frequent mechanical dyssynchrony at shorter QRSd related to males. This might explain the better CRT response rates at shorter QRSd in women (De Pooter et al., 2018). Despite the discordances, the LBBB pattern is currently the most robust ECG criterion in predicting improvement in symptoms and reduction in mortality. Consequently, the use of Strauss' stricter criteria appears warranted (Kanawati & Sy, 2018). Poposka et al. observed that the amplitude of R wave in V6, higher R/S ratio in V6 and higher computed variable (S1 + R6) - (S6 + R1) may predict the likelihood of response to CRT therapy in both LBBB-patients and non-LBBB

patients. Responders in non-LBBB patients kept the significant difference only in the height of R waves in V6. The R6/S6 ratio tended to be higher, but it did not reach a statistical significance (Poposka et al., 2018). Bear et al. evaluated the sensitivity of body surface mapping and ECG imaging to detect electrical dyssynchrony noninvasively, and experimentally using Langendorff isolated perfused in pig hearts with LBBB induced through ablation. They concluded that ECG imaging reliably and accurately detects electrical dyssynchrony, resynchronization by biventricular pacing, and the site of latest activation, providing more information than do body surface potentials (Bear et al., 2018). Finally, Pérez-Riera et al. suggested that VCG identifies more easily true LBBB, because mid-end conduction in the QRS loop is pathognomonic of true LBBB (Perez-Riera et al., 2018).

Variable definitions of LBBB used in different clinical and research settings

- I. AHA/ACCF/HRS recommendations (Surawicz et al., 2009): QRSd≥120 ms with wide notched or slurred R wave in leads I, aVL and V5 -V6; occasional RS pattern in V5-V6 by displaced transition of QRS complex and other cause; absence of q waves in leads I, V5-V6; R-wave peak time >60 ms in leads V5-V6 but normal in leads V1 to V3; discordant ST segment and T waves;
- II. Strauss's strict criteria definition (Strauss, Selvester, & Wagner, 2011): QRSd ≥140 ms in men and ≥130 ms in women. Additionally, QS or rS in V1 and V2, and mid-QRS notching or slurring in ≥2 contiguous leads of V1, V2, V5, V6, I and aVL;
- III. AHA/ACCF/HRS Class 1 Recommendation for CRT (Epstein et al., 2013): QRSd
 ≥150 ms. "LBBB morphology" as per AHA/ACCF/HRS recommendations;

- IV. ESC Class 1 Recommendation for CRT (Brignole et al., 2013): QRSd ≥120 ms with QS or rS in V1, wide (frequently notched or slurred) R wave in leads I, aVL,
 V5 or V6, absence of q waves in leads V5 and V6;
- V. ECG inclusion criteria for various major landmark CRT trials Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION)
 (Bristow et al., 2004): QRSd ≥120 ms;
- VI. Cardiac Resynchronization in Heart Failure (CARE-HF) (Cleland et al., 2005):

 QRSd between 120–150 ms + echo dyssynchrony;
- VII. Multicenter Automatic Defibrillator Implantation Trial with Cardiac Resynchronization Therapy (MADIT-CRT) (Moss et al., 2009): QRSd ≥130 ms.
- VIII. Resynchronization-Defibrillation for Ambulatory Heart Failure Trial (RAFT) (Tang et al., 2010): QRSd≥120 ms.
- 3. Dominant S wave in right precordial leads or QS pattern: QRS complexes in the right precordial leads (V1-V2) total or predominantly negative: rS (70%), QS (>29%) or qrS (<1%) (Figures 2A, 2B, 2C). An initial r wave of ≥1 mm in lead V₁ suggests intact left to right ventricular septal activation with existing conduction over the left bundle branch. This also identifies LBBB patients at low risk of complete heart block during right heart catheterization. These findings indicate that an initial r wave of ≥1 mm in lead V1, present in a ≈28% of ECGs with classically defined LBBB, may constitute a new exclusion criterion when defining complete LBBB (Padanilam et al., 2010). An increase of the voltage of the initial R wave in V₁ is occasionally seen with infarction of the ventricular septum in complicated LBBB.</p>
- 4. **Lateral leads:** a monophasic, broad mid-QRS notching or slurring R wave, recorded in the left lateral leads I, aVL and V5-V6 is the rule. The QRS transition zone is related

to the electrical axis of the heart in the horizontal plane and is easily determined from the precordial leads of a standard 12-lead ECG. The QRS transition zone is defined as the precordial lead where the QRS pattern changes from an rS to an Rs configuration, or the lead where an isoelectric RS pattern is present. A delayed transition is defined as the transition occurring at V5 or beyond; Delayed QRS transition in the precordial leads of an ECG seems to be a novel ECG risk marker for sudden cardiac death (SCD). In particular, markedly delayed transition was associated with significantly increased risk of SCD, independent of confounding factors (Aro et al., 2014) (Figures 2D, 2E, 2F, 2G).

- 5. QS pattern almost constantly followed by ST-segment elevation and a positive T wave in aVR.
- 6. Prolonged R-wave peak time (R-WPT) or ventricular activation time (VAT): ≥60 ms in leads V5 and V6 but normal in leads V1, V2 and V3 in cases of CLBBB. The nomenclature "intrinsicoid deflection" should be abandoned according to the last 2009 consensus (AHA/ACCF/HRS recommendations) (Surawicz et al., 2009).

Figure 3 shows an explanation for atypical LBBB with initial q wave in the left lateral leads (A) and prolonged ventricular activation time in CLBBB in lateral precordial leads (B).

7. Abnormalities in the ST segment and T wave: the ventricular repolarization abnormalities that occur as the direct result of changes in the sequence and/or duration of ventricular depolarization, manifested electrocardiographically as changes in QRS shape and/or duration, are referred to as secondary repolarization abnormalities. In uncomplicated LBBB, the ST segment and T wave are more frequently displaced

in a direction opposite to that of the main QRS deflection or "appropriate discordance" observed in ≈70% of cases. In right precordial leads is observed elevated ST segment has a straight upward slope, or an upward slope that is minimally concave-upwards followed by an upright T wave with asymmetrical limbs and a relatively blunt apex. Positive ST-segment displacement in the right precordial leads (V1 and V2) is much more difficult to evaluate in cases of acute coronary syndrome with ST segment elevation, since this elevation may also occur in uncomplicated LBBB. Stable ≥5 mm ST-segment elevation is occasionally found in leads with predominantly negative QRS complexes, particularly if they are of large amplitude in the absence of acute myocardial infarction (AMI). In such patients presenting with symptoms suggestive of AMI, further non-ECG confirmation of a probable underlying AMI should be sought for (Madias et al., 2001).

When QRS complexes in the left/lateral leads and the ST-segment/T-wave have the same polarity, the term cLBBB repolarization is used, and this is observed in ≈ 28 to 32% of cases (Padeletti et al., 2018). The definition of cLBBB is T-wave orientation concordant with QRS complex with a positive/diphasic T wave in at least two of the leads I and V5 or V6 (Padeletti et al., 2018) (Figure 4).

Ventricular repolarization in uncomplicated CLBBB

The ST- segment and T-wave vectors are more frequently opposite to the predominant deflection of the QRS: positive from V_1 to V_3 and negative in left leads I, aVL, V5 and V6. These are secondary repolarization abnormalities with a wide QRS-ST-T angle and normal ventricular gradient. The classic ventricular gradient concept introduced by Wilson et al. in 1931(Wilson, Macleod, & Barker, 1931) is of theoretical interest

concerning primary versus secondary repolarization abnormalities. The ventricular gradient in a single ECG lead is the net time integral of the ECG voltage from the beginning of the P wave to the end of the U wave. Its spatial counterpart is the ventricular gradient vector determined from the orthogonal XYZ leads. The practical utility of the ventricular gradient in differentiating primary from secondary repolarization abnormalities has not been demonstrated (Surawicz, 1988). When the direction of the QRS axis is normal, an abnormal direction of the T-wave axis is generally an indication of primary repolarization abnormalities.

The clinical implications of discordant and concordant LBBB are listed in Table 1.

Vectorcardiographic criteria for true CLBBB in the horizontal plane

- Narrow, long QRS loop usually with rotation in 8;
- The QRS loop duration ≥ 130 ms (women) or ≥ 140 ms (men), 65 or 70 dashes respectively (one dash = 2 ms);
- The QRS loop shape is elongated and narrow;
- The main body of the QRS loop is inscribed posteriorly and to the left within the range
 -90° to -40°;
- Maximal QRS vector located in the left posterior quadrant (between -40° to -80°) and of increased magnitude (>2 mV);
- Main portions of QRS loop of clockwise rotation. Counterclockwise rotation may indicate parietal CLBBB or associated lateral infarction or severe LVH;
- The efferent limb (II) located to the right with respect to the afferent limb (III and IV);
- Conduction delay noted in the mid and terminal portion: middle + end conduction delay;
- The main body of QRS loop is inscribed clockwise;

- The magnitude of the maximal QRS vector is increased above normal exceeding 2 mV;
- ST-segment and T-wave vector directed rightward and anteriorly in opposite direction
 with respect to the QRS loop: QRS-loop/ST-T angle ≥90° (discordant) or QRS-loop/ST-T angle <90° (concordant);
- T loop of counterclockwise or clockwise rotation. The clockwise rotation of T wave in this plane suggests CLBBB complicating LVH or myocardial infarction (Perez-Riera et al., 2018).

The prognosis in CLBBB

LBBB is a common ECG abnormality seen in patients, in whom cardiac conduction along the anterior, mid and posterior left fascicles of the His-Purkinje system is compromised. Although LBBB is often associated with significant heart disease and is often the result of myocardial injury or hypertrophy, it can also be seen in patients without LV disease. An isolated LBBB without cardiac symptoms or abnormalities does not necessarily impair the prognosis of the patient. However, LBBB can have markedly negative prognostic impact, especially in patients presenting with acute chest pain, syncope and in those suffering from heart failure with reduced LV ejection fraction. New onset LBBB should always be considered a sign of pathology and is a marker of acute myocardial infarction in a small proportion of patients. Although LBBB is no longer considered as an equivalent to ST-segment elevation MI equivalent in patients presenting with chest pain, concordant LBBB (Sgarbossa criteria), especially if new-onset, may indicate acute coronary occlusion.

LBBB is associated with poorer prognosis both in comparison to normal intraventricular conduction and RBBB (Baldasseroni et al., 2002; Freedman, Alderman, Sheffield,

Saporito, & Fisher, 1987; Hesse, Diaz, Snader, Blackstone, & Lauer, 2001; Schneider, Thomas, Kreger, McNamara, & Kannel, 1979).

Patients with LBBB have increased rates of cardiovascular mortality, sudden cardiac death and heart failure (Baldasseroni et al., 2002; Hesse et al., 2001; Rotman & Triebwasser, 1975; Schneider et al., 1979; Smith & Hayes, 1965).

Chronic BBB and nonfunctional atrioventricular (AV) block induced by incremental atrial pacing and/or infranodal conduction time (His to ventricle interval, HV) ≥70 ms had a significantly higher incidence of progression to spontaneous second- or third-degree AV block, with subjects with HV interval ≥100 ms presenting the highest risk (Petrac, Radic, Birtic, & Gjurovic, 1996; Scheinman et al., 1983; Scheinman et al., 1982).

Compared with concordant LBBB, discordant LBBB morphology was associated with more severe coronary artery disease (Khalil et al., 2016) and heart failure and worse prognosis, even in patients receiving a CRT with defibrillator capacity (Padeletti et al., 2018). Additionally, there was a trend towards more frequent occurrence of ventricular tachycardia/ventricular fibrillation/deaths in patients with discordant than in concordant LBBB, but statistical significance was not reached.

Isolated LBBB is associated with an increased risk of developing overt cardiovascular disease and increased cardiac mortality. The study included 110,000 participants in a screening program, 310 subjects with BBB without apparent or suspected heart disease were identified. Their outcome after a mean follow-up of 9.5 years was compared with that of 310 similarly screened age- and sex-matched controls (Fahy et al., 1996).

In a study by Eriksson et al. with 28 years of follow up with 7392 men without a history of myocardial infarction or stroke and without angina or dyspnea at baseline, men with LBBB had increased risk of developing AMI, heart failure, high-degree atrioventricular block and increased risk of coronary death, but not all-cause mortality. Thus, LBBB can

be a sign of a progressive degenerative disease that affects not only the conduction system but also the myocardium itself (Eriksson, Wilhelmsen, & Rosengren, 2005). It should be realized that one cannot exclude the possibility of undetected cardiovascular disease in patients with LBBB.

While the prognosis of isolated LBBB without associated cardiovascular disease varies from controversial to neutral, in otherwise normal hearts, LBBB leads to mechanical asynchrony with reduction of LV ejection fraction and redistribution of circumferential shortening and myocardial blood flow from the septum to the left lateral wall. It was shown in an animal model study that LBBB leads to asymmetric hypertrophy and dilatation of the left ventricle. Thus, LBBB can solely initiate remodeling in a normal heart (Vernooy et al., 2005).

Xia et al. developed a series of algorithms to automatically detect and measure parameters required for strict LBBB criteria and proposed a definition of QRS notch detection in signal-averaged 12-lead ECGs recorded from 612 LBBB patients (Xia et al., 2017). The proposed algorithms automatically measured QRS features for the diagnosis of strict LBBB and the study showed good performance in reference to manual results. However, to provide patients with the best standard of care, critical knowledge in ECG interpretation is necessary, and it requires close cooperation between clinical ECG experts and manufacturers of computer-interpreted ECG. Additionally, computer algorithms frequently present incorrect readings for conduction disorders.

Conclusion

The ECG characteristics of LBBB are important for therapeutic and prognostic purposes. In addition to the strict LBBB criteria introduced by Strauss et al, which include gender-specific cut-off for QRS duration and slurring/notching of the QRS. Additionally, the

vectorcardiogram may be decisive in differentiating between true and pseudo-LBBB by the presence (LBBB) or absence (LVH) of a mid- and terminal conduction delay of the QRS loop. The QRS loop discordance/concordance should also be taken into account for risk stratification.

Conflicts of interest

The authors declare that they have no conflicts of interest.

References

- Aro, A. L., Eranti, A., Anttonen, O., Kerola, T., Rissanen, H. A., Knekt, P., . . .
 Huikuri, H. V. (2014). Delayed QRS transition in the precordial leads of an electrocardiogram as a predictor of sudden cardiac death in the general population.
 Heart Rhythm, 11(12), 2254-2260. doi: 10.1016/j.hrthm.2014.08.014
- 2. Baldasseroni, S., Opasich, C., Gorini, M., Lucci, D., Marchionni, N., Marini, M., . . . Italian Network on Congestive Heart Failure, I. (2002). Left bundle-branch block is associated with increased 1-year sudden and total mortality rate in 5517 outpatients with congestive heart failure: a report from the Italian network on congestive heart failure. *Am Heart J*, 143(3), 398-405.
- Bear, L. R., Huntjens, P. R., Walton, R. D., Bernus, O., Coronel, R., & Dubois, R. (2018). Cardiac electrical dyssynchrony is accurately detected by noninvasive electrocardiographic imaging. *Heart Rhythm*, 15(7), 1058-1069. doi: 10.1016/j.hrthm.2018.02.024
- Belkin, M. N., & Upadhyay, G. A. (2017). Does Cardiac Resynchronization Therapy Benefit Patients with Non-Left Bundle Branch Block Prolonged QRS Patterns? *Curr Cardiol Rep*, 19(12), 125. doi: 10.1007/s11886-017-0929-8
- Bertaglia, E., Migliore, F., Baritussio, A., De Simone, A., Reggiani, A., Pecora, D., .

 Stabile, G. (2017). Stricter criteria for left bundle branch block diagnosis do not improve response to CRT. *Pacing Clin Electrophysiol*, 40(7), 850-856. doi: 10.1111/pace.13104
- 6. Breithardt, G., & Breithardt, O. A. (2012). Left bundle branch block, an old-new entity. *J Cardiovasc Transl Res*, 5(2), 107-116. doi: 10.1007/s12265-011-9344-5
- 7. Brignole, M., Auricchio, A., Baron-Esquivias, G., Bordachar, P., Boriani, G., Breithardt, O. A., . . . Wilson, C. M. (2013). 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*, 34(29), 2281-2329. doi: 10.1093/eurheartj/eht150
- Bristow, M. R., Saxon, L. A., Boehmer, J., Krueger, S., Kass, D. A., De Marco, T., .
 Defibrillation in Heart Failure, I. (2004). Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. *N Engl J Med*, 350(21), 2140-2150. doi: 10.1056/NEJMoa032423
- Cleland, J. G., Daubert, J. C., Erdmann, E., Freemantle, N., Gras, D., Kappenberger, L., . . . Cardiac Resynchronization-Heart Failure Study, I. (2005). The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med*, 352(15), 1539-1549. doi: 10.1056/NEJMoa050496
- De Pooter, J., Kamoen, V., El Haddad, M., Stroobandt, R., De Buyzere, M., Jordaens,
 L., & Timmermans, F. (2018). Gender differences in electro-mechanical characteristics of left bundle branch block: Potential implications for selection and response of cardiac resynchronization therapy. *Int J Cardiol*, 257, 84-91. doi: 10.1016/j.ijcard.2017.10.055
- 11. Derval, N., Duchateau, J., Mahida, S., Eschalier, R., Sacher, F., Lumens, J., . . . Bordachar, P. (2017). Distinctive Left Ventricular Activations Associated With ECG Pattern in Heart Failure Patients. *Circ Arrhythm Electrophysiol*, 10(6). doi: 10.1161/CIRCEP.117.005073
- 12. Epstein, A. E., DiMarco, J. P., Ellenbogen, K. A., Estes, N. A., 3rd, Freedman, R. A., Gettes, L. S., . . . Heart Rhythm, S. (2013). 2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American College of Cardiology

- Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol*, 61(3), e6-75. doi: 10.1016/j.jacc.2012.11.007
- 13. Eriksson, P., Wilhelmsen, L., & Rosengren, A. (2005). Bundle-branch block in middle-aged men: risk of complications and death over 28 years. The Primary Prevention Study in Goteborg, Sweden. Eur Heart J, 26(21), 2300-2306. doi: 10.1093/eurheartj/ehi580
- 14. Fahy, G. J., Pinski, S. L., Miller, D. P., McCabe, N., Pye, C., Walsh, M. J., & Robinson, K. (1996). Natural history of isolated bundle branch block. *Am J Cardiol*, 77(14), 1185-1190.
- 15. Freedman, R. A., Alderman, E. L., Sheffield, L. T., Saporito, M., & Fisher, L. D. (1987). Bundle branch block in patients with chronic coronary artery disease: angiographic correlates and prognostic significance. *J Am Coll Cardiol*, 10(1), 73-80.
- 16. Galeotti, L., van Dam, P. M., Loring, Z., Chan, D., & Strauss, D. G. (2013).
 Evaluating strict and conventional left bundle branch block criteria using electrocardiographic simulations. *Europace*, 15(12), 1816-1821. doi: 10.1093/europace/eut132
- 17. Garcia-Seara, J., Iglesias Alvarez, D., Alvarez Alvarez, B., Gude Sampedro, F., Martinez Sande, J. L., Rodriguez-Manero, M., . . . Gonzalez Juanatey, J. R. (2018). Cardiac resynchronization therapy response in heart failure patients with different subtypes of true left bundle branch block. *J Interv Card Electrophysiol*, 52(1), 91-101. doi: 10.1007/s10840-018-0363-x
- 18. Hesse, B., Diaz, L. A., Snader, C. E., Blackstone, E. H., & Lauer, M. S. (2001). Complete bundle branch block as an independent predictor of all-cause mortality:

- report of 7,073 patients referred for nuclear exercise testing. *Am J Med*, 110(4), 253-259.
- 19. Kanawati, J., & Sy, R. W. (2018). Contemporary Review of Left Bundle Branch Block in the Failing Heart Pathogenesis, Prognosis, and Therapy. *Heart Lung Circ*, 27(3), 291-300. doi: 10.1016/j.hlc.2017.09.007
- 20. Khalil, J., Bernard, A. S., Maurice, K., Zaheer, Y., Marwan, R., Abdallah, R., Hadi, S. (2016). Discordant vs. concordant left bundle branch block: A potential clinical significance. *J Electrocardiol*, 49(1), 69-75. doi: 10.1016/j.jelectrocard.2015.08.031
- 21. Lin, J., Buhr, K. A., & Kipp, R. (2017). Effect of PR Interval on Outcomes Following Cardiac Resynchronization Therapy: A Secondary Analysis of the COMPANION Trial. *J Cardiovasc Electrophysiol*, 28(2), 185-191. doi: 10.1111/jce.13131
- 22. Madias, J. E., Sinha, A., Ashtiani, R., Agarwal, H., Win, M., & Narayan, V. K. (2001).

 A critique of the new ST-segment criteria for the diagnosis of acute myocardial infarction in patients with left bundle-branch block. *Clin Cardiol*, 24(10), 652-655.
- 23. Mascioli, G., Padeletti, L., Sassone, B., Zecchin, M., Lucca, E., Sacchi, S., Sinagra, G. (2012). Electrocardiographic criteria of true left bundle branch block: a simple sign to predict a better clinical and instrumental response to CRT. *Pacing Clin Electrophysiol*, *35*(8), 927-934. doi: 10.1111/j.1540-8159.2012.03427.x
- 24. Medrano, G. A., Brenes, C., De Micheli, A., & Sodi-Pallares, D. (1970).
 [Simultaneous block of the anterior and posterior subdivisions of the left branch of the bundle of His (biphasic block), and its association with the right branch block (triphasic block). Experimental and clinical electrocardiographic study]. *Arch Inst Cardiol Mex*, 40(6), 752-770.

- 25. Moss, A. J., Hall, W. J., Cannom, D. S., Klein, H., Brown, M. W., Daubert, J. P., . . . Investigators, M.-C. T. (2009). Cardiac-resynchronization therapy for the prevention of heart-failure events. N Engl J Med, 361(14), 1329-1338. doi: 10.1056/NEJMoa0906431
- 26. Padanilam, B. J., Morris, K. E., Olson, J. A., Rippy, J. S., Walsh, M. N., Subramanian, N., . . . Steinberg, L. A. (2010). The surface electrocardiogram predicts risk of heart block during right heart catheterization in patients with preexisting left bundle branch block: implications for the definition of complete left bundle branch block. *J Cardiovasc Electrophysiol*, 21(7), 781-785. doi: 10.1111/j.1540-8167.2009.01714.x
- 27. Padeletti, L., Aimo, A., Vishenvsky, B., Schwartz, A., McNitt, S., Wang, P. J., . . . Zareba, W. (2018). The prognostic benefit of cardiac resynchronization therapy is greater in concordant vs. discordant left bundle branch block in the Multicenter Automatic Defibrillator Implantation Trial-Cardiac Resynchronization Therapy (MADIT-CRT). *Europace*, 20(5), 794-800. doi: 10.1093/europace/euw446
- 28. Padeletti, L., Valleggi, A., Vergaro, G., Luca, F., Rao, C. M., Perrotta, L., . . . Emdin, M. (2010). Concordant versus discordant left bundle branch block in heart failure patients: novel clinical value of an old electrocardiographic diagnosis. *J Card Fail*, 16(4), 320-326. doi: 10.1016/j.cardfail.2009.12.005
- 29. Penaloza, D., & Tranchesi, J. (1955). The three main vectors of the ventricular activation process in the normal human heart. I. Its significance. *Am Heart J*, 49(1), 51-67.
- 30. Perez-Riera, A. R., Barbosa-Barros, R., de Rezende Barbosa, M. P. C., Daminello-Raimundo, R., de Abreu, L. C., & Nikus, K. (2018). Left bundle branch block: Epidemiology, etiology, anatomic features, electrovectorcardiography, and

- classification proposal. *Ann Noninvasive Electrocardiol*, e12572. doi: 10.1111/anec.12572
- 31. Perrin, M. J., Green, M. S., Redpath, C. J., Nery, P. B., Keren, A., Beanlands, R. S., & Birnie, D. H. (2012). Greater response to cardiac resynchronization therapy in patients with true complete left bundle branch block: a PREDICT substudy. *Europace*, 14(5), 690-695. doi: 10.1093/europace/eur381
- 32. Petrac, D., Radic, B., Birtic, K., & Gjurovic, J. (1996). Prospective evaluation of infrahisal second-degree AV block induced by atrial pacing in the presence of chronic bundle branch block and syncope. *Pacing Clin Electrophysiol*, *19*(5), 784-792.
- 33. Poposka, L., Boskov, V., Risteski, D., Taleski, J., Janusevski, F., Srbinovska, E., & Georgievska-Ismail, L. (2018). Electrocardiographic Parameters as Predictors of Response to Cardiac Resynchronization Therapy. *Open Access Maced J Med Sci*, 6(2), 297-302. doi: 10.3889/oamjms.2018.092
- 34. Preda, I. (2013). [Results of randomized studies on cardiac resynchronization therapy and the reevaluation of cardiac ventricular activation in left bundle branch block]. *Orv Hetil*, *154*(18), 688-693. doi: 10.1556/OH.2013.29596
- 35. Rotman, M., & Triebwasser, J. H. (1975). A clinical and follow-up study of right and left bundle branch block. *Circulation*, *51*(3), 477-484.
- 36. Scheinman, M. M., Peters, R. W., Morady, F., Sauve, M. J., Malone, P., & Modin, G. (1983). Electrophysiologic studies in patients with bundle branch block. *Pacing Clin Electrophysiol*, 6(5 Pt 2), 1157-1165.
- 37. Scheinman, M. M., Peters, R. W., Suave, M. J., Desai, J., Abbott, J. A., Cogan, J., . . . Williams, K. (1982). Value of the H-Q interval in patients with bundle branch block and the role of prophylactic permanent pacing. *Am J Cardiol*, *50*(6), 1316-1322.

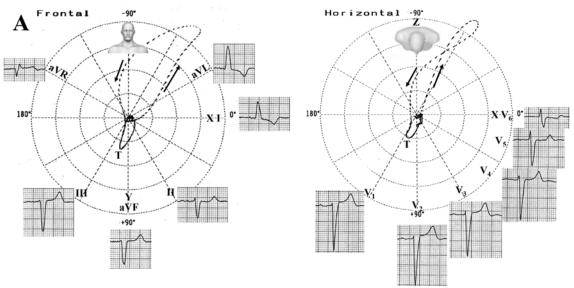
- Schneider, J. F., Thomas, H. E., Jr., Kreger, B. E., McNamara, P. M., & Kannel, W. B. (1979). Newly acquired left bundle-branch block: the Framingham study. *Ann Intern Med*, 90(3), 303-310.
- 39. Smith, S., & Hayes, W. L. (1965). The Prognosis of Complete Left Bundle Branch Block. *Am Heart J*, 70, 157-159.
- 40. Strauss, D. G., Olson, C. W., Wu, K. C., Heiberg, E., Persson, E., Selvester, R. H., . .
 Arheden, H. (2009). Vectorcardiogram synthesized from the 12-lead electrocardiogram to image ischemia. *J Electrocardiol*, 42(2), 190-197. doi: 10.1016/j.jelectrocard.2008.12.018
- 41. Strauss, D. G., Selvester, R. H., & Wagner, G. S. (2011). Defining left bundle branch block in the era of cardiac resynchronization therapy. *Am J Cardiol*, *107*(6), 927-934. doi: 10.1016/j.amjcard.2010.11.010
- 42. Surawicz, B. (1988). ST-T abnormalities. In P. W. MacFarlane & T. D. V. Lawrie (Eds.), *Comprehensive Electrocardiology* (pp. 511-563). New York, NY: Pergamon Books, Ltd.
- 43. Surawicz, B., Childers, R., Deal, B. J., Gettes, L. S., Bailey, J. J., Gorgels, A., . . . Heart Rhythm, S. (2009). 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*, *53*(11), 976-981. doi: 10.1016/j.jacc.2008.12.013
- 44. Tang, A. S., Wells, G. A., Talajic, M., Arnold, M. O., Sheldon, R., Connolly, S., . . . Resynchronization-Defibrillation for Ambulatory Heart Failure Trial, I. (2010).

- Cardiac-resynchronization therapy for mild-to-moderate heart failure. *N Engl J Med*, *363*(25), 2385-2395. doi: 10.1056/NEJMoa1009540
- 45. Tian, Y., Zhang, P., Li, X., Gao, Y., Zhu, T., Wang, L., . . . Guo, J. (2013). True complete left bundle branch block morphology strongly predicts good response to cardiac resynchronization therapy. *Europace*, *15*(10), 1499-1506. doi: 10.1093/europace/eut049
- 46. Vernooy, K., Verbeek, X. A., Peschar, M., Crijns, H. J., Arts, T., Cornelussen, R. N., & Prinzen, F. W. (2005). Left bundle branch block induces ventricular remodelling and functional septal hypoperfusion. *Eur Heart J*, 26(1), 91-98. doi: 10.1093/eurheartj/ehi008
- 47. Wilson, F. N., Macleod, A. G., & Barker, P. S. (1931). The T deflection of the electrocardiogram. *Trans Assoc Am Physicians*, 46, 29-38.
- 48. Xia, X., Ruwald, A. C., Ruwald, M. H., Ugoeke, N., Szepietowska, B., Kutyifa, V., . . . Couderc, J. P. (2017). Validation of an automatic diagnosis of strict left bundle branch block criteria using 12-lead electrocardiograms. Ann Noninvasive Electrocardiol, 22(2). doi: 10.1111/anec.12398

Figure legends

Figure 1 ECG/VCG correlation across the precordial leads

- A) ECG/VCG from CRT non-responder fulfilling inclusion criteria for major CRT clinical trials with QRSd of at least 120 ms (in this example exactly 120 ms), broad R wave in I, aVL, V5 and, V6, discordant ST segments and T waves, and absence of Q waves in I, V5 and V6. Also, the features broad mid-QRS notching or slurring of the R wave in the left leads I, aVL and V5-V6 in the strict Strauss' criteria are missing. Additionally, this VCG differentiates from true CLBBB by absence of middle-final delay (obligatory in true LBBB).
- B) The QRS loop shape is elongated and narrow; the main body of the QRS loop is inscribed posteriorly and to the left within the range 90 to 40°; conduction delay noted in the mid and terminal portion; the main body of QRS loop is inscribed clockwise (CW); the magnitude of the max QRS vector is increased above normal exceeding 2mV; ST segment and T wave vector are directed rightward and anteriorly (opposite to QRS-loop).



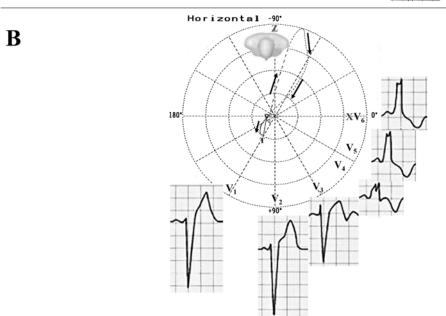


Figure 2 Examples of QRS complex patterns observed in the right (A, B, C) and left precordial leads (D, E, F, G)

rS in ~70% (A), QS in >29% (B) and qrS in <1% (C)

As the ventricles are activated sequentially (first right, then left) rather than simultaneously, this produces a broad or notched ('M'-shaped) R wave in the lateral leads (D). Additionally, there may be initial narrow q in aVL and exceptionally in I, but never in V5 and V6 (E), monophasic tall R wave without notch (F), and occasionally an Rs or rS pattern in V5 and V6 (G), which may indicate: a) displacement of the precordial transition zone of the QRS complex to the left; b) associated right ventricular hypertrophy (RVH); c) associated LAFB; d) associated myocardial infarction of the LV free wall.

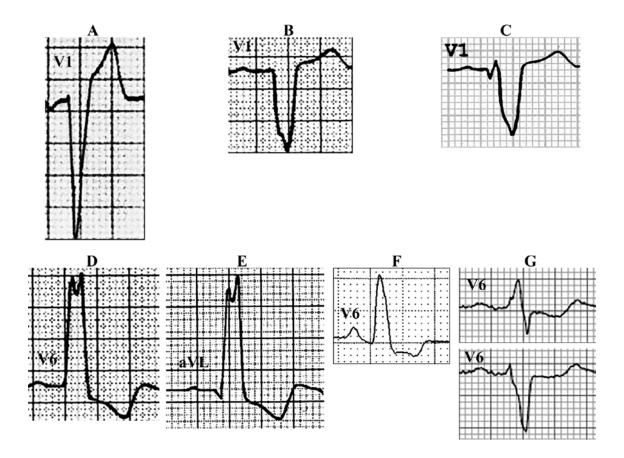


Figure 3 Fascicular or divisional CLBBB with initial q wave in the left leads (A) and prolonged ventricular activation time in CLBBB in lateral precordial leads (B)

Outline of CLBBB with initial q wave in the left lateral leads (Medrano et al., 1970). The LSF emerges before the bifascicular block area, preserving the first 10 ms septal vector, anteromedial (I_{AM}) vector or Penaloza-Tranchesi vector (Penaloza & Tranchesi, 1955). In these cases, the initial ventricular activation is normal, heading to the right and the front with qR in left leads (atypical CLBBB) (A). Ventricular activation time (VAT) \geq 60 ms in I and V_5 - V_6 but normal in V1-V2 and V3, when small initial r waves can be discerned in the right precordial leads (B).

LBB: left bundle branch; RBBB: right bundle branch; LAFB: left anterior fascicular block; LPFB: left posterior fascicular block; LSF: left septal fascicle; I_{AM}: first anteromedial vector.

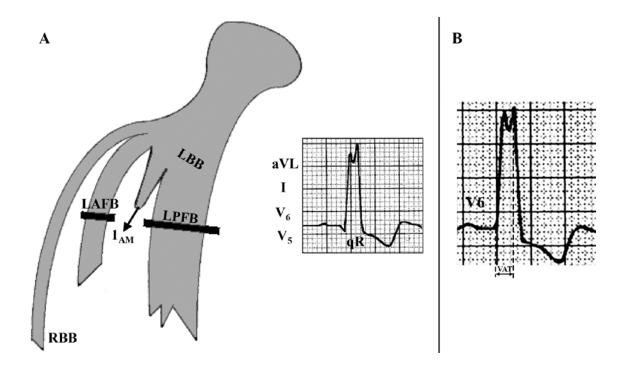


Figure 4 Concordant LBBB repolarization in left lateral leads (I, aVL, V5 and V6) and discordant LBBB: the ST segments and T waves go in the opposite direction to the main vector of the QRS complex

ECG tracings (25 mm/second; 10 mm/1 mV) showing cLBBB, characterized by a positive T wave in leads I, aVL, V5 and V6 (A); and dLBBB, characterized by ST-segment depression followed by a negative asymmetric T wave in at least two of the lateral leads (B).

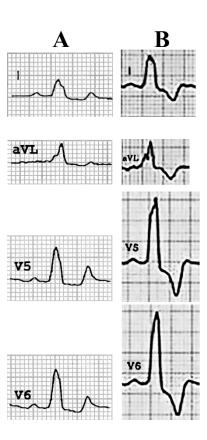


Table 1 Clinical implications of repolarization patterns in discordant and concordant LBBB (Khalil et al., 2016; Padeletti et al., 2018; Padeletti et al., 2010)

Tables

	Concordant LBBB	Discordant LBBB
% distribution	≈ 28-30%	≈ 68-70%
Age	Relatively younger	Relatively older (the only
		independent variable at
		multivariable analysis)
LV mass index (g/m ²)	Less	Greater
LVEF (%)	Higher (mean 51%)	Lower (mean 36%)
LV end-diastolic diameter	Smaller	Larger
Renal function	Better	Worse
Neurohormonal activation	Less	Higher
BNP level	Lower	Higher
Norepinephrine level	Less	Greater
Severity of LV disease	Milder	More severe
NYHA functional class	Lower	Higher
Degree of LV dysfunction	Lower	Higher
QRSd	Shorter (mean 151 ms)	Longer (mean 160 ms)
Left atrial dimension	Smaller (mean 4.0 cm)	Larger (mean 4.5 cm)
Coronary artery disease	Less	More frequent
Underwent CABG	Less frequent	More frequent
Moderate to severe mitral	Less frequent	More frequent
and tricuspid regurgitation		

Bi-ventricular	Less prominent	More prominent
dyssynchrony		
Prognosis	Better	Worse
Benefit of CRT	Less	Greater
Occurrence of VT/VF	Less frequent	More frequent (not
		statistically significant)

LBBB: left bundle branch block; LV: left ventricle; LVEF: left ventricular ejection fraction; QRSd: QRS duration; BNP: brain natriuretic peptide; NYHA: New York Heart Association; CABG: coronary artery bypass graft; CRT: cardiac resynchronization therapy; VT: ventricular tachycardia; VF: ventricular fibrillation