REVIEW ARTICLE

Episodic Left Bundle Branch Block—A Comprehensive Review of the Literature

George Bazoukis, M.D.,* Konstantinos Tsimos, M.D.,†
and Panagiotis Korantzopoulos, M.D., Ph.D.†

From the *Department of Internal Medicine, General Hospital of Athens “Elpis,” Athens, Greece, and †First Department of Cardiology, University of Ioannina, Medical School, Ioannina, Greece

Episodic (transient/ intermittent) left bundle branch block (LBBB) has been associated with different conditions such as bradycardia, tachycardia, anesthesia, acute pulmonary embolism, changes in intrathoracic pressure, chest trauma, cardiac interventional procedures, mad honey poisoning, and in other clinical settings. Of note, exclusion of an acute coronary syndrome in the setting of episodic LBBB is of great importance. Moreover, episodic LBBB is sometimes symptomatic and may be associated with left ventricular systolic and/or diastolic dysfunction or conduction disturbances leading to syncope. This review article provides a comprehensive overview of the conditions associated with episodic LBBB and discusses the clinical impact of this phenomenon.

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left bundle branch block; transient; Intermittent; rate-dependent; cardiac memory

Bundle branch blocks (BBBs) represent common and clinically important conduction disturbances. Apart from permanent BBBs, episodic BBBs (intermittent or transient) have been described in the literature.¹ By definition, transient BBB is an intraventricular conduction defect that subsequently returns to normal conduction while during intermittent BBB there are complexes showing BBB as well as normally conducted beats in a single electrocardiographic tracing.¹ The first case of transient BBB was reported by Sir Thomas Lewis in 1913² while its relation to structural heart disease was clearly established in 1938.³ Although it has been proposed that symptomatic patients with new or presumably new left bundle branch block (LBBB) and anginal pain should be treated as STEMI equivalents, in a recent registry the proportion of myocardial infarction was significantly lower among patients with LBBB (21%) compared to those without LBBB (32%).⁴ Apart from coronary

artery disease (CAD), other causes of LBBB include valve disease, dilated cardiomyopathy, infiltrative cardiomyopathy, hypertensive cardiomyopathy, congenital heart disease, degenerative conduction heart disease (Lenegre and Lev diseases), myocarditis, infective endocarditis, heart trauma/surgery, hyperkalemia, myxedema, and systemic sclerosis.⁵ Our review provides a comprehensive overview of transient or intermittent LBBB cases described in the literature and discusses its clinical impact.

STUDY SELECTION

A detailed PubMed search for relevant articles until May 2015 was performed. We used the following terms: “(intermittent OR transient) AND (left bundle branch block)” without language or date restrictions. Also, the reference lists of the retrieved studies were carefully checked in order to find additional relevant articles.

Address for correspondence: Dr. Panagiotis Korantzopoulos, 1st Department of Cardiology, University of Ioannina, Medical School, 45110 Ioannina, Greece. Fax: +30-26510-07017; E-mail: pkorantz@cc.uoi.gr

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INTERMITTENT/TRANSIENT LBBB

Rate Dependent LBBB

The most common cause of episodic LBBB is the change in heart rate (tachycardia or bradycardia). In Figure 1 we present the ECGs from a 60-year-old woman who developed transient rate-related LBBB (Fig. 1, authors archive). Another ECG strip obtained from a 73-year-old man shows rate-related LBBB with premature atrial contractions and supernormal conduction (Fig. 2, downloaded from <http://ecgguru.com/blog/jasons-blog-ecg-challenge-week-march-3rd-10th>). In fact, exercise induced LBBB is a phenomenon that occurs in approximately 0.38% of all patients undergoing exercise test.⁶ The exact heart rate that the BBB occurs is known as critical heart rate. This critical heart rate is also dependent upon the rate of change in cycle length. If the heart rate accelerates rapidly, the bundle branch block appears at slower rates. On the other hand, if the heart rate decelerates rapidly, normal conduction returns at more rapid rates. Usually, the heart rate of LBBB disappearance is lower than the rate of onset.

Transient BBB can have several mechanisms including phase 3 block, phase 4 block and concealed conduction.⁷ Phase 3 block (also called tachycardia-dependent block) occurs when an impulse arrives at tissues that are still refractory caused by incomplete repolarization. Transient LBBB is less common than right bundle branch block (only 25% of phase 3 aberration is of the LBBB type). Phase 4 block (also called bradycardia dependent block) occurs when conduction of an impulse is blocked in tissues after their normal refractory periods have ended. Phase 4 block is not commonly seen and is often associated with structural heart disease. Finally, aberration caused by concealed transeptal conduction occurs in several situations including perpetuation of aberrant conduction during tachyarrhythmias, unexpected persistence of acceleration-dependent aberration and alteration of aberration during atrial bigeminal rhythm.⁷ Rate-dependent BBB has also been attributed due to the "linking" phenomenon.⁸ Specifically, concealed delayed retrograde activation from the contralateral bundle branch maintains the functional antegrade block.⁹ Rosenbaum et al.,¹⁰ showed that bradycardia dependent intermittent BBB is related to hypopolarization of the involved

fascicle in the presence of spontaneous diastolic depolarization.

Apart from the aforementioned mechanisms which point to a benign etiology, rate dependent LBBB has been also described in patients with new-onset LBBB and ischemic chest pain, and therefore sometimes represents a clinical challenge.¹¹ A high prevalence of CAD and/or heart failure in patients who exhibit exercise-induced BBB has also been reported.^{6,12} Nevertheless noninvasive testing appears to have limited ability to detect or exclude CAD in patients presented with exercise-induced LBBB.¹³ Besides the appearance of LBBB during exercise, the opposite phenomenon, namely transient loss of complete BBB has also been reported.¹⁴ The underlying mechanism may be the exercise induced alternating conduction delay in the opposite bundle leading to more synchronous depolarization of alternating beats.¹⁴

Interestingly, Vieweg et al.,¹⁵ were the first to report a case of angina with rate dependent LBBB and a normal coronary arteriogram. A few years later, a case series of symptomatic rate dependent LBBB in patients with normal coronary arteriograms was presented.¹⁶ The underlying mechanism in such cases is suggested to be the microcirculatory ischemia or coronary vasospasm.¹⁷ In some instances, the chest pain due to episodic LBBB has been attributed to the sudden ventricular dysynchrony rather than to myocardial ischemia^{18,19} but coronary vasospasm may be the underlying cause in cases with normal coronary arteriograms.²⁰ Very recently, Shvilkin et al. described in detail 4 patients with painful LBBB syndrome and systematically analyzed 46 additional similar patients that have been reported in the literature.¹⁹ Importantly, certain criteria for the diagnosis of painful LBBB syndrome were proposed.¹⁹ These include: onset of chest pain the same time with LBBB development; resolution of symptoms with resolution of LBBB; normal 12-lead LBBB (although cardiac memory T wave changes may be evident); absence of myocardial ischemia; normal left ventricular function and low precordial S/T ratio during LBBB.¹⁹ Exercise training appears to be an effective treatment in cases of symptomatic exercise induced LBBB.²¹ Interestingly, right or biventricular pacing based on electrophysiological evaluation may be an effective measure to manage the painful LBBB syndrome.¹⁹

Figure 1. (A). ECG strips from a patient showing transient LBBB. (B) ECG strips from the same patient a few hours later showing normal QRS.

Episodic LBBB during Anesthesia

Cases of episodic LBBB during general, local, and epidural anesthesia have been described. LBBB during anesthesia may be related to blood pressure perturbations,²² and due to tachycardia²³⁻²⁵ or bradycardia²⁶ while its occurrence poses a diagnostic dilemma with regard to the presence or not of intraoperative myocardial ischemia or infarction.²⁷ In some cases, the occurrence of LBBB during anesthesia has been attributed to

the patients' medications such as lithium²⁸ or cardiotoxic drugs for cancer treatment.^{23,29} In addition, the impact of the anesthetic drugs in cardiac conduction system cannot be ignored.²⁹ Besides the occurrence of transient LBBB during general anesthesia, its appearance has been reported in cases of epidural,³⁰ local³¹ or combined general and epidural anesthesia.³² Interestingly, the previous history of exercise-induced LBBB may portend the appearance of LBBB during anesthesia.³³ Furthermore, athlete's heart has been associated with the

Figure 2. Rate-related LBBB with premature atrial contractions and supernormal conduction. ECG strip downloaded from: <http://ecgguru.com/blog/jasons-blog-ecg-challenge-week-march-3rd-10th>. Free license: <http://creativecommons.org/licenses/by-nd-nc/1.0/>.

appearance of anesthesia induced LBBB.³⁴ On the contrary, cases of transient LBBB disappearance during anesthesia have been reported.^{35,36} In conclusion, anesthesiologists should be aware of the possibility of episodic LBBB during anesthesia.

Transient LBBB in Acute Pulmonary Embolism

It is well-known RBBB is a common ECG sign of acute pulmonary embolism.³⁷ However, transient LBBB caused by sinus tachycardia can rarely be the prominent conduction abnormality in this condition.³⁸ On the other hand, transient LBBB disappearance in acute pulmonary embolism has been described.³⁹ A possible mechanism for this apparently bizarre phenomenon is the conduction delay along the right bundle branch which may result from acute pulmonary vascular obstruction and right ventricular strain. However, the appearance of a slower heart rate after pulmonary embolism is another possible explanation either because slower rates can slow conduction along the right bundle or because the previous "normal" heart rate is higher than the critical rate leading with that way to a rate-dependent LBBB which disappears in slower heart rates.³⁹

LBBB during Cardiac Interventions

Transient or permanent LBBB represents an uncommon complication of left cardiac catheterization.⁴⁰ Given that the trunk of left bundle branch is short and divides immediately it is believed that it is resistant to trauma whereas right bundle branch is sometimes injured during right-sided catheterization.⁴⁰ It has been demonstrated that sutureless aortic valve replacement (AVR) with the Perceval S bioprosthesis is complicated by transient LBBB in a minority of patients (10.7%).⁴¹ Also, recent data indicate that transcatheter aortic valve implantation (TAVI)-induced LBBB is transient in more than one third of patients.⁴² In addition, TAVI-induced LBBB negatively affects cardiac function and hospitalization, while its impact on mortality is still a matter of debate.⁴² In another recent study, TAVI-induced persistent LBBB was associated with higher mortality rates compared to transient LBBB.⁴³ However, very recently Urena et al. indicated that new onset persistent-LBBB after TAVI is not associated with increased risk of mortality (overall and cardiovascular) or rehospitalization (any cause or heart failure) at 1-year follow up but only with a higher rate of advanced or complete atrioventricular block requiring permanent pacemaker implantation while

it predicts a failure of LVEF improvement and poorer functional status after the procedure.⁴⁴

A case of Watchman device dislocation unmasked by intermittent LBBB has also been reported.⁴⁵ In that case the left atrial appendage device was dislocated to the left ventricular outflow tract. Finally, the presence of transient BBB (right or left) after performing an accessory pathway ablation for Wolff-Parkinson-White syndrome has been described.⁴⁶ The BBB that appears after ablation is frequent, transient, and benign while it is not associated with further consequences and seems to be a manifestation of cardiac memory.⁴⁶

Transient LBBB and Mad Honey Poisoning

Mad honey poisoning occurs after intake of honey derived from the nectar of *Rhododendron* species containing grayanotoxins.^{47,48} Several conduction disturbances including atrioventricular (AV) blocks, sinus bradycardia, nodal rhythm, asystole, long QT prolongation, and even acute coronary infarction due to mad honey poisoning have been documented.⁴⁸ Transient LBBB caused by tachycardia, bradycardia, or hypotension after mad honey poisoning have also been reported in two instances.^{47,48}

Drug-Induced Episodic LBBB

New-onset LBBB has been associated with different medications. A single oral dose of propafenone or flecainide can be administered to terminate acute-onset atrial fibrillation outside the hospital once treatment has been proved safe during hospitalization for selected patients ("pill-in-the-pocket" strategy).⁴⁹ A case of transient LBBB and first degree AV block after administration of propafenone 600 mg in a patient with a history of hypertension and recurrent paroxysmal AF and paroxysmal supraventricular tachycardia treated with carvedilol has been described.⁵⁰ Other drugs that have been implicated with episodic LBBB include propoxyphene hydrochloride poisoning,⁵¹ intravenous lisuride (a dopamine agonist),⁵² co-administration of propafenone and antineoplastic agents,⁵² flecainide,¹⁹ trastuzumab (Herceptin),⁵³ trimethaphan,⁵⁴ digitalis intoxication,⁵⁵ phenothiazines or tricyclic antidepressants,⁵⁶ and chloroquine.⁵⁷

Transient LBBB in Acute Pancreatitis

The development of electrocardiographic changes in intraabdominal pathologies is well documented.⁵⁸ More than 50% of the patients with acute pancreatitis have ECG abnormalities while electrolyte disturbances are present in about one-half of these cases.⁵⁹ Remarkably, cases of chest pain or abdominal pain with transient LBBB caused by acute pancreatitis have also been reported.^{58,60} Undoubtedly, in such cases the differential diagnosis between an acute coronary syndrome and other pathologies is challenging.

LBBB and Changes of Intrathoracic Pressure

Interestingly, Chow et al.,⁶¹ described a 66-year-old man with an intermittent LBBB triggered by laughter in the absence of heart rate changes. In that case, the patient was admitted because of syncope immediately after a bout of laughter and coughing. The coronary angiography showed triple vessel CAD with severe stenosis of the circumflex coronary artery, and revascularization was successfully performed. The exercise treadmill stress testing with a "laughter challenge" 6 weeks later showed no evidence of inducible LBBB. Therefore, it was speculated that changes in intrathoracic pressure during laughter may have led to compromised cardiac perfusion and attendant LBBB.

Episodic LBBB in Other Clinical Settings

Episodic LBBB has been reported in several diverse clinical conditions. These are the following: coronary fistulas connecting main pulmonary artery with coronary arteries,^{62,63} chest trauma,⁶⁴ cervical wound,⁶⁵ Guillain-Barre syndrome,⁶⁶ takotsubo cardiomyopathy,⁶⁷ Graves-Basedow disease,⁶⁸ hemorrhagic stroke,⁶⁹ myocarditis in enteric fever,⁷⁰ myocarditis along with acute ischemic cerebellar, pontine and lacunar infarction following viper bite,⁷¹ electroconvulsive therapy,⁷² endoscopic retrograde cholangiopancreatography,⁷³ athletic heart syndrome,⁷⁴ tachycardia induced cardiomyopathy,⁷⁵ endoscopic brachytherapy for lung cancer,⁷⁶ and propionic aciduria.⁷⁷

CLINICAL IMPACT OF EPISODIC LBBB

In regard to prognosis, individuals who develop exercise-induced LBBB during treadmill testing seem to have a significantly higher all-cause mortality compared to both individuals with normal and those with abnormal ST-segment depression.⁶ In keeping with these findings, another study showed that exercise-induced LBBB independently predicts a higher risk of death (29%) and major cardiac events (19%) compared with matched control group (25% and 10%, respectively).⁷⁸ Moreover, the rate in which exercise-induced LBBB occurs is suggested to be a prognostic factor (the onset of exercise-induced LBBB at a heart rate of ≤ 120 –125 bpm is correlated with the occurrence of CAD while the appearance of exercise-induced LBBB at a heart rate of ≥ 120 –125 bpm is correlated with a normal coronary arterial tree and a better prognosis.⁷⁹ However, if structural heart disease has been excluded, exercise-induced LBBB seems to have favorable prognosis.⁶ In this context, it has been shown that the prognosis of patients with exercise-induced LBBB and pain having normal coronary arteries is better compared to patients with LBBB and CAD.⁸⁰ The development of exercise-induced LBBB is predictive of subsequent progression to permanent LBBB.⁸¹ In a case series, 5 of the 8 patients with exercise-induced LBBB without coronary artery disease and 5 of the 12 patients with exercise-induced LBBB and coronary artery disease developed permanent LBBB. Additionally, progression to advanced AV block with the consequent need of pacemaker implantation was observed in one patient in each group.⁸⁰

LBBB has been associated with asynchronous left ventricular wall motion and secondary changes in the filling pattern.^{82,83} Of note, these abnormalities can lead to transient systolic and diastolic dysfunction and seem to be reversible after restoration of the normal conduction.⁸³ In this context, Donzeau et al.,⁸⁴ described three cases where sustained rate-dependent LBBB could induce syncope while no syncope happened when the same tachycardia at the same rate was associated with narrow QRS complexes. The prognosis of patients with painful LBBB is generally favorable.¹⁹

Patients with intermittent LBBB frequently have T wave inversions in the right and mid-precordial leads during normal conduction that usually do

not reflect coronary disease.^{85,86} The incidence of T wave inversions during periods of normal conduction has been reported to be as high as 50% in patients with intermittent LBBB.⁸⁷ This specific electrocardiographic abnormality can be explained on the basis of cardiac memory (also called Chatterjee phenomenon).^{88,89} Cardiac memory refers to electrocardiographic T wave abnormalities that occur on resumption of normal ventricular activation after a period of abnormal ventricular activation.⁹⁰ Moreover, the presence of cardiac memory has been associated with other alternating wide complex rhythms.⁹⁰ Specifically, other clinical conditions which can lead to cardiac memory phenomenon are intermittent ventricular pacing, intermittent ventricular preexcitation, and prolonged episodes of ventricular tachycardia.^{90,91} Sometimes the ECG changes associated with intermittent LBBB may mimic anterior wall ischemia due to high-grade left anterior descending coronary artery stenosis (Wellens' sign).⁹² The discrimination between cardiac memory phenomenon and myocardial ischemia is of great importance and some electrocardiographic clues have been suggested.^{93,94} The clinical implications of cardiac memory phenomenon include malignant ventricular arrhythmias such as torsade de pointes, predisposition to adverse mechanical remodeling of the human heart, and abnormal response to antiarrhythmic therapy.⁹⁴ Cardiac memory is associated with altered ion channel properties and therefore the action of antiarrhythmic drugs on specific ion channels is affected as memory evolves.⁹⁵ Notably, Haverkamp et al.,⁹⁶ reported a case of repolarization abnormalities appearance after catheter ablation which was attributed at least in part due to cardiac memory and contributed significantly to proarrhythmia. The adverse mechanical remodeling is thought to arise from dyssynchronous activation of the left ventricle which activates a cascade of signaling pathways that cause adverse structural remodeling.⁹¹

CONCLUSIONS

Episodic LBBB is an important electrocardiographic finding associated with different clinical conditions. The exclusion of an acute coronary syndrome in cases of episodic LBBB is imperative. The episodic LBBB may have a negative impact on ventricular performance and may cause

repolarization abnormalities implying cardiac memory. Clinicians should be aware of both the causes and consequences of this electrocardiographic entity.

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