Electrocardiographic markers of left ventricular systolic dysfunction in patients with left bundle branch block

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Abstract

Background: Although some patients with left bundle branch block (LBBB) have structural heart diseases, some patients with LBBB have "normal hearts". The electrocardiography (ECG) criteria of LBBB in reduced left ventricular ejection fraction (LVEF) have not been defined completely.

Aim: The main purpose of this study was to differentiate patients with reduced LVEF from patients with normal left ventricular systolic function simply by analysing 12-lead ECG.

Methods: Subjects admitted to our hospital with LBBB in their ECG were included in the study. The patients were categorised according to their left ventricular systolic function as group 1 (LVEF \geq 50%) and group 2 (LVEF < 50%). Duration of the QRS complex, residual conduction of left bundle branch, and concordance/discordance of T waves in leads V5, V6, or D1 were recorded. The ECG findings of the two groups were compared.

Results: One hundred consecutive patients with LBBB were included in the study (male/female: 56/44, age: 66 ± 15 years). In the whole group, there were 35 patients with normal left ventricular systolic function (LVEF \geq 50%), and 65 patients had LVEF below 50%. 80% of male patients with LBBB and 45% of female patients with LBBB had their LVEF below 50% (p < 0.001). Mean QRS durations of group 1 and group 2 were 132 ± 10 ms vs. 152 ± 22 ms, respectively (p < 0.001). The QRS duration of 140 ms was found to be the cut-off value to differentiate group 1 from group 2, with sensitivity and specificity of 72% and 75%, respectively. Twenty-one per cent of patients in group 1 and 69% in group 2 had discordant LBBB (p < 0.001). Residual conduction of left bundle branch was more frequent in group 2 (29% in group 1 vs. 52% in group 2, p = 0.03).

Conclusions: Male gender, QRS duration greater than 140 ms, discordant LBBB, and residual conduction in the left bundle branch seem to be markers of reduced LVEF in patients with LBBB.

Key words: heart failure, systolic dysfunction, left bundle branch block

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INTRODUCTION

Left bundle branch block (LBBB) is commonly associated with chronic heart failure, and it is an adverse prognostic finding in heart failure patients [1]. LBBB causes dyssynchronous ventricular contraction resulting in neurohormonal activation and left ventricular (LV) remodelling [2]. LBBB is frequently associated with cardiac pathologies affecting the conduction system and/or the myocardium, such as LV hypertrophy, coronary artery disease, cardiomyopathy, and drug effects [3–5]. In clinical practice, some patients with LBBB have no demonstrable cardiac disease with clinical investigation and echocardiographic evaluation. Although some electrocardiography (ECG) findings of LBBB are known to be associated with heart failure and adverse prognosis, no ECG criteria of LBBB have been systematically defined to differentiate patients with structural heart disease from those with "normal hearts". The main purpose of this study was to define markers of systolic dysfunction in patients with LBBB.

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METHODS Study group

The study was approved by the Local Ethics Committee (2013-26/7). Subjects admitted to our hospital with LBBB in their ECG were included in the study. Detailed medical history was taken from each subject. Physical examination, chest X-ray, laboratory investigations including complete blood count, blood biochemistry and thyroid function tests were routinely performed for each patient. The patients were categorised according to their LV systolic function as group 1 (left ventricular ejection fraction [LVEF] \geq 50%) and group 2 (LVEF < 50%). Patients who are free of any cardiac diseases other than LBBB were categorised as the control group.

Electrocardiographic examination

All ECGs were evaluated by two other cardiologists who were blind to the medical history and echocardiographic findings of the patients. LBBB was defined by the presence of QRS

complex duration of \geq 120 ms, presence of a QS or rS in V1, and broad, notched, or slurred R waves in leads D1, aVL, V5, and V6. Absence of g waves in leads D1, aVL, V5, and V6 was not strictly looked for in the diagnosis of LBBB because pathological q waves due to extensive anterior myocardial infarction are known to be associated with LBBB in these leads, and also q wave in aVL is allowable in current guidelines in defining LBBB [3]. LBBB was further categorised as either concordant or discordant according to positive or negative T waves, respectively, in leads V5, V6, or D1, respectively. Furthermore, LBBB was subdivided into LBBB with residual conduction of left bundle branch (those with an r wave in V1 \geq 1 mm and/or a q wave in $aVL \ge 1$ mm) and complete LBBB (those without either of these findings). Electrocardiographic recordings were examined independently by two cardiologists for the diagnosis and characterisation of LBBB as either "concordant" or "discordant", and either "residual left bundle branch conduction" or "complete LBBB" without interobserver variability (Figs. 1, 2).

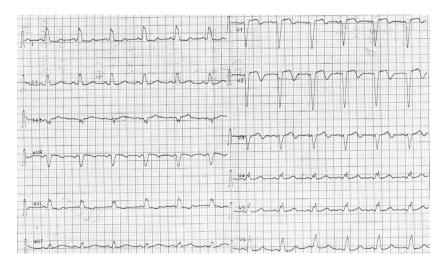


Figure 1. An example of an electrocardiogram (precordial leads) from a patient without any structural heart disease and with left bundle branch block. T waves are concordant with QRS complex in lead V6, and there is no sign of residual conduction of the left bundle branch

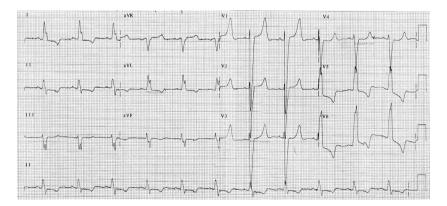


Figure 2. An example of an electrocardiogram (precordial leads) from a patient with non-ischaemic dilated cardiomyopathy. T waves are discordant with QRS complex in lead V6, and the amplitude of the wave in lead V1 is greater than 1 mm, demonstrating residual conduction in left bundle branch (distal left bundle branch disease)

Echocardiographic examination

Echocardiographic evaluation was made by recording a one-lead ECG continuously. Left ventricular end-diastolic and end-systolic diameters, ejection fraction (EF), interventricular septal and posterior wall thicknesses, and left atrial end-systolic diameters were measured from M-mode in the parasternal long axis views according to the standards of the American Society of Echocardiography. Left ventricular mass (LVM) was determined by Teichholz formula in each subject, and mass index was calculated by dividing LVM by body surface area. Left ventricular diastolic function was evaluated by mitral inflow velocities, namely E peak and A peak, and E/A ratio and also by deceleration time of the E wave and isovolumic relaxation time. Diastolic function was classified as normal, impaired relaxation (grade 1), pseudonormalisation (grade 2), and restrictive pattern (grade 3).

Statistical analysis

Distribution of the data was assessed by using one-sample Kolmogorov-Smirnov test. Continuous variables with normal distribution are expressed as mean \pm standard deviation, variables with skew distribution are expressed as median (minimum–maximum), and categorical variables are expressed as percentage. For comparison of categorical variables or percentages we used Fisher's exact and χ^2 tests. Differences between numeric variables were tested with Student's t-test or Mann-Whitney U-test. Correlation was tested with Pearson correlation coefficient. A p value below 0.05 was considered statistically significant.

RESULTS

One hundred consecutive patients with LBBB were included in the study (male/female: 56/44, age: 66 ± 15 years). In the whole group there were 35 patients with normal LV systolic function (LVEF \geq 50%), and 65 patients had LVEF below 50%. The clinical and echocardiographic characteristics of the patients are given in Table 1. Systolic dysfunction was found to be higher in male patients with LBBB compared to female patients (80% of male patients with LBBB and 45% of female patients with LBBB had EF < 50%; p < 0.001). Age, history of hypertension, hyperlipidaemia, diabetes, and smoking were similar between the groups. Coronary artery disease, and ischaemic and dilated cardiomyopathy were found to be more prevalent in patients with systolic dysfunction.

Body mass index was not significantly different between the groups. Although mean pulse rate was similar between the groups, mean systolic (SBP) and diastolic (DBP) blood pressure values were higher in group 1. There was a weak correlation between the LVEF and blood pressure measurements (LVEF and SBP: r = 0.388, p < 0.001; LVEF and DBP: r = 0.427, p < 0.001). Creatinine and blood urea nitrogen levels were also similar between the groups.

The mean LVEFs were 59 \pm 4% and 33 \pm 8% in group 1 and group 2, respectively (p < 0.001). End-systolic and end-diastolic diameters were also higher in group 2. There was no difference in LVM index between the groups. Grade 2 or more advanced diastolic dysfunction was more prevalent in group 2 (p < 0.001). The QRS duration of patients with normal LVEF was significantly lower when compared to that of patients with systolic dysfunction (QRS duration of group 1 vs. group 2: 132 ± 10 ms vs. 152 ± 22 ms, p < 0.001). There was a negative correlation between LVEF and QRS duration (r = -0.484, p < 0.001, Fig. 3). The QRS duration of 140 ms was found as the cut-off value for differentiating patients with normal systolic function from patients with systolic dysfunction, with the sensitivity and specificity of 72% and 75%, respectively. Receiver operating characteristic curve for QRS duration and EF is shown in Figure 4, and the data for different cut-off points are given in Table 2. The QTc interval was also higher in patients with LVEF < 50% (QTc interval: 437 ± 45 ms in group 1, 465 ± 42 ms in group 2; p = 0.003). Residual conduction of left bundle branch was more frequent in group 2 (29% in group 1 vs. 52% in group 2; p = 0.03). Discordant T wave-LBBB was also found to be more frequent in patients with EF < 50% (21% in group 1 vs. 69% in group 2; p < 0.001). When we applied multivariate analysis, male gender and discordant T wave-LBBB were found to be independent markers of lower EF (OR for male gender: 5.47, 95% CI 1.99-15.03; p = 0.001; OR for discordant T wave-LBBB: 9.87, 95% CI 3.44–28.29; p < 0.001).

In patients with ischaemic cardiomyopathy, residual conduction of the left bundle branch was not different from that of the left bundle branch in patients who were free of any cardiac diseases other than LBBB (considered as the control group). Discordant T waves were found to be more prevalent in patients with ischaemic cardiomyopathy compared to the control group (71% vs. 18%; p < 0.001). Patients with dilated cardiomyopathy had more residual conduction in left bundle branch and discordant T waves compared to the control group (59% vs. 32%; p = 0.045 for residual conduction; 63% vs. 18%; p = 0.001 for discordant T waves). These ECG findings were similarly prevalent in patients with coronary artery disease and hypertension with EF \geq 50% and the control group (Table 3).

DISCUSSION

The main findings of our study were the negative correlation between LVEF and QRS duration, and QRS duration of 140 ms as the cut-off value to differentiate patients with normal and decreased systolic function with acceptable sensitivity and specificity. We found that the width of the QRS complex is a relatively good discriminative ECG finding for LVEF in patients with LBBB. Some patients with LBBB have structural heart diseases with decreased EF, and some patients do not.

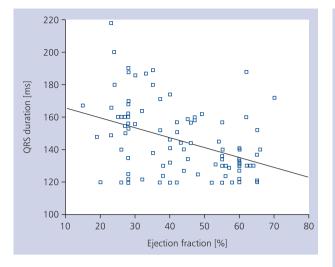
	Group 1 (n = 35)	Group 2 (n = 65)	Р
	$LVEF \ge 50\%$	LVEF < 50%	
Male/female	11/24	45/20	< 0.001
Age [years]	65 ± 12	67 ± 16	0.51
Body mass index [kg/m²]	29 ± 4	28 ± 5	0.81
Hypertension	27 (77%)	44 (68%)	0.32
Hyperlipidaemia	12 (34%)	26 (40%)	0.57
Diabetes	12 (34%)	22 (34%)	0.96
Smoking	12 (34%)	35 (54%)	0.06
Pulse rate [bpm]	75 ± 11	76 ± 14	0.74
Systolic blood pressure [mm Hg]	132 ± 18	123 ± 16	0.01
Diastolic blood pressure [mm Hg]	82 ± 11	74 ± 10	< 0.001
Creatinine [mg/dL]	1 ± 0.6	1.1 ± 0.3	0.50
Blood urea nitrogen [mg/dL]	19 ± 11	22 ± 12	0.35
QRS duration [ms]	132 ± 10	152 ± 22	< 0.001
QT interval [ms]	437 ± 45	465 ± 42	0.003
Residual conduction of left bundle branch	10 (29%)	34 (52%)	0.03
LVEF [%]	59 ± 4	33 ± 8	< 0.001
End-diastolic diameter [mm]	47 ± 5	62 ± 8	< 0.001
End-systolic diameter [mm]	31 ± 5	48 ± 10	< 0.001
Left ventricular mass index [g/m ²]	148 ± 40	152 ± 36	0.44
Diastolic dysfunction (n):			< 0.001
Normal	4	0	
Grade 1	30	15	
Grade 2	1	21	
Grade 3	0	29	
Coronary artery disease	8 (22%)	41 (63%)	< 0.001
Ischaemic cardiomyopathy	0 (0%)	39 (60%)	< 0.001
Dilated cardiomyopathy	0 (0%)	22 (34%)	< 0.001

LVEF — left ventricular ejection fraction

To our knowledge, ECG criteria of LBBB have not been fully defined to differentiate patients with normal and decreased systolic function until now.

Approximately one-third of patients with chronic heart failure have LBBB [1]. LBBB is known to be an adverse prognostic sign irrespective of LV systolic function, and it has been shown to be an independent risk factor for cardiovascular death in the general population [6]. It is also a risk factor of cardiovascular morbidity and mortality for patients with arterial hypertension and ischaemic heart disease [7]. LBBB is a strong adverse prognostic sign associated with total and sudden mortality in patients with heart failure [8]. LBBB alters the pattern of electrical activation of the LV. LBBB-induced electrical and mechanical dyssynchrony enhances LV dysfunction and remodelling. LBBB has been shown to reflect underlying myocardial structural disease [9]. It also contributes to functional impairment of myocardium and negatively affects perfusion, haemodynamics, systolic, and diastolic functions [10]. LBBB is usually accompanied by LV dilatation and reduced EF [11–13]. The perfusion of the septum is impaired in patients with LBBB even in the absence of coronary artery disease [14, 15]. The relation of causality between LBBB and heart failure is not completely known, and "the chicken and the egg" paradox is valid for this situation. Most probably, both situations give rise to each other.

The width of the QRS complex has been demonstrated to increase as the severity of LV systolic function advances, and baseline LBBB has been found to be associated with worse LV function and older age [16]. In the presence of LBBB, the QRS duration has been shown to have a significant inverse relationship with EF, and QRS duration greater than 170 ms is said to be a marker of significant LV systolic dysfunc-



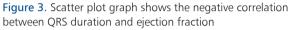


Table 2. The sensitivity and specificity values for different cut-off QRS duration values for differentiating patients with normal systolic function from patients with systolic dysfunction

QRS duration [ms]	Sensitivity [%]	Specificity [%]
130	80	34
140	72	75
150	60	91
160	39	93
170	17	100

tion [17]. The diagnostic evaluation of patients with isolated LBBB is challenging. In a recent study, 31% of patients with isolated LBBB and normal echocardiographic results have been found to have some pathological findings in cardiac magnetic resonance imaging [18]. In our study we found that patients with QRS duration of 140 ms or greater have EF less

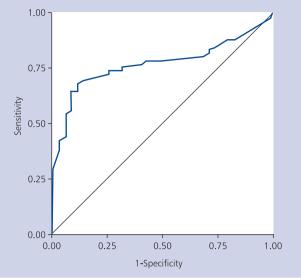


Figure 4. Receiver operating characteristic curve for QRS duration and ejection fraction

than 50% with sensitivity and specificity of 72% and 75%, respectively. Padanilam et al. [19] reported r wave \geq 1 mm in V1 and/or q wave \geq 1 mm in aVL as predictors of residual conduction in the left bundle branch. This ECG finding represents left-to-right activation of the interventricular septum. Residual conduction of the left bundle branch was found to be higher in group 2, which could be explained by distal and widespread involvement of the left bundle branch due to more marked intramyocardial disease [20]. LBBB may be caused by disease of the conduction system and/or myocardium. Normally, interventricular septum is depolarised from left to right resulting in septal q waves in lateral leads. If impulse conduction is blocked in the left bundle branch, the septal g wave disappears. Intraventricular conduction abnormalities associated with prior infarction, hypertrophy, or cardiomyopathy may result in QRS widening and atypical forms of LBBB [21].

Table 3. The frequencies of residual conduction and discordant T waves in different cardiac diseases

	Residual conduction in LBBB (positive)	Ρ	Discordant T wave (positive)	Ρ
Control group Ischaemic cardiomyopathy	32% 48%	0.149	18% 71%	< 0.001
Control group Dilated cardiomyopathy	32% 59%	0.045	18% 63%	0.001
Control group Coronary artery disease with EF ≥ 50%	34% 25%	0.612	17% 25%	0.620
Control group Hypertension with $EF \ge 50\%$	22% 35%	0.452	22% 17%	0.771

EF — ejection fraction LBBB — left bundle branch block

Left bundle branch block has been defined as concordant when T waves are positive, and discordant when T waves are negative in leads V5, V6, or D1 [22]. In systolic heart failure, discordant LBBB was found to be associated with worse clinical, neurohormonal, and prognostic profile [22]. The specific repolarisation pattern of discordant LBBB may be a sign of increased heterogeneity of the repolarisation process. A planar QRS-T angle $> 90^{\circ}$ has been shown to be a significant predictor of a composite end point of death, appropriate implantable cardioverter-defibrillator shock, or resuscitated cardiac arrest in non-paced, mild to moderately symptomatic patients with non-ischaemic cardiomyopathy. A widening QRS-T angle has been proposed to represent a continuum of worsening underlying pathology and outcome [23]. Discordant LBBB was more frequent in patients with EF < 50% in our study. Therefore, we think that in the case of the presence of discordant LBBB, the probability of having systolic dysfunction is higher compared to concordant LBBB.

Limitations of the study

This is a cross sectional study including patients with LBBB. Therefore, some patients with LBBB and normal EF may progress to overt heart disease and systolic dysfunction in the follow-up, which could not be diagnosed by echocardiography during inclusion. Echocardiography may not be a highly sensitive method of investigation to expose early-stage cardiac diseases. Magnetic resonance imaging may be more useful for this purpose, but its expense should be kept in mind.

CONCLUSIONS

In conclusion, LBBB could be an ECG finding of structurally normal hearts or demonstrable heart diseases. Since ECG is a simple and widely available diagnostic tool, defining some ECG criteria to differentiate patients with systolic dysfunction is of importance for cardiologists, internists, and general practitioners. Although male gender, QRS duration greater than 140 ms, discordant T wave-LBBB, and residual conduction in the left bundle branch were found to be markers of reduced EF in univariate analysis, only male gender and discordant T wave-LBBB were shown to be independent markers of reduced EF.

Conflict of interest: none declared

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Elektrokardiograficzne wskaźniki dysfunkcji skurczowej lewej komory u chorych z blokiem lewej odnogi pęczka Hisa

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Streszczenie

Wstęp: U niektórych pacjentów z blokiem lewej odnogi pęczka Hisa (LBBB) występują strukturalne choroby serca, jednak część chorych z LBBB ma "normalne serce". Kryteria elektrokardiograficzne (EKG) LBBB u pacjentów z obniżoną frakcją wyrzutową lewej komory (LVEF) nie zostały w pełni określone.

Cel: Głównym celem badania było odróżnienie pacjentów z obniżoną LVEF od osób z prawidłową czynnością skurczową lewej komory na podstawie analizy 12-odprowadzeniowego EKG.

Metody: Do badania włączono osoby przyjęte do szpitala, w którym pracują autorzy niniejszej pracy, z powodu cech LBBB w EKG. W zależności od czynności skurczowej lewej komory chorych przydzielano do grupy 1 (LVEF \geq 50%) lub do grupy 2 (LVEF < 50%). Zebrano dane dotyczące czasu trwania zespołu QRS, resztkowego przewodzenia w lewej odnodze pęczka Hisa oraz zgodności/niezgodności wychylenia załamków T w odprowadzeniach V5, V6 i D1. Porównano wyniki analizy EKG w obu grupach.

Wyniki: Do badania włączono 100 kolejnych pacjentów z LBBB (mężczyźni/kobiety: 56/44, wiek: 66 ± 15 lat). W całej badanej grupie było 35 osób z prawidłową czynnością skurczową lewej komory (LVEF \geq 50%) i 65 osób z LVEF < 50%. U 80% mężczyzn z LBBB i 45% kobiet z LBBB stwierdzono LVEF < 50% (p < 0,001). Średni czas trwania zespołu QRS w grupach 1 i 2 wynosił odpowiednio 132 \pm 10 ms vs. 152 \pm 22 ms (p < 0,001). Stwierdzono, że czas trwania zespołu QRS wynoszący 140 ms stanowi wartość graniczną pozwalającą zróżnicować pacjentów należących do grupy 1 i do grupy 2, a czułość i swoistość tego parametru wynoszą odpowiednio 72% i 75%. U 21% pacjentów z grupy 1 i 69% chorych z grupy 2 występowało przeciwstawne wychylenie załamków T i zespołów QRS (p < 0,001). Resztkowe przewodzenie w lewej odnodze pęczka Hisa obserwowano częściej w grupie 2 (29% w grupie 1 vs. 52% w grupie 2; p = 0,03).

Wnioski: Płeć męska, czas trwania załamków QRS powyżej 140 ms, LBBB z przeciwstawnym kierunkiem załamków T i zespołów QRS oraz resztkowe przewodzenie w lewej odnodze pęczka Hisa mogą być wskaźnikami obniżonej LVEF u chorych z LBBB. Słowa kluczowe: niewydolność serca, dysfunkcja skurczowa, blok lewej odnogi pęczka Hisa

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