ORIGINAL ARTICLE

Prolonged QRS duration: poor outcome for coronary artery disease

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Abstract: Objectives – The aim of our study was to analyze how an increase in QRS complex duration in left bundle branch block (LBBB) patients influence the risk for coronary lesions or arrhythmias. **Methods –** We prospectively studied 323 left bundle branch block patients admitted from January 2011 to June 2013 in Georgescu Institute of Cardiovascular Diseases. The median follow up was 7 days (hospitalization period). Patients were divided into two groups according to their QRS duration (<140 ms and ≥140 ms), in order to analyze how an increase in QRS complex duration affects mortality and baseline data in the study population. **Results –** The first important finding of our study is that prolonged QRS duration in LBBB patients is associated with a higher risk of coronary lesions, two and especially three coronary artery disease, an increased left ventricular systolic and diastolic dysfunction and an elevated risk of ventricular tachycardia. Those with a QRS duration ≥140 ms were more likely to have a decreased ejection fraction (EF) <50% (p= 0.001), more than half of them having an ejection fraction less than 30%. **Conclusions –** Our study demonstrates that a prolonged QRS duration is associated with a more reserved prognostic in LBBB patients.
Keywords: prognostic, LBBB, coronary lesions

Rezumat: Introducere – Scopul studiului a fost acela de a analiza dacă creșterea duratei complexului QRS la pacienții cu bloc de ram stâng influențează riscul de leziuni coronariene și aritmii. **Metodă –** Am studiat prospectiv 323 de pacienți cu bloc de ram stâng internați în perioada ianuarie 2011 – iunie 2013 în Institutul de Boli Cardiovasculare Iași. Perioada medie de urmărire a fost de 7 zile (durata de spitalizare). Pacienții au fost împărțiți în două grupuri, în funcție de durata complexului QRS (<140 ms and ≥140 ms), în vederea studierii modului în care durata complexului QRS influențează mortalitatea și caracteristicile pacienților. **Rezultate –** Cel mai important rezultat al studiului nostru este acela că o durată prelungită a complexului QRS la pacienții cu bloc de ram stâng este asociată cu un risc crescut de leziuni coronariene, în special bi- și tricoronariene, o creștere a disfuncției sistolice a ventriculului stâng și a riscului a tahicardie ventriculară. Pacienții cu o durată a complexului QRS ≥140 ms au avut mai frecvent o fracție de ejecție <50% (p= 0.001), mai mult de jumătate având o fracție de ejecție <30%. **Concluzii –** Studiul nostru demonstrează că o durată prelungită a complexului QRS este asociată cu un prognostic mai rezervat la pacienții cu bloc de ram stâng.

INTRODUCTION

The relation of QRS duration, specifically those with left bundle branch block (LBBB), to adverse outcome is controversial, but most studies show LBBB to be an independent prognostic marker for mortality[1]. In previous studies a prolonged QRS interval on a 12-lead electrocardiogram (ECG) has been associated with a higher incidence of sudden cardiac death and decrease in overall survival[2,3]. The aim of our study was to analyze how an increase in QRS complex duration in left bundle branch block (LBBB) patients affects the left ventricular function and the risk for arrhythmias or coronary lesions.

METHODS

With a view to assessing the meaning of left bundle branch block associated with ventricular dysfunction and atherosclerotic coronary disease, we prospectively studied all the patients admitted from January 2011 to June 2013 in Georgescu Institute of Cardi-

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ovascular Diseases and 323 of them had left bundle branch block.

All electrocardiograms were analyzed and the treating cardiologist determined the presence of left bundle-branch block. The electrocardiograms were classified according to the standardized guidelines, including LBBB not otherwise known to be old (new or presumably new LBBB) or LBBB known to be old. LBBB chronicity was determined by comparison with the most recent ECG available. If no prior ECG was available for comparison, patients were classified as having a presumably new LBBB. The ECG QRS duration was obtained from the ECG performed at admission, and was recorded based on the treating physician interpretation of QRS width.

Patients were excluded if they were younger than 30 years, have myocardial infarction, moderate or severe aortic or mitral stenosis, because their heart failure may have been at least partially by another etiology. We excluded patients with previous placement of a permanent pacemaker or automated implantable cardiac defibrillator (as ECG tracings were unavailable for review to assess whether cardiac pacing could have artificially widened the QRS interval). Also, we excluded patients which declined authorization for the use of their medical records for research.

According to their QRS duration (QRS duration <140 ms and QRS ≥140 ms), 323 patients with left bundle-branch block who met the inclusion and exclusion criteria mentioned above were divided into two groups:

- 159 patients with a QRS complex duration between 120-140 ms;
- 164 patients with a QRS complex duration ≥140 ms.

There wasn't a specific reason for a cutoff of 140 ms and this arrangement was made in order to be able to analyze how an increase in QRS complex duration affects mortality and baseline data in the study population.

The median follow up was 7 days (hospitalization period). Data collected included basic demographic information, characteristics of chest pain and associated symptoms, cardiac history and risk factors, medications, treatment, disposition, ECG, echocardiography, cardiac markers and angiographic data. All subjects were reviewed for the existence of hypertension, diabetes mellitus, hyperlipidemia, smoking, ischemic heart disease, cardiomyopathy, valvular heart disease and cerebrovascular disease.

Statistical analyzes were performed using the Statistical Program for Social Sciences (version 17.0 SPSS Inc.). Data were labeled as nominal or quantitative variables. Nominal variables were described using frequencies. Quantitative variables were tested for nominality of distribution by means of Kolmogorov-Smirnov test and were described by median and percentiles or by mean and standard deviation, whenever the case. The frequencies of nominal variables were compared with a chi-square test. Comparisons were made among patients with QRS duration <140 ms and those with QRS duration ≥140 ms. A p value of <0.05 was considered statistically significant.

The study was approved by the Committee on the Conduct on Human Research of University of Medicine and Pharmacy, Iași.

RESULTS

A sum-total of 402 patients with left bundle branch block was admitted between January 2011 and June 2013 in the Cardiovascular Diseases Institute Iasi, but only 323 were finally included in the study, after exclusion of subjects with valvular heart disease, permanent pacemaker or automated implantable cardiac defibrillator or myocardial infarction. According to the QRS duration using a cutoff of 140 ms, we divided the patients in two groups. A total of 159 subjects had QRS duration <140 ms and 164 had QRS duration ≥140 ms.

The baseline characteristics of patients with QRS duration <140 ms and those with QRS duration ≥140 ms are shown in Table 1. Patients with QRS duration ≥140 ms were older, predominantly males and with new or presumably new left bundle branch block. They were more likely to have a prior history of diabetes mellitus and cardiovascular events, including hypertension, congestive heart failure, angina and percutaneous coronary intervention. Statistically significant differences in terms of baseline characteristics were found in previously diagnosed or treated diabetes mellitus, prior congestive heart failure and angina pectoris, common in patients with QRS duration ≥140 ms ($p = 0.008$, $p = 0.001$ and $p = 0.017$). Most of the previous percutaneous coronary interventions in patients with QRS duration ≥140 were made on the left anterior descendent artery (LAD). Chest pain and dyspnoea were the most frequent symptoms at presentation. Out of the 323 LBBB patients in our study, 242 (74.92%) reported chest pain at presentation and 244 (75.54%) reported dyspnoea. Of the patients with QRS duration

≥140 ms, 135 (82.3%) presented with chest pain and 82 (60.74%) were men. The other symptoms, in order of frequency were palpitations and syncope, with statistically significant differences only for chest pain and palpitations (Table 1).

We also studied the echocardiographic characteristics of patients with left bundle branch block. Patients with QRS duration ≥140 ms were more likely to have a decreased ejection fraction (EF) <50% (111 patients (67.7%) vs. 81 (50.9%), p= 0.001), more than half of them having an ejection fraction less than 30%. There were also statistically significant differences between end-diastolic and end-sistolic diameters and volumes which were more elevated in those with QRS duration ≥140 ms (p = 0.003). We performed on each study participant the left atrial (LA) volume. Approximately 1 of 5 patients with QRS duration ≥140 ms had LA enlargement, but without statistically significant differences between the two groups (20.1% vs. 15.7%, p = 0.100). The baseline echocardiographic characteristics of patients with left bundle branch block divided in two groups are shown in Table 2.

In order to study the in-hospital outcome of patients with left bundle branch block according to their QRS duration, we found a more frequent association between a prolonged QRS duration ≥140 ms and the risk of ventricular tachycardia, but without statistically significant differences between the two groups, as shown in Table 3. All the patients were on telemetry wards and in all cases ventricular tachycardia was monomorphic, sustained or nonsustained, but hemodynamically stable.

In our study, conventional coronary angiography was performed in 49 (29.87%) patients with QRS ≥140 ms and 5 (3.04%) patients were evaluated using computed tomography angiography (CTA). This may be explained by the fact that in our study we excluded patients with myocardial infarction and almost half of patients with chest pain and new left bundle branch block have a myocardial infarction. Most of the patients with a QRS duration ≥140 ms, had no vessel disease (67.29%) and when this was the case, it was frequently localized on the left descendent artery (24.39%). In contrast, only 15.72% of patients with a QRS duration <140 ms, had

Table 1. Baseline characteristics of patients with left bundle branch block

Variable	QRS duration <140 ms (n=159)	QRS duration ≥140 ms (n=164)	P Value
Age (years)	64.86 ±10.39	66.86 ± 11.88	
QRS duration	124.93±11.49	144.45±12.34	
Men	92 (57.8%)	105 (64.1%)	0.305
Previously diagnosed or treated hypertension	74 (46.5%)	86 (52.4%)	0.525
Previously diagnosed or treated diabetes mellitus	22 (13.8%)	42 (25.6%)	0.008
Current/previous smoker	70 (44.1%)	67 (40.8%)	0.792
Previous congestive heart failure	62 (38.9%)	90 (54.8%)	0.001
Previous angina pectoris	4 (2.5%)	14 (8.5%)	0.017
Previous percutaneous coronary intervention	10 (6.2%)	17 (10.3%)	0.131
Chest pain	107 (67.2%)	135 (82.3%)	0.002
Palpitations	43 (27.1%)	18 (10.9%)	0.001
Syncope	20 (12.5%)	20 (12.2%)	0.917
Dyspnoea	113 (71.1%)	131 (79.8%)	0.071

Table 2. Echocardiographic characteristics of patients with left bundle branch block

Variable	QRS duration <140 ms (n=159)	QRS duration ≥140 ms (n=164)	P Value
Ejection fraction (<50%)	81 (50.9%)	111 (67.7%	0.001
Wall motion abnormalities	57 (35.8%)	97 (59.1%)	0.001
End-diastolic diameter of left ventricle (mm)	55.15±12.6	58.10±11.5	0.003
End-systolic diameter of left ventricle (mm)	40.78±12.5	44.83±11.9	0.003
End-diastolic volume of left ventricle (ml)	134.55±11.6	165.37±11.4	0.001
End-sistolic volume of left ventricle (ml)	88.57±10.6	111.72±11.8	0.003
Left atrial enlargement	25 (15.7%)	33 (20.1%)	0.100
Right atrial enlargement	14 (8.8%)	21 (12.8%)	0.090
Restrictive mitral profile	17 (10.6%)	22 (13.4%)	0.425

Table 3. In hospital arrhythmias of patients with left bundle branch block			
Variable	**QRS duration <140 ms (n=159)**	**QRS duration ≥140 ms (n=164)**	**P Value**
Ventricular extrasistolia	43 (27.04%)	40 (24.39%)	0.338
Atrial fibrillation	35 (22.01%)	29 (17.68%)	0.264
Atrial flutter	2 (1.25%)	5 (3.04%)	0.448
Ventricular tachycardia	17 (10.69%)	26 (15.85%)	0.193
Second-degree atrioventricular block	18 (11.31%)	9 (5.47%)	0.183
Complete atrioventricular block	7 (4.40%)	10 (6.09%)	0.620

coronary lesions. The majority of patients with QRS duration ≥140 ms had two or three-vessel coronary lesions (12.19% vs. 5.66%) (Table 4).

Of the patients with QRS duration ≥140 ms, 104 (63.41%) had final diagnoses of stable angina, 28 (17.07%) had cardiac diagnoses other than coronary artery disease and 32 (19.52%) were diagnosed with noncardiac chest pain. In patients with QRS duration <140 ms the most frequent final diagnostic was non-cardiac chest pain (49.69%) and the differences were statistically significant between stable angina and non-cardiac chest pain in these two groups (Table 5).

Patients with QRS ≥140 ms were more likely to receive diuretics, angiotensin converting enzime-inhibitors, beta-blockers, calcium channel blockers, aspirin, clopidogrel and statins. There was no difference in the utilization of antiaritmics and oral antiplatelet agents, between the two groups.

In this study we noticed that a prolonged QRS duration in patients with left bundle branch block is associated with an increased risk of coronary lesions and stable coronary disease. Also, patients with a QRS duration ≥140 ms had more severe coronary lesions, especially two or three-vessel coronary lesions. In the same time, these patients commonly receive coronary angioplasty as compared with patients with a QRS duration <140 ms.

DISCUSSION

The first important finding of our study is that prolonged QRS duration in patients with LBBB is associated with a higher risk of coronary lesions and stable co-

Table 4. Procedural characteristics of patients with left bundle branch block			
Variables	**QRS duration <140 ms (n=159)**	**QRS duration ≥140 ms (n=164)**	**P Value**
Computed tomography angiography (CTA)	7 (4.40%)	5 (3.04%)	0.364
Conventional coronary angiography	22 (13.81%)	49 (29.87%)	0.001
Number of diseased vessels on angiography			
• Without coronary lesions	134 (84.27%)	107 (67.29%)	0.001
• 1 coronary artery disease	9 (5.66%)	21 (12.80%)	0.001
• 2 coronary artery disease	7 (4.40%)	16 (9.75%)	0.001
• 3 coronary artery disease	9 (5.66%)	20 (12.19%)	0.001
LAD disease	20 (12.20%)	40 (24.39%)	0.005
RCA disease	10 (6.28%)	28 (17.07%)	0.002
LCX disease	10 (6.28%)	23 (14.02%)	0.017
Overall PCI use (including primary PCI, rescue PCI postlytics and elective PCI)	4 (2.51%)	13 (7.92%)	0.025
PCI on LAD	3 (1.88%)	6 (3.65%)	0.266
PCI on RCA	1 (0.62%)	8 (4.87%)	0.020
PCI on LCX	4 (2.51%)	9 (5.48%)	0.141
Abbreviations: * LAD = left descendent artery; LCX - left circumflex artery; RCA = right coronary artery; PCI = percutaneous coronary intervention			

Table 5. Final diagnostic of patients with left bundle branch block			
Final diagnostic	**QRS duration <140 ms (n=159)**	**QRS duration ≥140 ms (n=164)**	**P Value**
Stable coronary disease	41 (25.79%)	104 (63.41%)	0.001
Cardiac diagnosis other than coronary artery disease	39 (24.52%)	28 (17.07%)	0.128
Non-cardiac chest pain	79 (49.69%)	32 (19.52%)	0.001

ronary artery disease. Furthermore, in our study, patients with QRS duration ≥140 ms had more frequently critical coronary lesions, two and especially three coronary artery disease. In the same time, these patients were reffered for percutaneous coronary intervention more frequently that those with QRS duration <140 ms.

In previous studies, prolonged QRS duration was an independent predictor of cardiac death and nonfatal infarction[6-9] in patients referred for noninvasive evaluation of myocardial ischemia, and in patients with suspected acute coronary syndrome, QRS prolongation predicted in-hospital and 1-year mortality[10]. Because the rate of cardiovascular mortality in patients with coronary artery disease (CAD) and concomitant LBBB is higher than that of patients with a similar extent of CAD but without LBBB an effective method of identifying CAD in those with LBBB might be helpful[10.]

QRS duration is a readily available "front-line" clinical indicator of increased risk of sudden cardiac death, suggesting consideration of cardiac function assessment or evaluation of coronary artery disease in patients with suspected heart failure in particular[11-15].

In our study patients with QRS duration ≥140 ms were more likely to have a prior history of angina pectoris which may be a marker of an underlying coronary artery disease that progresses to adverse outcomes. However, several studies have failed to identify a relationship between the location of coronary stenosis and the presence of LBBB[16], and in a Framingham Study cohort, QRS duration was not a precursor of coronary disease over 18 years of follow-up[17]. In a recent study published by Aro et al. it has been suggested that, in a general population, intraventricular conduction delay, including LBBB is associated with an increased risk of cardiac and arrhythmic death. Although there were no differences in the history of myocardial infarction or angina pectoris between the groups, it is possible that LBBB to be a marker of an underlying subclinical coronary artery disease that progresses to adverse outcomes[18].

Another important finding from our study was that a QRS duration of ≥140 ms in patients with left bundle branch block is associated with an increased left ventricular systolic and diastolic dysfunction and an elevated risk of ventricular tachycardia.

It has long been recognized that when associated with heart disease, prolonged QRS duration in an ECG is an independent predictor of adverse outcome. In most patients with systolic left ventricular dysfunction, QRS prolongation presents as LBBB[3], and in these patients, increased QRS duration is associated with a worse prognosis[6,7]. For patients with coronary artery disease plus depressed ventricular function and nonsustained ventricular tachycardia, QRS prolongation resulting from LBBB has been associated with a 50% increase in the risk of both arrhythmic and total mortality[8]. The link between this ECG pattern and malignant arrhythmias is supported by accentuated repolarization abnormalities before the onset of arrhythmia. The prolonged QRS with the perturbed depolarization may play a direct role in sudden cardiac death via the facilitation of reentrant tachyarrhythmias[2]. In our study, there was no difference in the mortality, applied only to the hospitalization, between the two groups, only one person from each group died.

Our study is one of the fewest studies that evaluated the risk of atrioventricular blocks in patients with LBBB and we observed a more elevated, but not statistically significant, risk of third degree atrioventricular block in patients with a QRS duration ≥140 ms. Bradyarrhythmias may not be the most probable explanation for the increased mortality associated with prolonged QRS duration either in the previous studies. Even though future high-degree atrioventricular block is strongly associated with the presence of bundle branch block, especially LBBB, the risk of sudden death due to bradyarrhythmia is low even with high-risk BBB, and pacemaker treatment has not been found to diminish the risk of death in these patients[19-23].

The strengths of our study include the large number of baseline and echocardiographic characteristics of subjects. The diagnostic of coronary artery disease was based not only on past medical history and clinical examination, but also by conventional coronary angiography and computed tomography angiography.

A limitation of our study is the impossibility of long and complete follow-up of these subjects.

In conclusion, the results of our study sustain that patients with left bundle branch block in the setting of a prolonged QRS duration have a more reserved prognosis because of the left ventricular dysfunction and in-hospital arrhythmias. On the other hand, any patient with chest pain and LBBB should be evaluated through coronary angiography because of the high risk of critical coronary lesions, two and especially three coronary artery disease.

In particular, LBBB in a 12-lead ECG carries a substantial risk of subsequent cardiac death and sudden arrhythmic death, and its presence should alert phy-

sicians to the need for a careful evaluation, including echocardiography, of subclinical heart disease even in asymptomatic subjects.

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