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Original Article

Risk factors for coronary artery disease in left bundle branch block

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Abstract

Aim: The presence of left bundle branch block (LBBB) in the surface electrocardiogram makes the evalaution of patients for suspected angina pectoris difficult. A newly developed LBBB in patients with acute chest pain is an indication for primary percutaneous coronary intervention. However, it is difficult to evaluate the coronary artery disease (CAD) in stable patients with LBBB. In this study, we aimed to investigate the baseline demographic characteristics, electrocardiographic and echocardiographic findings in LBBB patients who had a preliminary diagnosis of CAD.

Material and Methods: We enrolled a total of 216 consecutive patients with a LBBB who had undergone coronary angiography. Of these patients, severe coronary artery disease did not find in 123 (56%) patients, while 93 (44%) patients had severe coronary artery disease

Results: The frequency of male sex, diabetes mellitus and hyperlipidemia were significantly higher in the CAD group (p=0.007, p=0.001, and p=0.012, respectively). Comparasion of electrocardiographic findings revealed no significant difference betweent the goups. In terms of the echocardiography findings, the left venticular ejection fraction was significantly lower and the left venticular end-diastolic volume was significantly higher in patients with CAD. We noted that patients with CAD had significiantly elevated creatinine levels compared to those who did not.

Conclusion: The significant risk factors for CAD among patients with LBBB included diabetes mellitus, elevated creatinine levels, male sex, advanced age, and low left venticular ejection fraction. These risk factors should be incorporated with non-invasive tests in patients with who had a preliminary diagnosis of CAD, and a conventional angiography should be considered in these patients in an attempt to increase the specificity and sensitivity of the available diagnostic tests.

Keywords: Left Bundle Branch Block; Coronary Artery Disease; Diabetes Mellitus.

INTRODUCTION

The presence of left bundle branch block (LBBB) in the resting electrocardiogram (ECG) makes the evalaution of patients for suspected angina pectoris difficult. The main causes of LBBB are aortic stenosis, dilated cardiomyopathy, acute myocardial infarction, coronary artey disease (CAD), advanced age, and hypertension. In general population, its prevalance is 0.43 % in men and 0.28 % in women (1,2). A newly developed left bundle branch block in patients with acute chest pain is an indication for primary percutaneous coronary intervention (3). However, it is a challenging to evaluate CAD in stable patients with LBBB.

Although conventional coronary angiography is the gold standart test for diagnosis of CAD, there are several non-invasive tests for risk stratification. These include exercise stress test, nuclear perfusion imaging, stress echocardiography, multislice computer tomography and stress cardiac magnetic resonance imaging. However, these tests have a different sensitivity and specificity based on the studied population. In this study, we aimed to investigate the baseline demographic characteristics, electrocardiographic and echocardiographic findings in LBBB patients who had a preliminary diagnosis of CAD

MATERIAL and METHODS

We enrolled the patients with LBBB who had undergone coronary angiography in our center between January 2016 and January 2018. We excluded the patients with a congenital heart disease, had a permanent pacemaker, and age under 18 years. In addition, patients with missing clinical data were excluded from the study. The patients' baseline demographic characteristics, electrocardiographic and echocardiographic as well as

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angiographic findings were retrospectiveley obtained from the hospital's electronic data. A total of 216 patients were enrolled, of whom 123 (56%) patients had no CAD, while 93 (44%) patients had coronary artery disease. Age, sex, hypertension, diabetes melitus, hyperlipidemia, smoking and family history were recorded as major risk factors for CAD. The history of atrial fibrillation was also recorded. The echocardiographic indices taken into consideration included the left ventricule ejection fraction, the left ventricule end-diastolic volume, the left ventricule end-diastolic diameter, the presence of left ventricular hypertrophy, and the left ventricule diastolic dysfunction. As for electrocardiography, the PR interval, QRS width, QT interval, and corrected QT interval that calculated with Bazzet Formula were recorded. In all patients, complete blood cell count, white blood cell subgroup analysis, creatinine, high density lipoprotein, triglyceride, low-density lipoprotein were recorded. A standardized questionnaire was used to collect clinical and demographic information, including medication history. The LBBB was defined when all of the following criteria were met;

1-QRS width >0.12 ms in the presence of normal sinus or supraventricular rhythm,

2-QS or RS complex in the lead V1,

3-The broad or notched R waves in the leads V5 and V6 or a RS pattern,

4-The absence of Q wave in the leads V5, V6, and I

Coronary angiography images were assessed by two experienced cardiologists who were blinded to the patients' clinical and demographic characteristics.The patients were included as a CAD group if they had at least one diseased vessel and/or a history of percutaneous coronary intervention and/or history of coronary artery bypass grafting. The patients with normal coronary arteries were categorized as the non-CAD group. Our study was approved by the local Ethics Committee of Başkent University Faculty of Medicine. A standardized questionnaire was used to collect clinical and demographic information, including medication history.

Statistical Analysis

Normally distributed continous variables were expressed as the mean ± standard deviation; non-normally distributed continous variabes were expressed as median (min-max); and categorical variables were presented as number (%). Student's T test was used for normally distributed variables, and Mann Whitney U test was used for non-normally distributed variables. Categorical data were analyzed with Fisher's exact test and the Chi-squared test. Backward stepwise logistic regression analysis method was used for multivariate analyses. The significant covariables in the univariate analysis were put in multivariate analysis. A P-value <0.05 was considered statistically significant. All analyses were performed using the SPSS statistical software package (version 17; SPPS, Chicago, IL, USA).

RESULTS

The mean age of the study population was 69.6 ± 12.9 years. We did not observe a significant difference in terms of age among the groups (p=0.315). The frequency of male sex, diabetes mellitus, and hyperlipidemia were significantly more common in the CAD group (p<0.05, for all) (Table 1).

Table 1. Comparison of the demographics and clinical characteristics

	CAD (-) n=123	CAD (+) n=93	p
Age, years	69.6 ± 12.9	73.3 ± 11.2	0.315
Male, n (%)	47 (38.2)	52 (55.9)	0.007
Hypertension, n (%)	87 (70.7)	74 (79.5)	0.093
Diabetes Mellitus, n (%)	24 (19.5)	38 (40.8)	0.001
Hyperlipidemia, n (%)	54 (43.9)	56 (60.2)	0.012
Smoking history, n (%)	38 (30.8)	31 (33.3)	0.348
Family history for CAD, n (%)	23 (18.6)	16 (17.2)	0.461
Atrial fibrillation, n (%)	28 (22.7)	14 (15.1)	0.090
Presence of LVH, n (%)	77 (62.6)	66 (70.9)	0.104
Presence of diastolic dysfunction in echo, n (%)	85 (69.1)	58 (62.3)	0.398
İschemia in MPS, n (%)	8	6	0.111

CAD: coronary artery disease, LVH: left ventricular hypertrophy, MPS:myocardial perfusion scintigraphy

The analysis of the electrocardiographic data revealed no significant difference with respect to the PR interval,the QRS width, the QT interval, and the corrected QT interval (p>0.05, for all) (Table 2).

The comparison of the echocardiography findings revealed a significantly lower left ventricule ejection fraction (41.3 ± 12.6 % vs. 46.9 ± 12.6 %), and a significantly greater left ventricule end-diastolic volume (122.5 ± 52.1ml vs. 103.3 ± 45.4ml) in patients with CAD (Table 2). The comparison of labarotory values revealed a significantly higher creatinine level in patients with CAD (1.34 ± 1.26 mg/dl vs. 0.97 ± 0.41 mg/dl). Low density lipoprotein was significantly lower in the CAD group. There was no significant difference between the groups in terms of other parameters (Table 2). Univariable risk factors for CAD were diabetes mellitus, creatinine level, hyperlipidemia, ejection fraction, male sex, and low density lipoprotein level and end diastolic volume in echocardiography. In multivariable logistic regression analysis, we found diabetes mellitus and creatinine level were independent risk factors for CAD in patients with LBBB (p=0.019, p=0.038, respectively) (Table 3).

Table 2. Comparison of electrocardiographic, echocardiographic and labarotory findings between two groups

	CAD (-) n=123	CAD (+) n=93	p
PR interval (msec)	170.9 ± 45.3	180.1 ± 39.8	0.145
QRS width (msec)	144.5 ± 16.1	146 ± 16.4	0.287
QT interval (msec)	440.1 ± 50.9	445.5 ± 36.4	0.389
QTc interval (msec)	480.3 ± 27.8	478.3 ± 30.7	0.608
Ejection fraction in echocardiography, n (%)	46.9 ± 2.6	41.3 ± 12.6	0.001
End diastolic volume (ml)	103.3 ± 45.4	122.5 ± 52.1	0.003
End diastolic diameter (mm)	47.7 ± 15.6	50.3 ± 11.7	0.187
Creatinine (mg/dl)	0.97 ± 0.41	1.34 ± 1.26	0.001
Hemoglobine (mg/dl)	14.4 ± 5.6	12.8 ± 2.1	0.159
White blood cell (x10^3/uL)	7.7 ± 2.6	7.7 ± 2.4	0.814
Platelets (x10^3/uL)	235 ± 68.5	211 ± 62.6	0.065
HDL-C (mg/dl)	48.1 ± 11.2	45.3 ± 13.0	0.088
LDL-C (mg/dl)	112.6 ± 33.6	101.8 ± 32.4	0.018
Triglyceride (mg/dl)	131.8 ± 55.1	149.5±105.1	0.142
RDW	13.8 ± 1.97	14.2 ± 2.17	0.660
N/L ratio	2.66 ± 1.95	2.97 ± 2.46	0.449

HDL-C, high density lipoprotein; LDL-C, low density lipoprotein; N/L ratio: neutrophil/lymphocyte ratio; RDW, red cell distribution width

Table 3. Multivariate regression analysis for defining the independent risk factors for CAD among patients with LBBB

Parameter	x^2	Confidency Interval %95	p value
Diabetes Mellitus	2.24	1.14-4.40	0.019
Creatinine	2.09	1.04-4.19	0.038
Hyperlipidemia	2.17	1.15-4.10	0.084
Ejection fraction	0.97	0.94-1.00	0.070
Male sex	1.64	0.85-3.14	0.132
Low density lipoprotein	0.99	0.98-1.00	0.443
End diastolic volume	1.001	0.99-1.01	0.889

DISCUSSION

In the general population, the prevalece of LBBB is approximately 0.5%. The LBBB has been linked to sudden cardiac death and adverse cardiac events (4). In the Framingham study, a CAD or heart failure developed in 48 % of patients with LBBB, and just 11 percent of patients were free of cardiovascular disease during an 18-years follow–up period (5). Besides this, patients with LBBB but without cardiovascular disease showed a slight increase in mortality compared to the general population (6). For these reasons, the presence of LBBB warrants further examination for structural heart disease. As the most common cause of LBBB is the CAD, the investigations are usually based on the exclusion of severe CAD.

The presence of LBBB causes a number of changes in the myocardial function, which profoundly affect the results of non-invasive tests. The delay of electrical activation of the left ventricle is presented as the widening of the QRS wave in the ECG. These results in an abnormal contraction in the interventricular septum compared to the posterior wall during the systole, causing a disturbance of ventricular synchrony. In rare circumsantences, this septal contraction abnormality can be observed as the impaired left ventricular wall motion in the echocardiography. In an experimental LBBB model, the induction of LBBB caused reduced septal systolic thickening and increased intramyocardial pressure, which leads to a relative decrease in the myocardial perfusion and a decrease in glucose uptake of septum relative to the lateral wall (7). This phenomenon has also been shown as hyperperfused lateral left ventricular wall due to the right ventricular pacing in patients with a permanent cardiac pacemaker (8).

Considering these effects of the LBBB on the myocardium, non-invasive tests may have difficulties in assessing the CAD and, thus causing decrease of the reliability of these tests. Because of the baseline electrocardiographic changes, an exercise stress test is not recommended for screening of CAD in patients with LBBB (9). Nuclear imaging methods, which are also frequently used for the diagnosis of CAD, have sensitivity of 87% and specificity of 73% for obstructive coronary disease in the general population (10). These rates are variable in patients with LBBB due to the abovementioned reasons. Some studies demonstrated that there is a higher incidence of ischemia in the territory supplied by the left anterior descending artery which can not be evaluated during the angiography (11,12). Dobutamine stress echocardiography has a similar sensitivity and specifity with SPECT in the general population (13). However, there are many false positive results in stress echo as in similar to SPECT in patients with LBBB, but in experienced hands, similar results have been reported among these patients (14).

In patients with LBBB, the risk factors for CAD have previously been reported. Ozeke et al. (15) studied 3 groups of patients; of which consisting of 51 patients with type-2 diabetes mellitus and LBBB, 51 patients with type-2 diabetes mellitus without LBBB, and 51 patients had isolated LBBB. The frequency of hypertension, serum creatinine levels, and cholesterol levels were significantly higher in patients with type-2 diabetes mellitus and LBBB. Furthermore, this group had higher Gensini scores, a lower left ventricule ejection fraction, and a higher incidence for 3-vessel disease. In our study, diabetes mellitus and serum creatinine level were found to be independent risk factors for CAD. Even though tle left ventricule ejection fraction and the frequency of hyperlipidemia were found statistically different between the groups as in previous studies, these risk factors were not found to be independently associated with CAD in our study. In a cross sectional study of 219 patients, Ghaffari et al. (16) showed that advanced age, male sex, and echocardiographic left ventricule ejection fraction of ≤50% were predictors for

CAD, while advanced age, male sex, diabetes mellitus history, and an angiographically documented CAD were the predictors for left ventricular systolic dysfunction. In our study, even if it was not statistically significant, the mean age was higher in the CAD group (73.3 ± 11.2 vs. 69.6 ± 12.9 years, p=0.315). The percentage of the male sex was also higher, which was hormany with the above-mentioned study (p=0.007). Moreover, in that study, diabetes mellitus was found to be an independent risk factor for CAD. According to our results, as mentioned to previous studies, we found diabetes mellitus as an independent risk factor for CAD in LBBB patients. And also, it is comprehensible that creatinine levels were significantly increased in CAD patients comparing to control group. Because we know that in chronic renal disease patients atherosclerotic process is faster than other patients. We did not find the other traditional risk factors as an independent variable; this may be due to number of patients participating in our study. However, it has shown that all the other traditional risk factors like male sex, left ventricule ejection fraction, hyperlipidemia, and low density lipoprotein levels were significantly different between the groups. In 2014, Anghel et al. (17) examined LBBB patients with and without hypertension; showed that in the hypertension-positive group, the CAD was more diffuse. However, the hypertensive group had also a significantly higher prevalence of diabetes mellitus than the normotansive group, thereby suggesting a strong contribution of diabetes mellitus to the CAD development. In another study (18), which consisted of 229 patients 99 patients were found to have CAD. Male sex, advanced age, and smoking history were shown as independent predictors for CAD. Similarly, a study investigating the role of myocardial perfusion imaging among patients with LBBB (19) demonstrated that male sex and reduced left ventricule ejection fraction were significant predictors of CAD. In that study, the patients without LBBB were included and, it was shown that LBBB itself was an independent risk factor for CAD. In another study investigating the predictors of CAD in patients with LBBB (20), CAD was detected in 54% out of 336 patients. Male sex, advanced age, diabetes mellitus, and echocardiographic left ventricule ejection fraction less than 50% were defined as risk factors for CAD. In our study, echocardiographic left ventricular ejection fraction was not categorized as over or below 50%, but it was compared as a numerical variable. The average of both groups was found to be below 50%, but it was significantly lower in the CAD group (46.9 ± 12.6% vs. 41.3 ± 12.6%, p=0.001). This suggests that LBBB with or without CAD may be a risk factor for heart failure. Moreover, our study demonstrated a significantly larger left ventricular end-diastolic volume in patients with CAD (122.5 ± 52.1 vs. 103.3 ± 45.4 ml; p=0.003). However, it was not an independent predictor of CAD (p=0.889). Strain and tissue Doppler echocardiographic studies demonstrated that these parameters may be helpful in the diagnosis of CAD in patients with LBBB (21). However, these parameters were not evaluated beacause of the retrospective design of the study. In our study, there was no relationship between the basal characteristics of electrocardiographic data findings and CAD. No previous study has yet demonstrated that the basal electrocardiographic parameters can predict CAD. Therefore, the surface ECG does not give an idea of CAD in the presence of LBBB.

CONCLUSION

There are some difficulties in evaluating the CAD in LBBB patients with non-invasive stress tests. For that this reason, baseline demographic characteristics, ECG, echocardiographic as well as laboratory findings were investigated in order to determine the patients who may have a greater risk before the diagnostic tests. The significant risk factors for CAD among patients with LBBB included diabetes mellitus, high creatinine values, male sex, advanced age, and low left ventricule ejection fraction. Based on these study findings, these clinical risk factors should be evaluated together with non-invasive tests in risky groups, and a conventional angiography should be considered in these patients in an attempt to increase the specificity and sensitivity of the available diagnostic tests.

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