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ORIGINAL ARTICLE

Predictors and Morphologic Characteristics of Ischemic Left Bundle Branch Block

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ABSTRACT

Background: The presence of left bundle branch block (LBBB) represents a major challenge in the non-invasive diagnosis of coronary artery disease (CAD), as demonstrated by primary tests including resting, stress electrocardiography (ECG) and stress echocardiography, which have conferred low diagnostic sensitivity and specificity. Thus, coronary angiography is usually required to confirm diagnosis. The aim of this study was to investigate the predictors of C AD among patients with LBBB and identify different ECG features of ischemic LBBB.

Methods: This was a retrospective descriptive study of the records of patients from Zagazig University Catheterization Laboratory, Egypt, from May 2019 to May 2022. Among 3000 patients who underwent elective coronary angiography, only 168 patients (5.6%) had LBBB in a preprocedural 12-lead ECG.

Patients with LBBB were classified according to presence of CAD on coronary angiogram into: Group I: Includes 96 patients with LBBB and CAD, 72 males and 24 females (mean age 60.9±4.2 years) which further was classified according to left ventricular ejection fraction (LVEF) into 2 subgroups: Subgroup A: with LVEF <50% and Subgroup B: with LVEF ≥50%. Group II: Includes 72 patients with LBBB without CAD, 42 males and 30 females (mean age 57.1±5.7 years). All patients with LBBB were reviewed with special focusing on clinical and demographic features, LBBB criteria, echocardiography (mainly LVEF) and coronary angiography (with special focusing on site, severity and number of coronary vessels affected).

Results: LBBB was attributed to CAD in 57.2% of LBBB patients. Patients with LBBB and CAD were older, more in males, with increased previous MI and PCI. Also, there are a significant decrease of EF when comparing group I with group II ($p<0.05$). Notching of upstroke of S wave in V3 was significantly present in CAD group. Multivariate logistic regression analysis among patients with LBBB performed to find the predictors of CAD showed that EF <50% was the most significant predictor of CAD after controlling for other factors [odds ratio 0.282, 95% confidence interval (CI 0.080-0.991)].

Conclusions: Coronary angiography is usually required for definitive diagnosis of coronary artery disease in patients with LBBB. Involvement of left anterior descending (LAD) coronary artery was most common followed by left circumflex artery (LCX), followed by right coronary artery (RCA). Low LVEF is the single most significant predictor of CAD among patients with LBBB. So, those patients with LBBB and reduced EF need aggressive evaluation and treatment.

Key Words: Left bundle branch block, Coronary artery disease, Left ventricular ejection fraction, Coronary angiography.

INTRODUCTION

An abnormality of the conductive system of the heart known as left bundle branch block (LBBB) frequently develops in patients who have no overt cardiac disease and is typically linked to coronary artery disease (CAD), aortic valve disease, myocardial inflammation, heart failure, and conductive system degeneration **[1]**. As tests like resting as well as stress electrocardiography (ECG), and stress echocardiography have low diagnostic predictive value **[2,3]**, the presence of LBBB represents a significant challenge for non-invasive diagnosis of CAD. Thus, coronary

angiography is typically needed to confirm the diagnosis **[4–8]**.

Unfortunately, due to inconsistent and ambiguous results from non-invasive diagnostic techniques, the absolute detection of ischemia in the presence of LBBB frequently requires invasive procedures, including coronary angiography **[9,10]**. The frequency of LBBB rises from 0.4% at age 50 to 5.7% at age 80 [11]. LBBB population have been found to have a greater prevalence of CAD than patients without LBBB **[12,13]**. Particularly in patients with concurrent CAD **[12,16,17]**, LBBB is an independent predictor of mortality **[14,15]**.

Although it may be challenging clinically, distinguishing between ischemia and non-ischemic left ventricular (LV) dysfunction is crucial for prognosis and treatment **[18]**. The non-invasive tests are generally unreliable in determining whether left ventricular failure is caused by non-ischemic or CAD in the presence of LBBB **[19]**. ECG-QRS morphologic characteristics in complete LBBB had low usefulness in separating ischemia from non-ischemic LV dysfunction, despite the fact that some ECG abnormalities were shown to be helpful **[20]**.

Because of intraventricular conduction defect or LBBB, patients with dilated cardiomyopathy commonly have a prolonged QRS duration (120 ms) (LBBB) **[21]**. In ischemic cardiomyopathy, LBBB may manifest early after myocardial infarction (MI), also later time due to remodeling **[22]**. To diagnose chronic MI in LBBB patients, different ECG criteria have been put out in the past. More precise reports demonstrate that these ECG criteria's specificity and predictive accuracy are too low **[23]**.

The aim of this study is to assess the prediction of CAD among patients with LBBB and to identify different ECG features of ischemic LBBB.

METHODS

This was a retrospective descriptive study of the records from Zagazig University Catheterization Laboratory, Egypt, from May 2019 to May 2022. Among 3000 patients who underwent coronary angiography, only 168 patients (5.6%) had LBBB in a preprocedural 12-lead ECG.

Informed consent and ethics committee/IRB approval: An informed consent has been obtained from patients. The Institutional Review Board (IRB), Zagazig University's School of Medicine, gave its clearance. A written informed consent was obtained from all participants, the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria: Patients who underwent elective coronary angiography who had LBBB in a preprocedural 12-lead ECG.

Exclusion criteria: Patients who presented with acute LBBB and managed as STEMI.

Patients with LBBB (168 patients) were divided according to presence of CAD on coronary angiogram into: **Group I:** Includes 96 patients with LBBB and CAD, 72 males and 24 females (mean age 60.9±4.2 years) which further was classified according to left ventricular ejection fraction (LVEF) into 2 subgroups: subgroup A: with LVEF<50%, subgroup B: with LVEF≥50%. **Group II:** Includes 72 patients with LBBB without CAD, 42 males and 30 females (mean age 57.1±5.7 years).

All patients were subjected to reviewing history and risk factors like: Age, sex, smoking, diabetes mellitus, hypertension, lipid profile and previous myocardial infarction or PCI. Hypertension defined as blood pressure levels of ≥140/90mmHg or patients on antihypertensive therapy. Total cholesterol levels >200mg/dl, LDL cholesterol level >130mg/dl or triglycerides levels >150mg/dl were categorized as dyslipidemia.

Left bundle branch block criteria: The 12-lead ECG was used to record left bundle branch block and to identify it in accordance with the criteria established by the New York Heart Association [24]. QRS interval 120 ms; slurred/notched wide and predominant R waves in leads I, aVL, V5 and V6; slurred, notched, and broad S waves in leads VI and V2 with absent or small R waves; mid-conduction delay defined as notching or a plateau in the mid-QRS wave; ventricular activation time >50 ms at the onset of the QRS interval; MM-shaped QRS variants without an initial Q-wave over the left precordium and occasionally wide R waves in V5 and V6.

Echocardiography: Transthoracic echocardiography was done using GE (vidid 5 pro) NORWAY. Two-dimensional echocardiography was done from the apical 4-and 2-chamber views. LVEF was assesses using biplane Simpson's method and considered impaired if the LVEF was <50% [25].

Coronary angiography: Multiple projections of selective coronary angiography were carried out; the existence of CAD was indicated by a major epicardial artery's luminal diameter narrowing by at least 70% or the left main coronary artery's luminal diameter narrowing by at least 50%.

Statistical analysis

Data was analyzed using SPSS (Statistical Package for Social Sciences) version 24. Qualitative data

was presented as number and percent. Comparison between groups was done by Chi-Square test. Quantitative data was tested for normality by Kolmogrov-Smirnov test. Normally distributed data was presented as mean ± SD. Student t-test was used to compare between two groups. Multivariate analysis using forward stepwise multiple linear regression was used to determine the independent predictor of CAD among patients with LBBB. $p<0.05$ was considered to be statistically significant.

RESULTS

The study showed that patients with LBBB were attributed to CAD in 57.2% of LBBB patients. Ischemic LBBB patients were older (60.9±4.2 VS 57.15±5.7, p: 0.008), significantly more in males (75% VS 25%, p: <0.005). There was statistically significant increase in CAD prevalence among LBBB patients who are smokers (56.3% VS 25%, p: 0.019) and in patients with history of previous MI (15.6% VS 4.1%, p: <0.001) and previous PCI. There was no statistically significant difference between both groups regarding diabetes, dyslipidemia, hypertension and atrial fibrillation (p: 0.147, 0.876, 0.876 and 0.5 respectively), as shown in table (1).

There was no statistically significant difference between both groups regarding QRS width (160±25 VS 170±30, p: 0.3), but notching of upstroke of S wave in V3 was significantly present in CAD group (63.5% VS 12.5%, p: 0.02), as shown in table (2).

There was a significant decrease of EF when compare group l with group ll (62.5% VS 33.3%, p: <0.05) as shown in table (3).

Among CAD group, coronary angiography showed single vessel disease (SVD) in 36 patients (37.5%), double vessel disease (DVD) in 30 patients (31.3%), three vessel disease (TVD) in 18 patients (18.8%) and left main disease (LMD) in12 patients (12.5%), as shown in table (4).

Table (5) showed that LAD is the main vessel affected followed by LCX, RCA and LMCA in descending order (75%, 56.3%, 43.8% and 12.5% respectively).

No statistically significant difference between both subgroups (A and B) regarding all clinical, echocardiographic and angiographic parameters was found, as shown in table (6).

On multivariate logistic regression analysis among patients with LBBB performed to find the predictors of CAD showed that EF <50% was the most significant predictor of CAD after controlling for other factors [odds ratio 0.282, 95% confidence interval (CI 0.080-0.991), p=0.018], as shown in table (7).

Table 1: Clinical characteristics of study groups

Variable	Group l (LBBB with CAD) (n=96: 57.2%)	Group ll (LBBB without CAD) (n=72: 42.8%)	p-value
Age (years) (mean ± SD)	60.9±4.2	57.15±5.7	0.008
Sex:			
Male	72 (75%)	42 (58.3%)	
Female	24 (25%)	30 (41.7%)	<0.005
Smoking	54 (56.3%)	18 (25%)	0.019
Diabetes mellitus	42 (43.8%)	18 (25%)	0.147
Dyslipidemia	42 (43.8%)	30 (41.7%)	0.876
Hypertension	54 (56.3%)	42 (58.3%)	0.876
AF	6 (6.25%)	6 (8.3%)	0.5
Previous MI	15 (15.6%)	3 (4.1%)	<0.001
Previous PCI	6 (6.25%)	_	

DM= Diabetes mellitus
HTN= Hypertension
AF =Atrial fibrillation
MI =Myocardial infarction
PCI =Percutaneous coronary intervention

Table 2: LBBB electrocardiographic morphologic characteristics of study groups

Variable	Group I (LBBB with CAD) (n=96)	Group II (LBBB without CAD) (n=72)	p-value
QRS width (duration: ms)	160±25	170±30	0.3
Notching of upstroke of S wave in V3 (n: %)	61 (63.5%)	9 (12.5%)	0.02

Table 3: Echocardiographic characteristics of study groups

Variable	Group I (LBBB with CAD) (n=96)	Group II (LBBB without CAD) (n=72)	p-value
LVEF<50% n (%)	60 (62.5%)	24 (33.3%)	<0.05
LVEF (mean ± SD)	52.9±6.6	59.2±8.2	0.032

LVEF =Left ventricular ejection fraction

Table 4: Coronary angiographic characteristics of study groups

Variable	Group I (LBBB with CAD) (n=96)	Group II (LBBB without CAD) (n=72)	p-value
Number of vessels involved:			
Single vessel disease (SVD)	36 (37.5%)	0 (0%)	_
Double vessel disease (DVD)	30 (31.3%)	0 (0%)	_
Three vessel disease (TVD)	18 (18.8%)	0 (0%)	_
Left main disease (LMD)	12 (12.5%)	0 (0%)	_

Table 5: The location of CAD in LBBB patients

LMCA	12 (12.5%)
LAD	72 (75%)
LCX	54 (56.3%)
RCA	42 (43.8%)

LMCA =Left main coronary artery

LCX =Left circumflex artery

LAD =Left anterior descending

RCA =Right coronary artery

Table 6: Background variables and risk factors in LBBB with CAD group according to LVEF

Variables	LVEF <50% (Subgroup A) (n=60)	LVEF ≥50% (subgroup B) (n=36)	p-value
Age (years)	61.3±3.9	60.3±4.8	0.543
DM	24 (40%)	18 (50%)	0.581
HTN	36 (60%)	18 (50%)	0.581
Dyslipidemia	24 (40%)	18 (50%)	0.581
SVD	30 (50%)	6 (16.7%)	0.059
DVD	18(30%)	12 (33.3%)	0.844
TVD	6 (10%)	12 (33.3%)	0.102
LMD	6 (10%)	6 (16.7%)	0.581
LAD	48 (80%)	24 (66.7%)	0.399
LCX	10 (50%)	8 (66.7%)	0.358
RCA	10 (50%)	4 (33.3%)	0.358

Table 7: Multivariate logistic regression analysis in patients with LBBB for detection of predictors of CAD

	Odds ratio	Confidence interval (95%)	p-value
Age <50	7.824	0.686-89.286	0.098
Gender (male)	0.647	0.161-2.606	0.540
DM	2.342	0.458-11.977	0.307
HTN	0.561	0.126-2.503	0.449
Smoking	3.564	0.983-12.918	0.053
EF (<50%)	0.282	0.080-0.991	0.018

DISCUSSION

According to previously published studies **[12,14,16,25]**, people who have CAD and concurrent left bundle branch block (LBBB) mostly die from cardiovascular causes than people who only have CAD. Therefore, determining the prevalence and severity of CAD in individuals with LBBB may be helpful in directing therapy and offering prognostic data **[26]**. The existence of LBBB is associated with more severe disease, more reduced LVEF and poor outcomes in individuals with CAD. LBBB has a significant influence by masking or imitating other electrocardiographic patterns **[27]**. Electrocardiographic, echocardiographic, or scintigraphic techniques make it difficult or impossible to detect CAD in the presence of LBBB [28], thus coronary angiography is typically needed to offer a conclusive diagnosis.

In our study, 5.6% of patients undergoing coronary angiography had LBBB (168 patients), LBBB was attributed to ischemia in 57.2% of LBBB patients, which was similar to those previously published studied **[29,30]**. Age, Gender, smoking, DM, HTN and dyslipidemia were not found to predict CAD well in this study, in contrast with the previous study conducted by Keles et al **[31]**. This may be because these are risk factors also for dilated cardiomyopathy which may result in LBBB, so they couldn't be used as independent predictors of CAD among LBBB population.

The many ECG morphologic characteristics that have been put forth in the past as MI indicators in the presence of LBBB are insensitive and inaccurate predictors of myocardial infarction. Additionally, there is a lot of interobserver variability that affects them **[32]**. A prolonged QRS length (170 ms) in the context of LBBB is an indicator of severe left ventricular failure, according to Das et al. There is a significant inverse relationship between QRS width and ejection fraction **[33]**.

As shown in table (2), there was no statistically significant difference between the two groups in our study regarding QRS width (p = 0.3), but Cabrera's sign (notching of the upstroke of the S wave in V3, may be also in V4, or V5) was significantly higher in the CAD group (p = 0.02). Wackers found that this sign had a diagnostic sensitivity of only 27% for prior myocardial infarction **[34]**.

In this study, among 168 patients with LBBB who were referred for coronary angiography, 72 patients (42.8%) had no CAD, 96 patients (57.2%) had significant CAD, and of those 96 patients, 36 (37.5%) had single vessel disease, 30 (31.3%) had double vessel disease, 18 (18.8%) had three vessel disease, and 12 (12.5%) had left main disease. In the study by Ghaffari et al. **[35]**, left main or three-vessel CAD was 16.9%; in the studies by Nguyen et al. **[28]**, about 13%; and Abrol et al. **[36]**, about 17%.

Single vessel disease, double vessel disease, and triple vessel disease were all present in 23%, 24%, and 37% of the participants in the study by Lashari et al. **[37]**. Single vessel disease was found in 25.8% of patients and triple vessel disease in 53.3% of patients in the Shareef et al. research **[38]**.

According to (Table 6), the LAD is the vessel that is most frequently affected (75%) followed by LCX (56.3%), RCA (43.8%), and then LMCA (12.5%). These results are comparable to those of Rahu et al. **[41]**, but in Lashari et al. **[37]**, the LAD was only affected in 16% of cases, LCX was in 4%, RCA was in 0%, and left main was in 13%. Therefore, comparable to other research, our analysis demonstrates a high incidence of single vessel disease and a high incidence of LAD involvement.

According to our research, patients with reduced LV function (EF 50%) did not differ significantly from patients with intact LV function (EF>50%) in terms of the number of vessels implicated or the specific artery impacted (Table 6). These findings concurred with those of Ghaffari et al. **[35]**, who discovered that the majority of patients with impaired LV function lacked left main or three vessel CAD.

Table 2's multivariate logistic regression analysis revealed that among patients with LBBB, reduced EF was the single most important predictor of CAD. The findings of Abrol et al. **[36]**, Keles et al. **[31]**, and Jeevanantham et al. **[39]** are comparable to those of these researchers.

These findings suggest that patients with LBBB and low EF (50%) have a substantially increased likelihood of developing CAD, emphasising the significance of early, proactive evaluation in these patients.

The present study had some shortcomings. First of all, this analysis was retrospective, which could have led to selection bias. Secondarily, some of the discrepancies between our results and those of earlier studies **[24,30,31]** may be explained by the existence of various demographic characteristics in this study sample. Thirdly, there are some drawbacks to generalizing these findings to all asymptomatic LBBB patients because our study cohort had at least intermediate odds of having CAD.

CONCLUSIONS

For patients with LBBB, coronary angiography is typically necessary for a conclusive diagnosis of coronary artery disease. The LAD was most frequently involved, followed by LCX and RCA. In ischemic LBBB, the Cabrera's sign (notching of the upstroke of the S wave in V3) occurs frequently. The only one most important indicator of CAD in patients with LBBB is lower LVEF. Therefore, patients with LBBB and diminished EF require proactive assessment and care.

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Financial Disclosures: No financial interests to disclose.

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