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Predictors of coronary artery disease in patients with left bundle branch block who undergo myocardial perfusion imaging

Vinodh Jeevanantham[1], Kavitha Manne[2], Mohan Sengodan[2], James M. Haley[2], David H. Hsi[2]

[1]Wake Forest University, Winston-Salem, NC, USA
[2]Unity Health System, Rochester, NY, USA

Abstract

Background: *Due to difficulties in diagnosing coronary ischemia in patients with left bundle branch block (LBBB), identifying clinical characteristics that might help to predict coronary artery disease (CAD) is important. Our study aimed to identify clinical predictors of CAD among patients with and without LBBB who undergo myocardial perfusion imaging (MPI).*

Methods: *All patients with LBBB who underwent MPI (LBBB group) from June 2005 to February 2007 were compared with patients with normal baseline electrocardiography who underwent treadmill MPI (non-LBBB group) during the same period.*

Results: *LBBB patients with CAD were younger and had lower ejection fraction (EF) compared to LBBB patients without CAD. Similarly non-LBBB patients with CAD had lower EF, but did not differ significantly in age compared to non-LBBB patients without CAD. Regression analysis among patients with LBBB showed that EF < 55% was the most significant predictor of CAD, after controlling for other factors. A regression analysis in non-LBBB patients showed that male gender and EF ≤ 55% were significant predictors of CAD. A regression analysis conducted in the combined data of both LBBB and non-LBBB groups showed male gender, EF ≤ 55% and LBBB to be the most significant predictors of CAD.*

Conclusions: *Patients with LBBB have a high probability of CAD based on MPI findings. Patients with LBBB and reduced EF have a much higher likelihood of CAD compared to patients without LBBB and normal EF. Further studies on early invasive approach in patients with LBBB and reduced EF seem warranted.* (Cardiol J 2009; 16, 4: 321–326)

Key words: left bundle branch block, coronary artery disease, myocardial perfusion imaging

Introduction

The prevalence of left bundle branch block (LBBB) in the general population increases from 0.4% at 50 years of age to 5.7% at 80 [1]. A higher prevalence of coronary artery disease (CAD) has been reported in patients with LBBB compared to those without LBBB [2, 3]. LBBB is an independent predictor of mortality [4, 5], especially in patients with concomitant CAD [2, 6, 7].

However, diagnosing coronary ischemia in patients with LBBB seeking medical attention is often a challenge using the electrocardiogram (ECG) [8], echocardiography, or sometimes even with scinti-

Address for correspondence: Vinodh Jeevanantham, MD, MPH, General Internal Medicine, Wake Forest University Health Sciences, Medical Center Blvd, Winston-Salem, NC 27157, USA, tel: 336 716 8212, fax: 336 716 7359, e-mail: vjeevanantham@gmail.com

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graphic studies [9, 10]. According to ACC/AHA guidelines [11], exercise treadmill testing is not reliable in detecting ischemia in patients with LBBB. Dipyridamole or adenosine based myocardial perfusion imaging (MPI) is recommended for cardiac stress testing in patients with LBBB [11].

Due to diagnostic difficulties, it is important to be aware of the clinical characteristics that might help identify LBBB patients with a high likelihood of CAD. Identifying such predictors may help to decide whether a patient needs non-invasive or early invasive testing. Our study aims to identify clinical predictors of CAD among patients with and without LBBB who undergo MPI.

Methods

Patient population

We conducted a retrospective chart review of all patients who underwent MPI between June 2005 and February 2007. The study was approved by the Unity Hospital Institutional Review Board. We compared patients with LBBB (LBBB group) *vs*. patients with normal baseline ECG who underwent MPI (non-LBBB group). Data on demographic variables, risk factors for CAD, digoxin or estrogen use, and indication for the test were collected.

Diagnosis of coronary artery disease

The diagnosis of CAD was based on the results of MPI in both groups. Exclusion criteria for both groups were patients with mild apical ischemia and normal left ventricular ejection fraction (EF). The exclusion criteria were based on the fact that Thallium-201 imaging has less spatial resolution than Tetrafosmin, thus the left ventricular apical region appears thicker and may cause false positive findings.

Statistical analysis

Statistical analyses were performed using the Statistical Program for Social Sciences (version 13.0 SPSS Inc., Chicago, Illinois, USA). Frequency analysis was done to identify the distribution of variables. An independent sample t-test was used to detect differences between continuous variables. Continuous variables are represented as mean ± standard deviation. χ^2 test was used to test association between categorical variables. A Fisher's exact test was used when appropriate. A p value of < 0.05 was considered statistically significant. Logistic (binary) regression analysis was used to identify independent predictors of CAD among LBBB patients, non-LBBB patients and in combined data of both groups. Based on correlation matrix analysis, univariate analyses and clinical correlation, the variables (age, gender, diabetes mellitus, hypertension, hyperlipidemia, EF ≤ 55%, history of LBBB, peripheral vascular disease and smoking) were included in the regression model.

Results

The total number of patients in the LBBB group was 130. The non-LBBB group was 538. Differences in clinical characteristics between patients with LBBB and the non-LBBB group are shown in Table 1. Patients with LBBB were older, more likely to be women and had a higher prevalence of diabetes, hypertension and peripheral vascular disease compared to the non-LBBB group (Table 1).

The mean EF was significantly lower in the LBBB group compared to the non-LBBB group (51.8 ± 13.2 *vs*. 58.4 ± 9.3, $p < 0.01$). These differences in mean EF were more prominent in LBBB patients with CAD compared to LBBB patients without CAD (Table 1). MPI was positive in 54.6% of patients with LBBB compared to 25.1% of the non-LBBB group ($p = 0.001$).

Table 2 shows the differences in clinical profile among LBBB patients with versus without CAD. Patients with LBBB and CAD were younger and had lower EF compared to patients with LBBB and without CAD (Table 2). Similarly, Table 3 shows the differences in clinical profile among non-LBBB patients with versus without CAD. Patients without LBBB and with CAD were more likely to be women with lower EF compared to non-LBBB patients without CAD.

Regression analysis performed to find the predictors of CAD among patients with LBBB showed that EF < 55% was the most significant final predictor of CAD among patients with LBBB after controlling for other factors [odds ratio (OR) 4.37, 95% confidence interval (CI 2.07–9.22), $p < 0.01$] (Table 4). Similarly a regression analysis performed to identify predictors of CAD among patients in non-LBBB group showed that male gender (OR 2.86, 95% CI 1.58–5.18, $p < 0.001$), and EF ≤ 55% (OR 5.8, 95% CI 3.6–9.5, $p < 0.001$) were the significant independent predictors of CAD after controlling for other factors such as diabetes, hypertension, smoking, hyperlipidemia and peripheral vascular disease (Table 5).

Table 6 shows the results of regression analysis to find predictors of CAD in the combined data of both LBBB and non-LBBB groups. Male gender (OR 2.37, 95% CI 1.46–3.84, $p < 0.01$), EF ≤ 55% (OR 5.69, 95% CI 3.73–8.68, $p < 0.01$), and LBBB (OR 4.05, 95% CI 2.41–6.79, $p < 0.01$) were found

Table 1. Differences in baseline variables between patients with left bundle branch block (LBBB) and normal baseline electrocardiography.

Variables	Normal baseline (n = 538)	LBBB (n = 130)	P
Age (years; mean ± SD)	57.1 ± 11.2	70.8 ± 12.3	0.01*
Women	212 (39.5%)	81 (62.3%)	< 0.01#
Diabetes	98 (18.2%)	35 (27.3%)	0.02#
Hypertension	313 (58.2%)	106 (81.5%)	< 0.01#
Hyperlipidemia	350 (65.2%)	83 (63.8%)	0.77#
Smoking	114 (21.2%)	17 (13.1%)	0.03#
Peripheral vascular disease	16 (3%)	19 (14.6%)	< 0.01#
Digoxin	7 (1.3%)	10 (7.7%)	< 0.01#
Estrogen	17 (3.2%)	2 (1.5%)	0.31#
Ejection fraction (mean ± SD)	58.4 ± 9.3	51.8 ± 13.2	< 0.01*
Ejection fraction (mean ± SD)			
MPI positive	51.2 ± 10.9	45.8 ± 12.4	0.02
MPI negative	61 ± 7.2	59.15 ± 10.2	0.08
CAD based on MPI	135 (25.1%)	71 (54.6%)	< 0.001

*p value based on t test; #p value based on χ^2 test; CAD — coronary artery disease; MPI — myocardial perfusion imaging

Table 2. Differences in baseline variables between patients with left bundle branch block (LBBB) with coronary artery disease (CAD) versus without diagnosed CAD.

Variables	LBBB with CAD (n = 71)	LBBB without CAD (n = 59)	P
Age (years; mean ± SD)	68.2 ± 12.7	73.8 ± 11.2	0.01*
Women	37 (52.1%)	44 (74.6%)	0.009#
Diabetes	23 (32.4%)	12 (21.1%)	0.152#
Hypertension	61 (85.9%)	45 (76.3%)	0.16#
Hyperlipidemia	49 (69%)	34 (57.6%)	0.18#
Smoking	10 (14.2%)	7 (11.9%)	0.71#
Peripheral vascular disease	10 (14.1%)	9 (15.3%)	0.85#
Digoxin	7 (9.9%)	3 (5.1%)	0.31#
Estrogen	1 (1.4%)	1 (1.7%)	0.89#
Ejection fraction (mean ± SD)	45.8 ± 12.4	59.1 ± 10.2	< 0.01*

*p value based on t test; #p value based on χ^2 test

Table 3. Differences in baseline variables between patients with non-left bundle branch block (non-LBBB) with coronary artery disease (CAD) versus without diagnosed CAD.

Variables	Non-LBBB with CAD (n = 135)	Non-LBBB without CAD (n = 403)	P
Age (years; mean ± SD)	56.8 ± 11.2	57.2 ± 11.2	0.73*
Women	115 (85.2%)	210 (52.2%)	< 0.01#
Diabetes	28 (20.7%)	70 (17.4%)	0.38#
Hypertension	81 (60%)	232 (57.6%)	0.62#
Hyperlipidemia	94 (69.6%)	256 (63.7%)	0.21#
Smoking	32 (23.9%)	82 (20.3%)	0.39#
Peripheral vascular disease	5 (3.7%)	11 (2.7%)	0.56#
Digoxin	4 (3.0%)	3 (0.7%)	0.05#
Estrogen	1 (0.7%)	16 (4.0%)	0.06#
Ejection fraction (mean ± SD)	51.2 ± 10.9	61 ± 7.2	< 0.01*

*p value based on t test; #p value based on χ^2 test

Table 4. Predictors of coronary artery disease using multivariate logistic regression analysis in patients with left bundle branch block.

Variable	Odds ratio	95% confidence interval	P
Age > 50 years	3.8	0.68–22.2	0.06‡
Male gender	2.0	0.82–4.8	0.13‡
Diabetes	1.58	0.64–3.9	0.32‡
Hypertension	2.2	0.62–7.6	0.22‡
Smoking	2.46	0.72–8.4	0.15‡
Hyperlipidemia	1.75	0.3–3.8	0.16‡
Peripheral vascular disease	1.3	0.39–4.37	0.66‡
Ejection fraction ≤ 55%	4.37	2.07–9.22	< 0.01*

*final independent predictors of coronary artery disease; ‡odds ratio before variable is removed from the backward binary logistic regression analysis

Table 5. Predictors of coronary artery disease using multivariate logistic regression analysis in non-left bundle branch block patients.

Variable	Odds ratio	95% confidence interval	P
Age > 50 years	1.18	0.71–1.96	0.53‡
Male gender	2.86	1.58–5.18	< 0.001*
Diabetes	1.19	0.67–2.14	0.55‡
Hypertension	1.4	0.89–2.24	0.14‡
Smoking	1.23	0.71–2.16	0.45‡
Hyperlipidemia	1.32	0.81–2.14	0.26‡
Peripheral vascular disease	1.02	0.28–3.65	0.96‡
Ejection fraction ≤ 55%	5.8	3.6–9.5	< 0.001*

*final independent predictors of coronary artery disease; ‡odds ratio before variable is removed from the backward binary logistic regression analysis

Table 6. Predictors of coronary artery disease using multivariate logistic regression analysis in combined data of left bundle branch block and non-left bundle branch block patients.

Variable	Odds ratio	95% confidence interval	P
Age > 50 years	1.07	0.65–1.76	0.78
Male gender	2.37	1.46–3.84	< 0.01*
Diabetes	1.25	0.77–2.03	0.35
Hypertension	1.38	0.89–2.13	0.15
Smoking	1.33	0.81–2.22	0.258
Hyperlipidemia	1.43	0.93–2.20	0.1
Peripheral vascular disease	1.15	0.47–2.69	0.75
Left bundle branch block	4.05	2.41–6.79	< 0.01*
Ejection fraction ≤ 55%	5.69	3.73–8.68	< 0.01*

*final independent predictors of coronary artery disease

to be the most significant predictors of CAD, after controlling for all confounding factors (Table 6).

Discussion

LBBB may result from systemic hypertension, coronary ischemia, or degeneration/lesions of the conduction system (Lenegre's disease) [12]. Other associated conditions reported are valvular heart disease, cardiomyopathy, myocarditis or auto-immune disorders such as systemic lupus erythematosis and systemic sclerosis [12]. However, in most cases, it is very difficult to identify the exact etiology. In clinical practice a large number of patients

with LBBB who present with chest pain are referred for coronary angiography due to diagnostic difficulties. Currently ACC/AHA guidelines recommend dipyridamole or adenosine based MPI for cardiac stress testing in patients with LBBB [11]. Therefore identifying LBBB patients who would benefit from non-invasive testing (MPI) *vs*. invasive coronary angiography is important.

In our study, patients with LBBB were older and a higher percentage were women compared to non-LBBB patients. In addition, the conventional risk factors (diabetes mellitus, hypertension) were more prevalent in LBBB patients. The prevalence of CAD in patients with LBBB was significantly higher than non-LBBB patients. These differences were more pronounced in patients with reduced EF. Although these differences could be partly attributed to the older age group, the differences are quite significant and may reflect an association. This is of importance because patients with diabetes mellitus and LBBB have been shown to have more severe and extensive CAD [13].

Among LBBB patients, those with CAD were younger and had lower EF compared to those without CAD. However, in the non-LBBB group, patients with CAD did not differ significantly in age, but had lower EF compared to non-LBBB patients without CAD. Multivariate regression analysis showed that lower EF was the single most significant predictor of CAD among patients with and without LBBB. Male gender was another significant factor which predicted CAD among non-LBBB patients. Regression analysis in the combined data showed that male gender, low EF and presence of LBBB were significant predictors of CAD. Based on these observations, it seems that patients with LBBB and reduced EF (≤ 55%) have a much higher likelihood of CAD compared to those without LBBB and normal EF.

Furthermore, Abrol et al. [14] showed that nearly 54% of patients with LBBB referred for angiogram had CAD. In addition, Nguyen et al. [15] showed that 16% of patients with LBBB and reduced left ventricular function had left main or three vessel disease compared to 8% of patients with LBBB and normal left ventricular function. These studies, along with our results, highlight the importance of early aggressive evaluation in patients with LBBB and reduced EF (≤ 55%).

Newer studies are looking at developing more accurate non-invasive testing for diagnosing CAD in patients with LBBB. 64-slice computed tomography angiography shows promise, with sensitivity of 95% and specificity of 97% [16], although further studies are needed before we adopt this as a routine alternative to conventional angiography [17]. Until then, further studies on early invasive approach in patients with LBBB and reduced EF seem warranted.

Recently, Ghaffari et al. [18] studied Iranian patients with LBBB and reported male gender, reduced EF and advanced age to be predictors of CAD. Similar findings were reported by Abrol et al. [14]. Our study is different from prior studies because the study population had an intermediate likelihood of CAD, whereas prior studies were done in patients with higher likelihood of CAD. Further, we had a comparison group with normal baseline ECG who underwent MPI, whereas the previous studies were done in patients with LBBB undergoing coronary angiogram without a comparison group.

The limitations of our study include its retrospective nature as well as the use of MPI to define CAD. Although defining CAD by angiogram is ideal, MPI is highly sensitive and specific (close on 90%) in diagnosing CAD [19]. Since our study population had at least intermediate likelihood of CAD, application of these findings to a general asymptomatic LBBB population has limitations.

Conclusions

Patients with LBBB have a high probability of CAD based on MPI findings. Patients with LBBB and reduced EF have a much higher likelihood of CAD compared to patients without LBBB and normal EF. Further studies on early invasive approach in patients with LBBB and reduced EF seem warranted. This may avoid unnecessary additional testing and allow for early identification of disease.

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