PJC Vol 23, No. 1 - 4
January — December 2012

ORIGINAL ARTICLE

INCREMENTAL PROGNOSTIC VALUE OF GATED SPECT MYOCARDIAL PERFUSION SCANS WITH DIPYRIDAMOLE STRESS IN PATIENTS WITH LEFT BUNDLE BRANCH BLOCK

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Objective: Gated single photon emission computerized tomography (GSPECT) myocardial perfusion imaging (MPI) has well validated incremental prognostic value. The aim of this study was to find out the prognostic value of abnormal dipyriodamole GSPECT MPI in patients with left bundle branch block (LBBB).

Methods: This was a prospective study conducted at Nuclear Cardiology Department of Karachi Institute of Heart Diseases (KIHD), Karachi from August 2010 till February 2011. Total 345 patients (135 with LBBB comprised Group A and 210 without LBBB comprised Group B) with adequate dipyridamole GSPECT MPI were included. These patients were followed-up for 18-24 months (mean 20 ±3 months) for fatal or non-fatal infarctions (MI).

Results: GSPECT scans were positive for abnormal in 47/135 (35%) in Group A and in 90/210 (43%) in Group B patients (non-significant p values). However, fixed perfusion defects were significantly higher in Group A (27%) than Group B (15%) while reversible defects were significantly higher in Group B (28%) than Group A (08%). Similarly incidence of transient ischemic dilatation (TID) was significantly higher in Group B (16%) than Group A (02%). Mean sum stress score (SSS) was higher in Group A (6 ±5) while mean sum difference score (SDS) was higher in Group B (4 ±2). Left ventricular ejection fraction (LVEF) was significantly lower in Group A (42 ±16) than Group B (58 ±8) with significantly higher end diastolic and end systolic volumes (EDV, ESV) in Group A. At 18-24 months follow up, 09 (4.3%) non-fatal events were reported in Group B while in Group A it was 04 (2.9%, non-significant p values). Total 8 (5.90%) fatal MIs were reported, all in Group A and none in Group B (significant p values). Kaplan Meier survival plot for non-fatal MI shows a similar event free survival in both groups with a Log Rank value 0.217 (non-significant p value) [Figure 2]. Kaplan Meier survival plot for fatal MI show significantly low event free survival for patients with LBBB (Group A) with a Log Rank value 10.552 (significant p value).

Conclusions: We conclude that dipyridamole GSPECT MPI provides important prognostic information in patients with LBBB. LBBB group had lower LVEF which was a strong predictor of cardiac deaths while perfusion parameters were predictors of non-fatal MIs in patients with or without LBBB.

Key words: Gated SPECT, LBBB, Prognostic value, dipyridamole, fatal myocardial infarctions

PJC 2012; 23: 25-31

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INTRODUCTION

The incidence of left bundle branch block (LBBB) in general population is low (0.6%) but almost 1/3rd of patients with chronic heart failure do have this abnormality.[1] Presence of LBBB poses a challenge for diagnosis of ischemia due to presence of baseline ST-T changes which makes

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electrocardiogram (ECG) non-diagnostic at rest and even during treadmill test.[2-3] Non-ischemic etiologies of LBBB include dilated cardiomyopathy, hypertensive heart disease, aortic valve disease and fibrosis of conduction fibers.[4] Studies have shown that a higher incidence of coronary artery disease (CAD) in patients with LBBB[5] and 3-4 fold increased in mortality in patients with known CAD.[6] Myocardial perfusion imaging (MPI) is a non-invasive imaging used for diagnosis and follow up of patients with CAD with good sensitivity but low specificity. This low specificity is caused by false positive septal defects[7] and specificity can be improved by using vasodilators and gating.[8] Gated single photon emission computerized tomography (GSPECT) allows assessment of myocardial perfusion and function in one study which ensures good diagnostic and prognostic strength for patients with CAD[9]. However, data is limited about the prognostic value of pharmacological (vasodilator) GSPECT in patients with LBBB with suspected or known CAD[4].

The aim of this study was to find out the prognostic value of abnormal dipyridamole GSPECT MPI in patients with LBBB.

METHODS

Study Design, Site and Duration: This was a prospective study conducted at Nuclear Cardiology Department of Karachi Institute of Heart Diseases (KIHD), Karachi, Pakistan from August 2010 till February 2011. It was duly approved by the ethical committee of the institute. We recruited 135 consecutive patients with LBBB on resting ECG who were referred for dipyridamole GSPECT scan for evaluation of known or suspected CAD. We also selected a control group of 210 patients without LBBB during the same time interval who had dipyridamole GSPECT. A positive GSPECT (with adequate dipyridamole intervention, i.e. increase in pulse rate ≥10/min or drop of systolic BP ≥10 mmHg from baseline) was defined as presence of perfusion defects on stress images with or without transient ischemic dilatation (TID) visually, abnormal left ventricular ejection fraction (EF < 50%), abnormal wall motion, sum stress score [SSS], sum rest score [SRS] and sum difference score [SD] all >2. All patients/families were interviewed on telephone (18-24 months follow up, mean 20 ±3 months) regarding MACE like fatal myocardial infarction (MI) and non-fatal events including MI and history of revascularization.

Study Population: Study included 345 consecutive patients who were referred for dipyridamole GSPECT MPI either for evaluation of chest pain or risk factor assessment. Out of these, 135 patients had LBBB on resting ECG (Group A) and 210 patients without LBBB (Group B). In Group A, mean age of the cohort was 58 ± 9 years with a male: female ratio of 77: 58 (57%: 43%). Risk factor assessment in Group A revealed that 93 (69%) were hypertensive, 49 (36%) were diabetic, 32 (24%) were dyslipidemic, 24 (18%) were smoker and positive family history for CAD was found in 39 (29%) [Table1]. In Group B, mean age of the cohort was 56 ± 12 years with a male: female ratio of 126: 84 (60%: 40%). Risk factor assessment in Group B revealed that 137 (65%) were hypertensive, 85 (40%) were diabetic, 55 (26%) were dyslipidemic, 24 (11%) were smoker and positive family history for CAD was found in 80 (38%) [all with non-significant p values, Table1].

Acquisition Protocol: All patients underwent same day (rest-stress or stress-rest) myocardial perfusion GSPECT using Tc-99m labeled Methoxy IsoButyl Isonitrile (MIBI). 10-15 mCi of Tc-99m MIBI was administered intravenously for first study (rest in rest-stress or stress in stress-rest protocol) and 25-30 mCi for second study (stress in rest-stress or rest in stress-rest protocol). Gated stress and non-gated rest SPECT acquisitions were performed using dedicated dual head cardiac (Cardio MD, Philips) gamma camera with low energy all purpose (LEAP) collimator,

32 projections around a 180 degree arc, a 64 x 64 matrix and 16 frames per cardiac cycle. Image reconstruction and LV functional parameters (EF, EDV, ESV and wall motion [WM]) were contemplated by using commercially available Astonish® and Autoquan® software packages respectively. An EF ≥ 50%, ESV ≤ 70 ml and WM score of zero (in a 17 segment model) were considered normal. Similarly, GMPI with SSS, SRS and SDS <2 were considered as normal.

Stress Protocol: Dipyridamole intervention was performed intravenously at a rate of 0.567 mg/kg for 4 minute in all patients. Tea, coffee and xanthine derivatives were stopped 24 prior to study. A rise in ≥10 beats/minute (from baseline) or drop of ≥10 mmHg of systolic blood pressure with or without symptoms or ST changes were considered as adequate response to dipyridamole. Tc-99m MIBI was given 3-4 minute after dipyridamole infusion. Intravenous aminophylline (75-125 mg) was given to all patient 2-3 minutes after radiotracer to antagonize the effect of dipyridamole.

Statistical Analysis: Comparisons between patient groups were performed using student-t test for continuous variables and the X^2 test for categorical variables. Continuous variables were described by mean ± standard deviation (SD).

Table-1: Demographic comparison of both groups (Group A=with LBBB, Group; B=without LBBB)

Variables	Group A (135) LBBB	Group B (210) Without LBBB	p-values
Age (mean ± SD) yrs	58 ± 9	56 ± 12	0.098
Male	77 (57%)	126 (60%)	0.659
Female	58 (43%)	84 (40%)	
Risk Factor			
Hypertension	93 (69%)	137 (65%)	0.515
Diabetes Mellitus	49 (36%)	85 (40%)	0.527
Dyslipidemia	32 (24%)	55 (26%)	0.772
Family history CAD	39 (29%)	80 (38%)	0.109
Smoker	24 (18%)	24 (11%)	0.092
LV Function			
%LV Ejection Fraction	42 ± 16	58 ± 8	<0.0001*
End Diastolic Volume (ml)	130 ± 20	98 ± 26	<0.0001 *
End Systolic Volume (ml)	75 ± 11	41 ± 15	<0.0001*
MPS findings			
Abnormal	47 (35%)	90 (43%)	0.171
Fixed	36 (27%)	31 (15%)	0.009*
Reversible	11 (08%)	59 (28%)	<0.0001*
TID	03 (2%)	33 (16%)	<0.0001*
SSS	6 ± 5	5 ± 3	0.021*
SDS	2 ± 1	4 ± 2	<0.0001*

*p<0.05
SD= Standard Deviation
MPS=Myocardial Perfusion Imaging
TID=Transient Ischemic Dilatation
SSS=Sum Stress Score
SDS=Sum Difference Score

Figure-1: Comparative fatal and non-fatal events among both groups

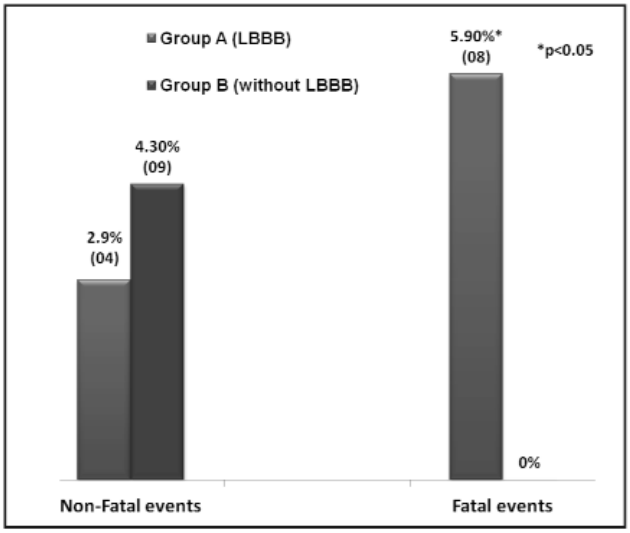
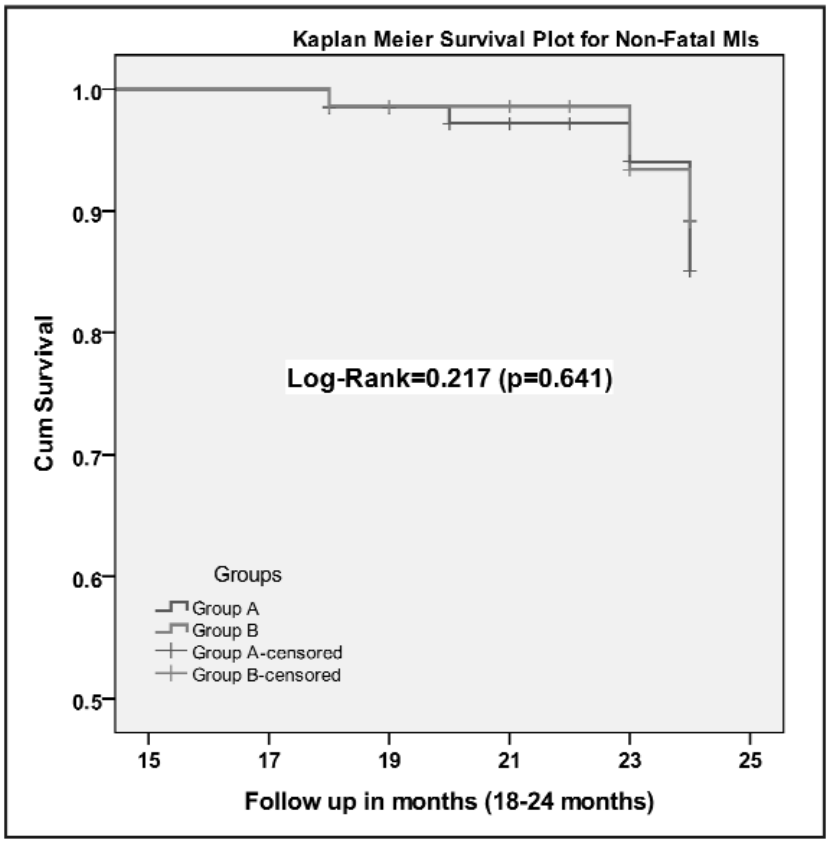
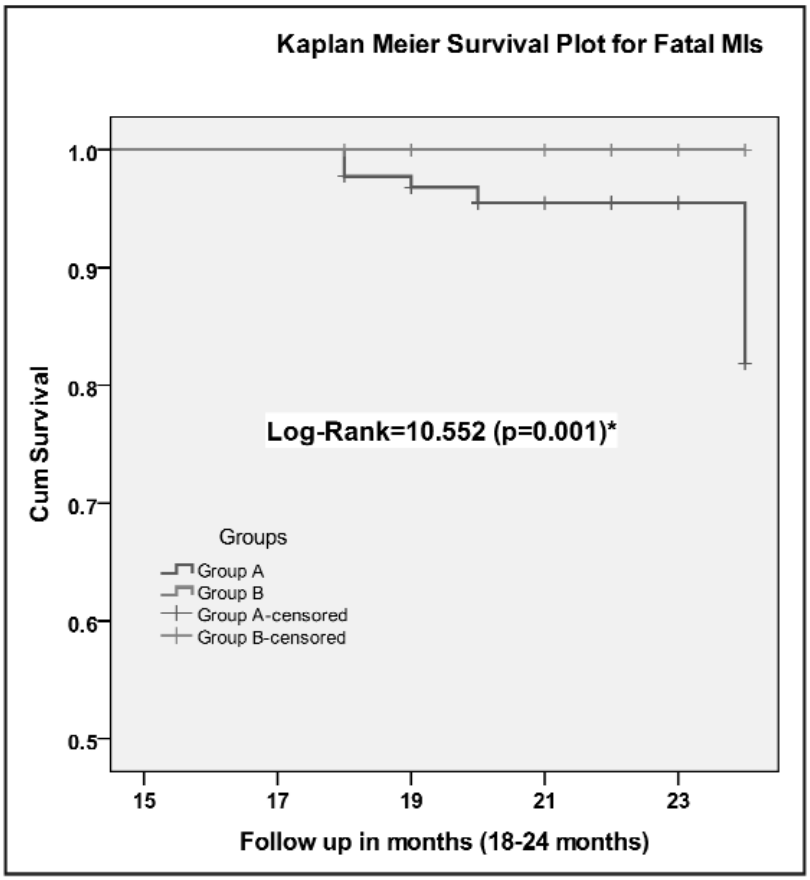


Figure-2: Kaplan Meier Survival Plot for Non-Fatal Myocardial Infraction among both groups (Group A=LBBB; Group B=without LBBB) in 18-24 months follow up.



Kaplan-Meier cumulative survival analysis for major cardiac events like fatal and non-fatal MI was performed, and survival curves were compared by the Logrank test. Statistical significance was defined as P<0.001.

Figure-3: Kaplan Meier Survival Plot for Fatal Myocardial Infraction among both groups (Group A=LBBB; Group B=without LBBB) in 18-24 months follow up



RESULTS

GSPECT scans were positive for abnormal perfusion findings in 47/135 (35%) in Group A and in 90/210 (43%) in Group B patients (non-significant p values). However, fixed perfusion defects were significantly higher in Group A (27%) than Group B (15%) while reversible defects were significantly higher in Group B (28%) than Group A (08%). Similarly incidence of TID was significantly higher in Group B (16%) than Group A (02%). Mean SSS was higher in Group A (6 ±5) indicting extent of CAD while mean SDS was higher in Group B (4 ±2) which shows higher ischemia burden in patients without LBBB (Group B). Left ventricular function parameters like LVEF (%) was significantly lower in Group A (42 ±16) than Group B (58 ±8) with significantly higher end diastolic and end systolic volumes (EDV, ESV) in Group A (Table 1).

At 18-24 months follow up, 09 (4.3%) non-fatal events were reported in Group B while in Group A it was 04 (2.9%). These non-fatal events included hospital admissions with chest pain culminated in revascularization 07 patients (05 in Group B and 02 in Group A). Total 8 (5.90%) fatal MI were reported in the studied population (all in Group A and none in Group B) [Figure 1). Kaplan Meier survival plot for non-fatal MI show a similar event free survival in both groups with a Log Rank value 0.217 (non-significant p value) [Figure 2]. Kaplan Meier survival plot for fatal MI show significantly low event free survival for in patients with LBBB (Group A) with a Log Rank value 10.552 (significant p value) [Figure 3].

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DISCUSSION

Gated SPECT with perfusion and functional parameters has an established incremental diagnostic and prognostic value in general population; however, data is scarce about its role in LBBB group. In this study abnormal GSPECT scans were non-significantly higher in Group B than Group A and most likely due to biased sampling. In Group A, incidence of fixed perfusion defects was significantly higher and this could be justified due to known anteroseptal defects associated with LBBB. Various mechanism have been proposed for this false positive finding like impaired diastolic flow to septum due to its delayed contraction,[10] short diastolic filling at higher rate[11] and decrease baseline and systole septal thickness with normal perfusion (partial volume effect).[12] Although we have used dipyridamole stress and gating to avoid it but studies have shown that these measures can reduce but not eliminate the incidence of false positive results.[13] In this study reversible perfusion abnormality was significantly higher in Group B (higher SDS) and also with higher incidence of TID. These findings are consistent with significant underlying CAD and this higher incidence could be due to biased sampling.

In Group A, the mean EF was low with raised EDV and ESV as compared to Group B with higher reversible ischemia burden. This is in accordance with various published studies,[14,15] as LBBB is often accompanied by LV dilatation even in absence of CAD and plausible mechanism is ventricular asynchrony which in long run leads to remodeling and dilatation[4]. Another important aspect of this study is significantly higher fatal MI in Group A and non-significant incidence of non-fatal events in both groups. If we closely observe the data than we come to realize that LVEF was the predictor of higher mortality in LBBB group while perfusion parameter like SDS was the predictor of non-fatal events in both groups. The SDS was significantly higher in Group B and that would be the reason of higher (although statistically non-significant) non-fatal events in Group B. These data are in accordance with a large published trial by Cedar Senai investigators[16] which revealed LVEF<45% as significant predictor of mortality while LVEF>45% had lower mortality rate irrespective of severity perfusion abnormalities on GSPECT. They also found that perfusion variables are powerful in predicting worsening of coronary disease. In our study mean SSS and SDS were in mild to moderate range in both groups and studies have shown differential risk stratification of lower score for non-fatal events and correlation of higher scores with fatal events.[17]

We conclude that dipyridamole GSPECT MPI provides important prognostic information in patients with LBBB. LBBB group had lower LVEF which was a strong predictor of cardiac deaths while perfusion parameters were predictor of non-fatal MIs in patients with or without LBBB.

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