SIGNIFICANCE OF PERFUSION DEFECTS ON DIPYRIDAMOLE THALLIUM CARDIAC SPECT IN PATIENTS WITH LEFT BUNDLE BRANCH BLOCK

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Background: Left Bundle Branch Block (LBBB) is a known cause of false positive results in myocardial perfusion studies. We aimed at investigation of correlation between degree of severity of perfusion defect on cardiac Single Photon Emission Computed Tomography (SPECT) and presence of coronary artery disease on angiography in patients with LBBB. **Study Design**: This was an analytical study and was carried out at Department of Nuclear Cardiology and Department of Cardiac Catheterisation of Punjab Institute of Cardiology, Lahore from January 2007 to April 2007. **Methods:** In this study patients having LBBB without known coronary artery disease (CAD) referred for myocardial perfusion studies to the Nuclear Cardiology Department from outpatient, indoor and emergency departments were included. Thallium^{201} stress/rest Single-Photon Emission Tomography (SPECT) acquisition scanning was performed. The myocardial perfusion pattern was classified as normal, fixed defect and reversible defect. Coronary angiography was used to confirm CAD only in patients with abnormal scan. **Results:** Thirty consecutive patients having LBBB were studied. All patients underwent myocardial perfusion imaging using dipyridamole pharmacologic stress. Fourteen patients (47%) revealed normal Thallium^{201} uptake and distribution at the septum. Reversible defects were noted in 13 (43%) patients. Fixed defects were noted in 3 (10%) patients. Among four patients with mild perfusion defects only 1 (25%) had significant coronary artery disease. In patients with moderate perfusion defects, coronary angiogram was positive for significant coronary artery disease in 1 (33%) patient. In six patients having severe perfusion defects significant coronary artery disease was noted in 5 (83%) patients. All patients with fixed defects had significant coronary artery disease. False positive studies were found to be significantly greater in patients with reversible defects particularly with mild to moderate defects. **Conclusions:** Patients with left bundle branch block showing moderate to severe reversible perfusion defects on dipyridamole thallium cardiac SPECT have high likelihood of coronary artery disease.

Keywords: Left bundle branch block, Coronary artery disease, Thallium^{201} stress test, Myocardial perfusion imaging, Single-photon emission computed tomography (SPECT).

INTRODUCTION

Patients with left bundle branch block often show a false positive ischaemic pattern in the interventricular septum on thallium stress-rest myocardial perfusion scintigraphy.[1,2]

In various international studies, 25–30% of patients presenting with left bundle branch block have significant coronary artery disease,[3,4] and therefore they should be screened for coronary artery disease. Thallium Stress-Rest Imaging being a relatively available, non-invasive modality, therefore this should be considered as a diagnostic tool to screen for CAD in LBBB.[5,6] Generally favourable prognosis has been seen in patients with LBBB and normal or near-normal myocardial perfusion scintigraphy.[7,8] In left bundle branch block, there is delayed septal activation and relaxation which adversely affects diastolic coronary flow regionally. With exercise the myocardium experiences decrease in diastolic perfusion time which yields decreased radiotracer uptake of septum relative to the lateral wall.[9] Thus these patients may have reversible septal/ anteroseptal defects which are more pronounced at higher heart rates.[10]

Pharmacological stress with dipyridamole or adenosine (which do not increase the heart rate significantly) has been suggested to be a more accurate stimulus for the detection of coronary artery disease by myocardial Thallium^{201} imaging in patients with LBBB.[11,12]

In Pakistan, very few studies have been carried out on patients with LBBB.[13] This study was designed to evaluate dipyridamole Thallium^{201} single photon emission computed tomography in detection of coronary artery disease in patients presenting with LBBB at Punjab Institute of Cardiology, Lahore and confirmation of coronary artery disease by coronary angiography.

MATERIAL AND METHODS

This analytical observational study was conducted with a non-probability consecutive sampling of patients with constant LBBB and without known

CAD who were referred for myocardial perfusion studies to the Nuclear Cardiology Department of Punjab Institute of Cardiology, Lahore, Pakistan, over a period of four months, i.e., from January 2007 to April 2007. All patients included in the study had permanent LBBB with mild to moderate pre-test likelihood for CAD (i.e., patients with at least one risk factor). Patients enrolled for study had no history of myocardial infarction or established coronary artery disease. LBBB was diagnosed on the basis of following criteria: (1) QRS duration greater than 0.12 sec, (2) Broad or notched R waves in left precardial leads or delayed intrinsicoid deflection of the QRS complex in lead I, and (3) Absence of septal Q waves in the left precardial leads. A Prism 2000 XP system equipped with low-energy, high-resolution collimators was used for image acquisition. Thallium^{201} stress/rest acquisition protocol was used in all patients. SPECT procedures were carried out using a 180 degrees clockwise circular orbit, beginning at 45-degree right anterior oblique projection and ending at 45-degree left posterior oblique projection. Studies were carried out in 32 projections in a continuous step-and-shoot mode, 31 seconds per step for stress and 39 seconds per step for rest, with a 64×64 matrix. Stress images were obtained 10 to 15 minutes after dipyridamole stress procedure. Trans-axial reconstruction was performed using filtered back-projection with a Butterworth filter with a cut-off frequency of 0.4 cycles/pixel. Short and long axes were displayed as well as polar maps, though quantitative data was not used in the analysis. Patients were subjected to pharmacological stress procedure with an intravenous infusion of dipyridamole (0.56 mg/Kg of body weight) over a 4-minute period. Three minutes after completing the infusion, Thallium^{201} was administered intravenously. Aminophylline was used when needed to relieve the adverse effects of dipyridamole.

Segmental uptake was classified using the five point model[14] as follows: 0=normal perfusion score, 1=mild reduction in tracer uptake-not definitely abnormal, 2=moderate reduction in tracer uptake definitely abnormal, 3=severe reduction in tracer uptake and 4=absent uptake. Radiotracer uptake at the septum was classified as normal when uptake at the anteroseptal and apical segments was above 50%. Fixed defect was defined as decreased tracer uptake with no change between rest and stress and reversible defect was defined as greater than two grade improvement of uptake in rest image compared to the stress image using the semi-quantitative scoring system previously described, or improvement of uptake to a score of 1 in the resting images.[14] Patients having positive Thallium^{201} scans were scheduled for coronary angiography in order to confirm the presence of significant coronary artery disease. The coronary angiography was not performed in patients who have normal myocardial perfusion scan because of low likelihood of disease. Angiography was considered significant when the anatomical stenosis was found to be ≥50% in at least one major vessel.

Myocardial perfusion Images were interpreted by consensus of at least two experienced observers who in the first reading were blinded to each other's data.

The data was analysed by using SPSS 14.0 for Windows. Categorical variables were expressed as numbers and percentages while continuous variables were expressed as mean ± standard deviation.

RESULTS

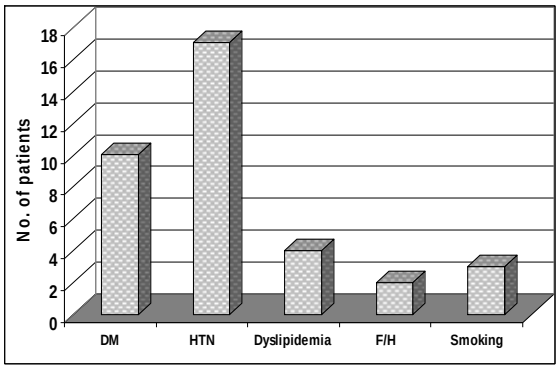
After fulfilling the inclusion criteria, 30 patients of LBBB were studied.

The mean age of the study population was 56.33±9.53 years. Sex-based division of the study population included 14 males and 16 female subjects, while Figure-1 shows the risk-factor distribution. Ten (33%) patients were diabetic on treatment, while 17 (57%) patients were known to have hypertension, 3 (10%) patients were smoker, 4 (13%) patients had high cholesterol levels, and 2 (7%) patients had a positive family history.

Majority of these 16 (53%) patients had one risk factor. Seven (23%) patients had two risk factors. Two (7%) had three risk factors, while five (17%) had no known risk factors.

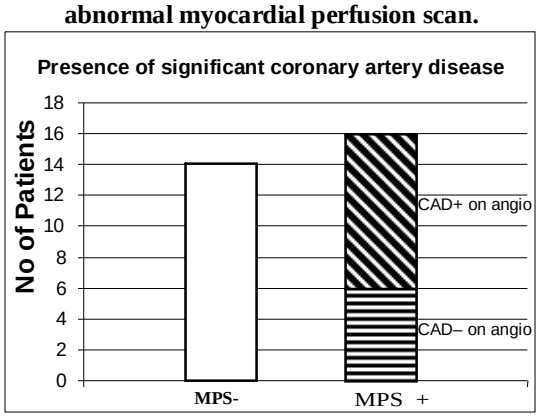
Patients were referred for cardiac imaging to rule out suspected CAD. During stress testing, 3 had a positive ECG response (>1 mm ST segment depression), and 8 patients had a positive clinical response to dipyridamole stress test (exertional chest discomfort and heaviness). Only 16 patients had perfusion defect on the myocardial perfusion scan and were considered to be abnormal and 14 subjects had normal perfusion scan. Out of 16 patients with abnormal scan, 4 had mild defects, 3 had moderate defects, 6 had severe defects and 3 had fixed defects. All of these patients underwent coronary angiography to confirm CAD. Only 10 out of 16 patients with abnormal perfusion scan had significant coronary artery disease (stenosis ≥ 50%), as shown in Figure-2. The summary of results of myocardial perfusion is shown in Table-1. When the results of myocardial perfusion scan and coronary angiography were compared, false positive results occurred in 6 cases (38%) as a whole, but comparison of subgroups (mild, moderate, severe and fixed defects) revealed varying incidence of false positive results, i.e., 75% in mild, 67% in moderate, 17% in severe, and 0% in fixed defects.

Figure-1: Risk factors of study population.



DM=Diabetes Mellitus; HTN=Hypertension; F/H=Family history.

Figure-2: Presence of CAD in patients with abnormal myocardial perfusion scan.



MPS=Myocardial perfusion scan; CAD=Coronary artery disease.

Table-1: Results of MPS and angiography in study population

Characteristics	Number of patients (n=30)
MPS+	16/30 (53%)
Reversible defects	13/16 (81%)
Mild	4/13 (31%)
Moderate	3/13 (23%)
Severe	6/13 (46%)
Irreversible defects	3/16 (19%)
Angiography + in MPS+ patients	10/16 (63%)
Mild	1/4 (25%)
Moderate	1/3 (33%)
Severe	5/6 (83%)
Fixed	3/3 (100%)

MPS=Myocardial perfusion scan.

Among 10 coronary angiography positive coronary artery disease patients diabetes mellitus was present in 4 (40%), hypertension in 3 (30%), smoking in 2 (20%) and family history in 1 (10%) patients. Among 20 coronary angiography negative patients diabetes was present in 6 (30%), hypertension in 14 (70%), Dyslipdemia 3 (15%), smoking in 1 (5%) and family history of ischaemic heart disease in 1 (5%) patients. Few patients had multiple risk factors.

DISCUSSION

In this study of 30 patients having LBBB, 47% patients revealed normal Thallium^{201} uptake and distribution while reversible defects were noted in 43% patients. Fixed defects were noted in 10% patients. One patient had significant coronary artery disease out of four patients with mild perfusion defects. Similarly one patient had significant coronary artery disease out for 4 with moderate perfusion defects. In six patients having severe perfusion defects significant coronary artery disease was noted in 5 patients. All patients with fixed defects had significant coronary artery disease.

Merlano *et al*[15] in their study of 130 patients reported that most of the patients with LBBB without coronary artery disease are likely to have normal patterns of myocardial perfusion at the septum while reversible defects were seen most patients with coronary artery disease. They observed reversible defects in 21% patients in dipyridamole pharmacological stress group and 29% defects in treadmill exercise stress test group while fixed defects were noted in 10% and 6% patients in the two groups respectively. In our study we observed reversible defects in 43% patients this could merely be due to more diabetic patients in our study as compared to Merlano *et al.*[15]

Afzal *et al*[13] in their study of 25 patients of LBBB and 10 normal subjects concluded that reduced septal thickening results in artefactual septal perfusion defects which can be eliminated by gating the perfusion scintigraphy and reporting perfusion status on diastolic frames in LBBB patients. Their study consists of relatively smaller number of patients and they have not performed coronary angiography to confirm CAD as we have in our study; however in our study we have not carried out gated scintigraphy.

Septal hypoperfusion may be observed on Thallium^{201} imaging in patients with LBBB and be resolved by gated studies.[16] Frequency of this finding in sestamibi myocardial perfusion imaging is still a matter of debate. In the case of Thallium^{201}, due to early imaging in contrast to sestamibi, higher number of false positive perfusion defects appear because of high heart rate at the time of imaging.[17-19] A few authors have shown that the incidence of false positive results in studies are reduced when the studies were considered to be positive only in the presence of reversible defects,[20] while Wagdy *et al* have observed that a low risk scan has an overall survival that was not significantly different from age-matched population.[21]

Moreover, in our study the false positive rate is higher in patients who had mild defects. Some

studies suggest that patients with left branch block have structural cardiovascular disease at the time of diagnosis of the electrical abnormality[22] and others have suggested that complete LBBB is an independent cardiovascular risk factor.[23] However, Gil and co-workers have reported 48% of normal scans among 142 patients with LBBB with mild to moderate likelihood for CAD, associated with a low rate of clinical events and no fatal outcomes.[24] Several other studies have also reported better outcomes among patients with permanent LBBB and normal scans or fixed defects without additional reversible defects.[7] In a group of 13 patients with LBBB and without coronary artery disease, Inanir *et al* have reported normal or near normal regional perfusion.[25]

Patients with LBBB without CAD may have minimally or moderately reduced uptake at the septum as a normal pattern. This result is in accordance with those studies, which have shown that most patients with LBBB and minimally reduced fixed defect at the septum did not have coronary artery disease[26,27] and also with those studies which reported excellent 2-year prognosis in patients with LBBB and no clinically overt CAD.[11] In our study three fixed defects which showed severely reduced uptake at the septum were due to tight vessel lesion or partial thickness myocardial infarction and it was confirmed by a severe coronary artery disease on coronary angiogram. Normal myocardial perfusion with Thallium[201] Dipyridamole has been found to be a good prognostic indicator in patients with complete LBBB and suspected CAD.[24] It could be anticipated that most patients with LBBB and no CAD will only have a mildly reduced uptake of Thallium[201] at the septum in both stress and rest images due to decreased myocardial perfusion as a result of augmented intramyocardial pressure in the septum, not necessarily associated to septal ischemia.[28,29] Hence, further Thallium[201] or Tc-99m Sestamibi myocardial perfusion studies using dipyridamole stress in the same group of patients followed by longer duration of follow-up are justified. Identification of true normal and true abnormal SPECT myocardial perfusion scan in LBBB patients provides prognostically important information. True abnormal myocardial perfusion scintigraphy carries poor prognosis whereas normal scans has been found to have a very good prognosis in patients with LBBB.[7,30] Hence in patients with LBBB, it might be prudent to reduce artifacts by gating the myocardial perfusion scintigraphy and report on end diastolic images.[13] By increasing the number of patients with LBBB considering their pre-test likelihood of disease and correlation of scintigraphic findings we can draw or formulate an algorithm for further management.

CONCLUSION

The results of this study have shown that most patients with LBBB and without coronary artery disease would have normal uptake of Thallium[201]. Patients with left bundle branch block showing moderate to severe reversible perfusion defects on dipyridamole thallium cardiac SPECT have high likelihood of coronary artery disease. Most patients with LBBB don't have coronary artery disease and many of them will have a good long-term outcome.

STUDY LIMITATIONS

It may be noted that this study was carried out in a relatively small number of patients and it is possible that just one false positive result might change the level of significance while comparing the two groups. Hence, in order to obtain more robust results, more number of patients should be studied in any future study. Secondly we performed coronary angiography only in those patients who had abnormal perfusion scan, so we cannot comment on false negative perfusion scans.

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