## VISUAL QUANTIFICATION OF ADENOSINE STRESS INDUCED TC-99M MIBI MYOCARDIAL PERFUSION SPECT IN LEFT BUNDLE BRANCH BLOCK AND IT'S COMPARISON WITH CORONARY ANGIOGRAPHY

#### Fida Hussain, Umer-i-Farooq\*, Safdar Abbas\*, Maryam Rehman\*\*, Ali Jamal

Armed Forces Institute of Pathology/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, \*Armed Forces Institute of Cardiology/National Institute of Heart Diseases/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, \*\*Combined Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan

#### ABSTRACT

**Objective:** To determine the role of visual quantification of Tc-99m MIBI myocardial perfusion SPECT in left bundle branch block as compared to coronary angiography findings.

Study Design: Prospective randomized controlled trial.

*Place and Duration of Study:* Department of Nuclear Medicine, Armed Forces Institute of Pathology and Armed Forces Institute of Cardiology/National Institute of Heart Diseases; Rawalpindi: Pakistan from 1st Sep 2016 to 31st Jan 2017.

*Material and Methods:* Thirty six patients with complete left bundle branch block and coronary angiography done within past 4 months were included in our study. Patients were divided in three groups on the basis of coronary angiographic findings. Six patients (4 males and 2 females) have normal LAD on coronary angiography, 18 (11 males and 7 females) have less than 50% LAD disease and 12 (9 males and 3 females) have more than 50% LAD lesions. Gated and non-gated pharmacological stress with adenosine myocardial perfusion SPECT was carried out in 1-day rest-stress protocol.

**Results:** There was no significant difference in the baseline data among all these three groups. Mean left ventricular ejection fraction (LVEF) values were lower in moderate LAD Disease group as compared to other two groups (42 ± 12.4 vs 58 ± 9.2 and 60.6 ± 10.6), left ventricular end diastolic volume (LVEDV) and left ventricular end systolic volume (LVESV) were greater in moderate LAD disease group as compared to other groups. There was no significant difference in LVEF, LVEDV, and LVESV between Normal LAD patients and minor LAD disease group. In normal LAD group 2 patients have normal myocardial perfusion scan; while rest of the 4 exhibit mild to moderate intensity fixed perfusion defects involving distal anteroseptal and distal inferoseptal walls. In Minor coronary artery disease group 4 patients scans show minor intensity fixed perfusion defect in distal anteroseptal and distal inferoseptal areas while rest of all the 14 patients studies demonstrate moderate intensity fixed perfusion scan showed moderate reversible myocardial ischemia in 8 patients and 2 patients studies show moderate to severe fixed perfusion defects in anteroseptal wall and apex while rest of the two showed severe reversible myocardial ischemia in LAD territory. The coronary angiography in these 4 patients showed >80 coronary artery disease.

**Conclusions:** Visual quantification of myocardial perfusion scan images is not only simple and easy way of myocardial assessment in LBBB patients but its results are statistically significant when compared with coronary angiography. Mild to moderate fixed perfusion defects in anteroseptal wall should be taken as normal in LBBB cases. However, reversible and sever fixed perfusion defects on myocardial perfusion study in the presence of LBBB must be further investigated and treated accordingly.

**Keywords:** Adenosine, Fixed perfusion defect, Mild coronary artery disease, Myocardial perfusion, Reversible perfusion defect, Sestamibi, Scintigraphy.

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

#### INTRODUCTION

Myocardial perfusion imaging (MPI) with

**Correspondence: Dr Fida Hussain**, Armed Forces Institute of Pathology, Rawalpindi, Pakistan

stress is the standard worldwide method for assessment of myocardial perfusion and function in coronary artery disease (CAD). The detection of myocardial ischemia in patients with left bundle branch block (LBBB) remains a challenge. Since LBBB may or may not accompanied with ischemic heart disease (IHD) and hypertension, diagnosis of CAD in LBBB patients is important<sup>1</sup>. Exercise stress test is inconclusive in LBBB patients. MPI is being used as an alternative method of diagnosis in these cases<sup>2-4</sup>. Despite utilizing pharmacologic stress with vasodilator agents many false positive results in LAD territory area have been reported. Coronary angiography could not be used as screening test in these patients because of its high cost and possible complications<sup>5</sup>. Many MPI studies with pharmacologic stress have reported frequent anteroseptal defects with MPS in patients with LBBB in the absence of significant left anterior descending (LAD) coronary artery disease6. Several mechanisms have been proposed to explain this false-positive phenomenon. Various interpretative methods and stress techniques have been evaluated in an attempt to improve the specificity of noninvasive studies for detecting LAD disease<sup>7</sup>. A number of software packages for quantifying myocardial perfusion are commercially available. In this study we emphasize that the simple visual quantification and a define method of interpretation could be easily utilized for better results.

# MATERIAL AND METHODS

Thirty Six patients with complete left bundle branch block and have coronary angiography done within past 4 months were included in our study. Patients with previous myocardial infarction and have any documented evidence of any cardiac problem after the coronary angiography were excluded. These patients were divided in three groups on the basis of coronary angiographic findings (table-I). Six patients (4 males and 2 females) have normal LAD on coronary angiography, 18 (11 males and 7 females) have less than 50% LAD disease and 12 (9 males and 3 females) have more than 50% LAD lesions. Gated and non-gated pharmacological stress with adenosine myocardial perfusion SPECT was carried out in 1-day rest-stress

protocol. Post stress electrocardiographic-gated acquisition was performed and non-gated study was acquired for resting images.

# Adenosine Infusion and Study Acquisition Protocols

Myocardial perfusion studies were acquired by using one-day rest and stress protocols (fig-1 a). Pharmacological stress study was acquired after the rest study. All the procedure was explained to the patients. Intravenous line was secured by using 22-gauge cannula with three way Y-connector attached. Patients were placed on coach in semi recumbent position by adjusting the back with essential gadgets attached. All baseline parameters like, heart rate, blood pressure, ECG were recorded on a designed sheet. Adenosine infusion was started at a rate of 140 mcg/kg/min for 6 minutes and radiotracer Tc-99m sestamibi 20-30 mCi was injected at mid-way of this infusion. ECG, blood pressure and heart rate were recorded at every 2 minute and continued till 4 minutes post infusion or till the cessation of any side effect. Any unwanted effect describes by the patient like, breathlessness, palpitations, flushing, nausea, headache, blurring of vision etc was also recorded. After the completion of stress, the patient was advised to take a glass of full cream milk or fatty diet.

The study was acquired on dual head gamma cameras, Symbia-E SPECT and Symbia T-6 SPECT/CT SPECT equipped with high resolution purpose parallel-hole general collimator at 30-45 min post injection. The acquisition parameters were based on guidelines and recommendations published by the American Society of Nuclear Cardiology<sup>8</sup>. A window of 20% centered on the 140-keV photo peak was used. The gated SPECT study was acquired using a non-circular orbit of 180°, starting at a 45° right anterior obligue angle and ending at a 45° left posterior oblique orientation. Acquisition was performed in a step-and-shoot mode, with a total of 32 projections of 40 seconds duration each.

#### **Image Processing and Analysis**

The tomographic images were processed by using Siemens Cardiology processing software. The Butterworth filter with a frequency cutoff of 0.40 cycles/pixel and an order of 6.0 for image reconstruction was utilized. The processed images were displayed and analyzed by using Corridor 4DM (Segami) v5.1, Cedars-Sinai quantitative perfusion SPECT (QPS4) and quantitative gated SPECT (QGS4.0). Polar plots of

Table-I: Characteristics of patient population.

and large; mild moderate and severely reduced tracer uptake. Reversibility was classified as completely reversible, partially reversible, or nonreversible (fixed).

#### **Statistical Analysis**

All the collected data were presented as mean ± SD or frequency, when appropriate. Comparisons between group means were determined by utilizing unpaired Student t-test. All calculations were made with the help of

	Normal LAD	< 50% LAD disease	>50% LAD lesion	
Age (years)	45 ± 10.4	51 ± 8.3	54 ± 11.5	
Gender (M:F)	4:2	11:7	9:3	
LVEF (%)	60.6 ± 10.6	58 ± 9.2	42 ± 12.4	
LVEDV (ml)	77 ± 12.6	84 ± 10.4	134 ± 13.4	
LVESV (ml)	32 ± 9.8	35 ± 9.7	74 ± 13.2	

LVESV (MI)32 ± 9.835 ± 9.774 ± 13.2Left anterior descending artery (LAD), Male vs female (M:F), Left ventricular ejection fraction (LVEF), Left ventricular end<br/>diastolic volume (LVEDV), Left ventricular end systolic volume (LVESV)

Table-II: Coronary angiography vs myocardial perfusion scan findings.

No of LBBB patients	Coroangio findings	MPI findings
6	Normal LAD	Mild to Moderate FPD in AS wall
14	<50% LAD disease	Moderate FPD in AS wall
4	<50% LAD disease	Mild FPD in AS wall
8	50-80% LAD disease	Moderate RMI in LAD territory
2	>80% LAD disease	Severe FPD
2	>80% LAD disease	Severe RMI

Left anterior descending artery (LAD), Fixed perfusion defects (FPD), Anteroseptal (AS), Reversible myocardial ischemia (RMI)

the left ventricle were created and divided into 20 segments. The tomographic slices were analyzed systematically in the short axis, vertical long axis and in the horizontal long axis. The visual analysis was performed systematically, dividing the heart into 9 regions: anterior, lateral, and inferior walls; septum, anteroseptal, anterolateral, inferolateral, and inferoseptal regions; and apex. These regions (except the apex) were further divided into basal, middle, and apical segments. The radiotracer uptake and diagnosis of reversible ischemia was based solely on qualitative visual analysis using a color scale. To be considered significant, a defect had to be confirmed in other tomographic cuts (short or long axis). The defects were described in relation to their extent and severity as small, medium,

software SPSS version 16. A *p*-value <0.05 was considered statistically significant.

#### RESULTS

The mean LVEF values were lower in moderate LAD Disease group as compared to other two groups ( $42 \pm 12.4 \text{ vs } 58 \pm 9.2 \text{ and } 60.6 \pm 10.6$ ). LVEDV and LVESV were greater in



Figure-1a: Resting first protocol.

moderate LAD disease group as compared to

other groups (table-I). There was no significant difference in LVEF, LVEDV, and LVESV between Normal LAD patients and minor LAD disease group.

# Myocardial Perfusion Scan Results

In normal LAD group 2 patients (1 male and 1 female) have normal myocardial perfusion scan while rest of the 4 exhibit mild to moderate intensity fixed perfusion defects involving distal anteroseptal and distal inferoseptal walls (fig-1b). In Minor coronary artery disease group 4 patients scans show minor intensity fixed perfusion defect in distal anteroseptal and distal inferoseptal areas while rest of all the 14 patients studies demonstrate moderate intensity fixed perfusion defects involving distal halves of anteroseptal and inferoseptal walls. In moderate LAD disease group myocardial perfusion scan show moderate reversible myocardial ischemia in 8 patients and 2 patients studies exhibit moderate to severe fixed perfusion defects in anteroseptal wall and apex while rest of the two showed severe reversible myocardial ischemia in LAD territory (fig-2). The coronary angiography in these 4 patients showed >80 coronary artery disease (table-II).

### DISCUSSION

In patients with LBBB, most the myocardial perfusion studies show false positive results which are wrongly interpreted as fixed or reversible perfusion defects in septal or anteroseptal region left ventricular of myocardium<sup>9</sup>. In that scenario further invasive tests or procedures are being performed for proper diagnosis and further treatment<sup>10-12</sup>. Many reported studies showed false positive interpretations leading invasive diagnostic procedures resulting prolonged morbidity and wastage of resources13,14. In most of the myocardial perfusion scan reports the intensity and extent of these defects are being mentioned as mild, moderate or severe. This quantification is visually or by utilization done either sophisticated software. In our study these fixed or reversible perfusion defects were

compared/correlated with conventional coronary angiography findings. Visual quantification of MPI images was assessed by two independent observers not knowing the coronary angiography results. The results showed that in cases of mild to moderate intensity fixed perfusion defects the coronary angiography showed normal results or mild CAD. In these patients no invasive intervention is required either. On the other hand, in cases of severe fixed perfusion defects or moderate or severe reversible myocardial perfusion defects the coronary angiography results showed >50% CAD.

In different reported studies many methods were utilized by the researcher for optimization of MPI results in LBBB. Among those reported studies analysis of Gated myocardial perfusion images and polar map presentations of end diastolic and end systolic images could give better clue of anteroseptal myocardial perfusion status<sup>15</sup>. Ali M et al in their study conclude that the patients with left bundle branch block



patient with normal LAD on coronary angiography.

Figure-2: MPI of the patient with 80% LAD disease on coronary angiography.

showing moderate to severe reversible perfusion defects on dipyridamole thallium cardiac SPECT have high likelihood of coronary artery disease<sup>16</sup>. The presence of reversible perfusion defect may or may not alter the indices of mechanical dyssynchrony by phase analysis<sup>17</sup>. Left bundle branch block and ventricular pacing may induce typical artefacts that appear as perfusion defects in myocardial perfusion single photon emission computed tomography. However, the long term prognosis and cardiac event remain same<sup>18</sup>.

On the basis of severity and extent of myocardial perfusion defect in LBBB the future cardiac event could also be predicted<sup>19-21</sup>. In our study where the perfusion defects were severe the coronary angiography showed >80% LAD lesion. In most of the nuclear cardiology departments gated studies are being acquired only for one set (either stress or rest) of images. In that scenario visual quantification give excellent results as a long term diagnostic and therapeutic solution for most of the LBBB patients. Quantification of regional radiotracer distribution in left ventricular myocardium could give better results but that need extra efforts, software and expertise which is not available in all of the nuclear cardiology departments in our setup. The visual quantification is not only easy but it also gives scientifically valid results as evident in our study. The prerequisites are essentially to be made for visual quantification like selection of patients and usage of pharmacological stress agents like adenosine or dipyridamole.

#### CONCLUSION

Visual quantification of myocardial perfusion scan images is not only simple and easy way of myocardial assessment in LBBB patients but its results are statistically significant when compared with coronary angiography. Mild to moderate fixed perfusion defects in anteroseptal wall should be taken as normal in LBBB cases. However, reversible and sever fixed perfusion defects on myocardial perfusion study even in the presence of LBBB must be further investigated and treated accordingly.

#### ACKNOWLEDGMENT

We acknowledge the work of all nuclear medicine department staff and stress testing technicians involved, without whom this project could not have been produced.

#### **CONFLICT OF INTEREST**

This study has no conflict of interest to declare by any author.

#### REFERENCES

- Edet-Sanson A1, Hitzel A, Guernou M, Véra P, Manrique A. Myocardial perfusion gated single-photon emission computed tomography in patients with left bundle branch block: comparison between the end-diastolic images and the ungated images. Nucl Med Commun 2009; 30(1): 62-7.
- Evangelista L1, Nai Fovino L, Saladini F, Saladini G, Razzolini R, Mormino GP, et al. Diagnostic and prognostic value of gated myocardial perfusion single-photon emission computed tomography in low-risk patients with left bundle-branch block Nucl Med Commun 2012; 33(5): 491-7.
- Fovino LN, Saladini G, Mormino GP, Saladini F, Razzolini R, Evangelista L. Risk stratification and prognostic assessment by myocardial perfusion-gated SPECT in patients with left bundle-branch block and low-intermediate cardiac risk. Ann Nucl Med 2012; 26(7): 559-70. Epub 2012 Jun.
- Soylu O, Celik S, Karakus G, Yildirim A, Ergelen M, Zencirci E, etal. Transthoracic Doppler echocardiographic coronary flow imaging in identification of left anterior descending coronary artery stenosis in patients with left bundle branch block. Echocardiography 2008; 25(10): 1065-70. Epub 2008 Sep.
- Jeevanantham V1, Manne K, Sengodan M, Haley JM, Hsi DH. Predictors of coronary artery disease in patients with left bundle branch block who undergo myocardial perfusion imaging. Cardiol J 2009; 16(4): 321-6.
- 6. Hell J Nucl Med. High accuracy of myocardial perfusion imaging in patients with left bundle branch block: comparison of four interpretation approaches 2009; 12(2): 132-7.
- Fallahi B, Beiki D, Eftekhari M, Gilani KA, Fard-Esfahani A, Gholamrezanezhad A, etal. High accuracy of myocardial perfusion imaging in patients with left bundle branch block: comparison of four interpretation approaches. Hell J Nucl Med 2009; 12(2): 132-7.
- Thomas A. Holly, MD, Brian G. Abbott, MD, Mouaz Al-Mallah, MD, Dennis A. Calnon, MD, Mylan C, et al. ASNC imaging guidelines for nuclear cardiology procedure. Published online 2010.
- Hayat SA, Dwivedi G, Jacobsen A, Lim TK, Kinsey C, Senior R. Effects of left bundle-branch block on cardiac structure, function, perfusion, and perfusion reserve: implications for myocardial contrast echocardiography versus radionuclide perfusion imaging for the detection of coronary artery disease. Circulation 2008; 117(14): 1832-41.
- Singh H, Patel CD1, Mishra S2, Bhargava B2. Stress-Rest Thallium-201 Myocardial Perfusion SPECT Pattern in Patients with Exercise Induced Left Bundle Branch Block. Nucl Med mol Imaging 2014; 48(3): 251-4.
- Uebleis C1, Hoyer X, Van Kriekinge SD, Schuessler F, Laubender RP, Becker A, et al. Association between left ventricular mechanical dyssynchrony with myocardial perfusion and functional parameters in patients with left bundle branch block. J Nucl Cardiol 2013; 20(2): 253-61.
- Nichols KJ, Van Tosh A, Siddiqi S, Chen J, Garcia EV, Palestro CJ, etal. Gated myocardial perfusion SPECT asynchrony measurements in patients with left bundle branch block. Int J Cardiovasc Imaging 2009; 25(1): 43-51.
- Kershaw MA, Rogers FJ2. Intermittent left bundle branch block: an overlooked cause of electrocardiographic changes that mimic high-grade stenosis of the left anterior descending coronary artery. J Am Osteopath Assoc. 2014; 114(11): 868-73.
- 14. Obiagwu C, Ariyarajah V, Apiyasawat S, Spodick DH. Correlation of echocardiographic left atrial abnormality with myocardial ischemia during myocardial perfusion assessment in

patients with left bundle branch block. Am J Cardiol 2013; 112(5): 660-3.

- 15. Afzal MS, Imran MB, Aslam N, Khurshid SJ, Khan MA, Irfan J, etal. Gated spect myocardial perfusion scintigraphy for identifying septal perfusion artifacts in left bundle branch block. J Coll Physicians Surg Pak 2006; 16(8): 504-8.
- Ali M, Mallick NH, Abid AR, Haq S, Ayub M. Significance of perfusion defects on dipyridamole thallium cardiac SPECT in patients with left bundle branch block. J Ayub Med Coll Abbottabad 2007; 19(4): 21-5.
- 17. Aljaroudi W, Koneru J, Heo J, Iskandrian AE. Impact of ischemia on left ventricular dyssynchrony by phase analysis of gated single photon emission computed tomography myocardial perfusion imaging. J Nucl Cardiol 2011; 18(1): 36-42.
- Ten Cate T, Kelder JC, Bogaard MD, Van Hemel NM, Fred Verzijlbergen J. The prognostic significance of typical perfusion

defects on vasodilator stress myocardial perfusion SPECT in patients with left bundle branch block or right ventricular apical pacing. Nucl Med Commun 2009; 30(3): 232-9.

- Pavlovic S, Sobic-Saranovic D, Djordjevic-Dikic A, Beleslin B, Stepanovic J, Artiko V. Comparative utility of gated myocardial perfusion imaging and transthoracic coronary flow reserve for the assessment of coronary artery disease in patients with left bundle branch block. Nucl Med Commun 2010; 31(4): 334-40.
- Usmani S, Khan HA, Zaman MU, Niyaz K. Prediction of cardiac events in patients having left bundle-branch block with/without chest pain using dipyridamole technetium-99m-sestamibi myocardial perfusion imaging. Med Princ Pract 2009; 18(4): 310-6.
- 21. America YG, Bax JJ, Boersma E, Stokkel M, van der Wall EE. Prognostic value of gated SPECT in patients with left bundle branch block. J Nucl Cardiol 2007; 14(1): 75-81.

.....