Original Article

DIFFERENCES IN PERFUSION AND REGIONAL FUNCTIONAL ABNORMALITIES IDENTIFIED BY REST GMPS IN DILATED CARDIOMYOPATHY PATIENTS WITH ISCHEMIC AND NON ISCHEMIC ETIOLOGY BASED ON CORONARY ANGIOGRAPHY RESULTS

Muhammad Shahzad Afzal*, Hamid Saeed**, M. Saeed Akhtar*, Muhammad Babar Imran*, Muhammad Iqbal*, Owais Bin Qadeer*, Faisal Ehsan Cheema*, Muhammad Naeem*
*Punjab Institute of Nuclear Medicine (PINUM), Jail Road Faisalabad.
**Faisalabad Institute of Cardiology, Faisalabad.

ABSTRACT: Dilated Cardiomyopathy (DCM) is a common problem and it is very important to differentiate its ischemic cause from nonischemic for management and prognostic purposes.

OBJECTIVE: To evaluate rest gated myocardial perfusion scintigraphy (GMPS) in patients with ischemic and nonischemic DCM, categorized on the basis of coronary angiography, and to compare mean summed perfusion score (SPS), mean summed thickening score (STS) and mean extent of perfusion abnormality (EPA) between them.

DESIGN: Descriptive case series.

PATIENTS & METHODS: This study was conducted at Nuclear Cardiology department of Punjab Institute of Nuclear Medicine (PINUM), Faisalabad over a period of six months from 01-01-2013 to 30-06-2013. Resting GMPS were performed in 102 known patients of DCM (aged 17 to 70 years with a mean age of 49.12 ± 11.8 years, 86 Male and 16 Female) by injecting 20 mCi of ^{99m}Tc-MIBI. Patients were subdivided into ischemic (n=74) and nonischemic subgroup (n=28) by using the coronary angiography results. Summed perfusion score (SPS), summed thickening score (STS) and extent of perfusion abnormality (EPA) were calculated by using twenty segment model. Results of GMPS were compared between ischemic DCM and nonischemic DCM by using independent samples t-test. P-value of <0.05 was taken as statistically significant.

RESULTS: SPS and EPA are significantly higher in ischemic than non ischemic sub groups (26.46 ± 10.80 Vs 7.86 ± 5.13 P<0.001, and 7.16 ± 1.97 vs 4.32 ± 1.70 P<0.001 respectively). STS was significantly higher in non ischemic group than ischemic group of DCM patients (33.21 ± 7.13 vs 23.99 ± 7.81).

CONCLUSION: Our study shows that there are statistically significant differences in the values of summed perfusion score, summed thickening score and extent of perfusion abnormalities between ischemic and non ischemic DCM groups, calculated by using rest gated myocardial perfusion scintigraphy. Combined evaluation of the perfusion and wall thickening on rest gated myocardial perfusion scintigraphy is useful to identify ischemic and nonischemic etiology of DCM.

KEY WORDS: Gated Myocardial perfusion Scintigraphy, MPS, GMPS. Dilated Cardiomyopathy, Coronary Angiography, Summed Thickening score, summed perfusion score, Extent of perfusion abnormality, SPS, STS, EPA. non ischemic, ischemic.

INTRODCUTION:

Dilated cardiomyopathy (DCM) is a common heart disease associated with geometric and functional findings of Left ventricle (LV) dilatation with depressed systolic function (i.e.

Corresponding Author:
Dr. Muhammad Shahzad Afzal.
Head Nuclear Cardiology Department, Punjab Institute of Nuclear Medicine (PINUM), Jail Road, Allied Hospital, Faisalabad, Pakistan
Mobile: 0321 6609811
Email: msamirza@yahoo.com

EF less than 45%)[1]. Its prevalence is 0.02%. DCM may be ischemic or non ischemic. In DCM patients, ischemic etiology is three times more frequent than non ischemic[2-3]. Differentiation of ischemic from non ischemic etiology of dilated cardiomyopathy is of prime importance to identify the group of patients whose cardiac status can be improved by revascularization of coronary arteries[4].

Stress echocardiography identifies the coronary artery disease in dilated cardiomyopathy, but the technique is operator dependent and further complicated by the conduction abnormalities like left bundle branch block (LBBB), with an accuracy of 70%[5-6]. Positron Emission Tomography (PET) studies have shown high accuracy but their limited availability and high cost are main limitations[7]. Role of MRI and CT scan in differentiating ischemic from non ischemic DCM is being evaluated by researchers[8-9]. Angiography with cardiac catheterization is considered gold standard[10]. Ischemic heart disease is diagnosed when at least one coronary artery has stenosis greater than 70%. Coronary angiography's invasive nature, high cost, limited availability in third world countries, operator dependency, high risk of complications in patients with DCM and higher mortality in patients with poor systolic function make it unsuitable to be used in every DCM patient.

Gated myocardial perfusion scintigraphy (GMPS) with Single Photon Emission Tomography (SPECT) technique offer potential for simultaneous assessment of myocardial perfusion and functions[11]. Studies have been conducted to evaluate the role of stress-rest myocardial perfusion scintigraphy in DCM patients which showed significant differences in its findings between ischemic and non ischemic groups[12], and identified Ischemic Heart Disease (IHD) with an accuracy of 80% [13]. A recent meta-analysis of large studies with either exercise or pharmacological stress tests, reported an average sensitivity of 87% and a specificity of 73% for the detection of angiographically significant CAD[14-15]. Complications of stress procedure used in nuclear cardiology are significantly higher in patients with poor LV systolic function; hence stress cannot be given to every patient with DCM. So there is critical need to introduce a noninvasive technique which is widely available, cost effective, and safe even when systolic function is poor, and can reliably differentiate ischemic from non ischemic DCM. In ischemic cardiomyopathy, affected segments have abnormal perfusion, wall motion and myocardial thickening. In non ischemic cardiomyopathy, myocardial motion and wall thickening is abnormal in spite of preserved perfusion [16]. As rest GMPS provides both functional as well as perfusion information of the myocardium, it is accepted to help in differentiation of ischemic from non ischemic dilated cardiomyopathy.

The rationale of our study is to investigate the differences in perfusion and regional functional abnormalities identified by rest GMPS in dilated cardiomyopathy patients with ischemic and non ischemic etiology ascertained on the basis of coronary angiography results. As only limited research work has been done in the past with rest GMPS in DCM patient, in our study differences between ischemic and non ischemic patients are expected to guide in deciding whether a DCM patient has ischemic or non ischemic etiology, which will help the cardiologist in decision making regarding type of management.

OBJECTIVES:

1. To determine the mean summed perfusion score (SPS), mean summed thickening score (STS) and mean extent of perfusion abnormality (EPA) in patients with dilated cardiomyopathy by using rest GMPS.
2. To categorize DCM patients into ischemic and non ischemic groups on the basis of results of coronary angiography and compare the means of above mentioned parameters between the two groups.

METHODS:

STUDY DESIGN: Descriptive case series

SETTINGS:

Study was conducted at Nuclear Cardiology department of Punjab Institute of Nuclear Medicine (PINUM), Faisalabad.

DURATION OF STUDY:

Study was conducted over a period of six months from 01-01-2013 to 30-06-2013.

SAMPLE SIZE:

Sample size was calculated by using WHO sample size calculator for two means taking power of the test 80%, level of significance 5%, population standard deviation 5, test value of population mean 6.7[17], and anticipated value of population mean 9.5[17]. Sample size is 102.

SAMPLING TECHNIQUE:

Consecutive sampling (non-probability) technique was used to select 102 patients of dilated Cardiomyopathy.

SAMPLE SELECTION:

INCLUSION CRITERIA:

- DCM Patients with age 18 to 80 years.
- Signs and symptoms of heart failure especially shortness of breath, orthopnea, ankle edema, raised JVP.
- Ejection fraction less than 45% and left ventricular diameter at end diastole more than 56 mm on echocardiography.
- Patient stable to undergo rest GMPS and coronary angiography.

EXCLUSION CRITERIA:

- Patients with primary valvular heart pathology.
- Patients with arrhythmias/ventricular premature contractions more than 10%.
- Patients with LBBB and RBBB.
- Patients in which Tc^{99m} MIBI scan is contraindicated e.g. pregnancy.
- Patients with severe systemic diseases.

DATA COLLECTION PROCEDURE:

The study protocol was approved by the hospital ethical committee. Patients were selected from those referred to PINUM by cardiologists for gated myocardial perfusion scintigraphy. Inclusion and exclusion criteria were strictly followed to control confounding variables. Written informed consent was taken from all patients after explaining the procedure, objective and benefits of the study. Patients included were thoroughly evaluated by taking detailed history and performing clinical examination. Patient's demographic data along with clinical information and investigation details were entered and designed Performa was filled. All the procedures at PINUM were performed free of cost and expenses were born by the institute. All selected patients underwent rest GMPS at PINUM followed by coronary angiography within seven days of rest GMPS study.

REST GMPS IMAGING:

Patients were asked to take light breakfast/meal at least 3 hours prior to the study. A 740 MBq ± 5% dose of ^{99m}Tc MIBI was injected by intravenous route. Rest GMPS was acquired forty five minutes after the injection of the radiopharmaceutical [Acquisition Parameters; step and shoot mode, 64 x 64 matrix, 1.45 zoom, 30 seconds per view, steps 60, 16 frames per cardiac cycle, 15% R-R interval window, 90° rotation with dual head detector configuration, circular orbit by a dual head gamma camera (GE, Infinia-4 USA) equipped with high resolution collimator).

Study of every patient was processed by iterative reconstruction using ordered-subset expectation maximization (OSEM) with Butterworth filter (cut off frequency 0.35 and order 20). Polar maps were generated by Quantitative Perfusion SPECT/Quantitative Gated SPECT (QPS/QGS) software. Twenty segment model was used and scores were allocated to all the segment of myocardium for the perfusion [0 = normal (uptake from 70-100%), 1 = mild decrease (uptake from 50-69%), 2 = moderate decrease (uptake from 30-49%), 3 = marked decrease (uptake from 10-29%), 4 = no uptake (< 10%)] and systolic wall thickening (0 = normal, 1 = mild reduced, 2 = moderate to severely reduced, 3 = absent) of the myocardium. Summed perfusion score and summed thickening score for each resting GMPS was calculated. Extent of perfusion abnormality for each study in terms of number of segments of myocardium with abnormal perfusion was calculated from polar map.

CORONARY ANGIOGRAPHY:

Coronary angiography of all patients was performed within seven days of resting MIBI study. Its results were used as gold standard to categorize every patient of dilated cardiomyopathy as ischemic (those having stenosis of at least one coronary artery greater than 70%) or non ischemic (those with absence of coronary artery stenosis or having stenosis less than 70%). Means of different parameters calculated from rest GMPS for ischemic and non ischemic groups were compared.

DATA ANALYSIS:

All data was entered and analyzed using SSPS version 17.0. Mean and standard deviation was calculated for all quantitative variables like age, SPS, STS and EPA in ischemic and nonischemic groups. Frequency and percentages was calculated for variables like sex.

Levene's test was used to see the variability of SPS, STS and EPA within these two groups. Independent samples t-test was applied on quantitative parameters like SPS, SMS and EPA, for comparison of quantitative parameters between ischemic and non ischemic dilated cardiomyopathy groups. P-value of <0.05 was taken as statistically significant.

RESULTS:

A total of 102 patients having age ranging from 17 to 70 years with a mean age of 49.12 ± 11.8 years (86 Male, 16 Female) with dilated cardiomyopathy were studied. In ischemic group (n=74) mean age was 53.49± 7.76 years (66 Male, 8 Female) while in nonischemic group n=28) mean age was 36.96 ± 12.68 years (20 Male, 8 Female).

The value of mean summed perfusion score (SPS) was more than 3 times higher in ischemic patients than non ischemic group (26.46 ± 10.80 Vs 7.86 ± 5.13). Levene's test (F=14.05, p<0.001) showed that variability of this parameter within these two groups is significantly different. Independent sample t-test for equality of means showed that there is statistically significant difference between the means of SPS in ischemic and non ischemic groups (df=94.8, p<0.001, mean difference = 18.60, SE difference=0.1.5, 95% confidence interval for difference lower=15.45 upper=21.75).

Mean Summed Thickening score (STS) was almost 1.4 times greater in non ischemic group than ischemic group of DCM patients (33.21 ± 7.13 vs 23.99 ± 7.81). Levene's test (F=2.77, p=0.0999) showed that variability in the values of this parameter between these two groups is not significantly different. Independent sample t-test for equality of means showed that there is statistically significant difference between the means of STC in ischemic and non ischemic groups (df=100, t=-5.452, p<0.001, mean difference = -9.23, SE difference=1.69), 95% confidence interval for difference lower=-12.59 upper=-5.87).

In DCM patients, mean value of EPA was almost 2 times higher in ischemic group than non ischemic group (7.16 ± 1.97 vs. 4.32 ± 1.70). Levene's test (F=1.41, p=0.239) showed that variability of this parameter in two groups is not significantly different. Independent sample t-test for equality of means showed that there is statistically significant difference between the means of EPV in ischemic and non ischemic groups (df=100, t=6.73, p<0.001, mean difference = 2.84, SE difference=0.42, 95% confidence interval for difference lower=2.0 upper=3.68).

DISCUSSION:

Differentiation of ischemic etiology of DCM from non ischemic is important and use of noninvasive techniques without stress, to distinguish these two entities is preferable because of high risk of complications with angiography and stress procedures in patients with poor systolic function. Although some work has been done in DCM patients with MPS, our study mainly focused on the segment based perfusion and thickening analysis of the myocardium by using rest gated MPS only.

Our study showed significantly higher summed perfusion score and extent of perfusion abnormalities in ischemic group than non ischemic group of DCM patients. While STS was significantly higher in non ischemic group than ischemic group of DCM

patients. In ischemic DCM, CAD results in reduced perfusion which causes myocardial infarction or ischemia, and is responsible for abnormal perfusion as well as abnormal motion and thickening in the affected myocardium only. Segments which are supplied by patent coronary arteries show normal perfusion and usually preserved wall motion and thickening. In non ischemic DCM, there is gradual fibrosis of the myocardium, and its extent is directly related to the degree of impairment in contractile function, whereas fibrosis and perfusion do not seem to be interrelated. The degree of impairment of hyperemic myocardial perfusion in non ischemic DCM patients is related to contractility and end-diastolic wall stress. So segments with impaired wall thickening and normal perfusion (mismatched) are more frequent in non ischemic DCM[18]. The presence of scar (matched perfusion and metabolic defects) in patients with advanced DCM is not always indicative of coronary disease[19]. It may be related to local inflammation and necrosis[20]. In patients with nonischemic dilated cardiomyopathy, the segmental perfusion abnormalities documented by MPS at rest although could be due to reduced viability as a result of local inflammation, vasculitis or scarring of the small segments, but may be related to a lower than normal wall thickness by partial volume effects and not to an excess in wall stress or tension, and may be unrelated to any insufficiency of myocardial perfusion[21]. Myocardial perfusion CT has showed altered function of the subresolution intramyocardial microcirculation[22]. Altered cardiac sympathetic innervations might also be playing a role in abnormal wall thickening in the presence of normal perfusion in patients with idiopathic DCM[23].

These mechanics are responsible for high summed perfusion score and larger area of diminished perfusion or EPA in ischemic DCM than non ischemic DCM, and higher STS in nonischemic DCM than ischemic DCM patients. In non ischemic DCM group, majority of the patients show mild and non-segmental distribution of perfusion abnormalities, while majority of the ischemic subgroup has perfusion abnormalities that distribute along the coronary vessel territories[24]. Non gated studies rely on the perfusion status of myocardium only, which can be hampered in some segments of myocardium of patients with simple cardiomyopathy in the absence of CAD, and hence yields only modest value to distinguish these two entities[25]. Stress MPS has shown higher values of summed stress, rest, and reversibility of perfusion defect scores in ischemic cardiomyopathy patients, compared with those of non ischemic cardiomyopathy[26]. Large severe defects have been observed in 90% of ischemic and in only 5% of nonischemic patients[27]. More frequent metabolic defects has also been observed with ^{123}I-BMIPP SPECT and ^{18}F-FDG PET in patients with severe left ventricular dysfunction secondary to coronary artery disease than in patients with nonischemic cardiomyopathy[23, 28].

Our study along with few other studies[18, 26] shows that most of the myocardium in non ischemic DCM group has normal perfusion with abnormal wall thickening. While in patients with ischemic DCM, affected myocardium has abnormal perfusion (due to ischemic insult or MI) and reduced thickening, but normally perfused myocardium show normal perfusion as well as wall thickening. When summed thickening score is taken into account, normal thickening of the normally perfused myocardium in ischemic DCM patients results in lower STS than in non ischemic DCM patients where there is global impaired thickening[26, 29].

Only limited work has been done with rest GMPS in the past to differentiate ischemic from non ischemic DCM. An average summed rest perfusion score of 6.7 ± 5 and 9.5 ± 5 and summed thickening score of 26± 7 and 17± 6 in non ischemic and ischemic dilated cardiomyopathy respectively has been reported[17]. In another study, the number of hypoperfused segments was significantly greater in patients with ischemic LV dysfunction than in those with non-ischemic LV dysfunction (9.3 ± 3.8 vs. 2.0 ± 2.8 segments, $P < 0.0001$)[30]. The same has been shown in our study by EPA parameter.

CONCLUSIONS:

Our study shows that there are statistically

significant differences in the values of summed perfusion score, summed thickening score and extent of perfusion abnormalities between ischemic and non ischemic DCM groups, calculated from rest gated myocardial perfusion scintigraphy. Combined evaluation of the perfusion and wall motion on rest gated myocardial perfusion scintigraphy can be used to identify ischemic and nonischemic etiology of DCM. However further studies are needed for clinical validation after defining criteria on the basis of our results.

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SR #	AUTHOR NAME	CONTRIBUTION
1	Dr. Muhammad Shahzad Afzal	Idea Conception, Data Collection
2	Dr. Muhammad Hamid Saeed	Manuscript Writing
3	Dr. Muhammad Saeed Akhtar	Data Collection
4	Dr. Muhammad Babar Imran	Data Collection & Analysis
5	Dr. Muhammad Iqbal	Proof Reading
6	Dr. Owais Bin Qadeer	Proof Reading
7	Dr. Faisal Ehsan	Proof Reading
8	Dr. Muhammad Naeem	Proof Reading