VALIDITY OF MYOCARDIAL PERFUSION IMAGING FOR THE DETECTION OF CORONARY ARTERY DISEASE

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ABSTRACT

OBJECTIVE: To determine the validity of myocardial perfusion imaging (MPI) for the detection of coronary artery disease (CAD).

METHODOLOGY: This hospital based observational study was conducted in department of Cardiology, Lady Reading Hospital, Peshawar, from May 2008 to Jun 2009. MPI was performed for all patients and invasive coronary angiography was used as gold standard for the detection of CAD.

RESULTS: A total of 50 patients were included in the study; their mean age was 53.8±9.7 years. Men were 35 (70%) and women were 15 (30%). Myocardial perfusion imaging was reported as normal in 5(10%) patients while 45 (90%) had evidence of CAD. Coronary angiography showed 44 patients (88%) had >50% stenosis in at least one coronary artery. Compared with coronary angiography, the sensitivity, specificity, positive predictive value and negative predictive values of myocardial perfusion imaging for detection of CAD were 98%, 67%, 95%, and 80% respectively. The sensitivity for the detection of ischemia in left anterior descending artery (LAD), right coronary artery (RCA) and left circumflex artery (CIRC) territories were 89.7%, 94.7% and 72.2% respectively.

CONCLUSION: Myocardial perfusion imaging has a high sensitivity but low specificity for identifying patients with coronary artery disease.

KEY WORDS: Myocardial perfusion imaging, Coronary artery disease, Coronary angiography.

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INTRODUCTION

For functional evaluation of patients with symptoms of coronary artery disease; different invasive and non-invasive stress tests are used[1-2]. Exercise testing (ETT) is performed as a primary screening test in those who are able to complete adequate level of exercise. It is the least expensive test[3-4] and has got both diagnostic and prognostic information[5-6-7]. It should be performed in patients with low pretest likelihood of CAD, in those who have normal resting ECG and in patients with a typical chest pain[8]. Exercise testing has a sensitivity and specificity for obstructive CAD of 68% and 77%, respectively, while sensitivity for left main/three-vessel CAD is 86%[9]. Therefore, exercise testing does not detect all patients with (severe) obstructive CAD and the finding of a negative test does not rule out the presence of CAD.[10] The addition of myocardial perfusion imaging (MPI) in conjunction with exercise stress improves the diagnostic accuracy and provides prognostic information, incremental to that obtained by clinical and exercise stress test parameters.[11] Overall sensitivity in the subset of patients undergoing angiography was 91% and overall specificity was 87%, with no significant difference between the tracers.[12]

MPI relies on the difference and distribution of a radioactive tracer such as thallium at rest and after stress. In patients with myocardial ischemia, uptake of tracers is reduced after stress and improves at rest.[13] Pharmacological stress have a proven role in patients with acute chest pain and with normal resting or stress ECG, normal enzymes level and with normal/ unchanged resting left ventricular function.[14] Scintigraphy is also useful in evaluating myocardial viability, in establishing the "culprit" lesion prior to revascularization, in assessing the completeness of revascularization, and in the risk stratification of patients with stable CAD, post myocardial infarction, post-unstable angina, and prior to vascular surgery.[15]

Coronary angiography remains the gold standard for identifying the presence or absence of arterial narrowing due to atherosclerosis. It is the only helpful modality in determining the choice of intervention either percutaneous or coronary artery bypass grafting.[16] Coronary angiography may be warranted in young patients with acute infarction to define the anatomy of the disease.[21]

But it cannot be applied as a screening test because it is invasive, costly and needs definite cardiac catheterization laboratory. The aim of this study was to know the sensitivity and specificity of MPI in patients with typical chest pain using coronary angiography as a gold standard.

METHODOLOGY

This hospital based observational study was conducted from May 2008 to Jun 2009, in the department of Cardiology, Lady Reading Hospital, Peshawar. Total number of patients was 50. Study was approved from ethical committee of the hospital. Informed consent was obtained from patients. It was non probability purposive sampling. Sample size was estimated by using WHO sample size estimating software, for stable angina patients at 95% confidence interval level with 5% margin of error. The expected prevalence of patients with stable angina was 3.5%. All patients irrespective of age and gender with stable angina and undergoing coronary angiography with or without past history of myocardial infarction were included. Patients with acute coronary syndrome (acute ST elevation Myocardial infarction, Non ST Elevation Myocardial Infarction and Unstable angina), valvular heart diseases, congestive heart failure, acute pulmonary embolism or pulmonary infarction, uncontrolled hypertension (systolic BP >190mmHg, diastolic BP >120), acute myocarditis or pericarditis, acute aortic dissection and uncontrolled arrhythmia) were excluded from the study.

Myocardial perfusion imaging procedure: A symptom-limited tread mill exercise stress test was performed. Technetium-99m Sestamibi was injected at peak stress and exercise was continued for an additional 60 seconds. Exercise stress endpoints were severe angina, physical exhaustion, dyspnea, sustained tachy-arrhythmias, exertional hypotension, or ischemic ST-T segment-depression of at least 0.2 mV and duration of 80 milliseconds. Exercise was considered inadequate if the physical validity of the patient was less than 80% of the predicted validity (workload) in the absence of angina or an ischemic ST-depression. Patients who were unable to perform a physical stress test or patients with a left bundle branch block underwent a pharmacological stress test. Technetium-99m Sestamibi was injected 3 minutes after start of infusion of the pharmacological agent. Horizontal or down sloping ST-segment depression of 1 mm or greater or up sloping of 1.5 mm or greater at 80 milliseconds after J point was considered positive for ischemia. In case of ST-T-segment abnormalities, registration of the stress ECG was continued until normalization of the ECG was seen. Tc-99m Sestamibi SPECT perfusion imaging same day and two day protocol was used. All acquisitions took place 30 to 45 minutes (stress) or 45 to 60 minutes (rest) post-injection. Gated SPECT acquisition protocol was performed post-stress. Quantitative SPECT analysis was performed on an ICON workstation computer (Siemens). The analysis was performed with the use of a completely automated software package, with the exception of a quality-control check to verify the maximum count circumferential profiles. Semi-quantitative visual interpretation of SPECT perfusion images used short-axis and vertical long-axis tomograms divided into 17 segments for each patient. Myocardial perfusion status was scored as follows: 0=normal radiotracer uptake; 1=mildly reduced uptake; 2=moderately reduced tracer uptake; 3=severely reduced tracer uptake; and 4=absent radiotracer uptake. Perfusion defect was considered fixed when there were no differences between rest and stress score, while reversible defect was defined as a segment with higher score on stress images. Ischemia was defined as a change of one or more grades between rest and stress images. Interpretation of tomographic images was done by consensus of two experienced observers unaware of other patient data.

Coronary Angiography: Coronary angiography was performed in all patients. Judkin's technique was used via right femoral artery approach. Coronary angiogram was evaluated by two independent observers, unaware of the MPI. A coronary stenosis was considered significant if the vessel diameter was narrowed by ≥50% in a major epicardial coronary artery or a major branch vessel. Visual estimation of percent diameter stenosis was performed in all patients. The view demonstrating the maximum stenosis was considered for analysis.

Statistical analysis: Categorical variables were presented as frequencies and percentages while quantative variables were expressed as mean ± S.D. Chi square test was used to compare the categorical variable while student T-test was used to compare numerical variables. Sensitivity, specificity, positive predictive values, negative predictive values were calculated according to standard definitions. P value of less than 0.05 was considered significant. Data was analyzed in SPSS version 11.

RESULTS

A total of 50 patients were included in the study, males were 35 (70%) and females 15 (30%). The age range was from 26 to 75 years, mean age with standard deviation was 53.8 ± 9.7 years.

On MPI, significant CAD was reported in 45(90%) patients. Double vessel disease (DVD) was found in 25 (50%) patients and triple vessel disease (TVD) was found in 7 (14%) patients (Table I). Left anterior descending artery (LAD) involvement was found in 35 (70%) and right coronary artery (RCA) in 30(60%) patients (Table II).

On coronary angiography, significant CAD was detected in 44 patients (88%). Fourteen (28%) had DVD, 9 (18%) had TVD and 4 patients (8%) had left main stem disease. (Table I) LAD involvement was found in 39 (78%) patients and RCA in 19(38%) patients (Table II).

TABLE 1: DISEASE FREQUENCY ON MYOCARDIAL PERFUSION IMAGING VS. CORONARY ANGIOGRAPHY

Number of Vessel involved	Number of diseased vessel on coronary angiography n (%)	Number of diseased vessel on myocardial perfusion imaging n (%)	P-Value
None	6 (12%)	5 (10%)	0.495
Single Vessel Disease	21 (42%)	13 (26%)	0.211
Double Vessel Disease	14 (28%)	25 (50%)	0.024
Tipple Vessel Disease	9 (18%)	7 (14%)	0.585
Total	50 (100%)	50 (100%)	

TABLE II: FREQUENCY OF DISEASED VESSEL ON CORONARY ANGIOGRAPHY VS. MYOCARDIAL PERFUSION IMAGING

Number of Vessel involved		Disease on coronary angiography n (n %) (n=50)	Disease on myocardial perfusion imaging n (n %) (n=50)	P - Value
LAD$	Present	39 (78%)	35 (74%)	0.440
	Absent	11 (22%)	13 (26%)	
RCA*	Present	19 (38%)	30 (60%)	0.028
	Absent	31 (62%)	20 (40%)	
CIRC#	Present	18 (36%)	19 (38%)	0.836
	Absent	32 (64%)	31 (62%)	

$left anterior descending artery, *right coronary artery #left circumflex artery

TABLE 3: SENSITIVITY AND SPECIFICITY OF MYOCARDIAL PERFUSION IMAGING FOR DIFFERENT VESSEL

Vessel involved	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
LAD$	87.1%	90.9%	97.1%	66.7%
RCA*	94.7%	61.3%	60.0%	95.0%
CIRC#	72.2%	81.3%	68.4%	83.9%

$left anterior descending artery, *right coronary artery #left circumflex artery

EFFICACY OF MPI FOR DIFFERENT VESSELS

Thirty seven patients were detected by MPI as having perfusion defects in LAD territory. Out of these, 35 were true positive and 2 patients were false positive. MPI was negative in 13 patients in which 9 patients were true negative and 4 were false negative. The calculated sensitivity & specificity for LAD were 89.7% and 81.8% respectively (Table III).

For right coronary artery, among 30 patients who were detected by MPI as having the disease, 18 were true positive and 12 patients were false positive, while 20 patients were not having the disease in this arterial territory. Nineteen patients were true negative and 1 patient was false negative. So the sensitivity & specificity were 94.7% and 61.3% respectively (Table III).

For left circumflex artery (CIRC), 19 patients were having the disease of which 13 were true positive and 6 were false positive. Thirty-one patients were reported as having the disease in this arterial territory in which 26 were true negative and 5 were false negative. The sensitivity and specificity were 72.2% & 81.3% respectively (Table III).

OVERALL EFFICACY OF MPI FOR DETECTION OF CAD:

Among 45 patients detected as positive for CAD by MPI, 43 patients were true positive, 2 patients were false positive. Five patients were reported as negative among which 4 were true negative and 1 was false negative. The overall sensitivity, specificity, positive predictive value, negative predictive values of myocardial perfusion imaging were 98%, 67%, 95% and 80% respectively.

DISCUSSION

In our study, the overall sensitivity, specificity, positive predictive value, negative predictive values of myocardial perfusion imaging were 98%, 67%, 95%, and 80% respectively.

The average sensitivity and specificity to detect significant CAD based on a pooled analysis of 79 studies in 8964 patients were found to be low as compared to our study i.e. 86% and 74%, respectively.17 The reason could be after the introduction of this technique in the early 1970s, the quality and accuracy of its images have improved substantially as a result of technical developments. In

general terms, however, the sensitivity of exercise MPI for detecting angiographically defined CAD is consistently above 70%, but in the better designed studies it is in the region of 85–90%. When dobutamine is used with MIBI, most studies have shown that the sensitivity is above 80% but the specificity ranges from 64% to 90%.[17] Protocols that include imaging in both the supine and prone positions increase sensitivity and specificity to 92 % and 86%, respectively, for both non obese and obese population.[18]

In our study the calculated sensitivity, specificity, positive predictive value and negative predictive value for LAD were 89.7%, 81.8%, 94.6%, 69.2% respectively. For right coronary artery, the sensitivity, specificity, PPV and NPV were 94.7%, 61.3%, 60.0% and 95.0% respectively. For left circumflex artery, the sensitivity, specificity, PPV and negative predictive values were 72.2%, 81.3%, 68.4% and 83.9% respectively. In comparing to our study, sensitivity of MPI in previous studies was 68% for the LAD, 50% for the LCX, and 88% for the RCA.[19-25] Corresponding specificity was 90%, 94%, and 81%, respectively. Specificity for detection of right CAD was lower than that for left anterior descending CAD ($P < 0.02$) and left circumflex CAD ($P < 0.0001$). The lower specificity in the RCA region may be explained by false-positive results related to diaphragmatic attenuation of the inferior wall. Sensitivity for detection of left circumflex CAD was lower than that for left anterior descending CAD ($P < 0.005$) and right CAD ($P < 0.0001$). The lower sensitivity for detection of disease in the LCX may be related to variation in coronary anatomy, with a small circumflex territory in some patients and the potential vascular overlap in the posteroinferior wall with the RCA.

Limitations: In our study the possible bias could be the patients with old myocardial infarction. Secondly majority of patients in our study were men (70%) in whom the prevalence of CAD is high, this could also have increased the sensitivity. Thirdly majority of our population (88%) had significant stenosis. This high prevalence of severe disease could also potentially raise sensitivity. Another reason for high sensitivity may be referral bias. Most of these patients were being referred for angiography because of high pretest probability of CAD. Fourthly the tracer activity below the diaphragm is commonly seen with Sestamibi, and this can reduce specificity, as seen in some studies. Fifthly the intensity of stress achieved, particularly with exercise, is another factor that may influence the observed diagnostic performance of MPI by increasing the number of false negative results.

CONCLUSION

Myocardial perfusion imaging has a high sensitivity but low specificity for identifying patients with coronary artery disease.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under

SBK: Conception and design, acquisition of data, Drafting the manuscript

SZ: acquisition of data,

AA: Analysis and interpretation of data,

MH: Critical revision, Final Approval of the manuscript

CONFLICT OF INTEREST

Author declares no conflict of interest

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