

Diagnostic Accuracy of Stress Myocardial Perfusion Imaging in Diagnosing Stable Ischemic Heart Disease

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Abstract

Objective: To determine the diagnostic accuracy of Stress Myocardial Perfusion Imaging (MPI) in diagnosing Stable Ischemic Heart Disease (SIHD).

Method: To analyze the sensitivity and specificity of Stress Myocardial Perfusion Imaging (MPI) in diagnosing Stable Ischemic Heart Disease (SIHD) by comparing with "gold standard" Coronary Angiogram.

Result: A total of 80 patients were studied (51 male, 29 female). 52 patients had significant stenosis in coronary angiography and 49 patients had reversible perfusion defect in myocardial perfusion imaging (MPI). MPI had a sensitivity of 88.46% and a specificity of 89.29% in diagnosing stable ischemic heart disease.

Conclusion: Coronary Angiography remains the near gold standard in diagnosing ischemic heart disease but is associated with serious complications like stroke, arrhythmias, acute renal failure, infection, etc. Though Myocardial perfusion imaging cannot replace coronary angiogram, it can be used as a reliable and sensitive non-invasive alternate investigation to diagnose stable ischemic heart disease in high risk individuals who are unwilling for angiogram.

Hence, there is an urgent and pressing requirement for reliable and safe investigation procedure for early and effective diagnosis of CAD. Coronary Angiography (CAG) remains the procedure of choice to diagnose ischemic heart disease but carries significant risk of stroke, arrhythmias, acute renal failure, infection, etc. Non-invasive Myocardial perfusion imaging (MPI) by nuclear medicine techniques is now widely applied for the evaluation of ischemic heart disease. Radioisotopes are injected at rest and also during stress which produces images of regional myocardial uptake proportional to the blood flow. There occurs a five-fold increase in myocardial blood flow with maximal exercise, above the resting condition.⁴ Due to critical narrowing of the epicardial arteries (coronary stenosis), the perfusion to myocardium is impaired and it cannot be increased further. Due to the stenosis, there occurs a differential flow to the territory supplied by the stenosed

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the past 40 years.² Rapid urbanization and change in lifestyle that occurred during the past two decades have led to the growing burden of coronary risk factors in India.³

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Received: 14.08.2017; Revised: 26.12.2017; Accepted: 19.04.2018

Table 1: Clinical classification of chest pain (Adapted from Braunwald et al¹⁸)

Typical Angina (Definite)	(1) Sub-sternal chest discomfort with a characteristic quality and duration that is; (2) provoked by exertion or emotional stress and; (3) relieved by rest or nitroglycerin
Atypical Angina (Probable)	Meets 2 of the above characteristics
Non-cardiac chest pain	Meets 1 or none of the typical anginal characteristics

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Hence, there is an urgent and pressing requirement for reliable and safe investigation procedure for early and effective diagnosis of CAD. Coronary Angiography (CAG) remains the procedure of choice to diagnose ischemic heart disease but carries significant risk of stroke, arrhythmias, acute renal failure, infection, etc. Non-invasive Myocardial perfusion imaging (MPI) by nuclear medicine techniques is now widely applied for the evaluation of ischemic heart disease. Radioisotopes are injected at rest and also during stress which produces images of regional myocardial uptake proportional to the blood flow. There occurs a five-fold increase in myocardial blood flow with maximal exercise, above the resting condition.⁴ Due to critical narrowing of the epicardial arteries (coronary stenosis), the perfusion to myocardium is impaired and it cannot be increased further. Due to the stenosis, there occurs a differential flow to the territory supplied by the stenosed vessel and uneven distribution of tracer isotopes.⁴

The results of myocardial perfusion imaging are compared to the results of invasive coronary angiography which is considered as a ‘gold standard’.

The diagnostic accuracy is finally determined by the comparison of results which is represented as ‘sensitivity’ and ‘specificity’ of MPI.

Several studies done across the globe to determine the diagnostic yield of MPI have yielded mixed results with majority of the studies showing a reasonable sensitivity and specificity. This study aims at establishing myocardial perfusion imaging as a reliable and accurate non-invasive investigation to diagnose stable ischemic heart disease (SIHD) in high risk individuals who are unwilling for coronary angiography apart from negating some of its serious complications.

Material and Methods

Place of study

The study was conducted in the Department of Cardiology in a tertiary care hospital setting.

Study design

A cross sectional study was undertaken.

Sample size

A total of 80 patients with stable ischemic heart disease were evaluated.

Selection of study population

The American College of Cardiology Foundation/American Heart Association (ACCF/AHA) has accepted the definition of Stable Ischemic Heart Disease (SIHD) to include Stable Angina or low risk unstable angina.^{5,6} Stable angina is chest pain or discomfort that most often occurs with activity or emotional stress (Table 1). Unstable Angina can be classified into Low risk, Intermediate risk and high risk unstable stable.

A total of 276 patients who visited

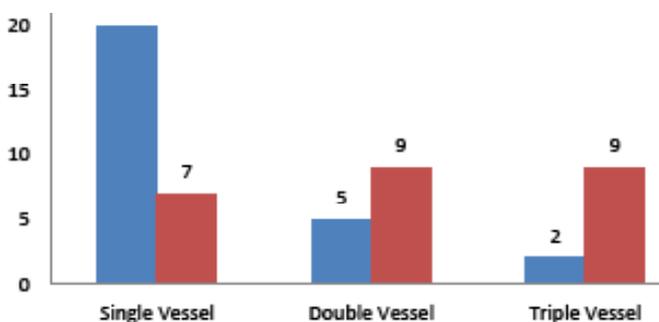


Fig. 1: Distribution and comparison of age and vessels involved

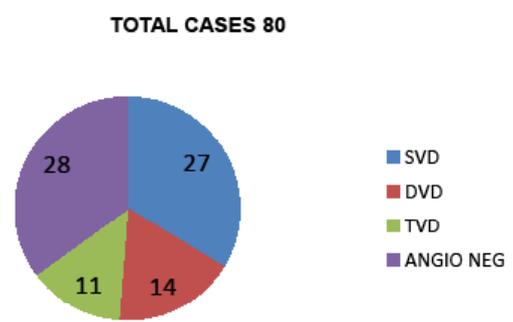


Fig. 2: Diagram depicting distribution of vessel involvement

Table 2: Age distribution of male and female study participants

Age	Single Vessel	Double Vessel	Triple Vessel	Normal	Chi square	P value
≤ 60	20	5	2	20	15.00	0.002**
>60	7	9	9	8		
Total	27	14	11	28		

the Cardiology OPD from Oct 2014 to Jul 2016 were identified to have stable ischemic heart disease. Of the 276 individuals who were selected for the study after analysing the inclusion and exclusion criteria mentioned below, 162 individuals were not willing to participate after explaining the course of the study in the language they understand.

The remaining 114 patients who consented to participate in the study after being explained, 34 patients withdrew their consent after undergoing myocardial perfusion imaging. Those who withdrew the consent were largely having a normal myocardial perfusion imaging.

Inclusion criteria

1. The study comprised of all consenting individuals having clinical signs of Stable ischemic heart disease
2. The probability of ischemic heart disease being > 5%.

Exclusion criteria

1. Patients who have undergone Cardiac intervention in the past.
2. Probability of ischemic heart disease < 5%
3. Patients with Acute MI and intermediate or high risk Unstable Angina (UA) / NSTEMI.
4. Patients with known valvular heart disease.
5. Evidence of Right or Left Bundle branch blocks (RBBB/LBBB).
6. Patients who have undergone device implantation.
7. Patients with known or freshly detected Cardiomyopathy.
8. All non-consenting individuals and individuals who withdrew consent during any part of the course of the study.

Patients with SIHD with pre-test probability more than 5% (combined Diamond/Forrester and Coronary Artery Surgery Study (CASS) data) are taken for Stress myocardial perfusion study with single day stress-rest protocol. Patient exercises on treadmill in Bruce or modified Bruce protocol

till the endpoints are achieved. Images are analyzed and classified as normal, reversible perfusion defect (inducible ischemia) and fixed perfusion defect (infarct area).

The extent of disease by Coronary Angiogram is defined as 1-vessel (single vessel disease), 2-vessel (double vessel disease), 3-vessel (triple vessel disease), or left main disease, with a significant stenosis 70% diameter reduction; left main disease, however, has been defined as a stenosis 50%.^{7,8}

Diagnostic accuracy of myocardial perfusion imaging is commonly represented by the terms *sensitivity* and *specificity*, which are calculated by comparing test results to the "gold standard" of the results of invasive coronary angiography.

Result

A total of 80 patients were studied (51 male, 29 female). 52 patients had significant stenosis in coronary angiography and 49 patients had reversible perfusion defect in myocardial perfusion imaging (MPI). Our study carried a sensitivity of 88.5% and specificity of 89.3% for myocardial perfusion imaging in diagnosing stable ischemic heart disease. Further, the positive predictive value (PPV) was 93.9% and negative predictive value (NPV) was 80.7%.

The accuracy of myocardial perfusion imaging as demonstrated by various studies worldwide showed sensitivity ranging from 85% to 97.8% and specificity ranging from 66.7% to 91%.⁹⁻¹²

Discussion

Total of 80 patients were included in the study of which 51 were Male (63.8%) and 29 were Female (36.3%). Out of 80 patients included in the study, mean age of Male was 58.05±11.42 years and Female was 58.06±14.17 years. Further, the age group between 51-60 years was most commonly affected constituting 28.75% of the total study population. Angiographic evidence of double and triple vessel disease were most commonly found in elderly

population (age more than 60 years) comprising 5 out of 9 patients for double vessel disease and 9 out of 11 patients for triple vessel disease. However, Angiographic evidence of single vessel disease involvement was most commonly found in patients less than 60 years of age (20 out of 27 patients) (Figure 1). The findings are similar to the results of the study conducted by Babu Ezhumalai et al.¹³

The INTERHEART case-control study done in 2006 identified eight common risk factors behind more than 90% of incident cases of Ischemic Heart Disease (IHD) in South Asian and Indian population.¹⁴ The risk factors include Dyslipidemia, smoking or tobacco use, Hypertension, Diabetes, abdominal obesity, physical inactivity, low fruits and vegetable intake and psychosocial stress.¹⁴ In our study, all 80 patients had atleast one of the risk factors indicated by INTERHEART study.

Further, Hypertension was the commonest risk factor present in our study population, present in 60% of the individuals compared to 29% in the study conducted by Gupta R et al.¹⁵ The risk of cardiovascular events is from two to three times higher in people with Type 1 or Type 2 diabetes.¹ Type 2 Diabetes was present in 44% of the individuals involved in the study. Other risk factors like Obesity, Dyslipidemia, smoking and family history of cardiovascular event were present in 55%, 50%, 43% and 26% respectively in the population under study. There was no significant difference in the prevalence of risk factors among Male and Female individuals except smoking. This may be due to the fact that smoking is relatively uncommon among female in Indian population.¹⁴ Also, many of the female patients hesitate to disclose smoking history as it carries significant social stigma.

Significant coronary vessel stenosis (suggested by CASS and modified by BARI study group) confirmed by coronary angiogram was present in 52 of the 80 patients studied (65.0%). Of the 52 patients, single vessel disease was the commonest type of vessel involved constituting 27 patients out of 52 (51.9%) followed by double and triple vessel disease constituting 14 out of 52 (26.9%) and 11 out of 52 (21.2%) respectively (Table 2).

Table 3: Analysis of sensitivity and specificity between MPI and CAG

MPI \ CAG	Positive (number)	Negative (number)	Total (number)
Positive (number)	46	03	49
Negative (number)	06	25	31
	52	28	80

Sensitivity: 88.5%; Specificity: 89.3%; Positive Predictive Value (PPV): 93.9%; Negative Predictive Value (NPV): 80.7%

When compared to age, vessel involvement showed a predominant single vessel disease among younger age group (age less than 60 years) with 20 out of 27 patients having single vessel disease are less than 60 years of age. Also, non-significant coronary stenosis (stenosis less than 70% diameter of LAD, RCA and LCx, less than 50% diameter of LMCA) or normal coronary vessels were also common among younger age group; 20 out of 28 patients having non-significant coronary vessel stenosis or normal angiogram were less than 60 years. In contrast, double vessel disease and triple vessel disease were more common in elderly group (age more than 60 years). 05 out of 09 patients (55.6%) having double vessel disease and 09 out of 11 patients (81.8%) having triple vessel disease were more than 60 years of age (Table 2).

A similar result was obtained by Babu Ezumalai et al in which 64.7% of normal angiogram patients were less than 55 years of age.¹³ However, all types of vessel involvement namely single, double and triple vessel disease were more common in patients more than 55 years of age. In their study, 55.2% of single vessel disease, 60.0% of double vessel disease and 66.7% of triple vessel disease were seen in patients more than 55 years of age.¹³

In our study, among single vessel disease, LAD (Left Anterior Descending) is the most commonly involved coronary vessel involving 15 of the 27 patients (55.6%) having single vessel disease. The other commonly involved vessels in single vessel disease are RCA (Right Coronary Artery) constituting 25.9% and LCx (Left Circumflex) constituting 18.5% of single vessel disease respectively. The findings are similar to the results of Robert M Califf et al and Koju R et al.^{16,17} The vessel involved in single vessel disease were LAD (47.6%), RCA (35.2%) and LCx (17.2%) in the study by Robert

M Califf et al and LAD (43.7%), RCA (37.5%) and LCx (21.9%) in the study by Koju R et al. In our study, there were 28 patients who showed negative for myocardial perfusion imaging. They were taken for coronary angiogram in spite of normal MPI as the pre-test likelihood of ischemic heart disease was high and the clinical signs and symptoms were suggestive of ischemic heart disease.

There were 06 false negative cases (normal myocardial perfusion imaging but positive angiographic finding) in the study. Of the 06 cases, 03 were single vessel disease involving RCA and the other 03 cases were triple vessel disease involving all three vessels namely LAD, RCA and LCx. Therefore, myocardial perfusion imaging is more likely to produce false negative results in patients having inferior wall ischemia (RCA territory of myocardium) and triple vessel disease.^{18,19}

However, in the setting of false negative result in triple vessel disease, though the perfusion imaging may be normal, there is decreased left ventricular ejection fraction (LVEF) which is unlikely for a normal myocardium. Low LVEF is associated with transient ischemic dilatation of left ventricle and increased tracer uptake by lungs which are indirect markers for ischemic heart disease with left ventricular dysfunction.¹⁸⁻²⁰ Since assessment of LVEF by myocardial perfusion imaging and tracer uptake by lungs are not under the scope of the present study, no further emphasis is made.

The present study carried a sensitivity of 88.5% and specificity of 89.3% for myocardial perfusion imaging in diagnosing stable ischemic heart disease. Further, the positive predictive value (PPV) was 93.9% and negative predictive value (NPV) was 80.7%, making myocardial perfusion imaging a reliable non-invasive investigation for diagnosing stable ischemic heart disease (Table 3).

Conclusion

The results conclude that MPI using ^{99m}Tc sestamibi is a reliable non-invasive investigation to diagnose stable ischemic heart disease. Though it cannot replace coronary angiogram which is considered a gold standard in detecting ischemic heart disease, the high sensitivity and specificity

of MPI makes it a useful and reliable screening procedure. Patients having high suspicion of stable ischemic heart disease may be subjected to MPI initially and if detected to have a reversible perfusion defect which implies a viable myocardium supplied by a stenosed coronary vessel, coronary angiogram may be performed with subsequent Angioplasty.

By making use of MPI as a gateway investigation to coronary angiogram, patients who are unwilling for angiogram can be evaluated with good sensitivity apart from evading some of the ill effects and complications of coronary angiogram.

Though the present study is not powered to make any recommendations, the results clearly indicate the need for further studies powered to make recommendations over the use of MPI as a screening investigation to coronary angiogram in detecting stable ischemic heart disease.

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