

**Research Article** 

# Comparison between Myocardial Perfusion Scintigraphy Using Technetium 99m Tetrofosmin and Conventional Coronary Angiogram in Assessing Coronary Artery Disease at Royal Hospital, Oman

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Received date: January 29, 2019; Accepted date: February 06, 2019; Published date: February 13, 2019

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#### Abstract

**Objectives:** To determine the sensitivity and specificity of MPS when compared to CCA in detecting coronary artery disease and compare it with published data. To compare myocardial perfusion findings (MPS) with conventional coronary angiography (CCA) results according to their territory.

**Methods:** The study included men and women >35 years of age who have undergone MPS and CCA within seven months due to suspected CAD with no interval major cardiac event or intervention between 2013 and 2014 at Royal Hospital, Oman.

**Results:** A total of 95 patients were included in the study. The sensitivity and specificity of MPS for detection of coronary artery stenosis (>=70%) were 95.45% and 47.06% respectively and for detection of coronary artery stenosis (>= 50%) were 82.76% and 43.24% respectively. The sensitivities and specificities of MPS for detection of Left anterior descending (LAD), Right coronary artery (RCA) and left circumflex (LCX) territory stenosis (>=70%) were (59.38% and 68.25%), (73.08% and 63.77%), and (42.31% and 81.16%) respectively. The agreement between MPs and CCA for coronary artery stenosis >=70% according to territory, the kappa value ranged 0.24- 0.30, p<0.0001.

**Conclusion:** The sensitivity and specificity of MPS at Royal Hospital for detecting critical stenosis was comparable with published data, 95.45% vs. (81%-93%), 47.09% vs. (38%-70%), respectively. There was a fair agreement in results between territory based MPS and CCA for coronary artery disease.

**Keywords:** Myocardial perfusion scan; Conventional coronary angiogram; Artery disease

#### Introduction

Hemodynamically significant coronary artery disease is an important indication for revascularization. Traditionally, the detection of coronary artery disease (CAD) is based on the assessment of stenosis in conventional coronary angiography (CCA) which is considered the gold standard test. However, because CCA visualizes coronary artery stenosis directly, rather than the hemodynamic significance of the lesions, the technique identifies atherosclerosis rather than ischemia [1].

To overcome this, some studies have use the threshold of FFR  $\leq 0.75$  to reliably identify inducible myocardial ischemia, and FFR of >0.80 to excludes myocardial ischemia. The benefits of this technique are that it is unaffected by fluctuations in heart rate, blood pressure, and myocardial contractility [2,3].

However, initial diagnostic invasive coronary angiography (ICA) in patients with stable CAD is not recommended. In their study, Patel and colleagues found that in current practice as many as 30% of patients undergo ICA with no symptoms (including no angina), 16% of patients undergo ICA without non-invasive testing, and an additional 15% undergo ICA even after normal non-invasive testing.

As a result, they predict that, 62% of stable patients without known CAD who undergo elective coronary angiography in the United States and 42% of patients in Europe have no significant stenosis [4].

Non-invasive imaging role in the evaluation of patients with suspected coronary artery disease (CAD), or stable CAD has increased over the past decades. Non-invasive imaging also plays an important role in risk stratification and selection of further treatment strategies, particularly in patients with an intermediate risk likelihood of CAD. Current guidelines do not indicate that functional imaging technique should be favoured; however it is recommended that the choice should consider local availability and expertise, the cost, and the risks of contrast agents and radiation exposure [5]. Citation: Al-Riyami K, Al-shammari A, Al-Zidjali M, Al-Shidi M, Al-Riyami A, et al. (2019) Comparison between Myocardial Perfusion Scintigraphy Using Technetium 99m Tetrofosmin and Conventional Coronary Angiogram in Assessing Coronary Artery Disease at Royal Hospital, Oman. J Nucl Med Radiat Ther 10: 394. doi:10.4172/2155-9619.1000394

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Stress myocardial perfusion imaging is an established non-invasive alternative to conventional coronary angiography in hemodynamically significant coronary artery disease. The strength of the test relies in its ability to detect hemodynamically significant ischemia rather than atherosclerosis [6,7].

Many studies have compared (MPS) to the gold standard in detecting CAD with overall sensitivities reaching up to 81%-93% and specificities of 38%-70%. Even those who were labeled as false positive MPS were evaluated by intra coronary ultra sound in one study which showed relative cross sectional plaque are >40% in 80% [8-11].

Thus far, a head-to-head comparison of data regarding the diagnostic accuracy of myocardial perfusion imaging by single-photon emission computed tomography, compared with invasive coronary angiography have never been obtained in the Omani population.

The aim of this study was to determine the sensitivity and specificity of MPS when compared to CCA in detecting coronary artery disease in intermediate and high risk patients and compare it with published data. Our second aim was to determine how these two techniques compare in localizing disease territory.

## **Material and Methods**

This is a retrospective, single-centre cohort diagnostic study. Institutional ethics committee approval was obtained.

## Patients

A retrospective evaluation was conducted on all MPS studies performed on consecutive patients referred for the evaluation of the presence of inducible ischemia between January 2013 and December 2014 at Royal Hospital, Oman.

**Inclusion criteria:** The study included patients above the age >=35, Had both MPS and CCA within 7 months with no cardiac event or intervention in between and no history of Coronary Artery Bypass Graft (CABG).

**Exclusion criteria:** Any patient with a gap of >7 months between MPS and CCA or patients with history of previous CABG or any intervention (surgery, Percutaneous Coronary Intervention -PCI) in between both studies

## Myocardial perfusion scan

In all patients, stress-rest MPS using adult two days' protocol; 450-500 MBq, Technitum-99m- labeled Tetrofosmin was performed with pharmacologic stress. Data were acquired using Siemens E-CAM Dual Head SPECT Gamma Camera with a low energy high resolution (LEHR) collimator. The energy window is set for 20% and centered at 140 KeV. The images are acquired in the LAO position. The matrix size is 64 x 64 with 1.45 zoom.

The acquisition is anterior, 25 sec per projection for a total of 32 and the number of frames/cycle: 8 bins per cardiac cycle. This was followed by reconstruction into long- and short-axis projections perpendicular to the heart axis; data were presented in polar map format (normalized to 100%), and a 17-segment model was used in which myocardial segments were allocated to the territories of the different coronary arteries). Perfusion defects were identified on the stress images (segmental tracer activity <75% of maximum) and divided into ischemia (reversible defects, with  $\geq$  10% increase in tracer uptake on the resting images) or scar tissue (irreversible defects). Accordingly, examinations were classified as being either normal or abnormal. The gated images were used to assess regional wall motion to improve differentiation between perfusion abnormalities and attenuation artifacts.

## Myocardial perfusion scan image evaluation

The MPS studies were accessed on PACS and read by 2 Nuclear Medicine physicians who were blinded to the results of the CCA and findings were recorded. Any difference in interpretation was resolved by consensus. The findings were defined initially as positive for Ischemia/infarct and negative for Ischemia/infarct and assessed for each coronary territory (LAD, RCA, LCX) using 17 segments method.

## Conventional coronary angiogram

The CCA reports were obtained from AL-SHIFA records and were also reported by two expert independent reviewers who used predefined criteria and were blinded to patient clinical information. Positive studies were determined at two cut off points, detection of lesion with  $\geq$ =50% stenosis, and  $\geq$ =70% stenosis. Each main coronary artery (RCA, LAD and LCX) were again further categorized as positive at critical stenosis  $\geq$ =70%.

The database for those patients was accessed *via* AL SHIFA, HIS (Health Information System) at Royal hospital and relevant clinical history was recorded.

### Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 22.0 (IBM Corporation, Armonk, NY, USA). Continuous variables were expressed as mean ( $\pm$  SD) or range. Categorical variables were expressed as numbers and percentages. Sensitivity, specificity, positive, and negative predictive values were calculated with 95% confidence intervals.

The diagnostic accuracy of MPS for the detection of myocardial events was expressed in terms of the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) and compared with CCA.

These values were calculated for all patients (males/females) and further categorized by coronary artery territory. Cohen's Kappa test was used to calculate the agreement per coronary territory between the two tests.

## Results

## **Baseline characteristics**

A total of 165 patients, were initially enrolled, 70 (42%) were subsequently excluded from the study as they did not meet the inclusion criteria. Thus, 95 patients (58%) completed the entire protocol and were included in the analysis. Patient characteristics are displayed in Table 1.

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Characteristic	Value		
Age, years	mean age 57.8 ± 8 years; range-years		
Gender	45 (47%) female and 50 (53%) male		
Diabetic	33 (35%)		
Hypertension	54 (57%)		
hyperlipidemia	21 (22%)		
Smoking history	17 (18%)		
History of myocardial infarction	8 (8%)		
History of PCI	13 (14%)		
Mean interval between MPS and CCA	1.45 months		

Table 1: Baseline characteristic.

## MPS and CCA analysis

MPS was positive in 69 (73%) of patients and negative in 26 (27%). Out of the reported positive cases 44 cases were males and 25 were females, while 6 males and 20 females were reported negative. In the category with CCA results with cut off lesion >=50%, CCA was positive in 58 (61%) patient and negative in 37 (39%). while using the higher cut off lesion >= 70%, resulted in reporting 44 (46%) cases as positive and 51 (54%) as negative.

Comparing the two test using the cut-off >= 50, MPS was true positive (TP) in 48 patients, true negative (TN) in 16, false positive (FP) in 21 and false negative (FN) in 10. The reported sensitivity and specificity of the test was 82.76%, (95% CI: 70.56-91.40) and 43.24%, (95% CI:27.11-60.51) respectively. The Positive Predictive and Negative predictive values were respectively 69.57% (95% CI: 62.76% -75.61%) and 61.54% (95% CI: 44.92% to 75.84%)

Comparing the two-test using the cut-off >= 70, MPS was TP in 42 patients, TN in 24, FP in 27 and FN in 2. The reported sensitivity and specificity of the test at this cut-off was 95.45% (95% CI: 84.50-99.31) and 47.06%, (95% CI: 32.93-61.54) respectively. The Positive Predictive and Negative Predictive values were respectively 60.87% (95% CI 54.37% - 67.01%) and 92.31% (95% CI: 75.02% - 97.96%).

We further classified the MPS study as positive or negative according to the involved coronary artery territory and compared it to CCA results (Table 2) and further sub-analysed according to sex (Figure 1).

LAD					
MPS		CCA			
+ve	-ve	+ve	-ve		
39 (41%)	56 (59%)	49 (52%)	46 (48%		
RCA					
MPS		CCA			
+ve	-ve	+ve	-ve		
44 (46%)	51 (54%)	31 (32%)	64 (68%)		

LCX					
MPS		CCA			
+ve	-ve	+ve	-ve		
24 (25%)	71 (75%)	31 (32%)	64 (68%		

**Table 2:** MPS and CCA results using the 70% threshold cut off value according to coronary territories.



**Figure 1:** MPS and CCA results according to patient sex and involved coronary artery territory using the CCA 70% threshold cut off. (MPI: Myocardial Perfusion Imaging; CCA: Conventional Coronary Angiography; Rx: Results; LAD: Left Anterior Descending; RCA: Right Coronary Artery; LCX: Left Circumflex; F: Female; M: Male)

In the left anterior descending artery category (LAD), MPS was TP in 19 patients, TN in 43, FP in 20 and FN in 13 with a reported sensitivity and specificity of 59.38%, (95% CI:40.65-76.29) and 8.25%, (95% CI:55.31-79.41) respectively. 8 male patients were reported as FP and 12 females.

In the right coronary artery category (RCA), MPS was TP in 19 patients, TN in 44, FP in 25 and FN in 7 with a reported sensitivity and specificity of 73.08%, (95% CI: 52.21-88.38) and 63.77%, (95% CI:

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51.31-75) respectively. In this category 14 male patient were reported as FP and 11 female patients.

Finally, the left circumflex artery category (LCX), MPS was TP in 11 patients, TN in 56, FP in 13 and FN in 15 with a reported sensitivity and specificity of 42.31%, (95% CI: 23.38-63.07), 81.16%, (95% CI: 69.94-89.56) respectively.

Cohen's Kappa test showed fair agreement in all coronary territory LAD: k=0.26, RCA: k=0.30 and LCX: k=0.24 when comparing MPS results with CCA results using the 70% threshold cut off value.

## Discussion

The sensitivity of MPS at Royal Hospital for detecting critical stenosis are comparable with published results 95.45% *vs.* (81%-93%), however, the specificity of MPS at Royal Hospital for detecting critical stenosis are at the lower limits of global results 47.09% *vs.* (38-70%) [8,10-18].

One explanation would be referral bias as patients with abnormal MPS are more likely to undergo CCA than those with normal MPS resulting in identification of almost all "false positive tests", whilst underestimating the number of "true negative" tests. Alternative to specificity, assessing normality rate would be more accurate: proportion of normal tests in a population with a low probability (<5%) based on clinical factors [19].

The lower sensitivity and specificity in the LAD and RCA territories respectively might reflect the implications of assessing patient related artifacts in these territories [20-22].

The majority of false positive cases in the LAD territory were in females, as expected due to breast attenuation and on the other hand the majority were males in the RCA territory likely due to diaphragmatic related artifact. The most frequent reported false negative tests were reported at the left circumflex artery territory which compares to previous studies [12].

The fair agreement with regards to coronary territory involvement, reminding us that MPS does not put into account anatomical variation in terms of coronary arterial supply to the myocardium. Additionally, the difficulty in allocating inferolateral defects to the RCA or to the LCX can reduce the agreement between territories [23].

There are a few limitations to the study which include being a retrospective single blinded study, small sample size and with and extended gap between the two tests (up to 7 months). A prospective, double blinded larger sample study with a gap limit of 2-3 months would increase the strength of the study

Furthermore, the results do point out the need to study the MPS findings in those who are false positive to determine the common appearances of patient related artifacts/misinterpretation in our population and "read around a defect".

Additionally, further assessment of the feasibility of adding CT attenuation correction when possible or alternatively a supine/prone protocol to help overcome artifacts. However, it should be kept in mind that reversible perfusion defects seen on SPECT images are often associated with angiographically unrecognized occult atherosclerotic changes and an abnormal vasodilation capacity of the coronary circulation. The propensity to disregard abnormal perfusion findings as false-positive in these patients may be unwarranted [9].

## Conclusion

The sensitivity of MPS at Royal Hospital, Oman in diagnosing critical stenosis is excellent when compared to published results. We recommend the use of CT attenuation when possible or prone imaging to overcome false positive results due to artifacts.

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