The role of myocardial perfusion imaging in the identification of the obstructive coronary artery lesions: a tertiary cardiology center experience

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ABSTRACT

Objectives: Because of the moderate accuracy of treadmill electrocardiogram and fear of a claim if a diagnosis is missed, cardiologists usually order Myocardial Perfusion Imaging (MPI) as a first-step test in most of patients with chest pain admitted to cardiology department. The performance of the MPI in diagnosing obstructive CAD depends on the population studied. Thus we aimed to assess the agreement between MPI and coronary angiography in the identification of the obstructive coronary lesion.
Methods: A total of 231 patients who underwent MPI due to suspicion of coronary ischemia and had a coronary angiogram within the last three months were included in this retrospective study. MPI and coronary angiography findings were analyzed to weigh the performance of MPI in determining obstructive coronary lesion.
Results: The mean age was 63.9 ± 8.9 years, 54.5 % being males. MPI showed a sensitivity of 0.86 in determining patients who had a significant (> 70%) coronary lesion. While evaluating the ability of MPI to detect ischemia in the left ventricle region which is supplied by the lesioned vessel, the sensitivity was found to be; 60% in determining anterior ischemia associated with significant LAD lesion, 77.4% in determining inferior ischemia associated with significant RCA lesion, and 44.4% in determining lateral ischemia associated with significant CX lesion.
Conclusions: Our findings have shown that MPI with visual assessment has 86% sensitivity for detecting significant coronary artery stenosis. However, the sensitivity of MPI in determining ischemia in the left ventricle region which is supplied by the lesioned coronary artery was found to be 44.4 to 77.4%.
Keywords: myocardial perfusion imaging, coronary angiography, obstructive coronary artery lesion

Coronary artery disease (CAD) has remained the leading causes of morbidity and mortality all over the world during the last five decades [1]. The initial diagnostic evaluation of patients presenting with chest pain and suspected obstructive CAD generally consists of an exercise electrocardiogram that has a sensitivity of 68% and a specificity of 77% in diagnosing obstructive CAD [2]. Nevertheless, the information obtained from the myocardial perfusion imaging (MPI) is more precise with respect to localization, extension, and severity of ischemia; thus it becomes a dominant non-invasive modality, usually a

gatekeeper test before coronary angiography, for the assessment of patients with suspected CAD in daily practice [3-4].

The performance of the MPI in diagnosing obstructive CAD depends on not only the prevalence of disease in the population studied but also individual characteristics of patients (i.e. likelihood of obstructive CAD) [4]. Thus clinical registries which weigh the performance of MPI among national cohort of patients provide important insights into the real-life health care.

The purpose of the present study was to assess the agreement between MPI and coronary angiography in the identification of the obstructive coronary lesion in patients with suspected CAD. Additionally, we intended to analyze the patient characteristics in whose MPI test was insufficient to detect the obstructive coronary lesions.

METHODS

Study Population

In this retrospective study, we initially searched the hospital database to find patients who had undergone both MPI and coronary angiography at our hospital between January 2018 and January 2019. The study protocol was approved by the local ethics committee. Patients who had previously undergone heart surgery, including coronary artery bypass grafting or prosthetic valve replacement and with a prior diagnosis of; heart failure, end-stage renal failure were excluded. Additionally, patients who experienced acute myocardial infarction or undergone revascularization within this period (January 2018 and January 2019), and who had insufficient data on patient cards were excluded. Finally 231 patients who underwent MPI because of clinical suspicion of CAD and were subsequently subjected to a coronary angiogram (owing to ischemia on MPI or ongoing symptoms) were found to be eligible. At this time, MPI records of recruited patients were analyzed to categorize those according to localization of ischemia. Afterwards angiographic findings were analyzed and categorized with respect to lesion localization and being significant (> 70%) or not. Then data were analyzed to weigh the performance of MPI in determining obstructive coronary lesion. The sensitivity of the MPI

was defined as the percentage of any level of ischemia in patients with evidence of obstructive (> 70%) lesions in one or more coronary arteries. Specificity of the MPI was determined as the percentage of normal images (without ischemia) in patients with normal angiography or with less than 70% stenosis in any coronary arteries.

Data with respect to demographic and clinical characteristics and laboratory parameters were collected from the medical records. The definition of hypertension was specified as a systolic pressure ≥ 140 mmHg and/or a diastolic pressure ≥ 90 mmHg or if the participant was taking an antihypertensive medication [5]. Diabetes mellitus was determined as a fasting glucose level > 126 mg/dl and/or if the patient was taking an anti-diabetic medication [6]. Participants who were recorded as smoker at the patient card were classified as smokers. Hyperlipidemia was defined as taking a lipid-lowering therapy. A history of CAD was determined as the existence of prior acute coronary syndrome, percutaneous coronary revascularization, and/or at least one attested coronary stenosis ≥ 50% luminal diameter on angiography [7].

Coronary Angiography Data

Angiographic data with respect to index coronary angiogram was conducted from the cardiac catheterization laboratory records. Angiographic images were visually assessed by two cardiologists who were blinded to the MPI data. Coronary slow flow phenomenon was defined with respect to corrected TIMI frame count, an objective and quantitative index of coronary flow [8].

Myocardial Perfusion Imaging Data
Stress Protocols

Exercise (treadmill) was the favored stress modality in patients who could exercise and reach sufficient exercise goals. Modified Bruce protocol was used in all of those. Pharmacologic stress with adenosine, dobutamine and dipyridamole was used in patients who could not complete or tolerate sufficient exercise, those with limited heart rate response, or left bundle-branch block. Patients were charged to discontinue taking nitrates for 6 hours, calcium channel blockers for 24 hours, and ß-blockers for 48 hours prior to the stress protocol. Tc-99m sestamibi was given through a venous access when the patient's heart rate achieved

85% of calculated maximum heart rate (both in exercise treadmill or pharmacologic stress). Exercise or pharmacological induction was continued for two minutes after the Tc-99m sestamibi injection.

Gated Single-photon Emission Computed Tomography (SPECT) Protocol

All patients underwent a Gated SPECT protocol according to current guideline [9]. MPI images were interpreted based on a 17-segment model [10]. All stored images were analyzed by a single, blinded, experienced observer. Images were categorized as either normal or ischemic. A score model was used to define reversible defects. According to this modality, the total score at stress, Summed Stress Score (SSS), reflected the extent and severity of the abnormality including ischemia and infarction. The difference between the SSS and Summed Rest Score (SRS) was defined as Summed Difference Score (SDS) that reflected a reversible defect. Semi-quantitative parameters were classed as follows; A SSS ≤ 3 was defined as a normal result, while a score of 4-8 as a mild defect, 9-12 as a moderate defect and > 12 as a severe defect. A SDS of 1-3 reported mild ischemia, 4-7

moderate ischemia and > 7 severe ischemia [11].

Statistical Analysis

The SPSS 22.0 (IBM Corporation, Armonk, New York, USA) was used for statistical analysis. Categorical variables were demonstrated as number and percentage. All quantitative data were expressed as mean ± SD unless otherwise stated. We compared continuous variables using student t-test or Mann-Whitney U test between groups. Categorical variables were summarized as percentages and compared with the Chi-square test. Diagnostic concordance with coronary angiogram and MPI data was analyzed was by using cross tabulations. A *p* value < 0.05 was considered as statistically significant.

RESULTS

Two hundred thirty-one patients were included in the present study. Baseline characteristics of the recruited patients are shown in Table 1. The mean age was 63.9 ± 8.9 years (55% males). 123 (53.2%) patients had non-significant coronary lesions, 54

Table 1. Baseline characteristics of the study patients

Parameters	n = 231
Age (years)	63.9 ± 8.9
Males	126 (54.5%)
History of CAD	127 (54.9%)
Diabetes mellitusy	97 (41.9%)
Hypertension	208 (90%)
Atrial Fibrillation	16 (6.9%)
Hyperlipidemia	125 (54.1%)
Laboratory parameters	
Hemoglobin (g/L)	13.8 ± 1.6
Low-density lipoprotein (mg/dl)	124.3 ± 44.7
Creatinine (mg/dl)	0.95 ± 0.57
Ejection Fraction on the Echocardiography (%)	56.6 ± 9.2
Indication of the Myocardial Perfusion Imaging	
Angina	164 (70.9%)
Searching ischemia (e.g. left branch bundle block, any symptom thought to be an equivalent of angina)	67 (29%)

Data are expressed as mean ± standard deviation for normally distributed variables and percentage (%) for categorical variables. CAD = coronary artery disease

Table 2. Diagnostic concordance between coronary angiography and myocardial perfusion imaging with respect to left anterior descending artery lesions

	Patients without significant LAD stenosis (< 70%) at angiography (n = 171)	Patients with LAD significant stenosis (> 70%) at angiography (n = 60)	*p value*
No ischemia at anterior wall	78 (45.6%)	24 (40%)	0.397
Mild ischemia at anterior wall	57 (33.3%)	22 (36.6%)	
Moderate ischemia at anterior wall	32 (18.7%)	10 (16.6%)	
Severe ischemia at anterior wall	4 (2.3%)	4 (6.6%)	

Data are expressed as percentage (%) for categorical variables. LAD = left anterior descending artery

(23.3%) patients had a significant stenosis in only one coronary artery, 38 (16.4%) patients had significant coronary lesions in two different coronary arteries, while 16 (6.9%) patients had three-vessel coronary artery disease. There were 14 (6%) patients with coronary slow flow who had not a significant lesion in any coronary arteries. A diaphragmatic attenuation was reported in 20 (8.6%) patients. Overall, MPI could identify 86% of patients who had a significant coronary lesion among our study population.

In the present study, coronary angiography showed a significant (> 70%) stenosis of LAD in 60 patients. However, MPI did not report any level of ischemia at the anterior wall in 24 (40%) of those, while mild ischemia at the anterior wall was reported in 22 (36.6%) of those. Moderate and severe ischemia at the anterior wall were found to be in 10 (16.6%) and 4 (6.6 %) of those, respectively. On the other hand, coronary angiography revealed a no or non-significant

stenosis of LAD in 171 patients. MPI did not report any level of ischemia at the anterior wall in 78 (45.6%) of those. But, mild, moderate and severe ischemia at the anterior wall were reported in 57 (33.3%), 32 (18.7%), and 4 (2.3%) of those, respectively (Table 2). Thus, sensitivity and specifity of MPI in identifying anterior ischemia associated with critical LAD lesion were found to be 60% and 45.6%, respectively.

Coronary angiography showed a significant (> 70%) stenosis of RCA in 62 patients. However, MPI did not report any level of ischemia at the inferior wall in 14 (22.5%) of those, while mild ischemia at the inferior wall was reported in 7 (11.2%) of those. Moderate and severe ischemia at the inferior wall were found to be in 29 (46.7%) and 12 (19.3 %) of those, respectively. On the other hand, coronary angiography revealed a no or non-significant stenosis of RCA in 169 patients. MPI did not report any level of ischemia

Table 3. Diagnostic concordance between coronary angiography and myocardial perfusion imaging with respect to right coronary artery lesions

	Patients without significant RCA stenosis (< 70%) at angiography (n = 169)	Patients with significant RCA stenosis (> 70%) at angiography (n = 62)	*p value*
No ischemia at inferior wall	72 (42.6%)	14 (22.5%)	< 0.001
Mild ischemia at inferior wall	25 (14.7%)	7 (11.2%)	
Moderate ischemia at inferior wall	68 (40.2%)	29 (46.7%)	
Severe ischemia at inferior wall	4 (2.3%)	12 (19.3%)	

Data are expressed as percentage (%) for categorical variables. RCA = right coronary artery

Table 4. Diagnostic concordance between coronary angiography and myocardial perfusion imaging with respect to circumflex artery lesions

	Patients without significant CX stenosis (< 70%) at angiography (n = 177)	Patients with significant CX stenosis (> 70%) at angiography (n = 54)	*p value*
No ischemia at lateral wall	127 (71.7%)	30 (55.5%)	0.001
Mild ischemia at lateral wall	17 (9.6%)	3 (5.5%)	
Moderate ischemia at lateral wall	31 (17.5%)	15 (27.7%)	
Severe ischemia at lateral wall	2 (1.1%)	6 (11.1%)	

Data are expressed as percentage (%) for categorical variables. CX = circumflex artery

at the inferior wall in 72 (42.6%) of those. But, mild, moderate and severe ischemia at the inferior wall were reported in 25 (14.7%), 68 (40.2%), and 4 (2.3%) of those, respectively (Table 3). Thus, sensitivity and specifity of MPI in identifying inferior ischemia associated with critical RCA lesion were found to be 77.4 % and 42.6%, respectively.

Additionally, coronary angiography showed a significant (> 70%) stenosis of CX in 54 patients. However, MPI did not report any level of ischemia at the lateral wall in 30 (55.5%) of those, while mild ischemia at the lateral wall was reported in 3 (5.5%) of those. Moderate and severe ischemia at the lateral wall were found to be in 15 (27.7%) and 6 (11.1 %) of those, respectively. On the other hand, coronary angiography revealed a no or non-significant stenosis of CX in 177 patients. MPI did not report any level of ischemia at the lateral wall in 127 (71.7%) of those. But, mild, moderate and severe ischemia at the lateral wall were reported in 17 (9.6%), 31 (17.5%), and 2 (1.1%) of those, respectively (Table 4). Thus, sensitivity and specifity of MPI in identifying lateral ischemia associated with critical CX lesion were found to be 44.4% and 71.7%, respectively.

While evaluating overall (regardless of the relationship between the vessel and its feeding area) sensitivity, MPI could identify; 85% of patients who had a significant LAD lesion, 88% of patients who had a significant RCA lesion, and 83% of patients who had a significant CX lesion.

While assessing patients with moderate-severe ischemia at the anterior wall (n = 50), there were not any significant difference on baseline characteristics

with respect to lesion severity in LAD. However among patients with moderate-severe ischemia at the inferior wall (n = 113), subjects who had a significant lesion on RCA were more likely to have a prior history of diabetes mellitus, coronary artery disease and be male (48.7 vs. 29.1; *p* = 0.042, 78% vs. 56.9%; *p* = 0.024, 9.7% vs. 38.8%; *p* < 0.001, respectively).

Coronary angiography demonstrated a significant (> 50%) stenosis of LMCA in 4 patients. One of them displayed moderate-severe ischemia at the anterior wall on the MPI; one of them displayed moderate-severe ischemia at the lateral wall while the other two patients revealed moderate-severe ischemia at the inferior wall.

DISCUSSION

The present study was an evaluation of patient characteristics and the agreement between MPI and coronary angiography in the identification of the obstructive coronary lesion (>70%) in patients with suspected CAD admitted to a tertiary referral hospital. The main results of the present study were as follows: 1) MPI showed a sensitivity of 0.86 in determining patients who had a significant coronary lesion; 2) The overall sensitivity was found to be 0.85 in determining significant LAD lesion while anterior ischemia associated with significant LAD lesion MPI showed a sensitivity of 0.6; 3) The overall sensitivity was found to be 0.88 in determining significant RCA lesion while inferior ischemia associated with significant RCA lesion MPI showed a sensitivity of 0.77; 4) The over-

all sensitivity was found to be 0.83 in determining significant CX lesion while lateral ischemia associated with significant CX lesion MPI showed a sensitivity of 0.44).

Modern cardiology has a broad range of clinical exploration methods available to assist the diagnosis and to stratify the risk of patients with suspected coronary artery disease. Basic (first-line) testing in those includes standard laboratory biochemical testing, a resting ECG, possible ambulatory ECG monitoring, and structural tests including resting echocardiography, and, in selected patients, cardiac magnetic resonance (CMR) [4]. In patients, with an intermediate probability of CAD and need to be tested noninvasively, an exercise ECG is the most widely used non-invasive method [12]. Although exercise ECG has advantages, easy to access and cheaper test comparing with the other non-invasive test options (stress CMR or stress echocardiography or MPI), because of the moderate diagnostic accuracy of it, clinicians usually could not be sure while excluding CAD with the result of the exercise ECG alone. Moreover, The National Institute for Health and Care Excellence (NICE) has recommended that exercise ECG testing should not be used alone for the diagnosis (or exclusion) of stable angina in patients without known CAD [13]. This recommendation has been followed in part by the latest European Society of Cardiology guideline on the management of chronic coronary syndromes, which suggests the use of functional imaging (stress CMR or stress echocardiography or MPI) over exercise ECG testing in patients with suspected CAD, in whom the results of exercise ECG are inadequate to diagnose or exclude CAD [4]. Although Stress CMR has some technical advantages, it is not easily accessible, it is contraindicated in patients who either have a pacemaker or severe renal failure, it is very sensitive to the rhythm of the heart thus it may not be interpretable in patients with atrial fibrillation [14]. On the other hand results of the stress echocardiography is usually challenging in patients with left bundle branch block or septal dyssynchrony [15]. As a result of those, cardiologists usually order MPI as a first-step test, even it is not recommended at this stage, in most of patients with chest pain admitted to cardiology department [12]. Thus the performance of the MPI, not only in recognizing coronary artery disease but also in detecting severe lesion, is important in daily practice. Previous studies evaluating the concordance of findings between coronary angiography and MPI reported different accuracy rates which were between 41.7% and 93.3% [16-17]. Hasbek *et al*. revealed a slightly low, 41.7%, diagnostic concordance between coronary angiography and MPI, in which treadmill test was the favored stress modality. However, they reported a 75.8% concordance rate in patients whom stress modality was a pharmacologic stress with adenosine [16]. Thus diagnostic accuracy of MPI depends on studied population and design of the works. Many of the previous studies defined culprit coronary lesion as 50% or more stenosis responsible for the symptoms while evaluating the concordance between coronary angiography and MPI. In other words, these studies were design to evaluate the power of MPI in detecting a coronary stenosis of 50% or above [16-20]. However current data has clearly revealed that only an estimated diameter stenosis > 70% in a coronary artery is classified as severe lesion and predicted to cause symptoms. Thus in the present study we aimed to evaluate the performance of MPI in determining a coronary stenosis > 70%.

In the present study, MPI could identify 86% of patients who had a significant coronary lesion that was very similar to previous studies [18, 21]. However while determining the lesion associated ischemic zone, sensitivity rates were fallen (e.g. 77% for RCA associated inferior ischemia, 60% for LAD associated anterior ischemia, and 44% for CX lesion associated lateral ischemia). This means that seven of every 100 patients with critical stenosis in RCA had an ischemia on another wall than inferior, 26 of every 100 patients with critical stenosis in LAD had an ischemia on another wall than anterior, and 42 of every 100 patients with critical stenosis in CX had an ischemia on another wall than lateral. The possible explanations for these findings are: I) existing collateral circulation; II) variation in coronary anatomy; III) heterogeneity of coronary hyperemia with pharmacologic stress [22]; IV) technical issues (As example; in normal SPECT images, the lateral wall often may appear brighter than the contra-lateral septum because of the camera is physically closer to the lateral myocardial wall (in proximity to the lateral chest wall) than to the septum. So that, the acquisition is associated with

more efficient count capture [22] - this may explain why MPI much more deviated in revealing lateral wall ischemia associated with CX lesion).

One of the remarkable findings of the present study was that patients who had a ischemia at the inferior wall, even if moderate, the possibility of critical stenosis in RCA was found to be considerably decreased if they were female or had not a prior history of diabetes mellitus or coronary artery disease. This finding is important because, physicians are everyday faced with such cases. The possible explanations for this finding are; I) breast attenuation; II) it is plausible that females who have a diabetes mellitus or coronary artery disease are more likely to be overweight and have large breasts that could affect the performance of MPI, in particular in evaluating inferior wall perfusion. Further studies need to be carried out in order to validate this finding.

Limitations

Our study has several limitations. First, we analyzed MPI images with visual analysis. Indeed published data has not clearly demonstrated improved sensi¬tivity or specificity of automated quantitative analysis systems programs over visual analysis. Moreover the visual analysis data are derived from experienced readers in laboratories have been found to be an excellent quality control [22]. However it would be better if every single patient were analyzed with an automated quantitative analysis program. Second, we did not analyze the results with respect to sub-group according to modality of stress (pharmacologic or treadmill) on MPI. Third, the present work is a single-center analysis; therefore, the generalisability of these findings is limited. Fourth, we did not evaluate the outcome of patients. Finally, we cannot exclude the possibility of unmeasured confounding factors.

CONCLUSION

In conclusion, the present study is an evaluation of patient characteristics and the agreement between MPI and coronary angiography in the identification of the obstructive coronary lesion (> 70%) in patients with suspected CAD. Our findings have shown that MPI with visual assessment has 86% sensitivity for

detecting significant coronary artery stenosis. However, the sensitivity of MPI in determining ischemia in the left ventricle region which is supplied by the lesioned coronary artery was found to be 44.4 to 77.4%.

Conflict of interest

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