

# Early Detection of Myocardial Damages for Patients with Chest Pain and Non-Diagnostic ECG in Emergency Department by Rest Myocardial Perfusion Imaging: A Preliminary Study

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## Abstract

**Background:** According to the World Health Organization (WHO), cardiovascular disease is the significant leading cause of mortality in adults. Some studies demonstrated that rest Myocardial Perfusion Imaging (rMPI) is a reliable test for ruling out myocardial ischemia/infarction in patients with inconclusive diagnostic data including non-diagnostic or normal Electrocardiogram (ECG) and troponin test result.

**Methods:** Patients who presented to the emergency department with chest pain underwent evaluation assay including inquiry about history, having abnormal ECG, troponin test result and physical examination. The patients with normal or non-diagnostic ECG and normal troponin were enrolled in our study. Then, they were referred to the department of nuclear medicine for rMPI. The patients with abnormal rMPI were asked to perform coronary angiography and the patients with normal rMPI were followed up for average of 12.8 months.

**Results:** In this study, 20 patients with mean age of  $46.15 \pm 12.7$  including 7 males and 13 females were enrolled. Among 20 patients, 14 (70%) patients had normal rMPI and 6 (30%) were abnormal. All patients with abnormal rMPI showed coronary disorders in angiography. Rest of them with normal rMPI were followed up and no cases with cardiac events were found among them. Sensitivity, specificity, positive and negative predictive value for MPI was 100%.

**Conclusion:** According to the data of this study, MPI has a good sensitivity and specificity for diagnosis of myocardial ischemia/infarction and the acute coronary syndrome that prevents unnecessary hospitalization. So, it can be included in the diagnostic protocol in emergency departments of developing countries.

**Keywords:** Acute coronary syndrome, Emergency departments, Chest pain, Myocardial perfusion imaging, Single-photon emission computed tomography (SPECT)

## Introduction

One of the most common causes for referring patients to Emergency Departments (ED) is chest pain with suspicion of the Acute Coronary Syndrome (ACS) (1). Based on the report of the World Health Organization (WHO), cardiovascular diseases are considered for the maximum number of non-communicable disease mortality (17.5 million deaths). Meanwhile, the major cause of death worldwide is cardiovascular diseases; their prevalence is constantly progressing for both men and women in developing and developed countries (2). The most leading diagnostic test of a cardiac event includes evaluation of chest pain history, Electrocardiogram (ECG), risk factors, patient age, and levels of serum markers of cardiac necrosis (1). Nevertheless, sometimes these measurements cause a missed diagnosis or an unessential hospital admission. Also, these clinical scores could be non-diagnostic or normal, therefore detection of coronary disease must be incorporated with imaging techniques. The quantitative assessment of abnormal myocardial perfusion could be performed by Single-Photon Emission Computed Tomography (SPECT) and myocardial perfusion imaging at rest and stress phases (3). Myocardial perfusion imaging is introduced as a most powerful prognostic and diagnostic test in increasing the accuracy and speed of detection in ACS patients with known and suspected ischemic heart disease (4,5). The rest Myocardial Perfusion Imaging (SPECT-MPI) with Tc-99m-Sestamibi as a single radiotracer has favorable properties compared with another prevalent radiotracer (thallium-201) in emergency situations in terms of lack of redistribution and better image quality (6). In this study, an attempt was made to investigate the detection effect of rMPI in the patients with possible ACS or myocardial infarction that referred to the emergency department with chest pain, normal ECG and troponin.

## Materials and Methods

### Patient selection

This cross-sectional study was performed in Bushehr Heart Medical Center from 2014 until 2018. The patients presenting with chest pain were referred to the emergency room. After the initial assessment the patients who had low-to-moderate risk [*e.g.*, normal ECG and cardiac serum biomarker (troponin T level)]

for ACS were specified. Patients with low to moderate risk for ACS were subjected to further evaluation after 6 hours. The tests were repeated and in case of similar results to previous ones and lack of history of angiography and heart or pulmonary diseases, they were referred to the department of nuclear medicine and underwent rMPI.

The institutional revision board approved the protocol of the study and written informed consent form was obtained from patients.

Exclusion criteria were the history of the previous cardiac ischemia, pregnancy, abnormal ECG indicating ischemia, clearly noncardiac pain, diseases such as liver and lung failure, cancer, and also percutaneous coronary intervention in the last six months, arrhythmia with suggested ischemia, and positive troponinT (TnT).

### **Rest myocardial perfusion imaging (SPECT-MPI)**

Rest myocardial perfusion imaging was carried out by using a dual-head gamma camera (Vertex ADAC plus) equipped with low energy high-resolution collimator. Next, 20 mCi Tc-99m-Sestamibi was injected into patients and images were acquired about 60 minutes after injection as well as according to imaging guidelines. Without any delay, after the imaging acquisition, data were processed through commercial standard protocols. Images were divided into three short-axis segmentations (basal, mid, distal) and one vertical long-axis (mid) slice. The sign of segment was scored visually using a standard 17 segment model and 5-spot scale system from 0 (normal) to 4 (the absence of myocardial uptake). The patients were visually examined in detail until the detected perfusion defect was considered abnormal (7). If there was any hypoactivity of inferior and anterior walls in rMPI SPECT imaging, few additional spot views to ascertain its diagnostic value were performed.

### **Follow up and study endpoints**

Patients were followed up to a period of an average of 12.8 months (minimum 6 months and a maximum 48 months). Follow-up was performed for all patients *via* the telephone calls from a physician to the patient or members of the family. The endpoints were myocardial infarction or cardiac death, nonfatal myocardial infarction, and admission due to ACSs.

### Statistical analysis

A standard statistical software package (SPSS version 21, Chicago, IL, USA) was applied for data analysis. Continuous variables are calculated as mean  $\pm$  SD, and categorical variables are calculated as numbers and percentages. The specificity and sensitivity values were calculated by true- or false-positive results for acute rMPI.

### Results

Twenty patients (7 men, 13 women) with persistent chest pain and suspected cardiac origin with negative troponin (cTnT) test as well as normal ECG assessment were selected for this study. All patients had a low to moderate probability for the ACS based on an initial evaluation, normal electrocardiogram, and first negative cTnT as a cardiac biomarker. Table 1 summarizes the baseline characteristics of the population, including sex, age, ECG, angiography, previous pain, current risk factors and a previous history of angina that relates these characteristics with the incidence of events. The mean age of the patients was  $46.15 \pm 12.7$  years and 35% of the populations were men, and also 21.9% had typical chest pain. History of angina was present in none of the patients. Perfusion images were classified as abnormal if the total rest perfusion score was 1 or more ( $\geq 1$ ). An abnormal acute rest perfusion image was present in 30% (6 patients) of the patients. In this group, there was 1 event during the 48-month

follow-up as recurring chest pain. All of the properties including the sensitivity, specificity, and Positive and Negative Predictive Value (PPV and NPV) of rMPI considering the occurrence of events were 100%.

### Discussion

The aim of this study was to evaluate the diagnostic value of rMPI SPECT in comparison with ECG, serum biomarkers and angiography. Myocardial infarction (MI) recognized as angina pectoris is described by substernal chest pain which is intensified by tension or exercise. Stable angina, unstable angina or non-ST-elevation MI (NSTEMI), and ST-elevation MI (STEMI) are an incidental cause of chest pain with the ACS origin that stable and unstable angina cannot have ST-elevation in ECG for chest pain condition. This study examined the patients with initial non-diagnostic or normal ECG for suspected ischemic and the initial normal troponin findings (no high sensitivity assay) for ACS or NSTEMI. These patients have been assumed at low-to-intermediate risk for acute coronary syndrome. It's suggested that the rest SPECT technique may be appropriate for definitive and accurate diagnosis according to data based on randomized trials. Rest myocardial perfusion imaging has a high negative predictive value in patients with a suspicious diagnosis. So, patients with normal acute rest MPI don't need admission to hospital for treatment and likewise that leads to potential cost saving for patients. In contrast, abnormal results are related to a high possibility of ACS and hospitalization for early measurement of treatment effect (8,9).

There are multiple studies that have justified the application of rest MPI in the management of suspected problems (9-12). These reports have concluded that the use of rest SPECT in the ED is related to lower expenditure as well as reduction of dispensable hospitalization. Until now, there are two important randomized trials that have been published. In a smaller trial, rest perfusion imaging improved clinical decisions for patients with indistinguishable ECG and suspected acute cardiac ischemia. Also, unnecessary hospital-care was reduced for these patients, without reducing suitable admission for patients with acute ischemia (9). In a much larger trial, tests performed and validated with randomized, prospective clinical trials showed an important

**Table 1.** Characteristics of population under study

Patient's demographics and biomarkers	All patients (n = 20)
Sex (male)	7(35%)
Mean age (years) $\pm$ SD	$46.15 \pm 10.4$ (min=30, max=62)
<b>Documented cardiac risk factors</b>	
Prior cardiac infractions (%)	0
Hypertension (%)	3(15%)
Diabetes (%)	2(10%)
Normal ECG (%)	20(100%)
Normal troponin	20(100%)
MPI-SPECT (%)	nor=14 abn=6
Abnormal rMPI (%)	6(30%)
Angiography (%)	6(30%)
Follow up (months)	12.8(min=6 , max=48)

influence on decisions of physicians. So in this experiment, patients were selected to receive standard care with or without rest MPI and they found that rest perfusion imaging can be great assistance in the diagnostic assessment of intermediate-risk patients with chest pain accompanied by nondiagnostic ECG findings. Rest-MPI evaluation provides the immediate identification of patients at a lower risk of ACSs who could safely be assessed in an outpatient situation. Normal myocardial perfusion images generally help clinicians in avoiding unnecessary interventional angiography and hospitalizations and no unfavorable effect of this diagnostic policy on patient problems is found during the primary hospitalization. However, more large scale studies to check improvements in myocardial salvage are required (11).

The results of the study by Duca *et al* compared the effect of acute rest MPI and individual serum marker for detecting myocardial injury and demonstrated that the acute rest MPI had better sensitivity and comparable specificity in symptomatic myocardial infarction when compared with serum troponin T and I (13). Heller *et al* evaluated the clinical application and cost-effectiveness of acute rest SPECT-MPI with technetium-99m tetrofosmin in patients with chest pain presenting to the emergency department. They concluded abnormal rest MPI imaging exactly predicts acute MI in patients with nondiagnostic ECG; in contrast, a normal result was associated with a very low risk cardiac event. Moreover, the use of this procedure in the emergency department unit can safely and considerably reduce the duration of unnecessary hospitalization (6).

In this study, rest myocardial perfusion imaging using the American Heart Association (AHA) guidelines was performed for the assessment and management of patients with acute chest pain presenting to the emergency department. In this technique, there is the least redistribution of the radiopharmaceutical in the

time interval between injection and imaging; imaging can be postponed for a while after the injection and it provides an accurate data about myocardial perfusion at the moment of injection, which reflects the area of myocardium at risk (14). Another study in 2012 by Better *et al* surveyed the efficiency of rest MP imaging in the managing of low to intermediate-risk patients with acute chest pain in the emergency department of developing countries. They found that rest MP imaging is a valid assessment test for ruling out myocardial infarction when used for patients in developing nations (15).

In this study, of the 6 abnormal rMPI cases, all were sent for angiography and the results showed significant coronary artery diseases with regard to abnormality observed in rMPI. Also, this study shows higher sensitivity and specificity for rMPI as well as other multiple cumulative experiences that confirm these results (16).

This study had several limitations; the most important ones are a small sample size, and lack of long follow-up studies to assess the survival analysis. Thus, further research necessitates larger number of patients to verify these findings.

## Conclusion

In patients with chest pain syndrome with normal ECG and troponin serum marker, rMPI SPECT has high sensitivity and specificity in diagnosis of MI and ACS. This method is cost effective and prevents unnesseray hospitalization of patients. So, it can be included in the diagnostic protocols in developing countries.

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