Brief Communications

Gated-SPECT Myocardial Perfusion Imaging for Evaluation of Patients with Acute Chest Pain and a Normal or Non-Diagnostic Electrocardiogram

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Abstract

Introduction: To assess the ability of rest gated single photon emission computed tomography (gated-SPECT) myocardial perfusion imaging (MPI), to rule out an acute coronary syndrome (ACS) in emergency room patients with a low to intermediate likelihood of coronary artery disease. This study is part of a coordinated multicenter protocol organized by the International Atomic Energy Agency (IAEA).

Methods: Forty-one patients (mean age: 55±12 years, 54% male), who presented to the emergency room of the Institute of Cardiology from December 2008 to July 2010, with chest pain and a normal or non-diagnostic electrocardiogram, without history of previous myocardial infarction (MI), were included. All underwent a rest gated-SPECT MPI, and were injected with 25 mCi of Tc99m-MIBI within 6 hours of the cessation of the index episode of chest pain. Blood samples for troponin-T measurement were collected. Coronary calcium score (CCS) was also indicated. The major study end-points at one-month follow-up (FU) were: cardiac death, non-fatal MI, cardiac revascularization on the same admission (not driven by a FU stress exam), and admission due to ACS. Secondary end-points were: non-cardiac death, positive stress test with imaging, and coronary angiogram with an epicardial coronary lesion equal or > 50%. Clinical FU was done at one, six and 12 months.

Results: Troponin-T was negative in all cases. Eleven patients (27%) showed an abnormal rest MPI. Mean CCS was 78±199. In four patients CCS was >100. Coronary angiogram driven by a positive rest MPI was performed in nine patients (22%), resulting in significant stenosis and percutaneous transluminal coronary angioplasty (PTCA) in seven cases (78%). Between two and four weeks after index event, stress MPI was performed in patients without PTCA, and it showed reversible perfusion defects in 31%. During FU, nine patients showed cardiac events during the first month: two (5%) ACS and seven (17%) revascularizations by PTCA. There was a weak concordance (kappa=0.279) between rest MPI and CCS, while between stress MPI and CCS it was poor (kappa=0.186). Patients with a normal rest MPI did not have cardiac events during the follow-up.

Conclusions: Patients presenting with acute chest pain and a low to intermediate likelihood of coronary artery disease, with a normal rest MPI during the acute event, have a very low probability of cardiac events one year after the index event.

Introduction

Chest pain accounts for approximately 6% of all emergency department (ED) visits [1]. Acute coronary syndromes (ACSs) cover a broad group, including ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI) and unstable angina [2]. It may take several hours after presentation before cardiac enzymes are positive and, additionally, it is well known that the electrocardiogram (ECG) can be normal in patients with acute myocardial infarction (MI) and unstable angina.

Thus, the timely identification, triage, and management of patients presenting to the ED with possible ACS remain a big concern. In addition of ECG and cardiac enzymes, cardiac imaging tests have also been used in the acute setting. Among them, acute rest myocardial perfusion imaging (MPI) in patients with suspected ACS has a high negative predictive value to exclude MI, as well as future cardiac events during medium-term follow-up (FU) [3-6]. Thus, in general, patients with normal acute rest MPI do not need to be hospitalized, avoiding unnecessary expenses. On the contrary, abnormal results are associated with a high probability of ACS and justify hospital admission for early initiation of treatment.

On the other hand, three previous studies have documented that coronary calcium score (CCS) is a rapid and efficient tool to screen patients presenting to ED with chest pain [7-9] with sensitivities of 98% to 100%, as well as high negative predictive values for identifying patients with acute MI, and very low event rates in patients with CCS=0.

Objectives

With the aim of evaluating the feasibility of performing rest gated-single photon emission computed tomography (gated-SPECT) MPI in emergency departments in developing nations, to rule out an ACS in patients presenting with chest pain and a low to intermediate likelihood of coronary artery disease (CAD), the International Atomic Energy Agency (IAEA) designed a multicenter study: “Diagnostic performance of gated-SPECT myocardial perfusion imaging at rest in patients presenting to the emergency room with chest pain and a normal or non-diagnostic ECG”. This study is still in progress.

The present work, part of this IAEA investigation, was designed with the secondary purpose of assessing whether there exists a concordance between MPI and the presence of coronary calcium in the acute chest pain setting.
Material and Methods

We studied 55 patients (mean age: 53±12 years, 58% male), who presented to the ED of the Institute of Cardiology from December 2008 to September 2010, with the following inclusion criteria: males and females 25 years of age and older that present with chest pain and a normal or non-diagnostic ECG; symptoms must have persisted for at least 15 minutes and must be present or have occurred in the six hours prior to injection of tracer; clinically stable. Exclusion criteria were: pregnancy; history of previous MI; clearly non-cardiac pain; known elevated troponin T; left ventricular bundle branch block or pacemaker.

The patient received usual care as per protocol in the institution. In addition, they were injected with 740 MBq of technetium 99m-methoxy-isobutyl-isonitrile (Tc 99m-MIBI) within six hours of the cessation of the index episode of chest pain, and a gated-SPECT MPI was performed. A multislice computed tomography for obtaining the coronary calcium score was also carried out. This study complies with the Declaration of Helsinki. The review board of the Institute of Cardiology approved the study, and written informed consent was obtained from all patients.

Patients were followed at one; six and 12 months after index event, taking into account the following:

- Major endpoints
cardiac death, non-fatal MI, admission due to ACS, and cardiac revascularization (during the first 30 days after index event).

- Secondary endpoints
non-cardiac death, positive stress MPI, and coronary angiogram with an epicardial coronary lesion ≥50%.

- Statistical Analysis
Categorical variables are expressed as numbers and percentages, and compared when necessary with the chi-square test and the McNemar test. Continuous variables are expressed as mean ± standard deviation (SD), and the non-parametric Kolmogorov-Smirnov normality test (K-S test) and Shapiro-Wilk's test were applied to check variables normalcy. According to the results, the Student t-test, the Mann-Whitney U test or the Wilcoxon's signed rank test were applied.

Relative risks (RR) were calculated with 95% confidence intervals (CI), as estimates of the risk of presenting adverse cardiac events associated with a particular variable. Concordance was assessed by the Kappa method, and the cumulative event rates were calculated by using Kaplan-Meier methods. A value of p <0.05 was considered significant.

Results

In 31 patients (56%) the index event was a typical chest pain, while in the other 24 the pain was atypical. The mean duration of the episode of pain was 35±20 minutes.

Twenty-eight patients (51%) showed a normal scan. In 16 patients (29%) the MPI was abnormal, and in 11 the perfusion result was equivocal (SRS ≤3). Mean left ventricular ejection fraction (LVEF) at rest was 68±10%. In 21 cases (38%) a stress MPI was carried out at 24±11 days after the index event. Of these, 48% had an abnormal MPI. The stress MPI was not indicated in 12 patients who were submitted to a coronary angiography. The other 22 patients refused.

Mean exercise duration was 8±2 minutes. Patients achieved a mean of 6.3±2.6 METS, with a 92±8% of maximal heart rate at peak stress. A weak concordance was found between stress test and MPI (kappa: 0.20). A post-stress LVEF increase appeared in 91% of patients; only two had a reduction, which coincided with an abnormal perfusion.

CCS was measured in 45 patients. Of these, 24 (53%) did not show coronary calcium, and 15 had CCS between 1 and 100. Only six patients (13%) had a high risk CCS, four with CCS higher than 400. Fifty percent of these high risk CCS patients had an abnormal MPI, as well as significant coronary lesions which were treated by percutaneous coronary intervention (PCI). Among patients with CCS between 0 and 100, seven had an abnormal MPI, and in one case there was an equivocal result. Four out of seven patients with abnormal MPI were treated by PCI. There was a weak concordance between MPI and CCS (kappa: 0.25).

Sixty-two percent of patients did not have an ACS. All ACS patients were admitted and coronary angiography was performed in 12: one presented ectasic coronary arteries with slow flow, one had non-significant stenosis and was followed by medical treatment, nine had significant coronary lesions (eight received stents and in the other the PCI failed), and the other one did not have epicardial coronary lesions.

No patients with normal MPI had events during the FU. The presence of a positive MPI (abnormal or equivocal results) was associated with the occurrence of events during the FU (positive vs. normal MPI: X =19.961, p<0.0001). For a patient presenting to ED with acute chest pain and a normal or non-diagnostic ECG, who had a positive MPI, the RR of having events during the first year was 7.5 (95% CI: 2.8-19.2), p<0.05. However, the presence of coronary calcium was not significantly associated with the occurrence of events in the FU (normal vs. abnormal CCS, p=0.28). For a patient presenting to ED with acute chest pain and a normal or non-diagnostic ECG, who has a positive CCS, the RR of having events during the first year was 1.77 (95% CI: 0.69-4.56), p=NS. Figure 1 shows the Kaplan-Meier curve at one-year FU.
Discussion

Our results show that the presence of a positive MPI (including both abnormal and equivocal results), was associated with the occurrence of events in the FU and, consequently, patients presenting to ED with acute chest pain and a low to intermediate likelihood of CAD, with a normal rest MPI during the acute event, have a very low probability of cardiac events one year after the index event. Nevertheless, CCS did not show an association with the occurrence of events at one-year.

MPI has been recognized by the American College of Cardiology / American Heart Association as a class IA indication for the assessment of myocardial risk in patients with possible ACS who have a non-diagnostic ECG and normal initial levels of serum markers, as well as class IB for the diagnosis of CAD in acute chest pain patients [10], with reported high sensitivity (93-100%) and negative predictive value (97-100%) [10, 11]. Thus, acute rest MPI is an important tool to identify high risk patients among those with a low risk presentation, and its evidence-based use improves prognosis and reduces costs.

In the present work, if we consider as abnormal rest MPI only those with SRS>3, 16 patients (29%) had abnormal rest perfusion; while 11 (20%) showed equivocal results (SRS ≤ 3). Our results are within the reported range: from 46% of abnormal MPI (30 out of 64 patients) [10]; 16% with abnormal perfusion and 15% equivocal [4], to only 9% (45 out of 479 patients) [6].

To consider an equivocal result as normal or abnormal may be debatable. In fact, it is difficult to consider it as normal in the course of an acute chest pain and, therefore, to not admit the patient (among our cases, in two patients -18% - with an equivocal result, a PCI was done during the first month after the index event). Another option could be to use the gated-SPECT segmental wall motion (WM) analysis. In accordance with this, Kontos et al [12] interpreted the MPI of 2 826 patients as abnormal in 40%, and as normal in 32%. The rest (patients with perfusion defects and normal segmental WM) were considered negative for ACS and classified as non-acute MPI. However, in our study this was not so useful, because mean LVEF at rest was 72% and only five cases exhibited regional WM abnormalities. Only four (44%) out of nine PCI cases showed regional WM abnormalities at rest. Nevertheless, it is important to point out that, as opposed to MI, rest ischemia does not necessarily produce regional WM abnormalities. Additionally, because of the time interval between tracer injection and image acquisition, it is possible that in some cases a transient period of ischemia that occurs at the time of injection could be resolved by the time of imaging, resulting in a perfusion defect with normal WM [12].

It is known that a normal CCS is frequently associated with a normal perfusion, but only 22% of those with abnormal or equivocal perfusion at rest had a CCS>100. A possible explanation is the mean age of our patients (53 years). CCS alone cannot rule out an ACS in the ED due to the possibility of soft vulnerable plaques. However, those patients with positive MPI and higher risk CCS have more probability of presenting significant stenosis.

Among our patients, 75% of those with abnormal MPI vs. 36% of those with equivocal results presented some kind of event during the FU, and no patient with normal MPI developed a cardiac event during the FU. Thus, a significant association was found between MPI at rest during the first six hours after the pain cessation and the occurrence of events during one year FU, with a RR of 7.5 of having some kind of event during the first year (p<0.05). This coincided with reported values of 71% and 1.5% of occurrence of events in patients with MPI abnormal and normal, respectively [4], where abnormal perfusion was the only predictor of events in multivariate analysis.

Limitation

A small sample of patients was included.
Conclusions
Patients presenting with acute chest pain and a low to intermediate likelihood of coronary artery disease, with a normal rest MPI during the acute event, have a very low probability of cardiac events one year after the index event. Coronary calcium score was not helpful to risk-stratify these patients.

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