Utility of myocardial perfusion SPECT for evaluation of patients from Chest Pain Unit

L. FRUTOS ESTEBAN, M.D. MARÍN FERRER, G. GUZMÁN MARTÍNEZ, J. RUIZ CANTADOR, C. DE PABLO AND L.M. MARTÍN CURTO

*Department of Nuclear Medicine. †Department of Cardiology. Hospital Universitario La Paz, Madrid. Spain.

SUMMARY.—The Chest Pain Units (CPU) are currently the best solution to improve management of patients with acute chest pain in the Emergency Room thanks to the use of reliable ischemia diagnostic detection tests and early treatment.

OBJECTIVE. To assess the value of myocardial perfusion SPECT (MPS) in the CPU in order to treat acute coronary syndromes (ACS) early and discharge patients with low risk of coronary artery disease (CAD) who can be treated as outpatients.

MATERIAL AND METHODS. We studied 629 patients from January 2003 to September 2005 with acute chest pain suggestive of angina, normal cardiac enzymes and normal or non-diagnostic ECG who had been referred to Nuclear Medicine for evaluation with a stress test for ischemia: 32 p treadmill stress testing and 597 p MPS (525 p exercise-rest and 72 p pharmacologic stress test). We compared the results with catheterization and clinical follow up for a 6-months period, evaluating new coronary events.

RESULTS. 76 % of MPS were normal and 24 % pathological. Only 1.5 % of the patients with normal MPS had CAD or coronary events in the follow-up, increasing to 35.2 % in patients with ischemia. A total of 45 catheterizations were performed, showing CAD 27 (24 with pathological MPS). A total of 2.6 % of the patients had coronary events during follow-up, 75 % of whom had pathological MPS.

CONCLUSION. The MPS improves diagnosis of ACS in the CPU, with a very low number of new coronary events at 6 months of the follow-up and permits safe discharge of these patients.

KEY WORDS: Chest Pain Unit, myocardial perfusion SPECT, acute coronary syndromes, ischemia detection test.

INTRODUCTION

Chest pain units (CPU) currently represent the most acceptable solution for improving the diagnosis and treatment of chest pain in the Emergency department.
Their main aim is to efficiently, rapidly and safely manage patients with chest pain who attend hospital emergency departments, classifying them in different risk groups, and having two fundamental objectives: to effectively detect acute coronary syndrome (ACS) early and to efficiently separate patients with low risk of coronary artery disease (CAD) who can be treated as outpatients.2,3

The final result translates to a better cost-effectiveness relationship, thanks to improvement in the quality of medical care, reduction in the number of inappropriate hospital discharges, reduction in the number of unnecessary admissions, and the reduction in medical costs.4

The diagnostic methods recommended in guidelines and protocols for use in CPU2,5-7 are serial electrocardiograms (ECG),2,5,6 chest X-ray,2 biochemical markers of myocardial damage,6,9 resting echocardiography,4,5 resting myocardial perfusion single photon emission tomography (MPS)4,10-13 and ischaemia provocation tests (conventional ergometry,14-17 stress echocardiography2,18,19 and post-stress/rest MPS20-25).

MPS currently constitutes a non-invasive, safe, precise and cost-effective diagnostic method in the assessment of CAD, and provides important information on myocardial perfusion and ventricular function, as well as prognostic information.

Its diagnostic efficacy is superior to conventional ergometry2,7 and similar in general terms to stress echocardiography,2,26-28 although its greater availability and experience in our hospital at present make MPS the ischaemia provocation test of choice.

As the creation and functioning of CPU in all Spanish hospitals is still not generalised, and due to the short time since its creation in the US in the eighties, the literature does not contain sufficient studies with large patient numbers and follow-up which justify the usefulness of MPS in these Units. The objective of this study therefore consists in demonstrating the usefulness of MPS in the CPU, in order to permit rapid diagnosis of patients attending the Emergency Department with acute chest pain, so that those patients with ACS are detected, thereby allowing both their admission and establishment of early treatment, and those patients with a low risk of CAD are ruled out, which will allow them to be discharged safely as a low incidence of coronary events was demonstrated in the following 6 months.

MATERIALS AND METHODS

Study group

Study and monitoring of all patients assessed by the CPU in the Emergency department of our hospital, and who were referred to the Nuclear Medicine Department for an ischaemia provocation test, were carried out from January 2003 to September 2005.

A total of 629 patients (60.6% men, 39.4% women), with a mean age of 62.5 years (standard deviation 12.3), who had attended the Emergency department with acute chest pain suggestive of coronary origin were included. The patients remained asymptomatic for at least 6 hours in the Emergency department; they did not show elevation of serial biochemical markers for myocardial damage (creatine kinase myocardial isoenzyme [CK-MB] and troponins) and the serial ECGs were normal or not diagnostic of ischaemia.

The cardiovascular risk factors (CVRF) detected in these patients are shown in figure 1; among them, the predominant factors were smoking (which included smokers and ex-smokers) and arterial hypertension.

Ischaemia provocation tests

The ischaemia provocation tests performed in our Department were (fig. 2): conventional ergometry in 32 patients (5 %) and MPS in 597 patients (95 %), of which post-exercise/rest MPS was performed in 525 patients and post-pharmacological stress/rest MPS was performed in 72 (64 patients were administered dipyridamole and 8 dobutamine).

![Fig. 1.—Distribution of cardiovascular risk factors. AHT: arterial hypertension; AMI: acute myocardial infarction; DL: dyslipidaemia; DM: diabetes mellitus; IC: ischaemic cardiopathy; SMOKE: smoking.](image-url)
Myocardial perfusion single photon emission tomography protocol

MPS was performed in all cases following the usual protocol. The patient first underwent an ergometric physical exercise test on a treadmill (modified maximum Bruce protocol) or a pharmacological stress test (using dipyridamole or dobutamine according to the patient’s clinical characteristics), in all cases with intravenous 99mTc-sestamibi (740 MBq) injection at the peak of maximum effort. One hour later, topographic images were acquired by a dual head gamma camera (Philips Axis) with rotating support and variable angle, using a 64 × 64 matrix and obtaining 64 images in a 180° elliptical orbit for approximately 20 minutes, using an attenuation correction device. The images acquired were then processed by reconstruction using filtered back projection, application of filters (low pass), repositioning of the cardiac axes, detection of possible artefacts and display of images following the short axis, horizontal long axis and vertical long axis of the heart. The resting study was then carried out according to the 2-day long protocol (the following day if the patient remained admitted or in a maximum of one week if they were discharged).

Interpretation of the myocardial perfusion single photon emission tomography

For interpretation of the images, a comparison was made between the results obtained with attenuation correction on effort and at rest, analysing 17 segments (manual or visual mode) in both studies, and correlating it with the coronary territories.

The results of these images were interpreted for the sake of simplicity as normal (no evidence of perfusion defects) and pathological, with the latter being divided into necrosis, ischaemia and necrosis plus ischaemia. The perfusion defects were classified according to their extent into small (one segment), medium (2-3 segments) and large (more than 3 segments).

Clinical management and follow-up

Patient management for the diagnosis of CAD was according to the decision tree used by the hospital CPU (fig. 3), so that after carrying out the stress MPS, the patients were reassessed to decide their treatment and clinical follow-up.

To that end, patients who were considered at high risk of having CAD according to the ergometry results (for example: early positive responses, presence of ventricular arrhythmias, hypotensive responses on effort), MPS results (severe perfusion defects and more than one segment) and/or clinical criteria (chest pain very suggestive of CAD) were admitted to complete their study and have catheterisation performed.

Patients considered to have intermediate risk (for example: late positive responses, mild/moderate diffusion defects or of one segment only) were discharged with medical treatment, underwent a resting study in the days following discharge to detect the presence of ischaemia and were then re-evaluated in the hospital’s CPU outpatients with these results for monitoring and/or changes in treatment.

Low risk patients (everything normal) were discharged with or without treatment according to the CVRF or clinical characteristics.

Patients were monitored a period of 6 months after discharge by:

1. Catheterisation results in the patients in whom it had been performed, either on diagnosis (in their hospital study by the CPU) or subsequently during the 6 month follow-up (performed as outpatients), considering as positive a catheterisation in which a level of coronary stenosis equal to or greater than 70% was detected.

2. Readmission to the Emergency department or the Cardiac Unit after discharge due to a new coronary event.
3. Clinical follow-up by telephoning patients without performing angiography or readmission to hospital in order to check satisfactory clinical evolution or detect new coronary events since discharge (unstable angina, acute myocardial infarction [AMI], death of cardiac origin).

**RESULTS**

**Ergometry results**

No significant adverse events occurred during the physical or pharmacological stress tests.

The results obtained in the 32 conventional ergometries were: 26 (81.3%) conclusive and 6 (18.7%) inconclusive, with a distribution of clinical responses (CR) and electrical responses (ER) as shown in table 1. In these 32 conventional ergometry patients, catheterisation was performed on only 2, who did not show coronary lesions, and only one patient (with negative CR and ER) had a coronary event (AMI) during follow-up, which was shown in the subsequent coronary angiography as an obstruction in the marginal oblique artery.

The results of the 597 MPS stress tests were: 407 (68.2%) conclusive and 190 (31.8%) inconclusive,
with a CR and ER distribution as shown in table 2, the results of which are analysed below.

**Myocardial perfusion single photon emission tomography results**

Of the 597 MPS performed, 451 (76%) were normal and 146 (24%) were pathological (fig. 4). Table 3 shows the relationship of the MPS results with catheterisation (cate) and coronary events (unstable angina, AMI and death).

A total of 45 catheterisations were performed, of which 27 showed coronary lesions (24 with abnormal MPS): 14 patients had lesion of one vessel, 9 had lesion of 2 vessels, 2 had lesion of 3 vessels and 2 had multivessel lesions. Six patients had a positive with a CR and ER distribution as shown in table 2, the results of which are analysed below.

**Table 1**

<table>
<thead>
<tr>
<th>CR – or Inconclusive</th>
<th>ER +</th>
<th>CR + or Inconclusive</th>
<th>ER – or Inconclusive</th>
<th>CR + or Inconclusive</th>
<th>CR – or Inconclusive</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conclusive</td>
<td>68.2 % (407 p)</td>
<td>64.9 % (264 p)</td>
<td>1.5 % (6 p)</td>
<td>25.5 % (104 p)</td>
<td>3.4 % (14 p)</td>
</tr>
<tr>
<td>Inconclusive</td>
<td>31.8 % (190 p)</td>
<td>60.0 % (114 p)</td>
<td>0.5 % (1 p)</td>
<td>31.0 % (59 p)</td>
<td>3.2 % (6 p)</td>
</tr>
</tbody>
</table>

CR: clinical responses; ER: electrical responses; p: patients.

**Table 2**

<table>
<thead>
<tr>
<th>MPS (597 p)</th>
<th>CATE –</th>
<th>CATE +</th>
<th>Angina</th>
<th>AMI</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>(451 p, 76%)</td>
<td>6</td>
<td>3* + 5 Ach</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Pathological</td>
<td>(146 p, 24%)</td>
<td>2</td>
<td>1*</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

*Two patients with impairment of one vessel and one patient with impairment of 2 vessels. *Impairment of one vessel. *Due to acute myocardial infarction. *Eight patients with impairment of one vessel, 6 with impairment of 2 vessels and one with impairment of 3 vessels. *Two patients with impairment of one vessel, 2 with impairment of 2 vessels, one with impairment of 3 and two with multivessel impairment.

Ach: acetylcholine test; AMI: acute myocardial infarction; CATE: catheterisation; I 1 seg: ischaemia of one segment; I 1 seg: ischaemia of more than one segment; N: necrosis; N + I: necrosis plus ischaemia.

**Table 3**

<table>
<thead>
<tr>
<th>MPS (597 p)</th>
<th>CATE –</th>
<th>CATE +</th>
<th>Angina</th>
<th>AMI</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>(451 p, 76%)</td>
<td>6</td>
<td>3* + 5 Ach</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Pathological</td>
<td>(146 p, 24%)</td>
<td>2</td>
<td>1*</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

*Two patients with impairment of one vessel and one patient with impairment of 2 vessels. *Impairment of one vessel. *Due to acute myocardial infarction. *Eight patients with impairment of one vessel, 6 with impairment of 2 vessels and one with impairment of 3 vessels. *Two patients with impairment of one vessel, 2 with impairment of 2 vessels, one with impairment of 3 and two with multivessel impairment.

Ach: acetylcholine test; AMI: acute myocardial infarction; CATE: catheterisation; I 1 seg: ischaemia of one segment; I 1 seg: ischaemia of more than one segment; MPS: myocardial perfusion single photon emission tomography; N: necrosis; N + I: necrosis plus ischaemia.
acetylcholine (Ach) test with absence of coronary lesions.

As can be seen in table 3, of the 451 patients with normal MPS, 444 (98.4%) did not undergo catheterisation or showed absence of coronary lesions in it, and none presented new coronary events in the follow-up time. 14 of these patients had catheterisation performed despite not noting alterations in the perfusion images: in 6 of these, this was due to positive ergometry (1 patient showed lesion of 1 vessel, 2 positive Ach test and the remainder of the patients had normal catheterisation); in 6 others it was due to clinical symptoms very suggestive of ischaemic cardiopathy (IC) with associated CVRF (1 patient with lesion of 1 vessel, 3 with positive Ach test and the rest normal); in 1 it was patient due to suspicion of progression of their CAD as they had a previous AMI with known non-significant coronary obstruction (lesion of 2 vessels on catheterisation) and in the last patient it was due to prior admission two months earlier with similar symptomatology (normal catheterisation).

Four patients with normal MPS had a new coronary event during the follow-up time: 3 anginas (2 patients with ergometry with positive CR and ER) without subsequent coronary angiography carried out and 1 non-Q AMI (negative ergometry) with revascularisation of the anterior descending artery.

Therefore, 1.5% of patients with normal MPS showed coronary lesions on catheterisation or had a new coronary event during follow-up.

One hundred and forty-six pathological MPS were obtained: 91 (62.3%) showed evidence of some reversible defect (ischaemia) and 55 (37.7%) had a fixed defect (necrosis).

Of the all patients with isolated necrosis without ischaemia, 1 patient showed coronary lesion of one vessel, 1 had angina (without subsequent coronary angiography), 1 AMI (with lesion of 3 vessels on the subsequent catheterisation) and 1 died due to cardiac causes (AMI during revascularisation surgery). One patient died due to a non-cardiac cause (pneumonia) during follow-up. Therefore, the total of coronary lesions shown or coronary events in these patients with necrosis on MPS was 7.3%.

A total of 91 patients with ischaemia were obtained (40 of these were ischaemia of one segment only and 24 were ischaemias associated with necrosis), so that the overall percentage of ischaemia in all the CPU patients with MPS was only 15.2%. 30 of these patients had catheterisation performed, which showed coronary lesions in 23 of them (76.6%). The remainder of the patients were treated medically and had favourable evolution. Nine patients with ischaemia on MPS (9.9%) had a coronary event (angina) in the follow-up time (5 with subsequent coronary angiography and coronary obstruction).

10% of patients with ischaemia of only one segment presented coronary lesions on the catheterisation or a new coronary event (angina).

Thus, the total percentage of coronary events or coronary lesions demonstrated in these patients with ischaemia on MPS was 35.2%.

The total percentage of coronary events during follow-up was 2.6% (16 patients): 13 cases corresponded to unstable angina, 2 to AMI and 1 to death of cardiac origin (AMI during revascularisation surgery). 75% of these patients who developed a coronary event had a MPS with evidence of perfusion alterations.

**DISCUSSION**

In our hospital, the CPU regularly carries out MPS stress tests as the ischaemia provocation test of choice for the study of its patients. Conventional ergometry was only performed when MPS was unavailable. Therefore, we will concentrate on analysing only the MPS stress tests. However, and although the study was not planned to compare conventional ergometry with MPS but to demonstrate the efficacy of our method in the CPU, we can briefly analyse and compare the gammagraphic results with the ergometry results.

Therefore, first analysing the results of the ergometry performed prior to obtaining the gammagraphic images in the 597 MPS, we observed a high percentage of negative CR and ER in these patients, as shown in results table 2 (64.9% in the conclusive and 60% in the inconclusive), which agrees with the fact that the patients assessed by the CPU are patients with low-moderate risk of CAD and which will usually be normal. However, it is worth noting that there is a considerable percentage of tests which are not diagnostic (25.5% of the conclusive and 31% of the inconclusive) as they present non-assessable or inconclusive ER with non-positive CR (negative or inconclusive), which if having carried out conventional ergometry only would have required
subsequently performing another more sensitive and specific ischaemia provocation test to reach a diagnosis.\textsuperscript{25}

As regards the MPS results and their correlation with catheterisation and coronary events, we can highlight various aspects:

1. The percentage of coronary events or CAD demonstrated by catheterisation was 1.5\% in patients with normal MPS, rising to 7.3\% in patients with necrosis and to 35.2\% in patients with ischaemia on the MPS, a result which was significantly higher than that obtained in patients with normal MPS. These values show that a normal MPS without perfusion alterations will allow us to safely discharge these patients from the CPU.\textsuperscript{22} On the other hand, it can be concluded from these results that not only must attention be paid to patients with ischaemia on the MPS, but those patients admitted to the CPU and who show necrosis must be closely monitored, due to the increase in the probability of events that we obtained in comparison to patients with normal MPS.

2. It is noticeable that only 30 of the 91 patients with ischaemia on the MPS had catheterisation performed, but it should be taken into account that 44\% of these ischaemias were of one segment only, so performing catheterisation was not clear and it was finally decided to opt for medical treatment and follow-up in these patients. However, it is worth noting that up to 10\% of these patients with ischaemia of one segment showed CAD on the catheterisation or had a new coronary event, which should be taken into account in management of these patients.

3. Of the 30 catheterisations carried out on patients with ischaemia on the MPS, 76.6\% (23 patients) showed coronary lesions. Once the perfusion images had been re-evaluated \textit{a posteriori} in these patients, we confirmed that the false positive results on MPS were attributable in all cases to attenuation artefacts\textsuperscript{30} which were not detected either because the attenuation correction had not been applied correctly in those patients, or because despite being applied correctly, other factors coexisted (extracardiac activity in the inferior wall in the resting study) which led to an error in interpretation of those studies.

4. Of all the patients with ischaemia on MPS, confirmed by the demonstration of coronary obstruction on the catheterisation or an event in the follow-up (32 patients), 23 (71.8 \%) had ergometry which was negative or non-diagnostic for ischaemia, which demonstrates the superior sensitivity of MPS in the assessment of CAD in comparison with conventional ergometry.\textsuperscript{25}

5. As a limitation of our study, we can highlight that the low percentage of catheterisations carried out does not allow us to reliably calculate the sensitivity, specificity and predictive values.

In addition, 8\% of patients were lost to follow-up and their evolution was not available, although in any case, these patients did not undergo catheterisation or readmission to our hospital, so we assume satisfactory evolution as they were patients with low risk of CAD.\textsuperscript{31}

Finally, in our study group we included patients with a history of IC which therefore had a higher probability of presenting perfusion alterations than the other patients. However, the objective of our study was to perform a global analysis of all the patients who had been assessed by the CPU (which includes patients with history of IC) to assess the usefulness of our method in this Unit, not to conduct a comparative study of the results according to the patients’ characteristics.

**CONCLUSIONS**

In patients who attend the Emergency department with acute chest pain suggestive of CAD, with normal serial cardiac enzymes and ECG normal or not diagnostic of ischaemia, observation in the CPU and performance of a stress MPS in the first 24 hours discriminates patients with CAD from those who do not suffer it.\textsuperscript{32} Therefore, the management of low-moderate risk patients with chest pain in a CPU allows correct stratification and early, safe patient discharge, with excellent prognosis in the short-mid term, and avoiding both inappropriate discharges and unnecessary admissions.\textsuperscript{2,4}

For the proper functioning of the CPU, it is essential to use action protocols\textsuperscript{2,6} which allow proper risk stratification to be made, as well as to have the collaboration of a multidisciplinary team composed of cardiologists, emergency physicians and nuclear medicine physicians.\textsuperscript{3}

MPS is currently the ischaemia provocation technique of choice in our hospital since it is a safe, reliable technique which improves the diagnosis of CAD in CPU patients, with a very low percentage of coronary events during the first 6 months after
discharge. Therefore, it allows high risk patients to be detected, who should be treated early or admitted to continue their study, while patients with normal MPS can be discharged with confidence, thereby reducing the hospital stay and the number of unnecessary admissions.

BIBLIOGRAPHY


