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Role of myocardial perfusion imaging in risk stratification

Sobhan Vinjamuri, Radhakrishnan Jayan

Nuclear Medicine Department, Royal Liverpool University Hospital, Liverpool, UK

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ABSTRACT

This review paper is based on a topic invited for review presented by the first author at the Annual Meeting of Society of Nuclear Medicine of Serbia and Montenegro, September 2003.

The optimal management of patients affected by coronary artery disease requires safe and cost-effective techniques for assessing the risk of subsequent cardiac events or the need for surgery. The ideal test should distinguish between high risk patients who will benefit from aggressive management and low risk patients who can be managed conservatively. Stress testing alone is believed to be inadequate for the assessment of risk. Nuclear Medicine techniques have routinely been used in the identification of patients with ischaemic heart disease and those with viable myocardium post myocardial infarction. While the essential methodology for the techniques remains same, the reporting and interpretation criteria for determining future risk are different. For instance, a fixed perfusion defect on stress myocardial perfusion imaging in a patient presenting cardiac-type chest pain to the cardiologists for the first time, has a different value from a similar patient being presented to the non-cardiologist for major vascular surgery.

A review of the literature concerning the current usage of nuclear cardiology techniques in risk stratification is presented.

Key words: myocardial perfusion imaging, risk stratification

The extent of myocardial ischaemia and left ventricular function are important factors that affect the prognosis in patients with Coronary Artery Disease (CAD). By possessing the ability to detect and quantify the extent of myocardial ischaemia and assessing left ventricular function, myocardial perfusion scintigraphy (MPS) has become an important tool to obtain prognostic information in patients with Coronary artery disease.

Many studies have shown that MPS in addition to being an independent prognostic marker also gives incremental prognostic information even when the results of clinical evaluation, exercise electrocardiogram and coronary angiography are available [1, 2].

Hachamovitch et al. [2] followed up 5183 patients who underwent MPS for the occurrence of cardiac death or myocardial infarction over a mean follow up of 642 $\pm$ 226 days. They found that patients with normal scans were at low risk and rates of both outcomes increased significantly with worsening scan abnormalities. Patients with normal MPS were found to have a low annual event rate (0.3% cardiac death and 0.5% nonfatal MI). As the severity of perfusion defects increased, so did the cardiac event rates. Patients with mildly abnormal scans were found to be at low risk of cardiac death but at intermediate risk of myocardial infarction. These patients were thought to benefit from medications proven to reduce the risk of myocardial infarction, whereas those with more severe defects needed a coronary angiogram and subsequent intervention. The number, extent and severity of perfusion defects, summed stress scores, the presence of a pattern suggestive of multivessel CAD and transient ischaemic dilatation were all significantly associated with the occurrence of cardiac events.

Hachamovitch et al also showed that in a patient population with no evidence of previous coronary artery disease at overall low risk, MPS adds incremental prognostic information and risk-stratifies patients even after clinical and exercise information is known [3].

Strattman et al [4] evaluated the role of Tc-99m sestamibi myocardial imaging compared to exercise ECG testing in patients referred for stable angina. During 1 year of follow-up, cardiac events occurred in only 0.5% of patients with normal MIBI scans compared with 7% of those with abnormal MIBI scans ($p < .001$). They demonstrated that as with exercise thallium-201 myocardial imaging, exercise stress technetium-99m MIBI myocardial tomography provides significant independent information concerning the subsequent risk of serious cardiac events (death, myocardial infarction) in patients with stable angina pectoris. The recognized imaging and radiotracer biokinetic differences between thallium-201 and technetium-99m MIBI do not appear to modulate the prognostic value associated with scintigraphic evidence of ischaemic myocardial jeopardy in the stable angina population.

Correspondence to: Dr. S. Vinjamuri
Nuclear Medicine Department
Royal Liverpool University Hospital
Prescot Street, Liverpool L7 8XP, UK
Tel : (+44) 151 706 44 62, fax : (+44) 151 706 58 44
e-mail: Sobhan.Vinjamuri@rlbuh-tr.nwest.nhs.uk

Gibbons et al. [5] found that in patients with intermediate risk Duke scores after treadmill testing (DTS), MPS was useful. In patients with intermediate DTS, there was an overall 2.5% event rate. Patients in this group with a normal or near normal MPS scan were found to be at a low risk of subsequent cardiac death (0.4%) and can be safely managed medically without the need for coronary angiography, whereas a severely abnormal scan raised the risk to 8.9%. This identification of subgroups at greater risk of cardiac events is important in patient management.

Quantitative and semi-quantitative analyses of myocardial perfusion images have been found to be helpful in classifying the level of risk associated with specific scan results.

The summed stress score (SSS), as determined by visual interpretation of images, is an evaluation of the extent and severity of abnormalities. It has been found useful in the risk stratification of cardiac patients. Interpretation is based on a typical 20-segment model and the scoring system increases from 0, which represents normal perfusion, to 4, which represents poor perfusion. Therefore, a higher SSS represents poorer perfusion and hence a poorer prognosis.

While clinical examination and patient history, exercise testing and coronary angiography have all been validated in the diagnosis and risk stratification of patients with known or suspected CAD, myocardial perfusion imaging has not only been validated but has been proven to provide both independent and incremental prognostic value over that provided by clinical, exercise and angiographic data.This was demonstrated by Pattillo [6] in his study of 732 patients referred for investigation of chest pain and followed up for a mean period of 41 months. These patients underwent symptom-limited exercise testing, coronary angiography and thallium imaging within 3 months of each other. The treadmill exercise score (TES) used is now known as the Duke treadmill score. The Gensini score served as a measure of the severity of angiographic disease. In this study, the prognostic power of perfusion imaging was greater than that of any of the other investigations in both independent and incremental analyses. The study highlights the independent predictive value of clinical variables, treadmill exercise scores, Gensini angiography scores and SPECT defect size. Results of MPI are significantly more predictive of future cardiac events.

Chatziiannou et al. [7] challenged the premise that high exercise tolerance is associated with a low cardiac event rate. Her group showed that high exercise tolerance does not predict a low cardiac event rate when abnormal myocardial perfusion is present. She studied 388 consecutive patients who underwent exercise MPS with dual isotope exercise-sestamibi/rest-thallium imaging and achieved at least Bruce stage IV. A follow-up at 18 $\pm$ 2.7 months tracked revascularization, myocardial infarction and cardiac death. At the follow-up, 6.2% of patients with an abnormal stress test and 5.5% of those with a normal stress test experienced a cardiac event. Patients with normal myocardial perfusion imaging had a 1.7% rate of adverse cardiac events. In contrast, 12.2% of patients with abnormal MPI experienced adverse cardiac events. Exercise ECG results, even with the addition of Duke treadmill score failed to approach the predictive power of myocardial perfusion imaging.

Sharir et al. [8] followed 1680 consecutive patients who underwent dual-isotope (rest-thallium/stress-sestamibi) gated SPECT for a period of 569 $\pm$ 106 days. They found that both post-stress left ventricular ejection fraction and post-stress left ventricular end systolic volume had incremental prognostic value over pre-scan and perfusion data in predicting cardiac death. They concluded that, compared to perfusion data alone, post-stress gated SPECT provide incremental prognostic information in patients with known or suspected CAD. Myocardial perfussion scintigraphy therefore, offers incremental prognostic value over clinical, exercise test and angiographic evaluations in predicting cardiac events and can risk stratify patients for cardiac death and MI regardless of presence or absence of known CAD. Its prognostic value is enhanced by post-stress LVEF and ESV measurement.

Up to this point the use of risk stratification has been discussed in general populations of patients with and without known CAD. However, several subgroups like women and diabetics have been found to present particular challenges and opportunities. In Hachamovitch's initial study, the incremental value of MPS over other diagnostic modalities were found to be more markedly evident in women, probably because of the inherent weakness of stress ECG in women.

Kang et al. [9] in 1999 studied the incremental prognostic value of adenosine stress MPS with sestamibi dual isotope myocardial perfusion imaging in women versus men and explored the prognostic impact of diabetes mellitus. They found a similar prognostic impact of MPS in both men and women and that MPS was appropriately influencing subsequent invasive management decisions in both genders.

They also found that diabetic patients experienced significantly more cardiac events over the follow-up period than did their non-diabetic counterparts. Hence, MPS plays a very important role in risk stratifying diabetics who are a high risk population for cardiac events.

Coronary artery disease represents a major risk in patients undergoing non-cardiac surgical procedures in whom the stress of surgery and postoperative recovery can represent a significant ischaemic burden. Leppo [10] recommends that MPS should have an important role in non-invasively assessing patients who are high risk according to clinical criteria especially before high-risk procedures such as vascular, intra-abdominal or thoracic and major orthopaedic operations. 15–20% of patients referred for an assessment with MPS can be expected to show severe defects requiring angiography and intervention.

The role of risk stratification before major surgery is to identify patients at low risk for events in whom surgery can proceed; to identify those patients with CAD who can safely undergo surgery with anti-ischaemic medications and perhaps with invasive monitoring, as required; and to identify those patients at high risk for cardiac complications in whom pre-operative angiography and revascularization may be required. Lette et al. [11] showed that the post-operative and long term cardiac event rate were 1% and 3.5% respectively, in patients with normal scans or fixed perfusion defects, and 17.5% and 22% in patients with reversible defects. Thus, there is clear clinical benefit to be derived in identifying those patients in whom risk for peri-operative and post-operative cardiac events is unacceptable and in whom steps need to be taken to mitigate the risk.

Myocardial perfussion scintigraphy has shown promise in evaluating chest pain in the setting of the emergency room. The current

guidelines of the American college of cardiology [12] also support this view and recommend a place for MPS in the algorithm of evaluation of patients presenting with chest pain to the emergency department. According to this algorithm, four risk levels are used for chest pain: non cardiac, chronic stable angina, possible acute coronary syndrome (ACS) and definite ACS. Radionuclide imaging is recommended as being most appropriate in the subgroup of patients with possible ACS. After the initial trial on the basis of symptoms, ECG, and history, rest SPECT imaging appears to be useful for identifying those at high risk (those with perfusion defects), who should be admitted, and patients at low risk (those with normal scans), who in general may be discharged home with a low risk of subsequent ischaemic events.

In conclusion, myocardial perfusion scintigraphy has been shown to have a proven value in risk stratification and predicting future cardiac events in both an unselected general population as well as specific high-risk groups such as diabetic patients.

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