Comparison of stress-only vs. stress/rest with technetium-99m methoxyisobutylisonitrile myocardial perfusion imaging

Daniel F. Worsley¹, Anthony Y. Fung², David B. Coupland¹, Cori G. Rexworthy¹, George P. Sexsmith¹, and Brian C. Lentle¹

¹ Divisions of Nuclear Medicine and ² Cardiology, Vancouver General Hospital, 855 West 12th Avenue, Vancouver, B.C. V5Z 1M9, Canada

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Abstract. Unlike conventional thallium-201 myocardial imaging. technetium-99m methoxyisobutylisonitrile (MIBI) requires separate stress and rest injections. We prospectively studied 148 consecutive patients referred for myocardial perfusion studies to determine the diagnostic value of rest images once normal exercise or dipyridamole tomographic images had been obtained. In patients referred with no history of previous myocardial infarction in whom the diagnosis of coronary artery disease was suspected, 45 of 109 (41%) patients had normal stress tomographic images. Obtaining rest images did not alter the final interpretation in any of these cases. From this we infer that in patients with normal images after exercise or dipyridamole administration and no past history of myocardial infarction, ^{99m}Tc-MIBI rest images are not required. This provides several advantages including increased speed of diagnosis, decreased patient radiation exposure, improved cost efficiency and decreased demand on tomographic camera time.

Key words: Coronary artery disease/diagnosis – Methyoxyisobutylisonitrile

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Introduction

Exercise thallous chloride ²⁰¹Tl myocardial perfusion imaging has been used extensively in the investigation and identification of patients with physiologically important coronary artery disease (CAD). The ability to identify patients with stress-induced ischaemia, and thus at subsequently increased risk for cardiac events, has important prognostic implications (Eagle et al. 1987; Iskandrian et al. 1986; Koss et al. 1987; Staniloff et al. 1986).

More recently, technetium-99m methoxyisobutylisonitrile (MIBI) has been used in the non-invasive assessment of myocardial perfusion in patients with CAD. When used in conjunction with single photon emission tomography (SPET) imaging, ^{99m}Tc-MIBI may be superior to conventional ²⁰¹Tl myocardial imaging (Hassan et al. 1990; Kahn et al. 1989; Larock et al. 1990). Both ²⁰¹Tl and ^{99m}Tc-MIBI uptake in the myocardium is, for practical purposes, proportional to coronary blood flow. However, unlike ²⁰¹Tl, the ^{99m}Tc-MIBI kinetics are such that once taken up by the myocardium no significant redistribution of the radiopharmaceutical occurs (Glover and Okada 1990; Marshall et al. 1990; Williams et al. 1989). As a consequence, separate injections at rest and after stress are required to differentiate persistent myocardial perfusion defects from transient ones. Several imaging protocols for stress ^{99m}Tc-MIBI myocardial perfusion have been proposed (Taillefer et al. 1989).

The purpose of this study was to determine whether or not rest images were required if normal ^{99m}Tc-MIBI SPET images after exercise or dipyridamole administration have been obtained.

Methods

We prospectively studied 148 consecutive patients referred for stress myocardial perfusion studies. For the purposes of the study, patients were divided into two groups. Group 1, the "diagnostic group", consisted of patients who were referred with no past history of myocardial infarction (MI) and in whom the dignosis of CAD was suspected. Group 2, the "prognostic group", consisted of patients who were referred with a past history of MI and in whom the diagnosis of reversible ischaemia was suspected. For patients to be included in the prognostic group, at least 2 of the following 4 criteria had to be met: a history consistent with myocardial infarction, definite electrocardiogram (ECG) evidence of infarction, documented increase in cardiac enzymes or akinetic wall motion as detected by ultrasound or radionuclide angiography.

In the diagnostic group there were 109 patients, comprising 65 men and 44 women. The mean age was 59 years (range 29-

Offprint requests to: A.Y. Fung

85 years). The prognostic group included 39 patients (28 men and 11 women). The mean age was 56 years (range 42–79 years).

The 99m Tc-MIBI used was the standard Dupont preparation, Cardiolite (Dupont, Billerica, Mass.). A maximum of 5600 MBq of sodium pertechnetate in 1–3 ml was added per vial. Radiochemical purity was measured by thin layer chromatography and was >95% in all preparations.

Imaging protocol. A 2-day protocol was employed in which exercise or dipyridamole images were performed on day 1, and rest images were obtained on the following day. Patients discontinued taking all cardiac medication, except nitrates, 48 h prior to testing. Methyl xanthine medication (theophylline) was discontinued 72 h, and caffeine 24 h, before imaging.

Exercise images were performed following a symptom-limited upright treadmill stress test, employing a standard Bruce protocol. Exercise was terminated due to worsening chest pain, development of dysrthymia, dyspnoea, fatigue or ST segment changes on the ECG. Approximately 1 min before the completion of exercise, 740 MBq of ^{99m}Tc-MIBI was given intravenously. Tomographic imaging was then performed 1 h later. Rest images were carried out the following day, again 1 h after the administration of 740 MBq of ^{99m}Tc-MIBI.

Patients who were unable to achieve 85% of their maximum predicted heart rate with an upright treadmill test were given 0.14 mg/kg·min dipyridamole intravenously over 4 min, followed by light isometric exercise. Four minutes following the completion of the dipyridamole infusion the patients received 740 MBq of 99m Tc-MIBI intravenously. Tomographic images were acquired 1 h later.

Following exercise or dipyridamole infusion, patients were given 250 ml of homogenized milk and instructed to eat a small fatty meal in order to aid hepatobiliary clearance of the radiopharmaceutical before imaging.

Image acquisition and data processing. Image acquisition was performed either on an Adac Genesys or Siemens Rota SPET system. Both cameras employed a 15% window centered over the 140 keV photopeak of ^{99m}Tc. Data were entered into an Adac 33,000 computer. Patients were positioned supine and imaged from left posterior oblique (LPO) 45 to right anterior oblique (RAO) 45 utilizing a step-and-shoot acquisition with 20 s/step and 60 steps. Images were collected onto a $64 \times 64 \times 16$ matrix. Non-corrected data were processed using filtered back-projection (Butterworth filter) to produce transverse, vertical and horizontal longitudinal tomographic images.

Interpretation was performed using a colour video display, and consensus was obtained from three observers. All of the images were of diagnostic quality. On viewing, the interpreters were not aware of the patients' clinical history and stress test findings. Exercise or dipyridamole images were interpreted prior to and independently of the rest images. Stress images were initially reported as normal, equivocal or abnormal. Subsequently, both stress and rest images were analysed, and a final interpretation was then arrived at.

Results

A total of 148 patients were studied. Thirty-two had equivocal, and 70 had abnormal stress images. Of the 46 patients who had normal stress images, all were also



Fig. 1. Normal stress-only interpretation, 100% of the patients with a normal stress-only interpretation also had a normal stress/rest interpretation



Fig. 2. Stress electrocardiogram (ECG) results in patients with a normal stress-only interpretation

normal on the final interpretation (Fig. 1). Obtaining rest images in these patients did not alter the final interpretation in any patient. Among patients with a previous MI, stress images were rarely normal (1/39). However, even for this single patient, obtaining the rest images did not alter the final interpretation. For patients in the diagnostic group, 41% (45/109) had normal stress images, and obtaining rest images did not add any further diagnostic information.

Of the 46 patients with normal stress images on stress-only interpretation, 14 had dipyridamole infusion, and 32 had undergone an exercise test. Exercise testing alone was unable to be used to discriminate patients who had normal exercise myocardial perfusion images. A positive or non-diagnostic exercise tolerance test was obtained in 50% (16/32) of patients who had normal stress images on stress-only interpretation (Fig. 2).

In patients whose stress-only images were reported as equivocal (n=32) or abnormal (n=70), 75% (24/32)and 5.7% (4/70), respectively, were reclassified as normal when the rest images were reviewed (Figs. 3, 4). The majority of the patients who were reclassified as normal (19/28) had an apparently decreased perfusion in the inferior wall of the myocardium. This apparently decreased perfusion was likely due to attenuation associated with supine imaging and the scanning table.



Fig. 3. Equivocal stress-only interpretation



Discussion and conclusion

With conventional ²⁰¹Tl-thallous chloride imaging, stress and redistribution images can be obtained from a single injection. Reinjection of additional thallium following rest imaging or after a 24-h delay has also been suggested (Dilsizian et al. 1989; Kait et al. 1988). These techniques appear preferable compared with conventional thallium imaging in assessing myocardial viability. In spite of normal stress-only ²⁰¹Tl images, abnormalities such as reverse redistribution can be identified when both the stress and 4-h redistribution views are examined (Wackers 1988). Since no appreciable redistribution occurs with ^{99m}Tc-MIBI, separate stress and rest injections are required.

Although interobserver variability calculations were not performed, there was generally good agreement among interpreters, particularly for patients with normal stress images. The interpreters' threshold for diagnosing a normal image based on the stress image alone was quite high. Only images which had a homogenous distribution of activity and no areas of defective or decreased perfusion were called normal (Fig. 5).

Patients who have had a previous MI rarely have normal stress images and will invariably require both stress and rest imaging. On the other hand, 41% of patients in our population who had not had a previous



Fig. 5. Normal short-axis stress and rest images. The diagnosis of a normal study can be made from interpreting just the stress images



Fig. 6. Suggested algorithm for technetium-99m methoxyisobutylisonitrite myocardial perfusion imaging

MI had normal stress tomographic images. Obtaining images after injection at rest in these patients does not add any further diagnostic information. As a consequence, we find no need to perform a rest examination in patients with normal stress-only myocardial perfusion images and propose the accompanying algorithm for ^{99m}Tc-MIBI myocardial perfusion imaging (Fig. 6).

In using the proposed algorithm, patient scheduling presents logistical problems. However, evaluation of the stress images immediately following acquisition, before the patient leaves the department, helps to overcome some scheduling problems. The other potential disadvantage of this algorithm relates to the inconvenience of the 2-day protocol. However, if time permits within the department, we feel that the improved quality of the images obtained justifies the inconvenience. In keeping with this, a study by Whalley et al. (1991) has suggested an improved detection of CAD with a 2-day imaging protocol compared with 2 different 1-day protocols.

The advantages of not having to obtain rest images in selected patients are quite clear and include increased speed of diagnosis, decreased patient radiation exposure, improved cost efficiency and expanded availability of SPET imaging devices for other investigations.

References

- Dilsizian V, Swain J, Dextras R, et al. (1989) Prediction of viable myocardium by thallium reinjection at rest after stress redistribution imaging: a pre and post revascularization study (abstract). Circulation 80:366
- Eagle KA, Singer DE, Brewster DC, et al. (1987) Dipyridamolethallium scanning in patients undergoing vascular surgery. Optimizing pre-operative evaluation of cardiac risk. JAMA 257(16):2185-2189
- Glover DK, Okada RD (1990) Myocardial kinetics of Tc-MIBI in canine myocardium after dipyridamole. Circulation 81(2):628-637
- Hassan IM, Mohammed MM, Constantinides C, et al. (1990) Segmental analysis of SPET ^{99m}Tc-methoxyisobutylisonitrile and ²⁰¹Tl myocardial imaging in ischaemic heart disease. Eur J Nucl Med 16(8–10):705–711
- Iskandrian AS, Hakki AH, Kane-Marsch S (1986) Exercise thallium-201 scintigraphy in men with non-diagnostic exercise electrocardiograms. Prognostic implications. Arch Int Med 146(11):2189–2193
- Kahn JK, McGhie I, Akers MS, et al. (1989) Quantitative rotational tomography with 201-Tl and 99m Tc 2-methoxy-isobutylisonitrile. A direct comparison in normal individuals and pa-

tients with coronary artery disease. Circulation 79(6):1282-1293

- Kait H, Berman DS, Maddahi J, et al. (1988) Late reversibility of tomographic myocardial thallium-201 defects; an accurate marker of myocardial viability. J Am Coll Cardiol 12:1456– 1463
- Koss JH, Kobren SM, Grunwald AM, et al. (1987) Role of exercise thallium-201 myocardial perfusion scintigraphy in predicting prognosis in suspected coronary artery disease. Am J Cardiol 59(6):531–534
- Larock MP, Cantineau R, Legrand V, et al. (1990) ^{99m}Tc-MIBI (RP-30) to define the extent of myocardial ischemia and evaluate ventricular function. Eur J Nucl Med 16(4-6):223–230
- Marshall RC, Leidholdt EM Jr, Zhang DY, et al. (1990) Technetium 99m hexakis 2-methoxy-2-isobutyl isonitrile and thallium-201 extraction, washout, and retention at varying coronary flow rates in rabbit heart. Circulation 82(3):998–1007
- Staniloff HM, Forrester JS, Berman DS, et al. (1986) Prediction of death, myocardial infarction, and worsening chest pain using thallium scintigraphy and exercise electrocardiography. J Nucl Med 27(12):1842–1848
- Taillefer R, Gagnon A, Laflamme L, et al. (1989) Same day injections of ^{99m}Tc-methoxyisobutylisonitrile (hexamibi) for myocardial tomographic imaging: comparison between rest-stress and stress-rest injection sequences. Eur J Nucl Med 15(3):113– 117
- Wackers FJT (1988) Myocardial perfusion imaging. In: Gottschalk
 A, Hoffer PB, Potchen EJ (eds) Diagnostic nuclear medicine,
 2nd edn. Williams and Wilkins, Baltimore, p 325
- Whalley DR, Murphy JJ, Frier M, et al. (1991) A comparison of same day and separate day injection protocols for myocardial perfusion SPECT using Tc-99m MIBI. Nucl Med Commun 12:99–104
- Williams SJ, Dragotakos DL, Okada RD (1989) Kinetics of ^{99m}Tchexakis *t*-butyl isonitrile in normal and ischemic canine myocardium. Eur J Nucl Med 15(6):287–291