

Short Communication

The positive predictive value of myocardial perfusion imaging in screening patients for suspected coronary artery disease

S ELLEMDIN, P SOMA

Summary

Background: In patients with known or suspected coronary artery disease, diagnosis and risk stratification can be aided by non-invasive tests for myocardial ischaemia. The main indications for the use of radionuclide perfusion imaging (sestamibi) rather than exercise electrocardiography include complete left bundle branch block, inconclusive stress electrocardiography and an inability to exercise. The published data on myocardial perfusion imaging is limited to eight studies of only 628 patients with widely varying ranges of sensitivities and specificities and the major problem being the bias created when patients with positive test results are referred far more frequently for coronary angiography than those with negative results. Furthermore, certain categories of patients are postulated to have a high number of false positives, especially obese patients and women, but this hypothesis has not been tested.

Methods and Results: A retrospective descriptive study on patients with positive sestamibi scans, who had coronary angiography within six months of each other, was performed. The study population consisted of 132 patients, 53.8% of whom were male and 44.7% had a body mass index of less than 28. The overall positive predictive value of the sestamibi scan in predicting significant coronary angiographic stenosis was 63.6%. This value increased significantly to 80.3% in males ($p = 0.000$). The positive predictive value did not differ in the different age categories, nor did it change with the different indications for sestamibi scanning.

Conclusions: The sestamibi scan remains a useful screen-

ing test for coronary artery disease in patients who are exercise intolerant or those with inconclusive stress electrocardiography. The test is highly predictive in males rather than females.

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In patients with known or suspected coronary artery disease (CAD), diagnosis and risk stratification can be aided by non-invasive tests for myocardial ischaemia. The three commonly used tests are exercise electrocardiography, myocardial perfusion imaging, and stress echocardiography.^{1,2}

The main indications for the use of radionuclide perfusion imaging (sestamibi) rather than exercise electrocardiography include² complete left bundle branch block (LBBB), electronically paced ventricular rhythm, pre-excitation syndrome, inconclusive stress electrocardiography, more than 1-mm ST-segment depression at rest on electrocardiogram (ECG), angina and a history of revascularisation, and an inability to exercise to an appropriate stage to give meaningful results to stress electrocardiography. At the present time, radionuclide imaging, single-photon emission computed tomography (SPECT) has an average sensitivity of 89 to 92% with a specificity of 78%.³

Methods

We undertook to establish what the positive predictive value of the methoxyisobutylisonitrile (MIBI) scan would be in predicting stable, yet significant CAD in patients at Pretoria Academic Hospital. A retrospective descriptive study on patients with positive sestamibi scans who had had coronary angiography within six months of each other was performed. The Pretoria Academic Hospital ethics committee approved this study. The study population, consisting of 132 patients, included all patients with ischaemic-type chest pain referred for sestamibi perfusion scans. Tc-99m (technetium)-sestamibi was used as the imaging agent in a two-day rest/stress protocol.

Both rest and stress SPECT images were qualitatively and semi-quantitatively assessed by a consultant nuclear physi-

Department of Internal Medicine, University of Pretoria, Pretoria

S ELLEMDIN, MB ChB, MMed (Int Med)

Department of Physiology, University of Pretoria, Pretoria

P SOMA, MB ChB, MSc (Clin Epidem)

cian and a resident nuclear physician independently, after which the two reports were collated by mutual consensus into a final report. Coronary angiogram results were reported as normal [ie, no visible epicardial CAD, normal left ventricular ejection fraction (LVEF), no dyskinetic segments] or abnormal (ie, insignificant coronary artery stenosis if less than 50% reduction in luminal diameter, significant coronary artery stenosis if more than 50% reduction in luminal diameter, decreased LVEF, dyskinetic segments present).

All statistical calculations were done with STATA version 8.0. Differences between groups were completed using the Wilcoxon rank sum test for continuous variables and the Fischer's exact for categorical variables. The positive predictive value (PPV) of MIBI scans in predicting significant coronary artery disease was calculated. The impact of gender, BMI ≥ 28 and indication for the MIBI scan on the positive predictive value (PPV) was assessed.

Results

During the designated time period, 380 sestamibi scans were performed. Of these, 165 were negative, precluding the need for further investigation by coronary angiography, the gold standard for the study. Six of these subjects did, however, ultimately have the latter test. Of the 215 positive sestamibi scans, 132 subjects subsequently underwent coronary angiography, while the remaining 83 did not. This is represented graphically in Fig. 1.

As shown in Table 1, the overwhelming indication for sestamibi scanning was exercise intolerance, as 66.7% of subjects fell into this category. The pre-operative evaluation category included mostly subjects older than 55 years of age requiring cardiac valve replacements. When classified into categories, gender was the only variable with a significant p-value. The uncategorised PPV of the sestamibi scan in predicting significant coronary stenosis was 63.6%. The PPV ranged from 49 to 80% when categorised according to age, gender, BMI and indication for sestamibi, as indicated in Table 1. The variable with the highest PPV was gender, with a value of 80.3%.

Only six of 165 negative sestamibi scan subjects had

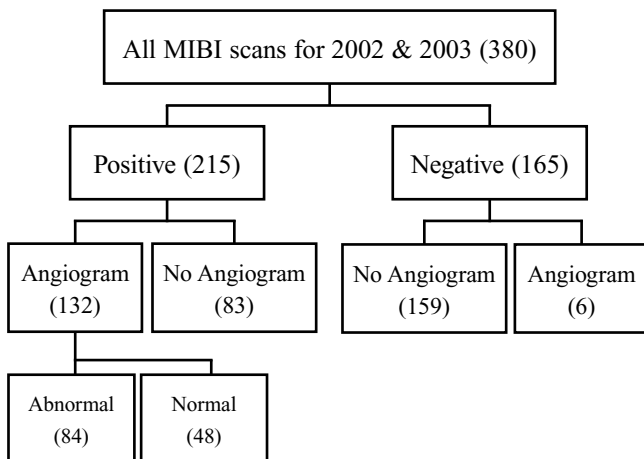


Fig. 1. Outline of the distribution of patients on whom MIBI scans were performed.

coronary angiography (3%) while of 215 positive scans, 132 subjects had coronary angiography (61%), which is approximately similar to that reported in the literature. This phenomenon is widely referred to in the literature as referral bias, namely, the outcome of the test in question determines the performance or non-performance of the gold standard.⁴ Because clinicians are influenced by the results of a diagnostic test, patients with an abnormal test are more likely to be referred for a definitive test, such as coronary angiogram, than those with a normal test.⁴

The study by Miller *et al.*⁴ concluded that referral bias has a marked effect on the apparent accuracy of the stress SPECT for the diagnosis of CAD. Adjustments for referral bias need to be made to yield better estimates so as to render the technique more accurate.⁴ Unfortunately, in our study, 39% of the patients with positive sestamibi scans did not have an angiogram, which was the gold standard.

Myocardial perfusion imaging is a useful adjunct to the non-invasive assessment of patients with stable angina, baseline ECG abnormalities, post-revascularisation assessment, and heart failure and in those unable to exercise.⁵ Our study showed PPVs of 62.5 and 64.3 for LBBB and pre-operative evaluation, respectively.

The limitations of this study included: firstly, the presence of left ventricular hypertrophy (by ECG or echocardiography) was not addressed although it has been reported to increase the number of false-positive sestamibi scans.⁶ Secondly, 39% of subjects were not referred for angiography after a positive sestamibi scan for various reasons including age, loss to follow-up, co-morbid disease, etc, but especially

TABLE 1. BASELINE CHARACTERISTICS OF THE 132 SUBJECTS WHO, AFTER A POSITIVE SESTAMIBI SCANNING, UNDERWENT ANGIOGRAPHY

Variable	n = 132 (%)	PPV	Mean	SD	p-value
Age (years)			57.6	10.4	0.757
< 60	71 (54)	61.9			
60-70	46 (35)	63.0			
≥ 70	15 (11)	73.3			
BMI (kg/m ²)			28.5	4.7	1.000
< 28	59 (45)	64.4			
≥ 28	73 (55)	63.0			
Gender					0.000
Females	71 (54)	49.3			
Males	61 (46)	80.3			
Indication for sestamibi					0.556
Exercise intolerance	81 (61)	66.7			
Inconclusive stress ECG	13 (10)	46.2			
LBBB	24 (18)	62.5			
Pre-operative evaluation	14 (11)	64.3			

SD = standard deviation; PPV = positive predictive value of the sestamibi scan in predicting significant coronary stenoses as categorised according to age, gender, BMI and indication.

because subjects were deemed unsuitable for a revascularisation procedure. Thirdly, sestamibi scans were not interpreted independently by the two nuclear physicians; the coronary angiograms were performed by several different cardiologists and were recorded mostly on VCR but some on CD, so variation in technical differences existed and also visual analysis was the method of quantification used when defining the percentage of stenosis on the angiograms. Finally, even though coronary angiography was used as the gold standard, cognisance is taken of the fact that ischaemia can be present in the absence of significant CAD (eg, microangiopathy in patients with diabetes, metabolic syndrome).

The accuracy of dipyridamole sestamibi SPECT imaging in detecting multivessel disease was similar for men and women.⁷ This was concluded in the study that evaluated the ability of perfusion imaging in correctly identifying individual coronary artery stenoses and multivessel disease in women versus men. In fact the sensitivity of dipyridamole sestamibi SPECT imaging in detecting disease of the left anterior descending artery was better in women.⁷ In addition, another study that explored the prognostic value of a normal Tc-99m sestamibi found that a normal stress Tc-99m sestamibi is highly predictive of a benign outcome, even in patients with an intermediate probability of CAD.⁸

Conclusion

The sestamibi scan remains a useful screening test for coronary artery disease in patients who are exercise intolerant or those who have inconclusive stress electrocardiography, especially if provision is made for BMI and gender. The test

is highly predictive in males rather than females, as shown in this study. One additional factor that may be a confounder is the presence of left ventricular hypertrophy, which needs to be addressed in future studies. In the appropriate patient, the sestamibi scan has the potential to avoid unnecessary angiography as well as to risk stratify patients with equivocal symptoms, exercise intolerance and inconclusive stress electrocardiography.

References

1. Kuntz KM, Fleischmann KE, Hunink MGM, Douglas PS. Cost-effectiveness of diagnostic strategies for patients with chest pain. *Ann Int Med* 1999; **130**(8): 709–728.
2. Lee TH, Boucher CA. Noninvasive tests in patients with stable coronary artery disease. *N Engl J Med* 2001; **344**(24): 1840–1845.
3. Verani MS, Willerson JT. Impact of nuclear cardiac imaging on the present and future practice of cardiology. *Eur J Nucl Med* 2000; **27**(Suppl): S21–S26.
4. Miller TD, Hodge DO, Christian TF, Milavetz JJ, Bailey KR, Gibbons RJ. Effects of adjustment for referral bias on sensitivity and specificity of SPECT for the diagnosis of coronary artery disease. *Am J Med* 2002; **112**(4): 290–298.
5. Sabharwal NK, Lahiri A. Role of myocardial perfusion imaging for risk stratification in suspected or known coronary artery disease. *Heart* 2003; **89**: 1291–1297.
6. Picano E, Palinkas A, Amyot R. Diagnosis of myocardial ischemia in hypertensive patients. *J Hyperten* 2001; **19**(7): 1177–1183.
7. Travin MI, Katz MS, Moulton AW, Miele NJ, Sharaf BL, Johnson LL. Accuracy of dipyridamole SPECT imaging in identifying individual coronary stenoses and multivessel disease in women versus men. *Journal of nuclear Cardiology* 2000; **7**(3): 213–220.
8. Soman P, Parsons A, Lahiri N, Lahiri A. The prognostic value of a normal SPECT dipyridamole Tc-99m sestamibi in suspected coronary artery disease. *J Nucl Cardiol* 1999; **6**: 252–256.