ORIGINAL ARTICLE

Evaluation of the American College of Cardiology Foundation/American Society of Nuclear Cardiology appropriateness criteria for SPECT myocardial perfusion imaging in an Asian tertiary cardiac center

Angela S. Koh, MBBS, Jennifer L. S. Flores, MD, Felix Y. J. Keng, MBBS, Ru San Tan, MBBS, and Terrance S. J. Chua, MBBS, FACC

Background. **Appropriate use criteria (AUC) for SPECT MPI have been published to address concern about the growth of cardiac imaging studies and the effective use of imaging, but there is no published data on its role outside the United States.**

Methods. **All consecutive patients referred to the MPI laboratory of our center from February 16 to June 19, 2009 were prospectively studied. Patients' medical records and stress data were collected and all imaging results were recorded. Based on AUC, MPI studies were classified into appropriate, inappropriate, uncertain, or unclassified. MPI studies were classified on the basis of their results into normal or abnormal scans.**

Results. **There were 1,623 patients (mean age 61 years ± 11, 61% males). Most common indications for SPECT were evaluation of ischemic equivalent for coronary artery disease (CAD), risk assessment post-revascularization, and preoperative evaluation for non-cardiac surgery. 10% of referrals were classified as inappropriate, 5% uncertain, and 3% unclassified. Women (48.4% vs 40.6% for men, $P = .063$) and asymptomatic patients (50.2% vs 14.3% for symptomatic, $P < .001$) had a higher proportion of inappropriate studies. The preoperative group had the highest proportion of inappropriate studies (59%). Appropriate referrals had a higher proportion of abnormal SPECT results than inappropriate referrals (40% vs 27%, OR 2.08, 95% CI 1.56-2.77, $P < .001$).**

Conclusions. **The pattern of referrals for SPECT MPI in an Asian center appears to vary from published reports in the United States. Preoperative evaluation for low-risk surgery appears to be the most common source of inappropriate referrals in our institution. Inappropriate referrals have a higher proportion of normal studies, but 27% were still reported as abnormal. (J Nucl Cardiol 2011;18:324–30.)**

Key Words: Myocardial perfusion imaging: SPECT • diagnostic and prognostic application • outcomes research • cost-effectiveness

INTRODUCTION

The increase in utilization of myocardial perfusion examinations in the United States has led to the development of imaging guidelines for nuclear cardiology by the American College of Cardiology Foundation (ACCF), American Heart Association, and American Society of Nuclear Cardiology (ASNC).[1] There are no data, and uncertainty about applicability of these criteria to patients and clinical situations outside the United States.

From the Department of Cardiology, National Heart Centre, Singapore, Singapore.

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Reprint requests: Terrance S. J. Chua, MBBS, FACC, Department of Cardiology, National Heart Centre, Mistri Wing, Third Hospital Avenue, Singapore 168752, Singapore; *terrance.chua.s.j@nhcs.com.sg*.

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The National Heart Centre in Singapore[2] is a tertiary cardiac center with academic affiliation. Single photon emission computed tomography myocardial perfusion imaging (SPECT MPI) has seen a yearly growth of 10% in National Heart Centre in Singapore[3] since 1996 (Figure 1). Hence, it is timely to assess the appropriateness for use of this imaging modality in our region of practice.

In addition, one previous retrospective single center study suggested that inappropriate studies were more likely to have normal SPECT results; but there was still a high proportion of such studies with abnormal findings.[4]

The aim of this prospective study was, therefore, to examine the patterns of referral for MPI in a large Asian tertiary cardiac center, so as to determine areas of appropriate and inappropriate use of MPI based on published criteria, and to correlate appropriateness grading with the outcome of MPI scans.

METHODS

Setting and Data Sources

All consecutive SPECT MPI studies referred to our MPI laboratory over a four-month period from February 16 to June 19, 2009 were prospectively analyzed according to the appropriateness criteria. The study was approved by the local institutional review board. Imaging was performed with a stress-rest protocol using either technetium 99m tetrofosmin or sestamibi. Stress testing was performed by exercise or dipyridamole with rest and post-stress gated SPECT imaging at the discretion of the nuclear cardiologist.

The patient's medical history and indications for testing were recorded on the day of their MPI appointment. Based on AUC, MPI studies were then immediately classified into appropriate, inappropriate, uncertain, or unclassified depending on their pretest probability of coronary artery disease (CAD) for symptomatic patients,[5-7] Framingham risk score[8,9] for asymptomatic patients, functional class, ability to exercise, and

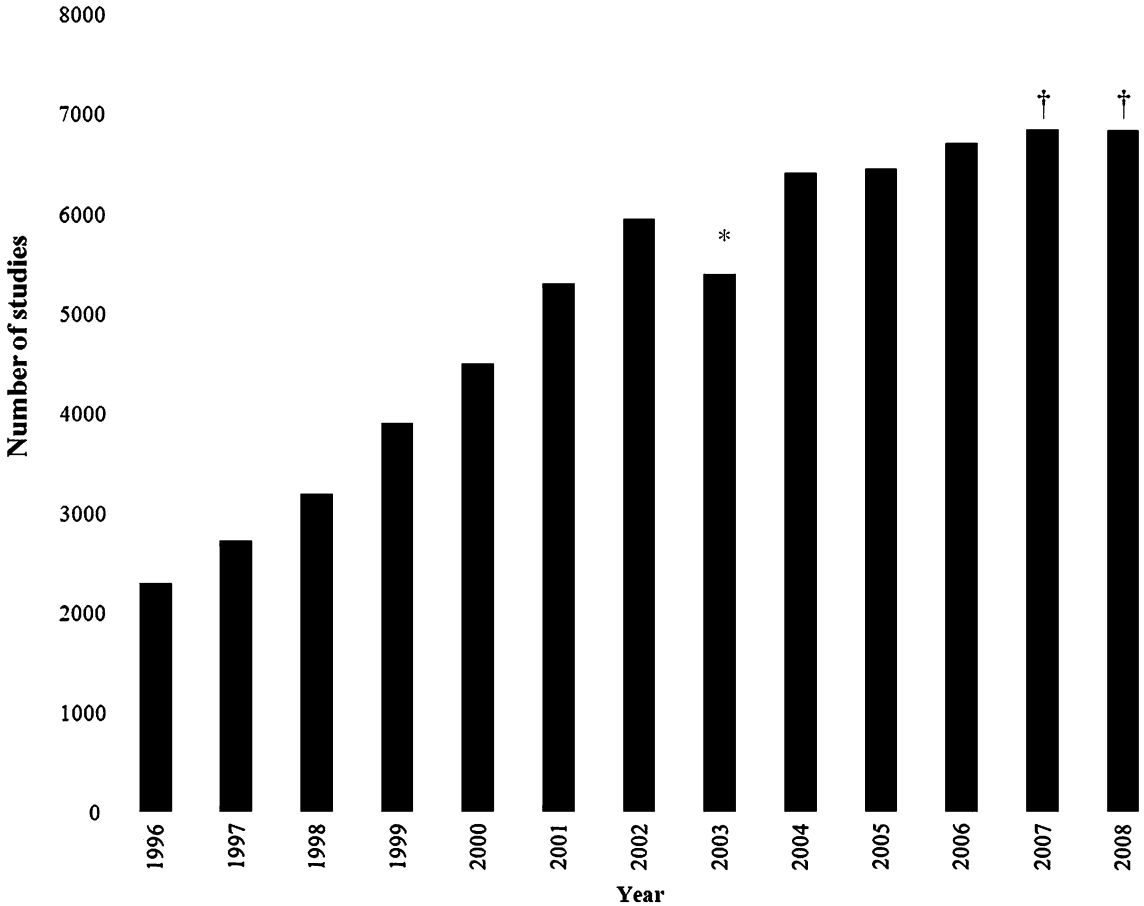

Figure 1. Trends in use of myocardial perfusion imaging in National Heart Centre, Singapore (1996-2008). Chart depicting the annual growth of MPI in our center since 1996. *The occurrence of Severe Acute Respiratory Syndrome (SARS) in 2003 led to a temporary closure of all non-urgent clinics and procedures, and a reduction of MPI use in that year. † In 2007, 64-slice cardiac computed tomography was introduced at our institution, and in 2008, services were interrupted by isotope supply problems.

surgical risk for preoperative patients.[9] For patients whose indications fell into more than one category, the primary indication as requested by the ordering physician was used. If the ordering physician had more than one indication for ordering the test, we utilized the hierarchy of potential test ordering from the appropriate use criteria[1] in this order: preoperative assessment, risk assessment within 3 months of acute coronary syndrome (ACS), prior percutaneous coronary intervention (PCI), or coronary artery bypass grafting (CABG), prior imaging, ischemia equivalent, and detection of CAD in asymptomatic individuals. Indications that were not addressed by the AUC were labeled as unclassifiable. Assessment of appropriateness was performed independently by two physicians (non-cardiologists). Disagreements were resolved by consensus. To minimize discordance, there was prior agreement that symptomatic patients were those who could have symptoms apart from typical angina for which the ordering physician has classified representative symptoms under ''chest pain syndrome.'' Categorization of functional level or effort tolerance would be assigned based on ordering physician's assessment from medical records.

Outcome Measurement

SPECT images were interpreted and scored by nuclear cardiologists, using a 20-segment scoring system with a 5-point score for severity (0 = normal, 4 = absent tracer uptake). For the purpose of the study analysis, each MPI study was categorized as normal or abnormal [fixed defect, completely reversible defect(s), or a partially reversible defect(s)].

Statistical Analysis

Categorical variables are presented as percentages and compared using chi-square/Fisher's exact test. Continuous variables are presented as mean ± standard deviation and comparisons were made by use of unpaired t test, the null hypothesis being that there was no significant difference between the appropriate, uncertain, or inappropriate groups. Statistical significance was assumed if $P < .05$. Agreement in the classification of indications between the two doctors was compared using kappa statistics. Multivariate logistic regression was performed to determine independent covariates associated with inappropriate referrals.

RESULTS

Overall

During the 4-month study period, 1,623 SPECT MPI studies were categorized. Agreement in the classification of the indications between two doctors was moderate ($\kappa = 0.64$). Stress-rest protocol was performed in all studies, using either technetium 99m tetrofosmin or sestamibi. Exercise stress (Bruce protocol) was preferred (59%); those who were unable to exercise received dipyridamole pharmacologic stress (41%). 59% of patients were males with mean patient age of 61 ± 11 years. Out of 1,623 patients, 71% had hypertension, 75% had dyslipidemia, 31% had diabetes mellitus, and 14% had a history of smoking. The ethnic distribution in our cohort of patients is similar to the overall Singapore population census (Chinese: 73% in our study vs 77% in the general population; Malays: 8% vs 14%; Indian 13% vs 8%, respectively).

Applying the AUC, 82% of our studies were categorized as appropriate, 10% as inappropriate, 5% as uncertain, and 3% as unclassifiable. 93% of the referrals at our institution were from cardiologists and the remaining 7% from non-cardiologists. Referrals were more likely to be graded as appropriate testing if patients were aged 61 years and above (51.2% vs 44.7%; OR 1.30, 95% CI 1.01-1.67; $P = .047$), had hypertension (72.7% vs 63.7%; OR 1.52, 95% CI 1.67-1.98; $P = .002$), dyslipidemia (76.4% vs 69%; OR 1.46, 95% CI 1.11-1.92; $P = .01$), diabetes mellitus (32.8% vs 23.3%; OR 1.60, 95% CI 1.20-2.15; $P = .001$), or a history of smoking (15.2% vs 9.7%; OR 1.67, 95% CI 1.11-2.52; $P = .013$). There were no differences in appropriateness grading between tests ordered by cardiologists (n = 1509) or non-cardiologists (n = 114).

Patients who were referred for symptomatic CAD were more likely to receive an appropriate grading than patients who were asymptomatic for CAD (50.2% vs 14.3%, OR 6.02 95% CI 4.28-8.46 $P < .001$).

Inappropriate testing was more common in women than in men (48.4% vs 40.6%, OR 1.37 95% CI 0.99-1.90 $P = .063$).

Indications Addressed by AUC

Table 1 shows the broad groups of indications for referral, their frequency, and proportions of studies that were graded as appropriate, inappropriate, and uncertain.

In the overall study population (n = 1623), 66% (n = 1067) of patients were referred for symptomatic indications while 14% (n = 223) patients were referred for asymptomatic indications.

In evaluating patients for coronary artery disease, there were 737 symptomatic patients and 117 asymptomatic patients (Table 1). Among the symptomatic group, 94% (n = 692) of the studies were classified as appropriate while 57% (n = 67) of the studies among the asymptomatic group were classified as appropriate ($P < .001$).

In the multivariate analysis of factors associated with inappropriate referrals (Table 2), age ≥ 61 years was most predictive of an inappropriate referral, associated with a fourfold increase in odds of having an inappropriate referral. An asymptomatic status was also predictive of an inappropriate classification, increasing the odds by twofold. As a whole, preoperative testing

Table 1. Classification of studies according to groups of indications for referral and their frequencies

Group	Number of studies (%) in order of frequency among all MPI referrals†	Number of studies (%) graded as appropriate*	Number of studies (%) graded as inappropriate*	Number of studies (%) graded as uncertain*
Evaluation of ischemic equivalent (non-acute)	737 (45.4)	692 (94)	35 (4.7)	10 (1.3)
Risk assessment post-revascularization	299 (18.4)	275 (92)	3 (1.0)	21 (7.0)
Preoperative evaluation for non-cardiac surgery	176 (11)	105 (60)	70 (39.3)	1 (0.7)
Risk assessment with prior test results	138 (8.5)	119 (86.2)	5 (3.6)	14 (10.2)
Detection CAD without ischemic equivalent	117 (7)	67 (57)	20 (17.5)	30 (25.5)
Risk assessment within 3 months of an acute coronary syndrome	92 (5.7)	90 (97.8)	0	2 (2.2)
Assessment of viability/ ischemia	11 (0.7)	11 (100)	0	0
Evaluation of ventricular function	5 (0.3)	5 (100)	0	0

Note that the indication with the highest proportion of inappropriate studies was the preoperative group.
All values expressed as n (%).
* The proportions of studies that were graded as appropriate, inappropriate, and uncertain among each indication.
† Other unclassifiable indications made up the remaining 3%.

Table 2. Multivariate analysis of factors related to inappropriate referrals

Variable	OR	95% CI	*P* value
Age ≥ 61 years	4.36	2.73-6.96	<.0001
Asymptomatic status	2.29	1.35-3.65	.002
Preoperative testing	1.57	1.10-1.62	<.0001
Female	0.90	0.43-0.93	.02
Smoking	0.88	1.11-3.53	.06
Hypertension	0.82	0.18-3.40	1.00
Dyslipidemia	0.63	0.71-1.63	.72
Diabetes mellitus	0.06	1.31-3.25	.002

CI, Confidence interval; *OR*, odds ratio.

increased the likelihood of being classified as inappropriate by 1.6 times compared to other referral indications.

Indications Not Addressed by AUC

Forty-eight studies were unclassifiable based on current AUC. These included evaluation for CAD post-heart transplant (44%), pretransplant workup for liver transplant (11%), and bone marrow transplant (11%), evaluation of premature ventricular complexes (22%), and evaluation for CAD prior to radiofrequency ablation procedures (11%).

Correlation of MPI Scan Result with Appropriateness Grading

Of 1,623 studies, 38% were reported as having abnormal results. We evaluated the relationship between appropriateness grading and the MPI results (Figure 2). Referrals graded as appropriate had a higher proportion of abnormal results than referrals graded as inappropriate ($P < .001$).

The top five groups of indications with the highest frequency of inappropriate referrals and proportions of abnormal scans in each category are represented in Table 3. Among the inappropriate referrals, the preoperative group contributed the highest proportion of referrals (59%), followed by evaluation of ischemic equivalent for coronary artery disease in low-risk patients (21%), detection of CAD in asymptomatic low-risk patients (11%), as well as risk assessment in asymptomatic patients with prior test results (3%), or post-revascularization (2%).

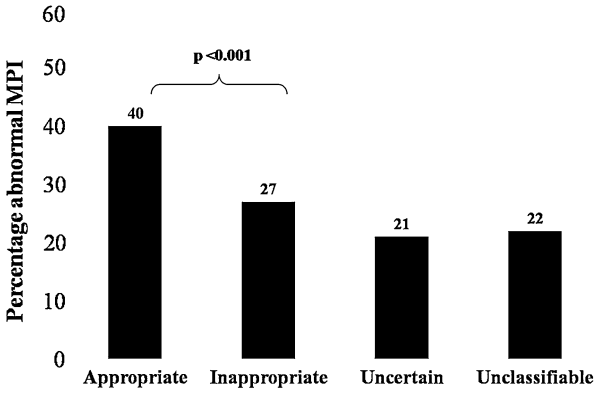

Figure 2. Relationship between appropriateness grading and MPI result. This chart shows the relationship between the appropriateness grading and the MPI results. Appropriate referrals had a higher proportion of abnormal result more than the inappropriate referrals ($P < .001$).

There were 176 referrals for preoperative evaluation. Referral for MPI in low-risk and intermediate preoperative risk patients with normal functional class is classified as inappropriate by AUC. 40% of these preoperative low and intermediate risk patients had an abnormal MPI result.

DISCUSSION

The rapid growth of imaging procedures has raised concerns about appropriateness of referrals to MPI and radiation exposure in the United States.[10,11] We have seen a similar growth of MPI use in our institution (Figure 1), despite a different health-care system[2] and cost structure.[12] In public hospitals in Singapore (including our center), approximately three-quarters of all referrals are in a ''subsidized'' class where the patient pays approximately US$145 per test, with no further direct payment to the institution for performing the test; hence, there is little incentive for the hospital to increase the total volume of tests. In addition, any cardiology consultant or cardiology fellow in our institution has the option to order MPI scans, but only 3 out of 40 cardiologists were involved in the interpretation of MPI scans or received any remuneration for reading scans. Given the relatively small proportion (<10%) of cardiologists reading scans, we believe that self-referral was unlikely to have contributed to the rapid growth of use of MPI scans. Hence, there is a need to better understand the patterns and appropriateness of referral for MPI.

To our knowledge, only three previous studies have documented the application of appropriate use guidelines for SPECT, all were at hospitals in the United States,[13-15] and two were retrospective[13,14] using the original 2005 guidelines.[16] To our knowledge, this is the first study in Asia to apply the recently published and updated 2009 ACCF/ASNC appropriate use criteria[1] and to prospectively examine the relationship between appropriateness and the outcome of the MPI result using these guidelines. As our data were collected prospectively and graded for appropriateness at the time of the

Table 3. Inappropriate indications for MPI testing and MPI scan results

Indication	Number (%) with studies graded as inappropriate	Number (%) with abnormal MPI results within each group*
Preoperative evaluation for non-cardiac surgery	95 (59)	38 (40)
Evaluation of ischemic equivalent (non-acute): low probability, interpretable ECG, able to exercise	34 (21)	3 (9)
Detection of CAD without ischemic equivalent: low risk, interpretable ECG	18 (11)	3 (17)
Risk assessment with prior test results: asymptomatic or stable symptoms with normal prior stress imaging study	5 (3)	3 (60)
Risk assessment post-revascularization: asymptomatic, less than 2 years after PCI	3 (2)	2 (67)
Total†	155 (96)	

All values expressed as n (%).
We examined the indications that were classified as being inappropriate.
Preoperative evaluation for non-cardiac surgery made up the largest proportion of inappropriate referrals, of which 40% had an abnormal MPI result.
* The top five most frequent inappropriate referrals and proportions of abnormal scans in each category.
† Of the inappropriate studies, other inappropriate indications made up the remaining 4%.

study and with the patient present (rather than retrospectively or through an online system), it was possible to ensure complete data capture.

In our center, the most common indications for referral were evaluation of ischemic equivalent for coronary artery disease (45%), followed by risk assessment post-revascularization (18%), and preoperative assessment for non-cardiac surgery (11%). Broadly speaking, our top two indications were similarly ranked among the top indications for SPECT MPI in other centers.[4,13,14] However, we found a high proportion of referrals for preoperative assessment, after referrals for ischemic equivalent for CAD and risk assessment post-revascularization. Notwithstanding differences in data collection and presentation between our analysis and earlier studies,[4,13,14] this is a notable finding, most likely due to differences in local clinical practice and referral patterns.

In our study the majority of referrals were classified as appropriate by AUC. The proportion of inappropriate studies in our cohort was 10%, which is similar to the proportion of inappropriate studies reported by Gibbons et al[13] (12%) and Mehta et al[4] (13%), as well as Hendel et al[14] (14%). However, the patterns and reasons for such referrals were very different. At our center, testing of low-risk symptomatic patients contributed only 11% of all inappropriate referrals, compared to 38% (Mehta et al[4]), 23% (Hendel et al[14]), and 48% (Gibbons et al[12]). Preoperative testing was much more common (59% of all such referrals) at our center as a cause of inappropriate referrals compared to these other studies. In fact, preoperative testing was the third strongest predictor of an inappropriate classification, in our multivariate analysis.

In our institution, cardiologists need to be consulted first before MPI can be ordered. Thus, the majority of tests were ordered by cardiologists, which might have influenced the proportion of studies classified as appropriate. Although this was a prospective study, referring physicians were not aware that their referring patterns were being graded and monitored; hence, the Hawthorne effect[15] probably did not contribute to the high proportion of appropriate referrals.

As this was a prospective study, we had complete data for all referrals, and hence, all referrals were assigned an appropriateness grading. The number of unclassifiable studies in our center is small (3%), possibly because it was a prospective study done on-site, with the patient and his records available to clarify any uncertainties. Most other centers have indications that were unclassifiable in the range from 3% to 10%.[4,13,14] Refinements in the AUC may potentially address these ambiguities; however, unclassifiable indications are wide-ranging, and may represent clinical situations that are peculiar to different clinical practices.

Several authors have alluded to the fact that while the AUC is developed upon existing ACC/AHA guidelines for certain indications,[14,16] it is partially based on expert opinion in areas where evidence is lacking, since not all clinical situations have been subject to randomized clinical trials.[17]

In their retrospective study, Metha et al[14] found that inappropriate referrals were significantly less likely to result in abnormal MPI scans. Our prospective study also found similar results: only 9% to 17% of symptomatic and asymptomatic low-risk patients who were evaluated for coronary artery disease, respectively, had abnormal scans. Since an abnormal scan is more likely to modify treatment than a normal scan, this finding appears in support of the concept of AUC in optimizing the utility of MPI in clinical practice, by avoiding its use in situations where most results would be normal.

However, the finding of a substantial proportion of abnormal scans in otherwise inappropriate referrals deserves comment. In evaluating our preoperative group, we found that 40% of inappropriate referrals within the preoperative group had abnormal MPI results. The high proportion of abnormal results might lead to the impression that testing is appropriate even in low-risk surgery groups. However, this is probably an inappropriate overgeneralization. An abnormal result in a patient with going for a low-risk procedure, e.g., cataract surgery, might not imply a high risk of cardiac events, since the overall risk might be small, and so the positive predictive value of the test in this setting might be low. Further work and outcome studies are needed to determine the significance of these findings. Based on these findings, our hospital has instituted education at meetings and protocols to improve appropriateness of referral, particularly for preoperative risk stratification.

LIMITATIONS

In our institution, a cardiology consult is required before an MPI test can be ordered. Whether higher rates of inappropriate use would be recorded had MPI been directly available to non-cardiologists is uncertain.

CONCLUSIONS

The ACCF/ASNC appropriateness use criteria for SPECT MPI appear useful and applicable in an Asian population, with 10% of referrals graded as inappropriate. In contrast to other reports, the patterns of referral for SPECT MPI differed significantly with preoperative risk stratification being the most common cause of an inappropriate referral. Inappropriate referrals have a higher proportion of normal studies. Elimination of the three most common causes of inappropriate referrals would reduce referral volume by 9%.

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