Are Shades of Gray Prognostically Useful in Reporting Myocardial Perfusion Single-Photon Emission Computed Tomography?

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Background—We have advocated the use of a 5-category “normal,” “probably normal,” “equivocal,” “probably abnormal,” and “definitely abnormal” approach to final interpretation of myocardial perfusion single-photon emission computed tomography (SPECT). The prognostic value of expressing levels of certainty compared with a dichotomous normal/abnormal classification or categories for summed stress scores is unclear.

Methods and Results—Myocardial perfusion SPECT (MPS) was visually assessed using a standard semiquantitative approach, yielding summed scores that were used for preliminary interpretation using 5 levels of certainty. The interpreter was permitted to then shift the level of certainty in the final interpretation by 1 degree, based on nonperfusion MPS variables and available clinical information. To examine the prognostic value of expressing levels of clinical certainty, we evaluated 20,740 unique consecutive patients who underwent rest Tl-201/stress Tc-99m sestamibi MPS (34.3% vasodilator stress), of whom 845 (4.4%) were lost to follow-up and 1,695 were excluded from prognostic analysis due to an early revascularization (<60 days after MPS). The remaining 18,200 patients (59.1% men; age, 65±13 years) were followed up for cardiac death for a mean of 2.7±1.7 years. During the follow-up, a total of 591 cardiac death events occurred. By univariable analysis, there were substantial differences in the distribution of follow-up cardiac death by the category of clinical MPS certainty. The clinical certainty was found to be an independent multivariable predictor of cardiac death in the study population and better identified patients at increased risk of cardiac death than the approaches based solely on the standard categories of summed perfusion scores or based solely on categories of segmental perfusion scores.

Conclusions—The use of multicategory reporting of MPS results incorporating nonperfusion MPS results and clinical information enhances risk stratification compared with both a dichotomous normal/abnormal approach or approaches based solely on segmental categories of perfusion scores. Whether this enhanced risk stratification based on the clinical certainty of the MPS interpretation leads to a more effective therapeutic regimen, tailored to the individual patient’s need, requires further prospective evaluation.

Key Words: myocardial perfusion imaging ■ image interpretation ■ prognosis

In formulating recommendations regarding the reporting of nuclear cardiology studies, there was debate regarding the issue of the reporting and final interpretation of the myocardial perfusion scan results. It is widely understood that in “real world” cardiology practice, busy specialists might prefer a simple yes or no answer to the question of the presence of coronary artery disease (CAD), and when they refer a patient for myocardial perfusion single-photon emission computed tomography (MPS), they might look for the word “normal” or “abnormal” in the report. In this regard, the recent American Society of Nuclear Cardiology consensus statement on reporting of MPS studies recommended, “the final interpretation must possess clarity and must state whether the study is “normal” or “abnormal.” The reader is encouraged to use those categories that provide the greatest clarity for the report.

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However, considering the complexity of the findings on MPS, we have advocated the use of a 5-category approach (“normal,” “probably normal,” “equivocal,” “probably abnormal,” and “definitely abnormal”) to final interpretation of...
myocardial perfusion SPECT, and this approach has been used by others. Furthermore, we have suggested that due to the subjectivity of semiquantitative visual interpretation, allowing flexibility of shifting by 1 category of clinical certainty in the final interpretation based on nonperfusion MPS findings and the available clinical information would enhance the clinical relationship between scan findings and patient outcomes. Nonetheless, the added value of expressing levels of certainty compared with a dichotomous normal/abnormal categorization or an approach based solely on summed perfusion scores is unclear.

The aim of our study was to assess the prognostic value of expressing various levels of certainty and of incorporating nonperfusion MPS findings in final myocardial perfusion SPECT interpretation in patients with known or suspected CAD as applied in a large population of patients with known or suspected coronary CAD undergoing stress MPS.

Methods

Study Population

All patients for this study were part of the ongoing prospective nuclear cardiology registry of patients who undergo stress Tc-99m sestamibi/rest thallium-201 MPS at Cedars-Sinai Medical Center and have consented to long-term follow-up. The initial study population comprised 20,740 consecutive patients who were enrolled in the registry after having exercise or vasodilator stress MPS. A total of 1695 patients were removed from further analysis due to early revascularization (<60 days after the index MPS); 845 patients were lost to follow-up; 485 pts (4.4%) were lost to follow-up. The final study population comprised 18,200 unique patients with complete follow-up (Figure 1).

Imaging Procedure

All patients underwent rest thallium-201/stress technetium-99m sestamibi MPS as previously described. Patients performed a symptom-limited exercise treadmill test (65.3%) or vasodilator (34.7%) stress MPS Acquisition Protocol

Stress MPS was performed using a dual-detector γ camera equipped with high-resolution collimators, obtaining noncircular 180° acquisition of 64 projections in the supine position for 25 seconds per projection followed immediately by prone acquisition for 15 seconds per projection. Rest Tl-201 acquisition was performed at 35 seconds per projection in supine position only. No attenuation or scatter correction was applied.

Image Interpretation and the Definition of Scintigraphic Indices

Semiquantitative visual interpretation of MPS images used short-axis and vertical long-axis tomograms divided into 20 segments for each patient. Each segment was scored by consensus of 2 expert observers using a 5-point scoring system (0 = normal to 4 = absence of segmental uptake). Three global perfusion indexes previously defined by our group (summed stress score [SSS], summed rest score [SRS], and summed difference score [SDS]) were used to derive global measures of perfusion defect extent and severity, and variables previously demonstrated to independently add prognostic information. Both supine and prone stress datasets were assessed and used to assign the final stress score to the LV segments, as previously described. Based on the previously published data, the following categories of the MPS were derived: normal perfusion (SSS 0 to 3); mildly abnormal (SSS 4 to 8); moderately abnormal (SSS 9 to 13); and severely abnormal (SSS >13). For the purposes of assessing certainty of interpretation based on SSS alone, a fifth category (“equivocal”) was also examined for SSS 2 or 3.

Definition of Levels of Clinical Certainty in MPS Interpretation

Preliminarily, perfusion defects represented by the perfusion scores at stress and rest, as described above, were used to form the interpretation of the MPS studies using the 5 levels of certainty: (1) normal; (2) probably normal; (3) equivocal; (4) probably abnormal; and (5) definitely abnormal, based simply on the various combinations of perfusion scores as shown in Table 1. For the final clinical interpretation, the interpreter was permitted to shift the level of certainty in the final interpretation by 1°, based on non-MPS clinical information; for example, a study considered equivocal by segmental scoring could be considered probably abnormal or probably normal, based on consideration of the nonperfusion findings and the available clinical information. The level of certainty of the final clinical interpretation was reported in all patients to the referring physician as a part of the clinical MPS report. Figure 2 demonstrates clinical examples of stress images and scoring representing the 5 different categories of clinical certainty of MPS interpretation.

Patient Follow-up

Patient follow-up was performed as previously described. Deaths were identified through our hospital-based patient-information system (WebVS) and the Social Security Death Index. To ascertain the cause of death, the information provided by WebVS and the death certificates obtained for all who died in Los Angeles County were reviewed conservatively in a blinded fashion by 2 experienced cardiologists. Cardiac death (CD) was defined as death from any cardiac cause (eg, lethal arrhythmia, myocardial infarction, or pump failure).
Survival was measured from the time of the original stress test. We used the date of last contact for patients who were not known to be deceased to calculate survival in the survival analysis. For the analysis of death from cardiac causes, we regarded death from other or unknown causes as censored observations.

Follow-up in the remaining patients was sought through a mailed questionnaire or a scripted telephone interview performed in a blinded fashion with patients who did not respond to the questionnaire or telephone interview or at least 1 year of data in the hospital electronic medical records. Patients who were not confirmed to have died and who had no follow-up information (obtained by means of the mailed questionnaire or telephone interview or at least 1 year of data in WebVS) were considered to be lost to follow-up.

**Statistical Methods**

In the study population, we analyzed differences in clinical, nuclear, and prognostic variables among the patients categorized into 5 groups according to the levels of clinical test certainty. In this regard, for purposes of univariable analysis, comparisons between patient groups were performed using a chi-squared test for categorical variables. Continuous variables were expressed as mean±SD and were compared using ANOVA. A probability value of <0.05 was considered significant.

**Calculation of the Net Reclassification Improvement (Pencina Index)**

To assess the usefulness of the proposed MPS interpretation classification, using the 5-point clinical certainty categories compared with the traditional dichotomous classification based on summed perfusion score, in which patients with summed stress scores ≤4 are grouped as normal, we calculated the net reclassification improvement index (NRI): the variable quantifying the correct movement in categories was defined by using a new classification (upward for events and downward for nonevents). If we define upward movement (up) as a change into a higher category based on the new classification and downward movement (down) as a change in the opposite direction, with (D) denoting the event indicator (1=event, 0=nonevent), then we may define the NRI as

\[
\text{NRI} = \frac{P(\text{up } D=1) - P(\text{down } D=1)}{P(\text{up } D=0) - P(\text{down } D=0)}
\]

The NRI in the study population was measured with regard to presence or absence of CD. The results were expressed as proportion and compared with the "no-change" status.

**Table 2. Clinical Characteristics of the Study Population**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Normal MPS (n=7871; 43.2%)</th>
<th>Probably Normal MPS (n=2748; 15.1%)</th>
<th>Equivocal MPS (n=1306; 7.2%)</th>
<th>Probably Abnormal MPS (n=1349; 7.4%)</th>
<th>Abnormal MPS (n=4926; 27.1%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>62±13</td>
<td>64±12</td>
<td>68±12</td>
<td>69±11</td>
<td>69±11</td>
</tr>
<tr>
<td>Female sex</td>
<td>48.2 (3794)</td>
<td>50.1 (1376)</td>
<td>44.8 (585)</td>
<td>35.1 (474)</td>
<td>24.7* (1216)</td>
</tr>
<tr>
<td>Exercise stress</td>
<td>74.1 (5829)</td>
<td>64.7 (1778)</td>
<td>59.0 (771)</td>
<td>57.8 (780)</td>
<td>55.4 (2730)</td>
</tr>
<tr>
<td>Known CAD</td>
<td>12.0 (947)</td>
<td>15.6 (429)</td>
<td>31.2 (408)</td>
<td>42.2 (569)</td>
<td>69.3* (3412)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10.1 (792)</td>
<td>14.9 (409)</td>
<td>17.3 (226)</td>
<td>17.6 (237)</td>
<td>21.8* (1076)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>44.0 (3460)</td>
<td>49.3 (1356)</td>
<td>48.8 (637)</td>
<td>54.8 (739)</td>
<td>51.4 (2533)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>44.4 (3492)</td>
<td>49.3 (1356)</td>
<td>48.8 (637)</td>
<td>54.8 (739)</td>
<td>51.4 (2533)</td>
</tr>
<tr>
<td>Smoking</td>
<td>11.8 (932)</td>
<td>14.4 (397)</td>
<td>12.7 (166)</td>
<td>11.0 (149)</td>
<td>13.8 (681)</td>
</tr>
<tr>
<td>Angina/shortness of breath</td>
<td>44.6 (3511)</td>
<td>45.7 (1256)</td>
<td>47.9 (626)</td>
<td>52.8 (712)</td>
<td>55.3 (945)</td>
</tr>
<tr>
<td>Ischemic ECG response</td>
<td>14.9 (1174)</td>
<td>13.0 (356)</td>
<td>14.2 (185)</td>
<td>18.1 (244)</td>
<td>19.2 (945)</td>
</tr>
<tr>
<td>Ischemic clinical response</td>
<td>4.0 (313)</td>
<td>3.7 (101)</td>
<td>8.7 (113)</td>
<td>8.2 (110)</td>
<td>12.7* (626)</td>
</tr>
</tbody>
</table>

Data are presented as % (n) or mean±SD.

*P<0.001 across groups.
Survival Analysis

Unadjusted as well as adjusted CD rates were assessed. For the latter, Cox proportional hazards analysis was applied to determine the independent prognostic value of clinical, historic, and nuclear parameters. Selection of variables for consideration for entry was based on both univariable statistical significance and clinical judgment. The threshold for entry of variables into the final model was \( P < 0.05 \). A statistically significant increase in the global \( \chi^2 \) of the model after the addition of the tested variables defined incremental prognostic value. Model assumptions of proportional hazards, linearity, and additivity were examined, and risk-adjusted survival and predicted CD rates were determined on the basis of the final model. A Cox proportional hazards regression model was used to evaluate adjusted predictive values for CD according to the perfusion defect and clinical MPS certainty category and to assess an incremental prognostic value of the level of clinical MPS certainty over other clinical information.

Finally, risk-adjusted CD-free survival curves, comparing patients with different levels of clinical MPS certainty as a function of time after the index MPS, were depicted using the final Cox proportional hazards multivariable model.

Results

Clinical Characteristics of the Study Population

Compared with patients with equivocal, abnormal, or probably abnormal MPS, those with MPS deemed to be normal or probably normal were in general younger and more frequently were female, underwent exercise stress, less frequently had angina or dyspnea, history of known CAD (prior myocardial infarction and revascularization), history of diabetes, abnormal rest ECG, and ischemic clinical and ECG response to stress (Table 2).

Of note, no significant differences in clinical and historic variables were noted among the study subgroups with normal and probably normal MPS results, except for slight differences in the perfusion scores (SSS=0 in normal versus SSS=0.96±1.30 in probably normal).

Table 3. Results of Net Reclassification Improvement Analysis (Pencina Index)

<table>
<thead>
<tr>
<th>Population</th>
<th>Patients With Shift “Up” in Their Classification</th>
<th>Patients Without Change</th>
<th>Patients With Shift “Down” in Their Classification</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without CD events</td>
<td>127</td>
<td>15 961</td>
<td>1521</td>
<td>17 609</td>
</tr>
<tr>
<td>With CD events</td>
<td>48</td>
<td>540</td>
<td>3</td>
<td>591</td>
</tr>
</tbody>
</table>

Prognostic Value of Multicategory Clinical MPS Certainty Compared With Standard Perfusion Score Categories

During a mean follow-up of 2.7±1.7 years, there was a total of 591 CD events (3.2%). Figure 3 demonstrates distribution of the CD events by the standard MPS results categorized using SSS.\(5,14\) Data distributed by summed scores allowed an excellent risk stratification of the patient population into 4 large groups with significant step-up in cardiac risk from category to category. The “normal” SSS category (SSS=0 to 3) was the largest, making up the majority of the patient population, and had a very low CD rate (0.4%). The event rate of the next SSS subgroup (4 to 8) had nearly 3 times the CD rate of the “normal” group, but even in this group, the CD rate was low (1.3%). Despite the low CD rate in these groups, 125 of 591 CDs (21%) occurred in the 1-3 group and 93 of 591 (16%) of the CDs occurred in the 4-8 group. From analysis of data not shown, in the SSS=0 to 3 group, categories of clinical MPS certainty other than normal or probably normal were associated with significantly higher cardiac mortality (relative risk of 2.8; \( P < 0.001 \)). In the SSS=4 to 8 group, there was also a progressive increase in CD as the category of clinical MPS certainty increased. Thus, there was additive prognostic information in these 2 groups, based on the categories of clinical MPS certainty over what would be derived by simple categorization as “normal” or “mildly abnormal” based on the SSS alone.

These results are confirmed by the calculation of the net gain in reclassification (NRI) (Table 3). Observed shift to the abnormal category in patients with events and shift into the normal category in those without events, using clinical MPS certainty categories, was associated with an overall 16%
improvement in reclassification ($P<0.001$), allowing a better stratification of 1 of every 6 patients in this study population.

Figure 4 demonstrates the CD rate in patients distributed by the levels of clinical MPS certainty based on the segmental perfusion scores alone compared with the levels of certainty in the final interpretation (“perfusion+shift”). Both methods allowed effective risk stratification (both $P<0.001$ across the scan certainty categories). However, implementation of the shift in the final clinical interpretation approach resulted in a significantly lower number of equivocal scans compared with the categorization based on perfusion scores alone ($P=0.01$); in addition, the risk of CD associated with equivocal scans identified using the final clinical interpretation protocol was significantly higher compared with that of normal or probably normal MPS, defined by perfusion score only, and was intermediate between the risks of the probably normal and probably abnormal categories. No differences in CD rate were found among the rest of the compared groups.

**CD by Category of Clinical MPS Certainty: Impact of Prior Known CAD**

When the patients without and those with known CAD were separately considered, slight differences were seen in the intermediate categories of interpretive certainty (Figure 5A and 5B). In both groups of patients, there appeared to be 3 clusters of mortality rates among the 5 possible categories of interpreter certainty. In the patients without known CAD, patients with normal and probably normal studies had similar low annualized CD rates. Patients with definitely abnormal scans had high annualized CD rates (2.4%/y). Patients with equivocal and probably abnormal scans had low-intermediate CD rates (1.1% and 1.2%, respectively). Among the patients with known CAD, the rates of CD were similarly low in the normal, probably normal, and equivocal categories, high-intermediate in the probably abnormal category (1/8%/y), and high in the definitely abnormal group (3.2%/y).

**Univariable Predictors of CD Events in the Study Population**

Thresholds of abnormal MPS, defined as SSS $>3$ and SSS $>0$, were the strongest univariable predictors of CD, followed by inability to perform an exercise stress, age, abnormal resting ECG, and history of CAD (prior myocardial infarction or revascularization). Other significant univariable predictors of CD were diabetes, hypertension, and symptoms of angina and/or shortness of breath, and male sex. Presence of reversible defects (ischemia) defined as SDS $>0$ was a significant predictor of CD, although less powerful compared with the stress perfusion defects, as defined by SSS (Table 4).

**Multivariable Predictors of CD Events**

When Cox proportional hazards analysis was applied to the study population, after taking in consideration of all of the significant univariable predictors of prognosis, the level of clinical MPS certainty in the final multivariable model remained a significant independent predictor of CD (Table 5).

It remained an independent and incremental predictor of cardiac mortality even when thresholds of SSS $>0$, SSS $>3$, and SDS $>0$ were considered. In the combined population (Figure 6), risk-adjusted survival curves for normal and probably normal scans overlapped and did not show separation, whereas survival curves for the equivocal, probably abnormal, and definitely abnormal scans demonstrated early separation and remained significantly different during the entire follow-up period. When analyzed separately, the impact of the clinical certainty level of the MPS interpretation on the risk-adjusted survival of patients with and with no known CAD demonstrated important differences (Figure 7, A and B).

**Table 4. Univariable Predictors of Cardiac Death in the Study Population**

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSS $&gt;3$</td>
<td>6.09</td>
<td>5.01–7.41</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SSS $&gt;0$</td>
<td>5.83</td>
<td>4.66–7.30</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pharm stress</td>
<td>5.57</td>
<td>4.62–6.70</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinical MPS certainty</td>
<td>5.16</td>
<td>4.04–6.58</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age $&gt;70$ y</td>
<td>3.53</td>
<td>2.96–4.21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Known CAD</td>
<td>3.49</td>
<td>2.95–4.13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Abnormal resting ECG</td>
<td>3.21</td>
<td>2.76–3.91</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SDS $&gt;0$ (any ischemia)</td>
<td>2.70</td>
<td>2.27–3.21</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.32</td>
<td>1.93–2.79</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Symptoms (angina/shortness of breath)</td>
<td>1.87</td>
<td>1.57–2.21</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.34</td>
<td>1.14–1.58</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male gender</td>
<td>1.25</td>
<td>1.08–1.53</td>
<td>0.004</td>
</tr>
</tbody>
</table>

HR indicates hazard ratio; MPS, myocardial perfusion SPECT.
In patients with no known CAD, survival curves of the patients with normal and probably normal scans were superimposed (Figure 7A). In accordance with the unadjusted data shown in Figure 5, the curves of equivocal and probably abnormal scans were also superimposed and were lower than the curves of the normal and probably normal groups. There was clearly lower survival in the patients with definitely abnormal scans than in the other groups. In patients with known CAD (Figure 7B), the survival curves of patients with normal, probably normal, and equivocal scans were similar (curves were superimposed), and survival was progressively lower in those with probably abnormal and definitely abnormal scans.

Discussion

This is the first study, to the best of our knowledge, attempting to assess the prognostic value of the various levels of reader certainty in MPS interpretation in patients with known or suspected CAD, although the prognostic implications of this approach were previously described for planar myocardial perfusion scintigraphy. Our findings show that the various levels of clinical MPS certainty have added value in prediction of CD over a dichotomous consideration of scans as “normal” or “abnormal” based on the SSS. In patients with MPS that would be defined as normal based on traditional SSS-based categorization, the various levels of clinical MPS certainty were able to reclassify a substantial proportion of patients at significantly increased risk of CD. Net reclassification improvement using new MPS interpretation classification was 16%, suggesting an improvement in the ability to risk-stratify patients by the clinical MPS certainty categories in every 1 of 6 patients. Furthermore, when compared with the clinical MPS certainty based on segmental score categories alone, the use of the final clinical MPS certainty categories (“perfusion + shift”) resulted in a smaller group of patients whose scans are deemed equivocal.

Our findings suggest that a simple, practical, clinical approach to the integration of perfusion and nonperfusion data into a single variable using the 5 categories of final interpretation may be useful both where the interpreting physicians performs semiquantitative or quantitative reading of the perfusion and in settings in which interpreting physicians provide a qualitative interpretation of the perfusion abnormality. This 5 category of clinical MPS certainty approach allows slight modification of MPS interpretation using patient-specific data that is not possible with a simple dichotomous classification (either quantitative or qualitative), based solely on the perfusion scan results. Potentially, the implementation of the clinically adjusted scan interpretation is generalizable to any type of ischemia testing, and, if implemented, would be in accordance with attempts of professional societies to standardize data from multiple diagnostic modalities.

Comparison With Prior Studies: Existing Controversies in the Expert Approach to the MPS Results Interpretation

Expert MPS interpretation in daily practice is a complex process. The clinical presentation, patient medical history, and physical examination, as well as expert knowledge and experience all are significant factors that are used to deter-

Table 5. Final Multivariable Cox Proportional Hazards Model for Prediction of CD

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR</th>
<th>95% CI</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, nonlinear</td>
<td>1.05</td>
<td>1.04–1.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pharm stress</td>
<td>2.76</td>
<td>2.27–3.37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Known CAD</td>
<td>1.25</td>
<td>1.03–1.50</td>
<td>0.021</td>
</tr>
<tr>
<td>Ischemic stress ECG</td>
<td>1.46</td>
<td>1.07–2.00</td>
<td>0.018</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.58</td>
<td>1.32–1.90</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Symptoms (angina/shortness of breath)</td>
<td>1.25</td>
<td>1.06–1.48</td>
<td>0.010</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.38</td>
<td>1.09–1.76</td>
<td>0.008</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>1.31</td>
<td>1.10–1.56</td>
<td>0.002</td>
</tr>
<tr>
<td>Digoxin therapy</td>
<td>2.04</td>
<td>1.67–2.50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinical MPS certainty</td>
<td>4.79</td>
<td>3.65–6.29</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinical MPS certainty (with SSS &gt;0 considered in the model)</td>
<td>4.09</td>
<td>2.70–8.92</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinical MPS certainty (with SSS &gt;3 considered in the model)</td>
<td>2.56</td>
<td>1.51–4.35</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinical MPS certainty (with SDS &gt;0 considered in the model)</td>
<td>5.78</td>
<td>4.18–7.99</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

HR indicates hazard ratio.

*Adjusted for age, gender, type of stress, symptoms (angina/SOB), history of CAD (prior MI/Revasc), diabetes, hyperlipidemia and ischemic ECG response.
mine the patient’s pretest likelihood of CAD. The post-test likelihood of CAD as well as predicted risk after MPS is significantly influenced by consideration of exercise stress data, vasodilator-induced heart rate changes, left ventricular ejection fraction or regional wall motion abnormalities, or transient ischemic dilation (TID), even in patients with perfectly normal perfusion.

With regard to endpoints of the study, previous reports demonstrated that extent and severity of the stress perfusion defect, expressed as SSS, are the best marker of hard events and CD, whereas extent and severity of the ischemia (expressed as SDS) is a predictor of myocardial infarction and of benefit with cardiovascularization. In this report, we focused on CD alone, and thus considered risk stratification based on SSS rather than SDS.

For physicians who use the recommended 17-segment interpretation, the use of the 5 levels of clinical MPS certainty may clarify their reporting. When the SSS is 0 (or even 1), the clinical implications are clear. When the SSS is ≥4, the study is considered abnormal. Further clinical decision-making would most likely consider CAD to be present. However, when the SSS is 2 to 3, the clinical implications are not clear. Most likely, physicians who use summed stress scoring consider these scores equivocal. By using the 5 levels of clinical MPS certainty in the final interpretation and permitting a single category shift, many such studies can be considered “probably normal” or “probably abnormal,” allowing the interpreter to convey a stronger message to the referring physician that can be used in further clinical decision-making than would have occurred by summed stress scoring alone. In our study, implementing the single category shift, there was a 17% reduction in the proportion of scans considered equivocal.

For interpreting physicians who do not read MPS with the semiquantitative scoring, adoption of the 5 levels of certainty provides a systematic way in which to take into account the clinical and stress findings when arriving at a final interpretation of an MPS study.

**Difference in the Interpretation of MPS Findings Between Those With and Those Without Known CAD**

In our previous research, we demonstrated that patients with known CAD who are referred to stress testing have clinical characteristics different from those with suspected CAD; their prognostic data also may differ, which usually requires a separate survival analysis of these clinical subsets.

In this study, in both populations (with and without known CAD), the prognosis associated with normal and probably normal final interpretations were the same. Although this distinction allows the reader to express that some minor unusual finding was present, clinicians should be advised that...
this minimal distinction does not have prognostic importance. In patients with known CAD, even the equivocal final diagnostic category was not associated with increased prognostic risk. In patient with no prior history of CAD, however, an equivocal final interpretation was associated with a significantly worse prognosis. Since the “one category shift” in the 5-category system would allow an otherwise probably normal study to be considered equivocal, it may provide a means of avoiding complete miscategorization of patients with high-risk anatomic findings. Given the relatively high proportion of CDs in our study that were in the normal scan group by normal/abnormal categories alone, this distinction may prove to be of clinical importance.

Study Limitations
Although this study is retrospective in nature, all data elements were collected and entered prospectively with the knowledge that they would become part of a research database. We used a 20-segment model on the left ventricle for the semiquantitative perfusion scan interpretation instead of the currently recommended 17-segment model. However, as demonstrated in our prior research, prognostic information from the summed scores on MPS derived on the basis of the 20-segment model is very similar to that obtained with the 17-segment model.

Ventricular function was not assessed in all the patients because gated MPS was not routinely performed in our center until 1995, and a large proportion of the database used in this study was obtained before this time. Future research is needed to evaluate the impact of ventricular function data derived from gated MPS on the level of clinical MPS certainty. Adding functional and any other novel nonperfusion risk marker data could allow further restratification of the patients who, by the traditional approach, will be considered otherwise at lower risk. Our approach of adjusting clinical certainty of the scan interpretation offers a mechanism allowing easy adjustment of the image reading and final impression to any novel risk markers evolving in the future.

Previous data suggest that MPS results may influence and intensity of medical therapy and outcomes, especially after the normal scan. We could not assess this important issue because of incomplete capture of the medical therapy regimen in the study population during follow-up. Finally, the study is based on data of a single nuclear cardiology center with interpretations by highly experienced cardiac imaging specialists with an agreed on, standardized approach to image interpretation, and the findings may not be applicable in other nuclear laboratories. To determine whether the 5-category approach to clinical MPS certainty incorporating 1 category shift would provide similar prognostic information if it were based on qualitative assessment alone compared to semiquanti
tative scoring, or whether it also applies when computer software-based qualitative analysis is performed would require further study.

Conclusions
In the large population of patients with known or suspected CAD referred for stress MPS, multicaregory level of the clinical MPS certainty was found to be an independent multivariable predictor of CD in the study population. The use of multicaregory reporting of MPS results incorporating nonperfusion MPS results and clinical information enhances risk stratification compared with a dichotomous normal/abnormal approach or an approach based solely on the categories of summed perfusion scores. Whether this enhanced risk stratification based on the clinical certainty of the MPI interpretation leads to a more effective therapeutic regimen, tailored to the individual patient’s need, requires further prospective evaluation.

Sources of Funding
This work was supported in part by grants from Bristol-Myers Squibb Medical Imaging Inc (Billerica, Mass) and Astellas Inc (Deerfield, Ill).

Disclosures
Dr Abidov received a research grant from William Beaumont Hospital-Oakland University Multidisciplinary Award and is a consultant on the advisory board for the Department of Imaging at Cedars-Sinai Medical Center. Dr Hachamovitch received research grants from Bracco Diagnostics, Astellas Pharma, Siemens Medical Solutions, and GE Healthcare and honoraria from Bracco Diagnostics and is a consultant on the advisory board at Lantheus Medical Imaging, Wyeth Pharmaceuticals. Dr Hayes is on the speakers bureau at Astellas. Dr Friedman is on the speakers bureau at Covidian and has ownership interest in Spectrum Dynamics, Cedars-Sinai Medical Center. Dr Thomson received honoraria from Bracco Diagnostics and is a consultant on the advisory board at Lantheus Medical Imaging, Wyeth Pharmaceuticals. Dr Slomka received a research grant from the National Institutes of Health (RO1 HL08976S-01) and is affiliated with Cedars-Sinai Medical Center. Dr Berman received research grants from Lantheus Medical Imaging, Astellas Healthcare, Medtronic, GE Healthcare, and Siemens, and honoraria from Lantheus Medical Imaging, Covidian, Astellas, Flouro Pharma, and Magellan, has ownership interest in Spectrum Dynamics, and is a consultant on the advisory board at Lantheus, Covidian, Astellas, Flouro Pharma, Magellan, and Cedars-Sinai Medical Center.

References
CLINICAL PERSPECTIVE

Myocardial perfusion single-photon emission computed tomography (MPS) is one of the most commonly used cardiac imaging tests, yet the way it is reported is not uniform. Although semiquantitative analysis of the global perfusion deficit has been shown to be prognostically important, it is not universally used, and the implication of nonzero scores that fall below the threshold of abnormal is unclear. We sought to determine whether expression of the level of certainty regarding presence of abnormality (5-point score, from definitely normal to definitely abnormal) had prognostic value. Based on the analysis of the clinical and prognostic data of 18,200 patients who underwent rest-stress dual-isotope MPS, we demonstrated that the final level of clinical scan certainty is an independent multivariable predictor of cardiac death in the study population. The use of multicategory reporting of MPS results incorporating nonperfusion MPS results and clinical information enhances risk stratification in comparison to both a dichotomous normal/abnormal approach and an approach based solely on summed perfusion scores and results in a smaller group of patients whose scans are deemed to be equivocal.
Are Shades of Gray Prognostically Useful in Reporting Myocardial Perfusion Single-Photon Emission Computed Tomography?

Aiden Abidov, Rory Hachamovitch, Sean W. Hayes, John D. Friedman, Ishac Cohen, Xingping Kang, Ling De Yang, Louise Thomson, Guido Germano, Piotr Slomka and Daniel S. Berman

Circ Cardiovasc Imaging. 2009;2:290-298; originally published online May 11, 2009;
doi: 10.1161/CIRCIMAGING.108.815811

Circulation: Cardiovascular Imaging is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2009 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-9651. Online ISSN: 1942-0080

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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