Risk Assessment Using Single-Photon Emission Computed Tomographic Technetium-99m Sestamibi Imaging

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Methods. We analyzed published reports in English on risk assessment using Tc-99m perfusion tracers.

Results. The largest experience is in patients with stable symptoms, comprising >12,000 patients in 14 studies. In these patients, normal stress SPECT sestamibi images were associated with an average annual hard event rate of 0.6% (death or nonfatal myocardial infarction [MI]). In contrast, patients with abnormal images had a 12-fold higher event rate (7.4% annually). Both fixed and reversible defects are prognostically important, and quantitative analysis shows increased risk in relation to the severity of the abnormality. These results are similar to those obtained with thallium-201.

Conclusions. Patients with stable chest pain syndromes and normal stress SPECT sestamibi images have a very low risk of death or nonfatal MI. It is highly unlikely that coronary revascularization can improve survival in such patients. Patients with abnormal images have an intermediate to high risk for future cardiac events, depending on the degree of the abnormality. Further prospective studies comparing aggressive medical therapy with coronary revascularization in these patients are warranted.

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coronary syndromes, patients undergoing major noncardiac surgery and patients with chest pain in the emergency department. All studies were performed with single-photon emission computed tomography (SPECT) but without gating or attenuation correction.

**Patients With Stable Chest Pain Syndromes**

A summary of the studies dealing with patients with stable chest pain syndromes is presented in Table 1 (16–29). The stress modalities included exercise in eight studies and pharmacologic modalities in six. In three studies from the same institution (16,19,20), a dual-isotope protocol (rest thallium and stress sestamibi) was used, but because the prognostic value was related to the stress images, these studies were included here. Four of the 14 studies were from the same institution, earlier studies (16,23). Cumulatively, there were >12,000 patients in these studies; 55% of patients were men, and the mean age of the patients was 61 years. Traditional coronary risk factors were present in many patients, such as remote MI in 22%, hypertension in 50% and diabetes mellitus in 16%. The average follow-up period was 20 months.

The annual rate of hard cardiac events (death or nonfatal MI) in patients with normal stress SPECT sestamibi images and in those with abnormal images is shown in Table 1. The average annual event rate was 12-fold higher in patients with abnormal images than in patients with normal images (7.4% vs. 0.6%) (Fig. 1). Therefore, patients with normal stress sestamibi images had a very low hard event rate of 1%/year, similar to the experience with stress thallium imaging. This event rate is comparable to that in the general population in the United States (30). In all studies, both fixed and reversible defects were prognostically important. Fixed defects are a more important predictor of death whereas reversible defects are an important predictor of nonfatal MI. Studies that included quantitative assessment of defect size (16,19,20,23) showed that the event rate was significantly greater in patients with severe than in those with mild abnormalities. For example, in one study (16), the annual hard event rate was 10.6% in patients with severe and 3.5% in patients with mild abnormalities and in another (19), the annual hard event rate was 6% and 3%, respectively. Furthermore, the prognostic power of

<table>
<thead>
<tr>
<th>Study (ref no.)</th>
<th>Year</th>
<th>No. of Pts</th>
<th>Mean Age (yr)</th>
<th>Men</th>
<th>Hx of Stress Tracer</th>
<th>Type of Stress</th>
<th>Tracer</th>
<th>F/U (mo)</th>
<th>Hard Events*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hachamovitch et al. (16)</td>
<td>1997</td>
<td>1,159</td>
<td>72</td>
<td>50%</td>
<td>18%</td>
<td>55%</td>
<td>66%</td>
<td>AD</td>
<td>275</td>
</tr>
<tr>
<td>Boyne et al. (17)</td>
<td>1997</td>
<td>229</td>
<td>58</td>
<td>50%</td>
<td>27%</td>
<td>—</td>
<td>—</td>
<td>Ex</td>
<td>Mibi</td>
</tr>
<tr>
<td>Nallamouthu et al. (18)</td>
<td>1996</td>
<td>412</td>
<td>57</td>
<td>65%</td>
<td>6%</td>
<td>43%</td>
<td>11%</td>
<td>Ex</td>
<td>Mibi</td>
</tr>
<tr>
<td>Hachamovitch et al. (19)</td>
<td>1996</td>
<td>2,113</td>
<td>61</td>
<td>60%</td>
<td>0</td>
<td>39%</td>
<td>9%</td>
<td>Ex</td>
<td>Dual†</td>
</tr>
<tr>
<td>Hachamovitch et al. (20)</td>
<td>1996</td>
<td>4,136</td>
<td>63</td>
<td>0</td>
<td>21%</td>
<td>—</td>
<td>—</td>
<td>Ex</td>
<td>Dual</td>
</tr>
<tr>
<td>Geleijnse et al. (21)</td>
<td>1996</td>
<td>80</td>
<td>61</td>
<td>0</td>
<td>13%</td>
<td>53%</td>
<td>13%</td>
<td>Dob</td>
<td>Mibi</td>
</tr>
<tr>
<td>Geleijnse et al. (22)</td>
<td>1996</td>
<td>392</td>
<td>60</td>
<td>56%</td>
<td>48%</td>
<td>43%</td>
<td>15%</td>
<td>Dob</td>
<td>Mibi</td>
</tr>
<tr>
<td>Berman et al. (23)</td>
<td>1995</td>
<td>1,702</td>
<td>62</td>
<td>61%</td>
<td>11%</td>
<td>—</td>
<td>10%</td>
<td>Ex</td>
<td>Mibi</td>
</tr>
<tr>
<td>Heller et al. (24)</td>
<td>1995</td>
<td>512</td>
<td>67</td>
<td>44%</td>
<td>27%</td>
<td>58%</td>
<td>25%</td>
<td>DP</td>
<td>Mibi</td>
</tr>
<tr>
<td>Zanco et al. (25)</td>
<td>1995</td>
<td>147</td>
<td>53</td>
<td>82%</td>
<td>40%</td>
<td>—</td>
<td>—</td>
<td>Ex</td>
<td>Mibi</td>
</tr>
<tr>
<td>Brown et al. (26)</td>
<td>1994</td>
<td>234</td>
<td>55</td>
<td>54%</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Ex/DP</td>
<td>Mibi</td>
</tr>
<tr>
<td>Stratmann et al. (27)</td>
<td>1994</td>
<td>521</td>
<td>60</td>
<td>98%</td>
<td>35%</td>
<td>48%</td>
<td>12%</td>
<td>Ex</td>
<td>Mibi</td>
</tr>
<tr>
<td>Stratmann et al. (28)</td>
<td>1994</td>
<td>534</td>
<td>65</td>
<td>97%</td>
<td>37%</td>
<td>59%</td>
<td>21%</td>
<td>DP</td>
<td>Mibi</td>
</tr>
<tr>
<td>Raiker et al. (29)</td>
<td>1994</td>
<td>208</td>
<td>59</td>
<td>52%</td>
<td>5%</td>
<td>—</td>
<td>—</td>
<td>Ex</td>
<td>Mibi</td>
</tr>
<tr>
<td>Total/average</td>
<td></td>
<td>12,360</td>
<td>61</td>
<td>55%</td>
<td>22%</td>
<td>50%</td>
<td>16%</td>
<td>—</td>
<td>Mibi</td>
</tr>
</tbody>
</table>

*Death or nonfatal myocardial infarction (MI). †Stress MIBI/rest thallium. AB = abnormal; AD = adenosine; DM = diabetes mellitus; Dob = dobutamine; DP = dipyridamole; Ex = exercise; F/U = follow-up; HTN = hypertension; Hx = history; Mibi = sestamibi; NL = normal; Pts = patients; ref = reference; SPECT = single-photon emission computed tomography; — = not available.
normal and abnormal stress images was equally important in men and women. In fact, women with severe abnormalities had a worse outcome than men with severe abnormalities (8% vs. 4% [5]). Incorporation of other SPECT variables, such as LV dilation (transient or fixed), LV ejection fraction (LVEF) and volumes (derived from gated SPECT), are likely to further enhance the prognostic power of SPECT imaging but require further study (7,9,10,15).

Classification of patients into low and high risk has been confirmed regardless of the pretest probability of CAD; that is, patients with a high pretest probability of CAD but normal stress SPECT images have a benign outcome, as do patients with a low pretest probability of CAD and normal images. However, because the overall risk in patients with a low pretest probability of CAD is low, stress imaging in this group is probably not cost-effective. The most cost-effective strategy is to study patients with an intermediate to high pretest probability of CAD (19,20). Furthermore, when quantitative analysis such as the summed stress score (determined by the extent and severity of abnormalities on the basis of a 20-segment model) was used, the risk of death and nonfatal MI varied according to the severity of abnormalities (19,31). For example, patients with mild abnormalities had an intermediate risk of nonfatal MI and a low risk for cardiac death, whereas patients with severe abnormalities had a high risk for death and an intermediate risk for nonfatal MI. These observations are important because coronary revascularization, including percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass graft surgery (CABG), have not been shown to lower the rate of nonfatal MI (32).

In our experience (5), events occurred ~2 years from the index stress test in patients with normal SPECT images. This finding may suggest that the “warranty” period for a normal stress sestamibi scan (i.e., duration of follow-up after a normal stress study) appears to be ~2 years; after that period, the event rate increases, probably reflecting the progressive nature of underlying CAD. However, the value of follow-up periodic testing in asymptomatic patients is still unclear because of improvements in medical therapy.

The prognostic value of stress testing with SPECT has also been confirmed in relation to the Duke treadmill exercise score. This score, which incorporates exercise duration and ST segment depression and angina during exercise, has been used to stratify patients into low, intermediate and high risk groups (33,34). The intermediate risk group comprised at least 50% of patients studied in a multicenter study of >4,581 patients (35). Patients with an intermediate Duke treadmill exercise score and normal SPECT images (50% of these were done with sestamibi) had an event rate of only 0.2%/year. American College of Cardiology/American Heart Association guidelines reports (36,37) have recommended that patients with an intermediate Duke score undergo either coronary angiography or an imaging modality (36,37). It is to be hoped that subsequent practice guidelines will carefully consider the new evidence and recommend the use of stress myocardial perfusion imaging in such patients.

It is equally important to note that the rate of early catheterization and coronary angiography was very low in patients with normal images (3.8% [16], 1% [19] and 1.4% [14]) and appropriately high in patients with abnormal images (17% [19] and 10% [16] for mild abnormalities, 42% [19] and 27% [16] for severe abnormalities).

### Noncardiac Surgery

Several guidelines have been published for risk assessment of patients undergoing major noncardiac surgery (38–41). This review is not intended to summarize these guidelines nor to critique them, but only to provide summary of published reports on the use of Tc-99m sestamibi. The risk after major noncardiac surgery includes perioperative and late events. The perioperative risk is exceedingly low in patients with normal stress sestamibi images. Similar to that in patients with stable symptoms, the late event rate is significantly higher in patients with abnormal than in those with normal scans (Table 2) (42–44).

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**Table 2. Summary of Studies on Risk Assessment Using Technetium-99m Sestamibi in Coronary Artery Disease**

<table>
<thead>
<tr>
<th>Study (ref no.)</th>
<th>Year</th>
<th>Study</th>
<th>No. of Pts</th>
<th>Mean Age (yr)</th>
<th>Men</th>
<th>% Abnormal Scan</th>
<th>Type</th>
<th>F/U</th>
<th>NL SPECT</th>
<th>AB SPECT</th>
<th>Type of Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stratmann et al. (49)</td>
<td>1995</td>
<td>UA</td>
<td>128</td>
<td>64</td>
<td>100%</td>
<td>77%</td>
<td>DP</td>
<td>16</td>
<td>5%</td>
<td>23%</td>
<td>D, MI</td>
</tr>
<tr>
<td>Stratmann et al. (48)</td>
<td>1995</td>
<td>UA</td>
<td>126</td>
<td>58</td>
<td>100%</td>
<td>59%</td>
<td>Ex</td>
<td>12</td>
<td>2%</td>
<td>14%</td>
<td>D, MI</td>
</tr>
<tr>
<td>Miller et al. (47)</td>
<td>1995</td>
<td>MI</td>
<td>274</td>
<td>62</td>
<td>77%</td>
<td>26%</td>
<td>Rest</td>
<td>12</td>
<td>0</td>
<td>7%</td>
<td>D</td>
</tr>
<tr>
<td>Travin et al. (46)</td>
<td>1995</td>
<td>MI</td>
<td>120</td>
<td>61</td>
<td>67%</td>
<td>80%</td>
<td>Ex</td>
<td>15</td>
<td>5%</td>
<td>30%</td>
<td>D, MI, UA</td>
</tr>
<tr>
<td>Miller et al. (45)</td>
<td>1994</td>
<td>MI/UA</td>
<td>137</td>
<td>65</td>
<td>92%</td>
<td>80%</td>
<td>DP</td>
<td>10</td>
<td>0</td>
<td>22%</td>
<td>D, MI</td>
</tr>
<tr>
<td>Maunoury et al. (44)</td>
<td>1996</td>
<td>Preop</td>
<td>43</td>
<td>64</td>
<td>47%</td>
<td>35%</td>
<td>AD</td>
<td>0.1</td>
<td>0</td>
<td>27%</td>
<td>MI, UA</td>
</tr>
<tr>
<td>Stratmann et al. (43)</td>
<td>1995</td>
<td>Preop</td>
<td>197</td>
<td>65</td>
<td>98%</td>
<td>56%</td>
<td>DP</td>
<td>21</td>
<td>3%</td>
<td>5%</td>
<td>D, MI, UA, PE</td>
</tr>
<tr>
<td>Stratmann et al. (42)</td>
<td>1996</td>
<td>Preop</td>
<td>229</td>
<td>67</td>
<td>99%</td>
<td>60%</td>
<td>DP</td>
<td>0.1</td>
<td>1%</td>
<td>14%</td>
<td>D, MI, UA, PE</td>
</tr>
</tbody>
</table>

*References 42 to 44 addressed perioperative evaluation, and references 45 to 49 addressed risk assessment in patients with acute coronary syndromes. AD = adenosine; D = death; PE = pulmonary edema; Preop = preoperative evaluation; UA = unstable angina; other abbreviations as in Table 1.*
Acute Coronary Syndromes

A limited number of studies in small groups of patients have evaluated the use of sestamibi imaging either at rest or during stress in patients with unstable angina or after acute MI. Again, patients with normal images or small defects have a significantly better outcome than patients with abnormal images or large defects (Table 2) (45–49). Patients with an acute MI may benefit from a single center study of 268 patients demonstrated (50) that early pharmacologic stress imaging may be useful for risk stratification in patients admitted with a diagnosis of acute MI. More studies in larger series of patients with and without thrombolytic therapy and angioplasty are needed.

Patients With Chest Pain in the Emergency Department

It is estimated that 6 million patients/year visit the emergency department in the United States for evaluation of chest pain (7% of all visits), and although only 10% to 15% of these patients have an acute MI, ~50% are admitted to the coronary care unit to rule out acute MI (51–56). Several studies show that patients with a low risk rest perfusion scan with Tc-99m sestamibi in the emergency department have a low subsequent cardiac event rate, whereas patients with a high risk scan have a higher probability of acute MI, revascularization or documentation of stenoses on cardiac catheterization (Table 3) (56–60).

Conclusions

Several studies show that patients with chest pain syndromes but normal stress SPECT perfusion images using Tc-labeled tracers have a very low event rate (<1%/year for death or nonfatal MI). It is therefore very unlikely that further invasive strategies, including PTCA or CABG, can improve the outcome. These results are similar to those for stress SPECT thallium imaging but differ from stress two-dimensional echocardiography. Multiple studies using stress echocardiography have shown (61) a higher event rate in patients with no evidence of ischemia. The difference between the prognostic value of different stress tests underscores the fact that outcome results by one method cannot be extrapolated to another. The risk of events is substantially higher in patients with abnormal than in those with normal SPECT imaging results. The management of patients with abnormal images as well as the frequency of testing are not clear and should at present be individualized; they deserve further study.

References

12. Schalet BD, Kegel JG, Heo J, Segal BL, Iskandrian AS. Prognostic Impli-

Table 3. Results of Rest Sestamibi Single-Photon Emission Computed Tomography in Patients With Chest Pain in Emergency Department

<table>
<thead>
<tr>
<th>Study (ref no.)</th>
<th>No. of Pts</th>
<th>Abnormal</th>
<th>Type of Study</th>
<th>NL Scan</th>
<th>AB Scan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varetto et al. (60)</td>
<td>64</td>
<td>47%</td>
<td>Rest mibi</td>
<td>0</td>
<td>43%</td>
</tr>
<tr>
<td>Hilton et al. (59)</td>
<td>102</td>
<td>31%</td>
<td>Rest mibi</td>
<td>0</td>
<td>41%</td>
</tr>
<tr>
<td>Hilton et al. (58)</td>
<td>102</td>
<td>22%</td>
<td>Rest mibi</td>
<td>0</td>
<td>8%</td>
</tr>
<tr>
<td>Tatum et al. (57)</td>
<td>442</td>
<td>24%</td>
<td>Rest mibi</td>
<td>0</td>
<td>7%</td>
</tr>
<tr>
<td>Kontos et al. (56)</td>
<td>532</td>
<td>32%</td>
<td>Rest mibi</td>
<td>0.6%</td>
<td>15%</td>
</tr>
</tbody>
</table>

Rev = coronary revascularization; other abbreviations as in Tables 1 and 2.

We thank Renee Brown for secretarial assistance.


38. Travin MI, Dessouki A, Cameron T, Heller GV. Use of exercise technetium-99m sestamibi SPECT imaging to detect residual ischemia and for risk stratification after acute MI. Am J Cardiol 1995;75:665–9.


61. Brown KA. Noninvasive cardiac risk stratification of patients with known or suspected coronary artery disease: do myocardial perfusion imaging and stress echocardiography provide the same information? Am J Cardiol. In press.