Preoperative Risk Stratification With Myocardial Perfusion Imaging in Intermediate and Low-Risk Non-Cardiac Surgery

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Background  Perioperative cardiac risk in high risk surgery is often stratified with myocardial perfusion single-photon emission computed tomography (SPECT). However, little and no data are available about intermediate and low-risk surgery, respectively.

Methods and Results  A total of 1,220 consecutive patients underwent electrocardiography-gated dipyridamole stress SPECT to evaluate myocardial perfusion and cardiac function before intermediate or low risk non-cardiac surgery. Variables predictive of perioperative cardiac events were determined and the usefulness of combining pretest information and the incremental prognostic value of SPECT was estimated. The frequency of all cardiac events depended on clinical risk factors and type of surgical procedures. After sorting the patients with clinical risk factors and surgical risk, assessment of myocardial perfusion or cardiac function yielded significant risk stratification in intermediate, but not in low-risk surgery. Adding functional data to perfusion variables offered an incremental prognostic value for patients with an intermediate clinical risk and scheduled intermediate risk surgery.

Conclusions  Integrating information about clinical risk factors, type of surgery, myocardial perfusion and cardiac function allows detailed preoperative risk stratification. Preoperative SPECT provides an incremental prognostic value in intermediate, but not in low-risk surgery. (Circ J 2007; 71: 1395–1400)

Key Words: Gated-single-photon emission tomography; Myocardial perfusion; Perioperative cardiac event; Preoperative risk stratification

Cardiac risk should be stratified in individual patients who are to undergo surgery, but it is difficult to assess the likelihood of perioperative cardiac events mainly because of complicated interrelationships between clinical risk factors and type of surgery. To overcome this problem, The American College of Cardiology/American Heart Association (ACC/AHA) Task Force published guidelines for perioperative cardiovascular evaluation for non-cardiac surgery in 1996 and 2002.1,2 These guidelines divide clinical risk factors into major, intermediate and minor categories, and surgical procedures into high, intermediate and low-risk types. These are then used to determine further preoperative examinations, preoperative therapy, operative performance and perioperative management. The guidelines regard myocardial perfusion imaging as a supplement to preoperative evaluation. Although there have been enough data concerning the use of myocardial perfusion single-photon emission computed tomography (SPECT) for perioperative risk stratification in high-risk surgery3–15 little and no data are available about intermediate12,14–18 and low-risk surgery, respectively.

The present study investigated the feasibility of assessing perioperative cardiac risk considering clinical risk factors, types of surgery and the results of cardiac testing. We sought variables predictive of cardiac events and estimated the usefulness of combining pretest information. We focused on the incremental prognostic value of preoperative cardiac testing in intermediate- and low-risk surgery.

Methods

This retrospective cohort study examined data collected from patients referred for preoperative stress myocardial perfusion SPECT before non-cardiac surgery. Written informed consent was obtained from all patients concerning the examination protocol, possible side-effects and the use of SPECT data for research purposes. The form to obtain consent was approved by the institutional committee.

Patient Population

Our database for preoperative risk stratification with myocardial perfusion SPECT was used to identify 2,402 consecutive patients who underwent preoperative dipyridamole stress SPECT between January 1997 and October 2005. All 1,339 patients in the database meeting the following criteria were selected to participate in the current study: scheduled non-cardiac surgery of intermediate or low risk, and having intermediate or minor clinical risk factors. The classifications of operation risk and clinical risk factors were based on the ACC/AHA Guidelines.1,2 Operation was cancelled or deferred after SPECT imaging in 119 patients, and 1,220 patients underwent surgery. The types of surgery and clinical risk of the 1,220 patients are indicated in Table 1 and demo...
graphic data are presented in Table 2.

**Myocardial SPECT Imaging**

Technetium-99m tetrofosmin or Sestamibi was the agent used for myocardial perfusion imaging. A rest/stress 1-day protocol was applied using doses of 300/850 MBq of tracer, and SPECT acquisition was started 30 min after injection. In the stress study, patients were continuously injected with 0.56 mg/kg of dipyridamole for 4 min, and then the perfusion tracer was administered 3 min after the completion of dipyridamole infusion. Myocardial perfusion and cardiac function were simultaneously assessed by electrocardiography (ECG) gating in 868 of the 1,220 patients. The remaining 352 patients underwent SPECT without gating because some of the gamma cameras in our laboratory were not fitted for ECG-gated acquisition at the early phase of the study period.

A 3-headed rotating gamma camera Toshiba GCA-9300 A/DI (Toshiba Corporation, Tokyo, Japan) was used for data acquisition and a medical image processor GMS-5500U/DI (Toshiba Corporation, Tokyo, Japan) was used for image processing. The gamma camera was rotated for 15 min per acquisition. SPECT images were reconstructed into a 128 × 128 matrix with a ramp filter after processing 90 projections over 360° with a Butterworth filter (order 8, cut-off 0.16 cycles/pixel). Gated-SPECT acquisition was implemented by dividing the cardiac cycle into 10 periods. Image data was resized to a 64 × 64 matrix before gated data analysis.

Rest and stress SPECT images were semi-quantified using 4-point scoring (0 to 3 for normal perfusion to defect) in the following 17 myocardial segments: 6 segments in a basal short-axis image, 6 segments in a mid short-axis slice and 4 segments in a long-axis image. The presence of perfusion abnormality was defined as the presence of a segment with a perfusion score of 1 or more. Rest and stress scores were defined as the total of the scores in the 17 segments from rest and stress images, respectively. The rest score reflects infarction severity, and the stress score includes information about infarction and ischemia.

Quantitative gated-SPECT (QGS) program was used for gated-SPECT analysis. Calculation of the left ventricular ejection fraction (LVEF) value was performed by means of automatic determination of endocardial and epicardial surfaces for all gating intervals in the cardiac cycle. We analyzed both rest and stress LVEF. The stress LVEF–rest LVEF value was also calculated to obtain an index reflecting post-ischemic stunning. The presence of wall motion abnormality was defined as the presence of a segment with a perfusion score of 1 or more. Rest and stress scores were defined as the total of the scores in the 17 segments from rest and stress images, respectively. The rest score reflects infarction severity, and the stress score includes information about infarction and ischemia.

**Medical Record Review**

We assessed cardiac events by reviewing medical records. Perioperative cardiac events were defined as those that occurred during, and within 1 month after surgery. Cardiac events included cardiac death, non-fatal myocardial infarction, unstable angina and congestive heart failure defined as follows. Cardiac death was defined as death as a result of

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>No. of patients (with each risk factor)</th>
<th>Event rate (in patients with each risk factor)</th>
<th>Relative risk</th>
<th>p value (based on univariate analysis)</th>
<th>p value (based on multivariate analysis)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 75 years</td>
<td>390 (32%)</td>
<td>15/390 (3.8%)</td>
<td>1.0</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>453 (37%)</td>
<td>21/453 (4.6%)</td>
<td>1.4</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>277 (23%)</td>
<td>14/277 (5.1%)</td>
<td>1.4</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>142 (12%)</td>
<td>6/142 (4.2%)</td>
<td>1.1</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>263 (22%)</td>
<td>15/263 (5.7%)</td>
<td>1.7</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>History of myocardial infarction</td>
<td>200 (16%)</td>
<td>11/200 (5.5%)</td>
<td>1.6</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>History of heart failure</td>
<td>63 (5.2%)</td>
<td>8/62 (13%)</td>
<td>3.8</td>
<td>&lt;0.01</td>
<td>NS</td>
</tr>
<tr>
<td>History of revascularization</td>
<td>110 (9.0%)</td>
<td>9/110 (8.2%)</td>
<td>2.4</td>
<td>&lt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td>History of stroke</td>
<td>56 (4.6%)</td>
<td>4/56 (7.1%)</td>
<td>1.9</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Renal failure</td>
<td>74 (6.1%)</td>
<td>6/74 (8.1%)</td>
<td>2.3</td>
<td>&lt;0.05</td>
<td>NS</td>
</tr>
<tr>
<td>ST change at rest</td>
<td>226 (19%)</td>
<td>14/226 (6.2%)</td>
<td>1.9</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Perfusion abnormality</td>
<td>472 (39%)</td>
<td>25/472 (5.3%)</td>
<td>1.8</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>Wall motion abnormality</td>
<td>346 (28%)</td>
<td>31/346 (9.0%)</td>
<td>4.9</td>
<td>&lt;0.0001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>250 (26%)</td>
<td>26/250 (10%)</td>
<td>3.1</td>
<td>&lt;0.0001</td>
<td>NS</td>
</tr>
</tbody>
</table>

The second parentheses in operation risk show the breakdown by the clinical risk groups.
myocardial infarction, heart failure or arrhythmias. The diagnostic criteria for myocardial infarction were based on changes in ECG and the serum creatine kinase value: new ECG Q-wave $\geq 1$ mm or creatine kinase myocardial-bound $\geq 5\%$ or both. Unstable angina was defined as electrocardiographic ST changes (ST-segment depression or elevation of $\geq 1$ mm on 12-lead ECG) with cardiac symptoms. Congestive heart failure was defined as radiographic evidence of pulmonary edema and cardiac enlargement requiring inotropic support. Non-fatal arrhythmias were excluded from cardiac events. Hard events comprised cardiac death and myocardial infarction.

Statistical Analysis
For univariate analysis, we used Fisher’s exact test to compare the frequency of cardiac events between patients with positive and negative test results or risk factors. The same analysis also compared event frequency between intermediate and minor risk factors and between intermediate and low-risk surgeries. Stepwise logistic regression models were used in multivariate analysis to identify independent predictors of cardiac events (Stat View ver. 4.5, Abacus Concepts, Inc, Berkeley, CA, USA). A p-value of $<0.05$ was considered statistically significant in all analyses.

Results
Overall Cardiac Events
Cardiac events developed in 47 (3.9\%) of 1,220 patients and hard events occurred in 7 (0.6\%) patients. Six patients died of the following non-cardiac causes during the perioperative period: multiple organ failure, sepsis, pneumonia, bleeding (n=2) and cerebral infarction. Among these 6 patients, myocardial perfusion and cardiac function were normal in 5, and perfusion was abnormal in 1 without a wall motion abnormality. Of the 119 patients whose surgery was cancelled or deferred, perfusion images from 68 (57.1\%) were positive; this proportion was significantly higher than the rate among patients who underwent surgery (57.1\% vs 28.4\%: $p<0.0001$). Surgery for 55 of the above 119 patients (intermediate and low-risk surgery, 50 and 5, respectively) was cancelled or deferred mainly because of high cardiac risk estimated.

Clinical Risk Factors Predictive of Cardiac Events
Table 2 shows the characteristics of the patients and the results of univariate and multivariate analyses for seeking variables predicting perioperative cardiac events. A history of myocardial infarction, heart failure, revascularization, renal failure, perfusion and wall motion abnormalities presented significant risk stratification in univariate analysis. The multivariate analysis uncovered only perfusion abnormality as an independent predictor of cardiac events.

Clinical Risk, Surgical Procedures and Cardiac Events
Figs 1A and B show the frequency of cardiac events (all and hard events) in each risk group. Although the frequency of hard events did not significantly depend on clinical or surgical risk, the frequency of all cardiac events was dependent on clinical risk factors and type of surgical procedures. Fig 1C depicts risk stratification after combining clinical risk factors and surgical risk. Patients with an intermediate clinical risk undergoing an intermediate risk operation developed a higher frequency of cardiac events compared
with other subgroups.

**Prognostic Value of SPECT**

Fig. 2 shows the incremental prognostic value of gated-SPECT in predicting all cardiac events. Patients were divided into 3 groups (closed, hatched and unfilled bars) in each subgroup in each panel using threshold values of perfusion scores or LVEF. Adding information about myocardial perfusion or cardiac function offered significant risk stratification in patients undergoing intermediate risk surgery and having intermediate or minor clinical risk factors. In contrast, gated-SPECT did not provide significant risk stratification in low risk surgery. The risk of hard events was not sorted by gated-SPECT (data not shown).

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Fig 2. Incremental value of information about myocardial perfusion or cardiac function in predicting all cardiac events. Stratification with rest perfusion score (A), stress perfusion score (B), left ventricular ejection fraction (LVEF) at rest (C), and LVEF after stress (D). In each panel, patients were divided into 4 subgroups according to clinical risk factors and operation risk. In each subgroup, patients were sorted again into 3 groups (closed, hatched and unfilled bars) according to the following threshold values of single-photon emission computed tomography indices. Closed bar, (A) rest perfusion score ≥7, (B) stress perfusion score ≥9, (C) and (D) LVEF ≤45%; hatched bar, (A) 1 ≤ rest perfusion score ≤6, (B) 1 ≤ stress perfusion score ≤8, (C) and (D) 46% ≤ LVEF ≤ 59%; unfilled bar, (A) rest perfusion score =0, (B) stress perfusion score =0, (C) and (D) LVEF ≥60%; *p<0.05; **p<0.01 (comparison between the unfilled bar and others). The total numbers of patients are 1,220 in (A) and (B), and 868 in (C) and (D). The threshold values (stress score=9, rest score=7, LVEF=45%) were determined on the basis of the mean and standard deviation: approximately mean+SD in perfusion scores, and mean–SD in LVEF.

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Fig 3. Combining perfusion and functional data for stratifying risk in intermediate risk surgery. Patients were classified into 2 groups (closed and unfilled bars) according to the following criteria. Unfilled bar, stress score =0; closed bar, stress score ≥1 in the classification of ‘perfusion only’. Unfilled bar, stress score =0 and without regional wall motion abnormality; closed bar, remaining patients in the classification of ‘+ function’. The numbers in parentheses are the number of patients with cardiac events/the total number in the category.
To determine the prognostic power of post-ischemic stunning, we classified patients into 2 groups according to the stress ejection fraction (EF) – rest EF value and compared their event rates. The stress LVEF value was lower than that at rest in 186 and 110 patients in intermediate and low-risk surgery, respectively. The event rates in these patients were 11/186 (5.9%) and 9/110 (0%), and those among patients with stress LVEF equal to or exceeding rest LVEF were 24/397 (6.0%) and 3/175 (1.7%) in intermediate and low-risk surgery, respectively. Thus, event rates between the groups of patients with and without a post-stress EF depression did not significantly differ.

Fig 3 combines perfusion and functional data to stratify risk in 583 patients referred for gated-SPECT and undergoing intermediate risk surgery. Normal perfusion and wall motion resulted in very low frequencies of all cardiac events. Adding functional data to perfusion variables offered an incremental prognostic value for patients with an intermediate clinical risk and scheduled intermediate risk surgery. In low-risk surgery, this combination also did not provide significant risk stratification (data not shown).

Discussion

Although much is understood about the use of myocardial perfusion imaging for preoperative risk stratification in high-risk surgery, data about intermediate-risk surgery are limited and no data is available in low-risk surgery. The present study showed that gated myocardial perfusion SPECT has an incremental prognostic value in intermediate, but not in low-risk, non-cardiac surgery.

Many investigators have identified preoperative clinical markers related to postoperative cardiac events, the most frequent being advanced age, hypertension, diabetes, angina pectoris, cardiac arrhythmias, history of myocardial infarction, congestive heart failure, previous CABG and abnormal baseline ECG. Fig 1A indicates that the event rate among patients with intermediate cardiac risk is significantly higher than that of patients with minor cardiac risk. The event rate was also dependent on the risk grade of surgical procedures (Fig 1B), suggesting the feasibility of the ACC/AHA criteria. For further risk stratification with preoperative waiting time because low-risk individuals can be exempted from further cardiac testing, including catheterization, and proceed directly to surgery. However, the clinical value of stratifying risk with gated-SPECT is limited for low-risk surgery, because of the low frequency of cardiac events regardless of perfusion and functional findings.

Study Limitations

The first limitation is that we retrospectively analyzed consecutive patients who had undergone SPECT imaging instead of consecutive patients who had undergone surgery. It was impossible to conduct a prospective study of SPECT on consecutive patients undergoing surgery. The pretest probability of cardiac events differs between these 2 groups of patients. To reduce this referral bias, we assigned the patients to different risk groups according to the clinical risk factors and the type of surgery based on the guidelines, and the prognostic value of SPECT was analyzed in each subgroup. Next, surgeons and anesthesiologists were not blinded to the results of cardiac testing. This availability of

that cardiac risk is reduced by such choices. However, the results of the current study suggest that preoperative evaluation of myocardial perfusion and cardiac function has limited clinical value for patients who are scheduled for low-risk surgery.

Differences between rest and stress functional variables are markers of stress-induced ischemia. However, we found that a post-stress EF depression was not associated with adverse outcome in terms of perioperative cardiac events. This is probably because we used dipyridamole instead of exercise stress, which increases myocardial oxygen consumption and facilitates the likelihood of post-ischemic stunning. However, dipyridamole stress causes ischemia through coronary steal that develops mainly in patients with severe coronary stenosis. Most of the patients in the present study underwent SPECT for preoperative risk stratification as a screening procedure, and only a few of them have severe coronary artery disease. Therefore, we believe that the EF depression after dipyridamole infusion had limited prognostic value for this cohort. We used dipyridamole stress because most of the patients in the present study were elderly and often unable to exercise. Adenosine can be a substitute for dipyridamole.

In addition, the incremental value of dipyridamole stress to rest perfusion imaging was not clear when comparing Figs 2A and B. This is probably because of cancellation of surgery and preoperative coronary revascularization for patients with findings of stress-induced ischemia in dipyridamole SPECT. These patients were excluded from the analysis (included in the 119 patients whose surgery was cancelled or deferred). This intervention is thought to lower the prognostic value of the stress perfusion score, and further investigation is required to clarify the value of dipyridamole stress by comparing the event rate of patients operated after revascularization with that of risk-matched patients with ischemia without preoperative revascularization.

Preoperative stress myocardial perfusion imaging provides excellent negative predictive values in forecasting perioperative cardiac events. As indicated in Fig 3, the present results also suggest that normal perfusion and wall motion ensure a very low likelihood of perioperative cardiac events in intermediate-risk surgery. Accurate identification of low-risk patients facilitates reductions in cost and preoperative waiting time because low-risk individuals can be exempted from further cardiac testing, including catheterization, and proceed directly to surgery. However, the clinical value of stratifying risk with gated-SPECT is limited for low-risk surgery, because of the low frequency of cardiac events regardless of perfusion and functional findings.
results had an influence on decisions regarding performance of operation and perioperative patient management, including the use of a ß-blockade, which could lower the cardiac event rate and underestimate the prognostic value of SPECT. Finally, patients with major clinical risk factors (unstable coronary syndromes, decompensated heart failure, significant arrhythmias and severe valvular disease) were not included in the current study, because most of these patients proceed to surgery after treating their clinical conditions, or surgery is cancelled as indicated in the guidelines without undergoing cardiac testing.1,2

Conclusion

Detailed preoperative risk stratification was achieved by integrating information about clinical risk factors, type of surgery, myocardial perfusion and cardiac function. Assessing myocardial perfusion and cardiac function yields an incremental prognostic value in intermediate, but not in low-risk surgery.

References