Influence of ageing on perioperative cardiac risk in non-cardiac surgery

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Abstract

Background: ageing is known to augment perioperative cardiac risk in non-cardiac surgery. However, it remains unclear whether the increased risk is attributable to ageing itself or to the associated cardiac risk factors and coronary artery disease.

Methods: this retrospective study enrolled 1,351 patients who underwent non-cardiac surgery after dipyridamole stress myocardial perfusion scintigraphy. These patients were divided into the following four groups: Group 1-E (aged 75 or more, normal single photon emission computed tomography (SPECT)), Group 1-Y (aged less than 75, normal SPECT), Group 2-E (aged 75 or more, abnormal SPECT) and Group 2-Y (aged less than 75, abnormal SPECT). Clinical risk factors, scintigraphic findings and occurrence of perioperative cardiac events were analysed.

Results: the older cohorts had a significantly higher number of risk factors than their younger counterparts. No significant difference was observed in the degree of perfusion abnormality between Groups 2-E and 2-Y. Although the event rates were comparable in Groups 1-E and 1-Y, Group 2-E yielded a significantly higher rate than Group 2-Y. Ageing was an independent predictor of cardiac events in Group 2 in multivariate analysis.

Conclusions: ageing has no influence on perioperative cardiac risk in patients without overt myocardial infarction or ischaemia. The likelihood of cardiac events is increased by ageing, independently of other variables, in patients with perfusion abnormality.

Keywords: ageing, dipyridamole stress, elderly, Myocardial perfusion scintigraphy, perioperative cardiac event, SPECT

Background

Recently, the number of aged patients undergoing surgical treatment has increased corresponding to the extension of their lifespan. Ageing affects cardiovascular risk factors, incidence and clinical manifestation of cardiac disease, treatment strategies and prognosis [1]. A number of investigators have pointed out that ageing increases the likelihood of perioperative cardiac events in non-cardiac surgery, and that age is an independent predictor of perioperative events [2–5]. On the other hand, advanced age is listed as a minor clinical predictor in the American College of Cardiology/American Heart Association (ACC/AHA) Guidelines for Perioperative Cardiovascular Evaluation for Non-cardiac Surgery [6, 7]. In these guidelines, minor predictors are defined as markers for cardiovascular diseases that have not been proved to independently increase perioperative risk. In addition, some authors have reported that advanced age is not an independent predictor of perioperative outcome [8, 9].

With few exceptions, which enrolled only patients without coronary artery disease [10], most studies analysed a combination of patients with and without overt coronary artery disease by introducing multivariate analyses of various clinical risk factors, including advanced age [1–5, 8, 9]. To separate the influence of ageing from that of associated coronary artery disease often seen in the elderly, the subjects had to be divided into different groups according to their likelihood of having ischaemic disease. However, the preoperative diagnosis of ischaemic heart disease is difficult in the elderly because of reduced
Ageing and perioperative cardiac risk

physical activity resulting in the reduction of demand angina and sub-optimal performance in exercise cardiac testing [1]. In such patients, a pharmacological stress test incorporating myocardial perfusion SPECT (single-photon emission computed tomography) or echocardiogram is often of greater diagnostic or prognostic accuracy [10–12]. Although Dhond et al. recently assessed perioperative and long-term cardiac risk in the elderly, with negative findings in dobutamine stress echocardiography [10], the number of subjects involved was limited to 82, consisting of 41 elderly and 41 younger patients with similar risk factors, and the patients with positive echocardiographic findings were not analysed.

The aim of this retrospective study was to investigate whether the increased perioperative cardiac risk in the elderly was attributable to ageing itself or to the associated cardiac risk factors and coronary artery disease whose frequencies increase with advancing age. Dipyridamole stress myocardial perfusion SPECT was employed to separate the patients without overt coronary artery disease from those with it.

Methods

Patients

From our database, we retrospectively collected data of 1,570 consecutive patients who had undergone dipyridamole stress myocardial perfusion SPECT before non-cardiac surgery (from January 1997 through December 2004). Patients were referred for the perfusion examination because of concern about cardiac risk. Written informed consent had been obtained from all patients after explaining about the stress-induced cardiac risk and the future use of the data for research purposes. The form used to obtain consent was approved by the institutional committee of Keio University Hospital. Surgery was performed on 1,351 patients and was cancelled or deferred in 219 patients. Therefore, 1,351 patients were analysed finally (Table 1). Of the reasons for cancellation in the 219 cases, 95 were estimated high cardiac risk, 109 were non-cardiac clinical problems, 15 were other than clinical problems, such as failure to obtain consent for operation, and so on. All the surgical procedures were classified as high or intermediate risk operations according to the ACC/AHA guidelines [6, 7]. The subjects were divided into the following four groups on the basis of their age and SPECT findings: Group 1-E (aged 75 or more, normal SPECT finding), group 1-Y (aged less than 75, normal SPECT), group 2-E (aged 75 or more, abnormal SPECT) and group 2-Y (aged less than 75, abnormal SPECT). The definition of ‘normal SPECT’ is given in the section on image analysis. Clinical characteristics of the patients are indicated in Table 1.

Protocol

Technetium-99m tetrofosmin or sestamibi was the imaging agent. A rest/stress one-day protocol was employed for imaging. In the rest study, all patients were injected with 300 MBq of the tracer, and SPECT acquisition was performed 30 min after injection. In the stress study, patients were continuously injected with 0.56 mg/kg of dipyridamole for 4 min, and then 850 MBq of the perfusion tracer was administered 3 min after the completion of dipyridamole infusion. Stress SPECT images were obtained 30 to 60 min after administration.

Instrumentation

A three-headed SPECT system (GCA-9300A/DI, Toshiba Corporation, Tokyo) was employed for data acquisition and a medical image processor (GMS-5500U/DI, Toshiba Corporation, Tokyo) was employed for image processing. Data acquisition continued for 15 min. The acquired data was reconstructed into SPECT images with a 128 × 128 matrix with a ramp filter after reducing the image noise using a Butterworth filter (order 8, cut-off 0.15 cycles/pixel).

Table 1. Clinical characteristics of 1,351 patients

<table>
<thead>
<tr>
<th></th>
<th>1-E</th>
<th>1-Y</th>
<th>2-E</th>
<th>2-Y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>270</td>
<td>729</td>
<td>93</td>
<td>259</td>
</tr>
<tr>
<td>Age</td>
<td>78.9 ± 3.1***</td>
<td>63.3 ± 9.5</td>
<td>79.4 ± 4.2***</td>
<td>65.0 ± 7.5</td>
</tr>
<tr>
<td>Hypertension</td>
<td>34%*</td>
<td>26%</td>
<td>39%*</td>
<td>27%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>11%</td>
<td>11%</td>
<td>28%</td>
<td>22%</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>4.8%</td>
<td>7.4%</td>
<td>11%</td>
<td>8.9%</td>
</tr>
<tr>
<td>Chest pain</td>
<td>17%</td>
<td>16%</td>
<td>19%</td>
<td>26%</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>19%*</td>
<td>14%</td>
<td>14%</td>
<td>12%</td>
</tr>
<tr>
<td>History of myocardial infarction</td>
<td>3.7%</td>
<td>1.8%</td>
<td>41%</td>
<td>44%</td>
</tr>
<tr>
<td>History of heart failure</td>
<td>7.0%**</td>
<td>2.1%</td>
<td>6.3%</td>
<td>5.8%</td>
</tr>
<tr>
<td>History of re-vascularisation</td>
<td>4.1%</td>
<td>2.7%</td>
<td>11%</td>
<td>19%</td>
</tr>
<tr>
<td>Q waves</td>
<td>9.3%</td>
<td>10%</td>
<td>24%**</td>
<td>31%</td>
</tr>
<tr>
<td>ST changes at rest</td>
<td>36%</td>
<td>32%</td>
<td>47%</td>
<td>48%</td>
</tr>
<tr>
<td>Number of high-risk surgery</td>
<td>42%</td>
<td>45%</td>
<td>41%</td>
<td>45%</td>
</tr>
</tbody>
</table>

E, elderly; Y, young; *, P<0.05; **, P<0.001; †, P<0.0001 in comparison between 1-E and 1-Y, or 2-E and 2-Y using univariate analysis. *, independent predictor of cardiac events in Group 2 in multivariate analysis.
Image analysis

Rest and stress SPECT images were visually interpreted by two radiologists to determine whether the SPECT findings were normal or not. A consensus interpretation was arrived at in case of disagreement. A normal SPECT finding implies no regional hypoperfusion in both rest and stress images, suggesting no evidence of myocardial ischaemia or infarction.

In addition, the images were semi-quantitatively assessed using a 4-point scoring system (0 to 3, for normal perfusion to perfusion defect) in the following 17 myocardial segments: 6 segments in a basal short-axis image, 6 segments in a mid short-axis image, 4 segments in an apical short-axis image and 1 apical segment in a vertical long-axis image. Scores in the 17 segments were added to calculate stress and rest total perfusion scores. Ischaemic score was defined as (stress total perfusion score—rest total perfusion score), which reflects the severity of myocardial ischaemia. Therefore, stress, rest and ischaemic scores were 0 in all patients in Group 1.

Medical record review

We assessed clinical risk factors by reviewing the medical records. Clinical variables taken into account were age, hypertension, diabetes mellitus, hypercholesterolemia (serum cholesterol > 6.20 mmol/l), chest pain, preoperative arrhythmias, history of myocardial infarction, history of congestive heart failure, history of coronary re-vascularisation, electrocardiographic analysis including pathological Q waves and ischaemic ST change at rest.

The outcome of this study was perioperative cardiac events that occurred during operation or within 1 month after surgery [13]. This information was also obtained by reviewing the medical records. Cardiac events included cardiac death, non-fatal myocardial infarction, unstable angina and congestive heart failure with the following definitions [4, 14]. Cardiac death was defined as death due to myocardial infarction, heart failure or arrhythmias. Diagnoses of myocardial infarction were based on the changes of ECG and the serum creatine kinase value: new ECG Q wave > 1 mm or CK-MB > 5% or both. Unstable angina was defined by the ST changes on electrocardiogram (ST-segment depression or elevation of >1 mm on the 12 lead ECG), with cardiac symptoms. Congestive heart failure was defined as radiographic evidence of pulmonary oedema and cardiac enlargement requiring inotropic support. Non-fatal arrhythmias were excluded from cardiac events. Hard events comprised cardiac death and myocardial infarction.

Statistical analysis

In univariate analysis, we used Fisher’s exact test to compare the percentage of patients having risk factors and the frequency of cardiac events between elderly and younger cohorts. Stepwise logistic regression models were employed in multivariate analysis to elucidate whether or not ageing is an independent risk factor and to identify independent predictors of cardiac events (Stat View ver.4.5, Abacus Concepts, Inc., Berkeley). The above multivariate analysis was carried out separately in Group 1 and 2 patients. $P<0.05$ was considered statistically significant in each analysis.

Results

Of the total 1,351 patients, cardiac events were observed in 80 patients (5.9%), including 26 with hard events (1.9%).

Among the 219 patients who were not operated on, 106 (48.4%) manifested positive perfusion images; this proportion is significantly higher than the rate of positive perfusion images in patients who were operated on (48.4% versus 26.1%; $P<0.0001$). In both groups with normal and abnormal SPECT, there was no significant difference in the proportion of the elderly between operation and cancellation cohorts (operation cohort: Group 1 (270/999, 27.0%), Group 2 (93/352, 26.4%); cancellation cohort: Group 1 (34/113, 30.1%), Group 2 (30/106, 28.3%).

Table 2 shows the comparison between older and younger groups for the event rate, scintigraphic scores and the number of risk factors. In both groups with normal and abnormal SPECT, the older cohorts had a significantly higher number of risk factors than their younger counterparts. In contrast, no significant difference was observed in the scintigraphic scores in Group 2. Although the event rates in the older and younger subjects in Group 1 were comparable, the older group yielded a significantly higher rate for all cardiac events than the younger one in Group 2. The classification of event rates by surgical procedures is as follows (not included in Table 2). Cardiac event rates are 4.4% (Group 1-E), 4.2% (Group 1-Y), 26.3% (Group 2-E) and 15.4% (Group 2-Y) in high-risk operations, and 0.6% (Group 1-E), 2.3%...
(Group 1-Y), 18.2% (Group 2-E) and 9.9% (Group 2-Y) in intermediate risk operations (not statistically significant between the younger and older groups).

Table 1 shows the results of univariate and multivariate analyses comparing the risk factors in the older and younger groups and the predictability of cardiac events with clinical risk factors. Age, hypertension and diabetes were independent predictors of cardiac events in Group 2 according to the results of multivariate analysis. On the contrary, there was no independent predictor in Group 1.

Discussion

The frequency of epicardial coronary artery stenosis increases with advancing age. This coronary artery stenosis may cause myocardial ischaemia, infarction or other cardiac events. Cardiac risk factors, which are more often present in the elderly than the younger population, are thought to facilitate the progression of epicardial coronary artery stenosis and to affect the coronary microcirculatory function [15]. Besides these vascular conditions, age-related cardiac changes include decrease in contractility, increase in stiffness and ventricular filling pressures, decrease in beta-adrenoceptor and beta-adrenoceptor-mediated modulation of inotropy and chronotropy, increase in left atrial pressure/size and action potential time and decrease in coronary flow reserve [1]. All of the above changes are possible candidates for explaining increased perioperative cardiac risk in the elderly. Moreover, these factors affect each other, which makes the situation more complicated.

Although most of the existing reports indicate the impact of ageing on surgical risk, it is difficult to judge which kinds of aged patients are susceptible to perioperative cardiac events. Solving this problem is important to reduce the cardiac events due to inappropriate operation on the elderly with high risk and to avoid inappropriate cancellation of operation resulting from an overestimation of the cardiac risk. As mentioned above, we analysed cardiac risk factors after sorting the subjects with findings of myocardial perfusion SPECT to distinguish the influence of the underlying epicardial coronary artery disease from that of other factors associated with ageing. The reason we used myocardial perfusion SPECT lies in its usefulness in assessing ischaemia and estimating prognosis in the elderly [10–12, 16, 17].

It has invariably been reported that preoperative stress myocardial perfusion imaging provides excellent negative predictive values in forecasting perioperative cardiac events, which implies that a normal stress perfusion study has powerful prognostic utility [18]. The excellent prognostic utility of negative SPECT was also observed in the older patients in this study. Furthermore, in patients without overt ischaemia or infarction, the frequency of perioperative cardiac events in the aged was comparable with the younger cohort, even though ageing increased the number of clinical risk factors (Table 2). Consequently, various age-related cardiac changes mentioned here and the increased number of clinical risk factors have no significant influence on perioperative cardiac events in patients without overt ischaemia or infarction. Therefore, the applicability of surgical treatment in the aged can be discussed almost in the same manner as it is applicable to their younger counterparts, in terms of perioperative cardiac problems, if the subjects manifest negative SPECT findings.

On the other hand, ageing increased the frequency of cardiac events in patients with positive SPECT findings and was proved to be an independent predictor of cardiac events. However, perfusion score was not remarkably different between the older and younger groups. These results suggest that ageing augments cardiac risk only with the existence of overt myocardial ischaemia or infarction and that this influence was not due to increased clinical risk factors in the aged people or different severity of coronary artery disease. Therefore, if abnormal SPECT findings are observed, patients undergoing non-cardiac surgery should be treated with special attention (e.g. use of beta blockers) to avoid perioperative cardiac events.

Regarding the application of preoperative SPECT, the results in this study indicate that it stratifies risk at least in patients undergoing intermediate or high-risk operation. As for clinical risk factors and the use of SPECT, ACC/AHA guidelines recommend that patients with intermediate or minor clinical predictors undergo non-invasive cardiac testing including SPECT scanning [6].

There are some limitations inherent in the current study. First, we retrospectively analysed consecutive patients who had undergone SPECT imaging because it was impossible to conduct a prospective study to perform SPECT on consecutive patients undergoing surgery. This may have resulted in higher event rates because of the selection bias of high-risk cohort for SPECT. In this situation, it is important to compare event rates with concomitant comparisons of risk factors and severity of reduced myocardial perfusion, which were indicators of the cardiac characteristics of the selected subjects.

The second limitation is that surgeons and anesthesiologists had known the SPECT results before decision-making. This must have influenced their decisions regarding performance of operation and perioperative management, which may have contributed to the lowering of cardiac event rate. Since the percentages of aged patients in the operation and cancellation groups are similar, this bias does not seem to have considerable influence on the comparison of event rates between older and younger populations.

In conclusion, ageing itself has no appreciable influence on perioperative cardiac risk in patients without overt myocardial infarction or ischaemia. In contrast, in patients with myocardial ischaemia or infarction documented by SPECT, the likelihood of cardiac events increases independently of other clinical variables following ageing. Dipyridamole stress myocardial perfusion SPECT offers a
prognostic value in elderly patients undergoing non-cardiac surgery.

Key points
- It remains unclear whether the cause of increased perioperative cardiac risk is attributable to ageing itself or to the associated cardiac risk factors and coronary disease.
- To separate the influence of ageing from that of associated coronary artery disease, patients were divided into different groups according to their age and SPECT findings.
- Ageing itself has no appreciable influence on perioperative cardiac risk in patients with normal myocardial perfusion. In contrast, in patients with perfusion abnormality, the rate of cardiac events increases following ageing, independently of other clinical variables.

Competing interests
None.

References