The Influence of Aging on the Prognostic Value of the Revised Cardiac Risk Index for Postoperative Cardiac Complications in Vascular Surgery Patients


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Objective. The Lee-risk index [Lee-index] was developed to predict major adverse cardiac events [MACE]. However, age is not included as a risk factor. The aim was to assess the value of the Lee-index in vascular surgery patients among different age categories.

Methods. Of 2642 patients cardiovascular risk factors were noted to calculate the Lee-index. Patients were divided into four age categories; ≤55 (n = 396), 56–65 (n = 650), 66–75 (n = 1058) and >75 years (n = 538). Outcome measures were postoperative MACE (cardiac death, MI, coronary revascularization and heart failure). The performance of the Lee-index was determined using C-statistics within the four age groups.

Results. The incidence of MACE was 10.9%, for Lee-index 1, 2 and >3; 6%, 13% and 20%, respectively. However, the prognostic value differed among age groups. The predictive value for MACE was highest among patients under 55 years (0.62) and lowest among those aged >75 years (0.57). The prediction of MACE improved in elderly (aged >75) after adjusting the Lee-index with age, revised risk of operation (low, low-intermediate, high-intermediate and high-risk procedures) and hypertension (0.62 to 0.69).

Conclusion. The prognostic value of the Lee-index is reduced in elderly vascular surgery patients, adjustment with age, risk of surgical procedure, and hypertension improves the Lee-index significantly.

Keywords: Cardiac Risk; Vascular surgery; Prognosis; Elderly.

Introduction

Peripheral atherosclerotic disease [PAD] is becoming an increasingly important health issue in the Western society. A clear increase of PAD is observed in elderly subjects. In The Rotterdam Study the prevalence of PAD increases from 6.6% in patients aged 55–59 years to 52% aged >85 years. As life expectancy improves, the prevalence of PAD is on the increase leading to 16,000 hospital admissions annually in the Netherlands, 6% of all admissions due to cardiovascular diseases. Postoperative outcome is related to the presence and extent of coronary artery disease as well as the regulation of risk factors for coronary artery disease such as diabetes mellitus, hyperlipidaemia, and hypertension. Commonly, patients are screened prior to surgery using the Revised Cardiac Risk Index, which includes ischemic heart disease, heart failure, cerebrovascular disease, insulin dependent diabetes mellitus, renal dysfunction, and high-risk surgery. However, this risk index may have a potential limitation for preoperative cardiac risk assessment in vascular surgery patients as age is not included and only 21% of the original study population underwent vascular surgery. In this study we evaluated the prognostic value of the Revised Cardiac Risk Index and determined if the accuracy could be improved by the addition of different age categories and additional risk factors.
Method

Study design and patient selection

Between January 1993 and June 2006, 2,730 open non-cardiac vascular surgical procedures were performed in patients above 18 years old at Erasmus MC, Rotterdam, the Netherlands. Patients were divided into four categories according to their age: ≤55, 56–65, 66–75 and >75 years respectively. We excluded 88 procedures that were conducted within 30 days after the index procedure. The postoperative outcome of the remaining 2,642 procedures, performed in 2,298 different patients, was analyzed. Over the 13-year observation study, 250 patients had multiple surgical procedures. The procedure and not the patient was the unit of analysis because this approach is consistent with clinical practice, wherein the risk of perioperative complications is assessed in relation to a specific procedure. The Medical Ethics Committee of the Erasmus MC was informed about the study protocol, and per institutional practice no official approval was requested.

Revised Cardiac Risk Index factors

The Revised Cardiac Risk Index [Lee-index] assigns 1 point to each of the following 6 characteristics: high-risk surgery, ischemic heart disease, history of heart failure, cerebrovascular disease, renal insufficiency and insulin dependent diabetes mellitus. Ischemic heart disease was defined as a history of MI or positive stress test, current complaint of ischemic chest pain, or use of nitrate therapy, or Q waves on the electrocardiogram, but patients with a history of coronary artery bypass grafting [CABG] or percutaneous coronary intervention [PCI] were included only if they had current complaints of chest pain presumed to be due to ischemia; heart failure was defined as a history of heart failure, pulmonary edema, or paroxysmal nocturnal dyspnea, or a chest radiograph showing pulmonary vascular redistribution; renal insufficiency was a creatinine level >177 μmol/L; high-risk surgery as AAA, r-AAA and LLR procedures; and cerebrovascular disease was defined as a history of a stroke or transient ischemic attack. Notably, due to the high surgical risk of LLR, AAA and r-AAA surgery, by definition no Lee-index of 0 points was reported in these patients. This resulted in three categories according to the number of Lee risk index points: 1, 2 and ≥3.

Clinical follow-up and end points

Perioperative clinical information was retrieved from an electronic database of patients maintained in our hospital. From the municipal civil registries, we obtained the survival status. The follow-up was complete in 98.2%. The primary outcomes were major adverse cardiac event [MACE] and all-cause mortality, occurring within 30 days after surgery. The secondary outcome was all-cause mortality during long-term follow-up. MACE within 30-days after surgery, was defined as cardiac death (which was defined as any death with a cardiac complication as the primary or secondary cause, including deaths following myocardial infarction, cardiac arrhythmia and heart failure), myocardial infarction or coronary revascularization (PCI or CABG). Sudden death in a previously stable patient was considered as cardiac death. Myocardial infarction was defined as the presence of 2 out of the following 3 criteria: (1) typical chest-pain complaints, (2) electrocardiographic changes including acute ST elevation followed by appearance of Q waves or loss of R waves, or new left bundle branch block, or new persistent T wave inversion for at least 24 hours, or new ST segment depression which persists >24 hours, and (3) a positive troponin T, ie >0.10 ng/ml (>0.1 ug/L), or peak creatinine phosphokinase -MB >8% of an elevated total creatinine phosphokinase with characteristic rise and fall. Heart failure was defined according the New York Heart Association classification. In addition, the causes of death

Other risk factors

Other baseline risk factors recorded of all patients were age, gender, hypertension (defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg and/or use of anti-hypertensive medication), chronic obstructive pulmonary disease [COPD] according to symptoms and pulmonary function tests (i.e. forced expiratory volume in 1 second <70% of maximal age and gender predictive value), body mass index, smoking status, hypercholesterolemia (total cholesterol of >5.2 mmol/L) and medication (including statins, diuretics, angiotensin-converting-enzyme inhibitors, calcium antagonists, nitrates, beta-blockers, aspirin and anti-coagulants). All prescription and over-the-counter medications were noted on the day of admission.

Procedures

All patients underwent open vascular surgery, respectively: carotid endarterectomy [CEA], elective infrarenal abdominal aortic surgery [AAA], acute infrarenal AAA surgery [r-AAA] and lower limb arterial reconstruction procedures [LLR].
occurred within 30 days after surgery were grouped into three different categories: (1) cerebro-cardiovascular death [CCVD], (2) non-cerebrocardiovascular death [non-CCVD] and (3) unknown cause of death. Cerebro-cardiovascular death was defined as any death with a cerebro-cardiovascular complication as the primary or secondary cause and included deaths following myocardial infarction (MI), serious cardiac arrhythmias (defined as the presence of a sustained cardiac rhythm disturbance that required urgent medical intervention), congestive heart failure, stroke [cerebro vascular accident (CVA) or transient ischemic attack (TIA)], surgery-related fatal bleeding complications and others. Non-CCVD was defined as any death with a principal non-cerebro-cardiovascular cause, including infection, malignancy, respiratory insufficiency and others. The cause of death was ascertained by reviewing medical records, the computerized hospital database, autopsy reports, or by contacting the referring physician or general practitioner.

Results

Patient characteristics

A total of 2,642 procedures were performed (21% CEA, 8% r-AAA, 34% AAA and 38% LLR). The mean age was 66 ± 11 years and 75% of the patients were men. Of these patients, 396 (15%) were ≤55, 650 (25%) were 56–65, 1,058 (40%) were 66–75 and 538 (20%) were >75 years. Men were 0.97 years older than were female (p < 0.052). With increase of age, higher incidences of hypertension, COPD, ischemic heart disease and r-AAA and AAA surgery were observed (Table 1). No patients were reported with a Lee-index score of 0, as all patients with CEA had a positive history of cerebrovascular disease and/or presence of another risk factor used in the Lee risk index. The majority of patients had a score of 1 point (52%), followed by 30% and 18%, respectively 2 and ≥3 points (Table 2).

Primary end-point

A total of 287 (10.9%) patients had a major adverse cardiac event, for Lee-index 1, 2 and ≥3 respectively 6.2%, 13.2% and 20.5%. Increasing rates of MACE were found with increased age, with a slight drop of incidences within patients aged >75 years. Within each age category, the Lee-index was significantly associated with incidences of MACE. A correlation of all-cause mortality and Lee-index was found in all patients (p < 0.03). However, no correlation of the Lee-index and all-cause mortality was found within each age category. Cerebro-cardiovascular events (116 (76%)) were the major cause of death which included: MI 19%, heart failure 10%, cardiac arrhythmia 10%, stroke 6%, fatal bleeding 26% and others 5%. The non-cerebro-cardiovascular (36 (24%)) events included: infection 14%, malignancy 0%, respiratory insufficient 6% and others 4%. None patients had an unknown cause of death. In total, 58 (39%) patients died because of cardiac complications within 30 days after surgery.

In univariate analysis, the Lee-index was associated with an increased risk of MACE as its individual components (Table 3). The prospective C-statistic for the prediction of MACE was 0.65. The predictive value of the Lee-index was significantly superior in patients aged ≤55 years compared to patients aged >75 years (area under the curve 0.76 vs. 0.62, p < 0.01). When more detailed information, including type of surgery (low, low-intermediate, high-intermediate and high risk of surgery), age (≤55, age 56–65, age 66–75 and
>75 years) and history of hypertension, was added to the model, the overall C-statistics improved to 0.71. Importantly, after the introduction of these additional risk factors no difference in the C-statistics was observed between each age category ≤55, age 56–65, age 66–75 and >75 years), respectively 0.71, 0.71, 0.69 and 0.69. The prediction of MACE in elderly patients improved from 0.62 to 0.69 (p = 0.02).

Important differences in incidence of MACE were observed in relation to type of surgery. Overall incidences of MACE according to low-risk (CEA), low-intermediate (LLR), high-intermediate (AAA) and high-risk (r-AAA) surgery were 2.4%, 11.6%, 12.3% and 24.0%, respectively (p < 0.001) (Fig. 1).

Within each type of surgery, the Lee-index was significantly associated with risk of MACE.

When we perform our analysis applied only to patients having a single procedure (n = 2,298, 66 ± 11 years, 75% were men), our results remained the same. For example, incidences of hypertension were 38%, 43%, 46% and 47% for age category ≤55, 56–65, 66–75 and >75 years respectively (p = 0.03). The prospective C-statistic for the prediction of MACE was also 0.65 (0.76, 0.66, 0.64 and 0.62 for each age category (≤55, age 56–65, age 66–75 and >75 years)). After the introduction of our additional risk factors no difference in the C-statistics was observed between each age category, respectively 0.74, 0.73, 0.71 and 0.71. The multivariate analysis showed the same results as presented in Table 3. Because of these findings, we concluded that the influence of patients with multiple procedures on the overall results does not have an important impact on our results.

Secondary end-point

Although the Lee-index was originally developed to predict perioperative cardiac complications, a clear association was found between the Lee-index and all-cause mortality during follow-up (Fig. 2). A total of 1,454 (55%) patients died during mean period of 6.4 ± 3.9 years. Annual mortality rates of patients with a Lee-index score of 1, 2 and ≥3 were 5.2%/year, 6.4%/year and 7.3%/year respectively (p < 0.001). In multivariate analysis, adjusting for the four age categories, risk of surgery (low, low-intermediate, high-intermediate and high risk), year of operation,
chronic obstructive pulmonary dysfunction, hypercholesterolemia, smoking status, body mass index, gender, hypertension and cardiovascular medication, the risk of all-cause mortality was 1.45 (95% CI): 1.28–1.65) for Lee-index 2 and 1.90 (95% CI: 1.63–2.22) for Lee-index ≥ 3, compared with Lee-index 1. When analysis was performed to patients with a single procedure, the risk of all-cause mortality was 2.01 (95% CI: 1.37–2.94) for Lee-index 2 and 3.11 (95% CI: 1.94–4.97) for Lee-index ≥ 3, compared with Lee-index 1.

**Table 3. Unadjusted and adjusted predictors of estimate risk of major adverse cardiac events**

<table>
<thead>
<tr>
<th></th>
<th>Unadjusted HR, (95% CI)</th>
<th>Adjusted HR*, (95% CI)</th>
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<tbody>
<tr>
<td>Lee-index 1 (reference)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Lee-index 2</td>
<td>2.30 (1.71–3.11)</td>
<td>1.94 (1.37–2.73)</td>
</tr>
<tr>
<td>Lee-index ≥ 3</td>
<td>3.89 (2.83–5.33)</td>
<td>2.92 (1.92–4.44)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.84 (1.36–2.48)</td>
<td>1.51 (1.11–2.06)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>1.76 (1.26–2.45)</td>
<td>1.53 (1.09–2.14)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>2.51 (1.80–2.97)</td>
<td>1.70 (1.30–2.22)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>2.43 (1.60–3.68)</td>
<td>1.31 (0.84–2.06)</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>2.24 (1.64–3.05)</td>
<td>1.71 (1.24–2.36)</td>
</tr>
<tr>
<td>Age ≤ 55 years (reference)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Age 56–65 years</td>
<td>2.27 (1.30–3.94)</td>
<td>2.44 (1.34–4.42)</td>
</tr>
<tr>
<td>Age 66–75 years</td>
<td>3.51 (2.10–5.89)</td>
<td>3.49 (1.99–6.10)</td>
</tr>
<tr>
<td>Age &gt; 75 years</td>
<td>3.13 (2.10–5.40)</td>
<td>2.56 (1.41–4.65)</td>
</tr>
<tr>
<td>Low-risk surgery (reference)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Low-intermediate risk</td>
<td>5.56 (2.99–9.60)</td>
<td>4.04 (2.17–7.54)</td>
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<tr>
<td>High-intermediate risk</td>
<td>5.76 (3.21–10.34)</td>
<td>4.14 (2.23–7.68)</td>
</tr>
<tr>
<td>High-risk</td>
<td>12.95 (6.84–24.52)</td>
<td>10.45 (5.22–20.95)</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>2.15 (1.67–2.77)</td>
<td>1.70 (1.25–2.31)</td>
</tr>
</tbody>
</table>

HR = hazard ratio; CI = confidence interval.
* Adjusted for the the four age categories (≤ 55, 56–65, 66–75 and >75 years), risk of surgery (low, low-intermediate, high-intermediate and high risk), hypertension, year of operation, chronic obstructive pulmonary dysfunction, hypercholesterolemia, smoking status, body mass index, gender and cardiovascular medication.

**Fig. 1.** Incidences of major cardiac events, according to type of operation and the Revised Cardiac Risk score. MACE = major adverse cardiac events; r-AAA = acute infrarenal AAA surgery; AAA = elective infrarenal abdominal aortic surgery; LLR = lower limb arterial reconstruction procedures; CEA = carotid endarterectomy. *Lee-index that assigns one point to each of the following characteristics: ischemic heart disease, history of heart failure, high-risk surgery, history of cerebrovascular disease, renal insufficiency and diabetes mellitus.
surgery patients. Of all patients, only 21% underwent vascular surgery and all procedures were considered as high-risk. However, postoperative morbidity and mortality varied considerably among different vascular surgical procedures. In order to improve the predictive value of the Lee-index, we specified the type of vascular surgery into four categories: low, low-intermediate, high-intermediate and high-risk.

However, the main limitation of the Lee-index is that age is not included. The number of patients referred for vascular surgery is increasing with a substantial number of septo- and octogenarians. The average age of AAA surgery increased from 69 to 72 years during 1980–2000. In addition, this aging population presents with complex co-morbidity associated with increased postoperative mortality rates.

Several risk indices have been developed to stratify vascular surgery patients based on age and clinical cardiac risk factors. In 1994, Samy et al. developed a scoring system in 500 patients scheduled for abdominal aortic aneurysm surgery for the prediction of postoperative mortality: the Glasgow aneurysm score. This score included myocardial disease, cerebrovascular disease, renal dysfunction and age as a continuous variable as risk factors. Age was an independent risk factor for postoperative mortality ($p = 0.02$). Steyerberg et al. constructed the Leiden Risk Model in 246 patients undergoing abdominal aortic aneurysm surgery and included age per decade (<60, 60–70 and >70 years) as a risk factor. Age had only a moderate predictive value for all-cause perioperative mortality (OR 1.9; 95% CI: 0.9–4.2). In addition, L’Italien et al. developed a risk model among 1081 patients undergoing different vascular surgical procedures, with an overall predictive value for cardiac death and non-fatal myocardial infarction of 0.74 (C-statistic). They included advanced age (>70 years) as a dichotomous risk factor. The limitations of these studies are the low number of patients included, none of the studies had MACE as their end-point and the focus is predominantly on aortic surgery.

Preoperative cardiovascular risk stratification has been an area of intense interest for identifying patients at higher cardiac risk. Patients classified as high risk can be refrained for surgery or should be considered to undergo less invasive surgery (like endovascular procedures). Additional cardio protective therapy in elderly (like beta-blockers and statins) in reduction of perioperative cardiac complications has improved in recent years. In addition to the immediate postoperative outcome, prognostic indices should be considered to assess long-term prognosis, as patients should live long enough to enjoy the benefits of surgery. As shown in the follow-up of patients undergoing major vascular surgery with

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**Discussion**

The main finding of our study is that the prognostic value of the Revised Cardiac Risk Index [Lee-index] is reduced in the very elderly patients (>75 years) undergoing vascular surgery. The Lee-index was introduced to assess perioperative cardiac risk among a large number of patients. Risk factors included are high-risk surgery, ischemic heart disease, history of heart failure, cerebrovascular disease, renal insufficiency and diabetes mellitus. Importantly, age was not included in the index. In addition, only a low number of vascular surgery patients were included. Our study showed that if additional information was added to the Lee-index (e.g. age, a more detailed classification of type of vascular surgery and history of hypertension), the accuracy of the Lee-index to predict postoperative MACE improves significantly in vascular surgery patients, among the entire strata of age.

The Lee-index is a modification of the original Goldman risk index, developed in the 1990s and validated in numerous clinical studies and is currently considered the best available risk model. Although the Lee-index was developed using clinical data of 4315 consecutive patients undergoing non-cardiac surgery, the model has shortcomings for vascular surgery patients. Of all patients, only 21% underwent vascular surgery and all procedures were considered as high-risk. However, postoperative morbidity and mortality varied considerably among different vascular surgical procedures. In order to improve the predictive value of the Lee-index, we specified the type of vascular surgery into four categories: low, low-intermediate, high-intermediate and high-risk.

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**Fig. 2.** All cause long-term mortality in 2,642 patients who underwent major vascular surgery, according to the Revised Cardiac Risk score. Lee-index that assigns one point to each of the following characteristics: ischemic heart disease, history of heart failure, high-risk surgery, history of cerebrovascular disease, renal insufficiency and diabetes mellitus.
different cardiac risk index scores, annual mortality rates increased by each risk factor added, ranging from 5.2%/year in patients with 1 risk factor, to 6.4%/year and 7.3%/year for 2 and ≥3 risk factors respectively. This indicates that the prognosis is related to underlying cardiovascular disease. Postoperative surveillance of patients among the high-risk scores with aggressive anti-ischemic therapy is indicated to improve long-term outcome.

A major limitation of our study is the retrospective analysis of prospectively collected data. Changes in the perioperative management have evolved markedly over time and were not taken into account in our analysis. These include multiple factors ranging from preoperative management, such as drug therapy, anesthesiological and surgical techniques to intensive post-surgical care management. We tried to adjust for this confounding to add the year of operation in our multivariate analysis, resulting in Table 3.

In conclusion: this revision of the Lee-index, now including age, risk of surgery and hypertension, clearly stratifies vascular surgery patients into low, intermediate and high risk. In addition, this model provides long-term prognostic value.

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