Age-Specific Performance of the Revised Cardiac Risk Index for Predicting Cardiovascular Risk in Elective NonCardiac Surgery

Charlotte Andersson, MD, PhD; Mads Wissenberg, MD; Mads Emil Jørgensen, MB; Mark A. Hlatky, MD; Charlotte Mérie, MD, PhD; Per Føge Jensen, MD, PhD, MHM; Gunnar H. Gislason, MD, PhD; Lars Køber, MD, DSc; Christian Torp-Pedersen, MD, DSc; Charlotte Andersson, MD, PhD; Mads Wissenberg, MD; Mads Emil Jørgensen, MB; Mark A. Hlatky, MD; Charlotte Mérie, MD, PhD; Per Føge Jensen, MD, PhD, MHM; Gunnar H. Gislason, MD, PhD; Lars Køber, MD, DSc; Christian Torp-Pedersen, MD, DSc

Background—The revised cardiac risk index (RCRI) holds a central role in preoperative cardiac risk stratification in noncardiac surgery. Its performance in unselected populations, including different age groups, has, however, not been systematically investigated. We assessed the relationship of RCRI with major adverse cardiovascular events in an unselected cohort of patients undergoing elective, noncardiac surgery overall and in different age groups.

Methods and Results—We followed up all individuals ≥25 years who underwent major elective noncardiac surgery in Denmark (January 1, 2005, to November 30, 2011) for the 30-day risk of major adverse cardiovascular events (ischemic stroke, myocardial infarction, or cardiovascular death). There were 742 of 357,396 (0.2%), 755 of 748,899 (1.0%), 521 of 119,211 (4%), and 257 of 31,466 (8%) major adverse cardiovascular events occurring in RCRI classes I, II, III, and IV. Multivariable odds ratio estimates were as follows: ischemic heart disease 3.30 (95% confidence interval, 2.96–3.69), high-risk surgery 2.70 (2.46–2.96), congestive heart failure 2.65 (2.29–3.06), cerebrovascular disease 10.02 (9.08–11.05), insulin therapy 1.62 (1.37–1.93), and kidney disease 1.45 (1.33–1.59). Modeling RCRI classes as a continuous variable, C statistic was highest among age group 56 to 65 years (0.772) and lowest for those aged >85 years (0.683). Sensitivity of RCRI class >I (ie, having ≥1 risk factor) for capturing major adverse cardiovascular events was 59%, 71%, 64%, 66%, and 67% in patients aged ≤55, 56 to 65, 66 to 75, 76 to 85, and >85 years, respectively; the negative predictive values were >98% across all age groups.

Conclusions—In a nationwide unselected cohort, the performance of the RCRI was similar to that of the original cohort. Having ≥1 risk factor was of moderate sensitivity, but high negative predictive value for all ages. (Circ Cardiovasc Qual Outcomes. 2015;8:00-00. DOI: 10.1161/CIRCOUTCOMES.114.001298.)

Key Words: cardiovascular diseases • decision support techniques • preoperative care • surgery

Noncardiac surgery is a significant risk factor for major adverse cardiovascular events (MACE). An individual’s propensity for MACE depends on the burden and type of risk factors, including surgery type, and subclinical and clinical cardiovascular disease. For patients at higher risks of MACE, preoperative cardiac evaluation and medical optimization may translate into better outcomes. Cardiac evaluation is, however, unlikely to be cost-effective in patients at low pretest probability of MACE (but may instead pose a risk of false-positive findings, unnecessary downstream testing, and postponement of surgery). Selection of the appropriate patients for preoperative cardiac evaluation is, therefore, paramount.

The revised cardiac risk index (RCRI) by Lee et al often holds a central role for initial risk screening. The RCRI has a class IB recommendation in the European Society of Cardiology guidelines on preoperative risk assessment and the American College of Cardiology/American Heart Association guidelines use it to define intermediate risk factors for MACE in surgery. The score assigns 1 point for each of a history of ischemic heart disease, cerebrovascular disease, congestive heart failure, preoperative use of insulin, elevated creatinine (>2 mg/dL), and high-risk surgery (comprising thoracic, intra-abdominal, or suprarenal aortic surgery). The RCRI was aimed for prediction of a composite end point of myocardial infarction, pulmonary edema, ventricular fibrillation or primary cardiac arrest, and complete heart block. It was developed on a cohort of patients who were aged ≥50 years and scheduled for major nonemergency, noncardiac surgery.
WHAT IS KNOWN

- The revised cardiac risk index (RCRI) is widely used for preoperative risk assessment in noncardiac surgery.
- The RCRI was developed to predict a composite end point of myocardial infarction, pulmonary edema, ventricular fibrillation or primary cardiac arrest, and complete heart block.

WHAT THE STUDY ADDS

- We validated the usefulness of the RCRI for predicting major adverse cardiovascular events (comprising ischemic stroke, myocardial infarction, or cardiovascular death) in an unselected cohort of Danish patients undergoing elective noncardiac surgery, with specific focus on different age groups.
- The discriminatory ability of the RCRI to predict major adverse cardiovascular events in our cohort was similar to that of the original study of the risk index.
- The negative predictive value of having no risk factors was >98% across all ages, supporting that RCRI may be used to identify people at low risk for perioperative major adverse cardiovascular events around noncardiac surgery.

with an expected length of hospitalization of ≥2 days at a tertiary-care teaching hospital. It is, however, frequently used outside the frame on which it was developed, including on both younger and older patients. In the latter context, age is an important contributor to MACE risk; but despite so, no previous study has specifically addressed the performance of RCRI in different age groups, which was the aim of the present Danish nationwide study. Of note, the end points used in our study differed slightly from the original end points and included nonfatal ischemic stroke in addition to nonfatal myocar-
dial infarction and cardiovascular death. We chose this broader definition of hard end points because they are well defined and because ischemic stroke have overlapping pathophysiology with cardiac events.

Methods

Medical care in Denmark is tax-financed and is accessible to all citizens (≈5.5 million people) without copayment. The government keeps complete records of several healthcare-related variables, including all hospitalizations, claimed prescriptions, surgeries, and dates and causes of deaths. The Danish government keeps track of all Danish citizens through a permanent civil registration number that is used in every hospital contact. We used 5 of these registries for the present study. In brief, we used the Danish National Patient Registry to obtain information on comorbidity and surgery. Because hospital departments are reimbursed based on correct diagnostic and procedural registration, these data are assumed to be complete and accurate. All surgical procedures performed at public hospitals are registered according to the Nordic classification system for surgeries (NOMESKO NCPS), and medical conditions are coded according to the International Classification of Diseases system (ICD; the 10th revision has been used since 1994). We identified all neuro, eye, ear-nose-throat, breast, orthopedic, abdominal, plastic, gynecological, endocrine, thoracic (noncardiac), urologic, and vascular surgeries requiring anesthesia performed between January 1, 2005, and November 30, 2011 (surgery codes are available in Table I in the Data Supplement). We defined high-risk surgeries as intra-abdominal (excluding hernia repairs), intrathoracic, or suprainguinal aortic surgery, in accordance with the original classification. From the National Population Registry, we obtained information on causes of deaths (based on death certificates) occurring within 30 days of surgery. We obtained information on the use of insulin (anatomic therapeutic classification code A10A) from the Danish Registry of Medicinal Product Statistics, which holds information on all claimed prescriptions from Danish pharmacies since 1995. Because of partial reimbursement of medical expenses, the registry is accurate. We obtained information on all anesthetic procedures from the Danish Anesthesia Registry. This registry has existed since the end of 2004. Information available includes whether the surgical procedure was of acute or elective type (this has been registered as a part of clinical work).

Population and Definition of Variables in RCRI

The study population included those who were aged ≥25 years at the time of surgery and who had only 1 anatomic region involved during the same surgical session (eg, people with concomitant surgery on the spleen and bladder were excluded). For individuals who had ≥1 surgical procedure performed within 30 days, we only considered the first surgery in each such 30-day period.

We identified comorbidities by previous discharge diagnoses in the National Hospitalization Registry at any time ≤5 years before the index date. In accordance with the RCRI score, we assigned 1 point for each of ischemic heart disease (ICD-10 code I20-25), a history of cerebrovascular disease (ICD-10 I60-69), a history of congestive heart failure (I11, I11.0, I11.1, I11.2, I11.3, I11.5, I11.8, I11.9), chronic obstructive pulmonary disease (I43), diabetes mellitus (E11-E14), hypertension (I10-I13), atrial fibrillation, and congestive heart failure (I50), heart failure with reduced ejection fraction (I50.1), and complete heart block.

Anesthesia Registry. This registry has existed since the end of 2004. From the National Anesthesia Registry, we obtained information on all anesthetic procedures from the Danish Anesthesia Registry. This registry has existed since the end of 2004. Information available includes whether the surgical procedure was of acute or elective type (this has been registered as a part of clinical work).

Outcomes

We evaluated the 30-day risk of MACE, defined as nonfatal acute myocardial infarction (ICD-10 code I21), nonfatal ischemic stroke (ICD-10 code I60-I69), or cardiovascular death (ICD-10 codes I00-I99). For the nonfatal myocardial infarction and ischemic stroke end points, we only considered in-hospital diagnoses because these have been shown to be accurate in our registries.

Ethics

In Denmark, retrospective register-based studies do not need ethical approval. The study was approved by the Danish Data Protection Agency (ref. no. 2007-58-015/I.suite no. 02737 GEH–2014–019).

Statistics

All surgeries were treated as independent observations. We used logistic regression models (proc logistic) with RCRI included as a continuous variable to estimate discrimination (by c statistic) in overall population and in age-stratified subgroups. 95% confidence intervals of c statistic were derived from the roc statement in SAS proc logistic. To evaluate the odds ratios associated with individual variables
from the risk score, we used a multivariable logistic regression model including all 6 variables in the same model. A 2-sided \( P \) value <0.05 was considered significant for all statistical tests. All statistical analyses were performed in SAS version 9.3 (SAS Institute, NC). The diagnostic test evaluations were performed using http://www.medcalc.org/calc/diagnostic_test.php.

**Results**

A total of 447,352 surgeries were included (Table 1). Mean age and proportion of men increased with higher RCRI scores. Approximately 80% of the population was classified as RCRI class I. The distribution of surgeries differed slightly for the RCRI groups with orthopedic and female reproductive surgery being the most common surgeries among those with RCRI class I, whereas abdominal surgery was among the most common surgery subtypes in patients with RCRI class II to IV.

MACE occurred in 2275 individuals (0.51%). Rates increased with higher RCRI classes and were comparable with those seen in the original cohort (Table 2; Figure). Discrimination was similar to that of the original cohort (c statistic 0.761 in the present cohort and 0.759 in the original RCRI cohort). Odds ratios associated with the individual variables of the risk score are presented in Table 2.

**Age-Specific Performance of the RCRI**

In total, 86% of patients aged ≤55 years were in RCRI class I. The proportion of patients with RCRI class I was lower for higher age groups, and only 63% of people aged >85 years were classified as RCRI class I (Table 3). In general, older patients had higher MACE rates associated with low RCRI classes than young patients. For example, patients aged >85 years with RCRI class I had similar observed MACE rates (125/6499 [1.9%]) as patients aged ≤55 years with RCRI class III (34/1674 [2.0%]). The negative predictive value of not having any risk factors, ie, having an RCRI class I, was however high across all age groups (98.1% in the age group >85 years; Table 4). Analyses of the performance of the RCRI classes in different age groups yielded highest discrimination among those aged 56 to 65 years (c statistic 0.772) and a little lower for the very elderly (c statistic 0.683 among those aged >85 years; Table 3). RCRI class >I was associated with MACE rates ranging from 0.3% for the youngest to 6.8% for the oldest (Table III in the Data Supplement). Odds ratios associated with the individual variables from the RCRI stratified by age is available in Table IV in the Data Supplement.

<table>
<thead>
<tr>
<th>Table 1. Baseline Characteristics</th>
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<tbody>
<tr>
<td>Class I</td>
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<tr>
<td>----------------------------------</td>
</tr>
<tr>
<td>Sex, men (%)</td>
</tr>
<tr>
<td>Age, y</td>
</tr>
<tr>
<td>Congestive heart failure (%)</td>
</tr>
<tr>
<td>Ischemic heart disease (%)</td>
</tr>
<tr>
<td>Cerebrovascular disease (%)</td>
</tr>
<tr>
<td>Kidney disease (%)</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
</tr>
<tr>
<td>Acute myocardial infarction (%)</td>
</tr>
<tr>
<td>Use of insulin (%)</td>
</tr>
<tr>
<td>Surgery types</td>
</tr>
<tr>
<td>----------------------------------</td>
</tr>
<tr>
<td>Ear-nose-throat</td>
</tr>
<tr>
<td>Major orthopedic</td>
</tr>
<tr>
<td>Minor orthopedic</td>
</tr>
<tr>
<td>Abdominal (bowel)</td>
</tr>
<tr>
<td>Abdominal (nonbowel)*</td>
</tr>
<tr>
<td>Breast</td>
</tr>
<tr>
<td>Plastic</td>
</tr>
<tr>
<td>Endocrine</td>
</tr>
<tr>
<td>Eye</td>
</tr>
<tr>
<td>Female reproductive</td>
</tr>
<tr>
<td>Male reproductive</td>
</tr>
<tr>
<td>Intracranial</td>
</tr>
<tr>
<td>Neuro</td>
</tr>
<tr>
<td>Nonarterial vessels</td>
</tr>
<tr>
<td>Thoracic</td>
</tr>
<tr>
<td>Urologic</td>
</tr>
<tr>
<td>Vascular</td>
</tr>
</tbody>
</table>

*The majority of surgeries in this group were cholecystectomies or hernia repairs.
associated with the different risk factors were similar across all age groups (a history of cerebrovascular disease was associated with an odds ratio of 45.1 [95% confidence interval, 32.0–65.5] among people aged \( \leq 55 \) years versus 3.40 [2.68–4.31] among people aged >85 years and insulin therapy was associated with an odds ratio of 0.87 [0.39–1.95] among people aged \( \leq 55 \) years versus 1.82 [1.11–3.00] among people aged >85 years).

Discussion

In this study, we evaluated the performance of the RCRI in an unselected Danish population undergoing elective, noncardiac surgery between 2005 and 2011. We observed that the RCRI had similar discrimination in our cohort as in the original cohort although the renal disease definition and MACE end point differed a bit (end point in original RCRI cohort was defined as myocardial infarction, pulmonary edema, ventricular fibrillation or primary cardiac arrest, and complete heart block). We also observed that the odds ratios associated with the individual risk factors of the RCRI were comparable with those of the original cohort, apart from a history of stroke, which had higher odds ratio in our study (10.0) than in the original RCRI cohort (3.2). This may likely be explained by the inclusion of ischemic stroke in our MACE end point because people with a history of stroke have a well-known substantial risk of recurrent stroke. Although not part of the original RCRI, we chose to include ischemic stroke in the end point because this is a clinically important event that shares pathophysiological pathways and risk factors with, for example, acute myocardial infarction. In contrast, we decided not to include softer end points, such as pulmonary edema, because the validity of such diagnoses in our registries is unknown.

C statistic for RCRI have previously been reported to range from 0.683 in a recent European multicenter study of patients aged >55 years undergoing major surgery with additional risk factors for adverse cardiovascular events (the end point was a combination of death, acute myocardial infarction, cardiac arrest, cardiopulmonary resuscitation, and acute decompen-sated heart failure) to 0.746 (with moderate calibration) in a sample from the American College of Surgeons’ 2008 National Surgical Quality Improvement Program database (outcomes were cardiac arrest or myocardial infarction). Efforts have been made to create alternative and more detailed risk scores, but none has gained similar popularity to RCRI because it is easy to use. Our observations suggest that the discriminatory power of the RCRI is acceptable for all ages,
but that the absolute MACE rates differ across ages for any given RCRI class. Age-specific reference values of MACE rates may, therefore, be warranted when evaluating patients preoperatively.

When evaluating the usefulness of any risk score, the first question that needs be asked is for what it is intended to be used for. The RCRI can perhaps particularly be used to select the appropriate group patients whom may safely undergo surgery without further cardiac evaluation. Our data indicated that RCRI class I captures ≈80% of the population and can, with a negative predictive value >98%, rule out perioperative MACE. The second thing that should be asked about a risk score is whether higher discriminatory power and reclassification of patients by inclusion of additional variables will lead to changed clinical management and improved outcomes. This is difficult to answer for the RCRI, because unlike, for instance, the pooled cardiovascular risk calculator (which is used for defining primary prevention strategies with statins) or the CHADS2-VASc score (which is used for defining the appropriate prevention strategy of stroke and thromboembolism in atrial fibrillation) no definite cut off values are established that will affect clinical treatment decisions (ie, that will guide downstream clinical testing and preventive interventions). As such, cardiac biomarkers, such as high-sensitivity troponin T or B-type natriuretic peptide, have shown to add significant prognostic value beyond the RCRI although there is yet no evidence suggesting improved clinical outcomes or lower preoperative testing costs associated with this practice.12,14,15

Approximately 41% of all MACE were observed within the RCRI class I group among people aged ≤55 years. In younger individuals, future research may, therefore, be needed to investigate whether a greater proportion of people at true risk of MACE could be captured by consideration of additional clinical information, such as body mass index, family history of premature cardiovascular disease, familial hypercholesterolemia, smoking, and type 2 diabetes mellitus (treated with oral glucose-lowering medications), which are not captured by the RCRI. An RCRI class >I captured 71% of all MACE in those aged 56 to 65 years and nearly as many, 67% among those aged >85 years. Within the higher age groups, more people were, however, classified as having RCRI class >I, which would translate into high preoperative diagnostic costs if all such patients were to undergo additional testing. Furthermore, among those with RCRI class > I MACE rates were still rather modest/moderate (6.8% among people aged >85 years), and many people are therefore classified as at risk, even though absolute event rate is not high. It is, therefore, perhaps likely that additional risk stratification tools, such as cardiac biomarkers, could add information that would be of value for defining optimal treatment strategies in this elderly segment. Nevertheless, in summary, our study demonstrated that the RCRI performs as intended with an acceptable discrimination. It seems, therefore, reasonable to continue to use this risk score for initial risk assessment across adults of all ages undergoing elective, noncardiac surgery.

### Strengths and Limitations

The main strength of this study was the comprehensive study population comprising all Danish patients undergoing elective noncardiac surgery between 2005 and 2011 and the inclusion of hard, validated end points. A major limitation of our study was, however, the lack of systematic assessment of myocardial infarction postoperatively by troponins. Some myocardial infarction may, therefore, have been missed. A previous study has shown that many postoperative myocardial infarctions do not present with classical angina symptoms.16 Yet, missed

### Table 3. Observed Major Adverse Cardiovascular Events Rates in Different Age Groups

<table>
<thead>
<tr>
<th>RCRI Class</th>
<th>≤55</th>
<th>56–65</th>
<th>66–75</th>
<th>76–85</th>
<th>&gt;85</th>
</tr>
</thead>
<tbody>
<tr>
<td>n total</td>
<td>214,776</td>
<td>96,793</td>
<td>81,936</td>
<td>43,491</td>
<td>10,356</td>
</tr>
<tr>
<td>I</td>
<td>70,184,890 (0.04%)</td>
<td>95,765,855 (0.12%)</td>
<td>191,603,314 (0.32%)</td>
<td>261,291,108 (0.90%)</td>
<td>125,649,912 (1.92%)</td>
</tr>
<tr>
<td>II</td>
<td>55,278,866 (0.20%)</td>
<td>122,16,870 (0.72%)</td>
<td>209,16,954 (1.23%)</td>
<td>230,10,465 (2.20%)</td>
<td>139,27,060 (5.14%)</td>
</tr>
<tr>
<td>III</td>
<td>34,167,4 (2.03%)</td>
<td>77,27,06 (2.85%)</td>
<td>145,365,3 (3.97%)</td>
<td>178,30,08 (5.92%)</td>
<td>87,88,0 (9.89%)</td>
</tr>
<tr>
<td>IV</td>
<td>10,326 (3.07%)</td>
<td>29,624 (8.98%)</td>
<td>80,101,5 (7.88%)</td>
<td>100,910 (10.99%)</td>
<td>38,271 (9.77%)</td>
</tr>
<tr>
<td>C statistic</td>
<td>0.739 (0.700–0.778)</td>
<td>0.772 (0.745–0.779)</td>
<td>0.746 (0.726–0.766)</td>
<td>0.701 (0.681–0.720)</td>
<td>0.683 (0.657–0.710)</td>
</tr>
</tbody>
</table>

C statistic with 95% confidence intervals refers to logistic regression modeling with RCRI class as continuous variable. RCRI indicates revised cardiac risk index.

### Table 4. Sensitivity, Specificity, Positive and Negative Predictive Values, and Positive and Negative Likelihood Ratios of Having ≥1 Risk Factor (ie, RCRI Class >I vs RCRI Class I) for Predicting Major Adverse Cardiovascular Events

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>≤55 y</th>
<th>56–65 y</th>
<th>66–75 y</th>
<th>76–85 y</th>
<th>&gt;85 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity, %</td>
<td>58.3 (50.8–66.1)</td>
<td>70.6 (65.3–75.5)</td>
<td>64.2 (60.0–68.3)</td>
<td>66.1 (62.6–69.4)</td>
<td>66.7 (61.6–71.4)</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>86.1 (86.0–86.3)</td>
<td>79.3 (79.0–79.5)</td>
<td>74.0 (73.7–74.3)</td>
<td>67.5 (67.1–68.0)</td>
<td>64.0 (63.0–64.9)</td>
</tr>
<tr>
<td>Positive predictive value, %</td>
<td>0.3 (0.3–0.4)</td>
<td>1.1 (1.0–1.3)</td>
<td>1.6 (1.4–1.8)</td>
<td>3.5 (3.2–3.9)</td>
<td>6.5 (5.8–7.3)</td>
</tr>
<tr>
<td>Negative predictive value, %</td>
<td>&gt;99.9 (&gt;99.9–&gt;99.9)</td>
<td>99.9 (99.9–99.9)</td>
<td>99.7 (99.6–99.7)</td>
<td>99.1 (99.0–99.2)</td>
<td>98.1 (97.7–98.4)</td>
</tr>
<tr>
<td>Positive likelihood ratio, %</td>
<td>4.2 (3.7–4.8)</td>
<td>3.4 (3.2–3.7)</td>
<td>2.5 (2.3–2.6)</td>
<td>2.0 (1.9–2.1)</td>
<td>1.9 (1.7–2.0)</td>
</tr>
<tr>
<td>Negative likelihood ratio, %</td>
<td>0.5 (0.4–0.6)</td>
<td>0.4 (0.3–0.4)</td>
<td>0.5 (0.4–0.5)</td>
<td>0.5 (0.5–0.6)</td>
<td>0.5 (0.5–0.6)</td>
</tr>
</tbody>
</table>

Absolute numbers of true and false-positive and false-negative tests are available in Table IV in the Data Supplement. RCRI indicates revised cardiac risk index.
myocardial infarctions are known to carry a poor prognosis with high mortality rates in postsurgical patients (1 study reported that 61% of patients who experienced a myocardial infarction died within 30 days),11 which would have been captured by our composite end point, including cardiovascular mortality. We also did not have values on serum creatinine levels for the whole study population, and we, therefore, used a diagnosis of renal disease as a proxy for elevated creatinine. Although the specificity of capturing patients with creatinine concentrations >2 mg/dL was excellent (>99%), the sensitivity was moderate (45%). However, given the large study sample and the relatively low prevalence of creatinine concentrations >2 mg/dL, the estimated odds ratios associated with renal disease (and negative predictive values of having no risk factors) would likely be unaffected by such moderate sensitivity. Finally, it is likely that some people within the higher RCRI classes may have undergone preoperative cardiovascular evaluation and optimization, which perhaps would have led to lower observed MACE rates.

Acknowledgments

Dr Andersson was responsible for data analyses, wrote the initial draft of the article, and takes full responsibility for the accuracy of analyses and integrity of the data. All authors contributed to study design, interpretation of the data, and critical revision of the article. All authors approved the final article.

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Disclosures

Dr Gislason has received speaker fees from AstraZeneca, Bristol-Myers Squibb, and Pfizer but unrelated to the topic of the current study.

References


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Data Supplement (unedited) at:
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SUPPLEMENTAL MATERIAL

Online appendix Table 1, specification of surgery codes

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<tr>
<th>Surgery:</th>
<th>Code:</th>
</tr>
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<tbody>
<tr>
<td>Intracerebral</td>
<td>KAA</td>
</tr>
<tr>
<td>Neuro</td>
<td>KAB-D</td>
</tr>
<tr>
<td>Endocrine</td>
<td>KB</td>
</tr>
<tr>
<td>Eye</td>
<td>KC</td>
</tr>
<tr>
<td>ENT</td>
<td>KD</td>
</tr>
<tr>
<td>Thorax (pulmonary)</td>
<td>KG</td>
</tr>
<tr>
<td>Breast</td>
<td>KH</td>
</tr>
<tr>
<td>Abdominal (bowels)</td>
<td>KJC, KJD, KJE, KJF, KJG, KJH,</td>
</tr>
<tr>
<td>Abdominal (non-bowels)</td>
<td>KJA, KJJ, KJK, KJJ, KJM</td>
</tr>
<tr>
<td>Urological</td>
<td>KKA, KKB, KKC, KKD, KKK</td>
</tr>
<tr>
<td>Male reproductive</td>
<td>KKE, KKF, KKG</td>
</tr>
<tr>
<td>Female reproductive</td>
<td>KLA, KLB, KLC, KLD, KLG</td>
</tr>
<tr>
<td>Orthopedic major</td>
<td>KNA, KNB, KNE, KNF, KNG</td>
</tr>
<tr>
<td>Orthopedic minor</td>
<td>KNC, KND, KNH</td>
</tr>
<tr>
<td>Vascular</td>
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</tr>
<tr>
<td>Non-arterial vessels</td>
<td>KPH, KPJ</td>
</tr>
<tr>
<td>Plastic</td>
<td>KQ</td>
</tr>
</tbody>
</table>

Footnote: These 17 surgery subgroups were created according to extent of surgery, based on clinical impression. “Thoracic” surgery included pulmonary, mediastinal, and pleural surgery, “abdominal (bowel)” surgery included esophageal, gastric, duodenal, small intestine, colon, and rectal surgery, “abdominal (non-bowel)” included all other kinds of abdominal surgeries, “urology” included surgery of kidneys, ureters, and bladder, “male reproductive” included surgery to penis, urethra, scrotum, and prostate/seminal glands, “orthopedic minor” included hand, antebrachial, and foot surgery, “orthopedic
“major” included all other orthopedic surgeries, and “vascular (arteries)” included the whole arterial system.
Online supplemental Table 2 – serum creatinine concentrations by a registry diagnosis of renal disease

<table>
<thead>
<tr>
<th></th>
<th>No renal disease</th>
<th>Renal disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine ≤2 mg/dL</td>
<td>30114</td>
<td>261</td>
</tr>
<tr>
<td>Creatinine &gt;2mg/dL</td>
<td>875</td>
<td>737</td>
</tr>
</tbody>
</table>
**Online supplemental Table 3 – classification of patients with or without MACE risk factors (i.e., RCRI class I vs. >I)**

<table>
<thead>
<tr>
<th></th>
<th>≤ 55 years</th>
<th>56-65 years</th>
<th>66-75 years</th>
<th>76-85 years</th>
<th>&gt;85 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCRI class I</td>
<td>184,890 (86.1%)</td>
<td>76,585 (79.1%)</td>
<td>60,314 (73.6%)</td>
<td>29,108 (66.9%)</td>
<td>6,499 (62.8%)</td>
</tr>
<tr>
<td>RCRI class &gt;I</td>
<td>29,886 (13.9%)</td>
<td>20,208 (20.9%)</td>
<td>21,662 (26.4%)</td>
<td>14,383 (33.1%)</td>
<td>3,857 (37.2%)</td>
</tr>
<tr>
<td>True negative</td>
<td>184,820 (&gt;99.9%)</td>
<td>76,490 (99.9%)</td>
<td>60,123 (99.7%)</td>
<td>28,847 (99.1%)</td>
<td>6,374 (98.1%)</td>
</tr>
<tr>
<td>True positive</td>
<td>99 (0.3%)</td>
<td>228 (1.1%)</td>
<td>343 (2.0%)</td>
<td>508 (3.5%)</td>
<td>250 (6.8%)</td>
</tr>
<tr>
<td>False negative</td>
<td>70 (0.04%)</td>
<td>95 (0.1%)</td>
<td>191 (0.3%)</td>
<td>261 (0.9%)</td>
<td>125 (1.9%)</td>
</tr>
<tr>
<td>False positive</td>
<td>29,787 (99.7%)</td>
<td>19,980 (98.9%)</td>
<td>21,188 (98.0%)</td>
<td>13,875 (99.1%)</td>
<td>3,593 (93.2%)</td>
</tr>
</tbody>
</table>

Footnote: A “test” result refers to the presence or absence of risk factors (i.e., belonging to RCRI class I vs. >I). Thus, a “true negative” is a person who belongs to RCRI class I and does not have an event; a “true positive” is a person who belongs to RCRI class >I and has an event. A “false positive” is a person who belongs to RCRI class >I but has no event, and a “false negative” is a person who belongs to RCRI class I but has an event.
Online supplemental Table 4 – odds ratios associated with individual risk factors in the RCRI stratified by age groups

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>≤ 55 years (95% CI)</th>
<th>56-65 years (95% CI)</th>
<th>66-75 years (95% CI)</th>
<th>76-85 years (95% CI)</th>
<th>&gt;85 years (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-risk surgery</td>
<td>2.55 (1.79, 3.63)</td>
<td>3.32 (2.62, 4.20)</td>
<td>2.74 (2.30, 3.26)</td>
<td>2.43 (2.07, 2.86)</td>
<td>1.91 (1.49, 2.44)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>4.62 (2.78, 7.70)</td>
<td>2.63 (1.93, 3.58)</td>
<td>2.11 (1.72, 2.59)</td>
<td>2.07 (1.74, 2.45)</td>
<td>1.94 (1.52, 2.47)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1.24 (0.48, 3.18)</td>
<td>1.66 (1.04, 2.66)</td>
<td>2.34 (1.79, 3.07)</td>
<td>2.13 (1.72, 2.65)</td>
<td>1.56 (1.16, 2.08)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>45.08 (31.99, 65.52)</td>
<td>13.36 (10.46, 17.07)</td>
<td>7.82 (6.54, 9.34)</td>
<td>4.10 (3.47, 4.86)</td>
<td>3.40 (2.68, 4.31)</td>
</tr>
<tr>
<td>Insulin therapy</td>
<td>0.87 (0.39, 1.95)</td>
<td>1.33 (0.85, 2.09)</td>
<td>1.80 (1.34, 2.42)</td>
<td>1.88 (1.41, 2.50)</td>
<td>1.82 (1.11, 3.00)</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>2.17 (1.60, 2.94)</td>
<td>1.69 (1.35, 2.11)</td>
<td>1.40 (1.19, 1.64)</td>
<td>1.20 (1.03, 1.39)</td>
<td>1.38 (1.13, 1.69)</td>
</tr>
</tbody>
</table>