British Journal of Anaesthesia **107** (2): 133–43 (2011)
Advance Access publication 30 June 2011 · doi:10.1093/bja/aer194

BJA

Utility of clinical risk predictors for preoperative cardiovascular risk prediction

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Editor's key points

- Cardiovascular risk prediction is a desirable objective in anaesthesia.
- All current approaches have some limitations and lack specificity for an individual patient.
- The use of additional variables, such as age, is proposed.
- Risk assessment should be repeated through the perioperative period and not just preoperatively.

Summary. Cardiovascular risk prediction using clinical risk factors is integral to both the European and the American algorithms for preoperative cardiac risk assessment and perioperative management for non-cardiac surgery. We have reviewed these risk factors and their ability to guide clinical decision making. We examine their limitations and attempt to identify factors which may improve their performance when used for clinical risk stratification. To improve the performance of the clinical risk factors, it is necessary to create uniformity in the definitions of both cardiovascular outcomes and the clinical risk factors. The risk factors selected should reflect the degree of organ dysfunction rather than a historical diagnosis. Parsimonious model design should be applied, making use of a minimal number of continuous variables rather than creating overfitted models. The inclusion of age in the model may assist partly in controlling for the duration of risk factor exposure. Risk assignment should occur throughout the perioperative period and the risk factors chosen for model inclusion should vary depending on when the assignment occurs (before operation, intraoperatively, or after operation).

Keywords: clinical risk factors; complications, myocardial infarction; modelling; risk

Preoperative risk stratification as stated by the American College of Cardiology/American Heart Association (ACC/AHA)[1] in their 'Perioperative cardiovascular evaluation and care for noncardiac surgery' is aimed at 'providing a risk profile' while the European Society of Cardiology/European Society of Anaesthesiology's (ESC/ESA) guidelines for preoperative cardiac risk assessment aim to generate an 'individualized cardiac risk assessment'.[2] These risk assessments are then used to assist with both short- and long-term patient investigation and to direct further perioperative management.

Clinical risk factors play an important role in this process, providing a cheap and readily accessible tool by which to perform preoperative risk stratification. The first major contribution to perioperative cardiovascular risk prediction was made when Goldman and colleagues[3] developed the original perioperative cardiovascular risk index, later modified by Detsky and colleagues.[4] Subsequent indices showed similar performance in predicting cardiovascular risk[5] until the development of Lee's Revised Cardiac Risk Index (RCRI).[6] The RCRI performed significantly better than previous indices and was validated outside its derivation population (Table 1).[7] This led to its incorporation into the ACC/AHA perioperative algorithm, and also into the ESC/ESA guidelines for preoperative cardiac risk assessment and management for non-cardiac surgery. This has established the RCRI as the primary clinical cardiovascular risk stratification tool in perioperative medicine.[1 2]

The aim of this review is to evaluate the utility and limitations of the RCRI clinical risk factors as they are currently used in preoperative evaluation guidelines for risk stratification and directing further preoperative investigation.[1 2] We have attempted to identify areas of clinical risk prediction which could be improved on in the future.

Performance of the current clinical risk stratification tools

The goal of preoperative risk assessment is to assess an individual patient's cardiac risk in order to direct further testing and treatment, and to perform this process as cost-effectively as possible. Current perioperative cardiovascular evaluation algorithms follow a stepwise process making use of clinical factors and test results together with an estimation of the size of the surgical stress response to arrive at an 'individualized cardiac risk assessment'.[1 2]

The first four steps in both the European and American guidelines are directed at assessing patient-specific risk. These steps determine (i) the presence of active or unstable cardiac conditions, (ii) the patient's functional capacity, (iii) the urgency, and (iv) associated cardiac risk of the surgery. They are tailored to the individual patient and the surgery they have to undergo. The presence of active cardiac conditions, high-risk surgery, or poor effort tolerance all greatly increases a patient's risk for a postoperative cardiac complication.

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Table 1 Cardiovascular outcomes associated with Lee's RCRI. CVS, cardiovascular. Clinical risk factors include high-risk surgery, ischaemic heart disease, history of congestive cardiac failure, history of cerebrovascular disease, insulin therapy for diabetes, and a preoperative serum creatinine of >177 μmol litre^{-1}.[6]

Number of CVS risk factors	Major CVS complications (95% CI)[6] (%)	Cardiovascular death[7] (%)
0	0.5 (0.2–1.1)	0.3
1	1.3 (0.7–2.1)	0.7
2	3.6 (2.1–5.6)	1.7
≥3	9.1 (5.5–13.8)	3.6

Patients are then clinically stratified using the RCRI clinical risk factors.[6] In contrast to the preceding steps of the algorithms, the RCRI is a population-derived risk index. As a result, it cannot be used to assign individual patient risk but is rather used to stratify patients into risk categories, which forms the basis for further perioperative management. To perform this role adequately, the RCRI risk factors must successfully discriminate higher risk from lower risk patients in this already triaged population.

Two statistical methods may be used to evaluate the discrimination of the RCRI. The first is by means of likelihood ratios (LRs). LRs reflect a test's ability to create risk categories, by expressing these categories as ratios. Clinically useful discrimination is seen with ratios <0.2 or >10.[8] An added advantage of the LR is that it may be used to determine post-test probability, using Fagan's nomogram.[9] The second commonly used method is the area under the receiver-operating characteristic (ROC) curve (AUC).[10] The AUC (also known as the *c*-statistic) is expressed as a percentage and reflects the probability that a positive test will experience an event when compared with a negative test.[10] The ACC/AHA guidelines use the RCRI to create three risk categories (3 or more, 1 or 2, no risk factors) to guide further investigation, while the ESC guidelines make use of only two risk categories (≥3 risk factors or <3 risk factors).[1 2] An assessment of the RCRI determined that the only clinically significant LRs were achieved when a patient had no clinical risk factors (LR of 0.16).[8] The presence of one risk factor fell just outside the clinically useful range with a negative LR of 0.34. For patients with either two, or three and more risk factors, the discrimination was found to be poor with an LR of 2.7 and 4.8, respectively.[8] When applied to a large retrospective database study (108 593 patients) of non-cardiac surgery population, the RCRI was able to discriminate four individual risk groups in which the risk of cardiac death was statistically different (0.3%, 0.7%, 1.7%, 3.6%). However, the clinical utility of these findings is questionable as the resultant *c*-statistic for the AUC was only 0.63.[7]

To improve on this discriminatory ability, patients have been grouped into low (0 or 1 risk factors) and intermediate–high (≥2 risk factors) risk categories. The ability of the RCRI to predict perioperative cardiac complications [cardiac death, myocardial infarction (MI), non-fatal cardiac arrest] or death within 30 days of surgery was reviewed in a recent large meta-analysis of predominantly observational cohort studies (792 740 patients in 24 studies).[11] It found moderate discrimination between patients at high *vs* low risk for cardiac events [AUC 0.75 (95% CI 0.72–0.79), with a positive LR of 2.78 (95% CI 1.74–4.45) and a negative LR of 0.45 (95% CI 0.31–0.67)].

When used for vascular surgery alone, the RCRI showed significantly poorer discrimination for predicting cardiac events in this meta-analysis, than with other types of non-cardiac surgery, with an AUC of 0.64 (95% CI 0.61–0.66), a positive LR of 1.56 (95% CI 1.42–1.73), and a negative LR of 0.55 (95% CI 0.53–0.82).[11] Interestingly, these findings echo those in Lee's original prospective observational study of 4315 non-cardiac surgical patients aged ≥50 yr, where they identified the limited discriminative utility of the RCRI in aortic surgery [AUC 0.543 (0.092)].[6] Other data also suggest that the performance of the RCRI is influenced by the nature of the surgical procedure and is particularly compromised by higher risk surgeries. A retrospective database review found that the separation of low-to-intermediate risk surgeries from the intermediate-to-high-risk surgeries changed the AUC from 0.68 to 0.56, respectively.[7] A recent prospective observational study of 10 081 vascular surgical patients, which evaluated the same patient outcomes of the original RCRI confirmed that with vascular surgical procedures of increasing cardiovascular risk, the RCRI progressively underestimated the associated cardiovascular complications.[12]

Thus, the RCRI, as a preoperative population-derived risk stratification tool, is at best able to crudely risk stratify patients. In addition, the RCRI's discrimination is best in patients with no risk factors, and not in the higher risk categories as used in the ACC/AHA or the ESC guidelines,[8 11] or in vascular surgical patients.[6 11] It would seem that the RCRI's greatest utility lies in its ability to exclude low-risk patients rather than in predicting events in intermediate-to-high-risk patients. Indeed, the need to undertake high-quality studies to evaluate the RCRI's ability to predict perioperative cardiac risk has been suggested,[11] and Goldman[13] in his editorial on the paper suggests that the RCRI is accurate enough for preoperative risk stratification, although he too suggests that it may benefit from an improvement in its diagnostic accuracy.

The poor discrimination in high-risk (≥3 risk factors) patients would not be a concern, if subsequent non-invasive testing was able to reliably risk stratify these patients. Unfortunately, the evidence suggests that non-invasive investigations are not able to do this. A single, prospective, randomized trial of 208 vascular surgical patients has addressed this issue. In patients with ≥2 RCRI risk factors, one group was managed as per the AHA/ACC preoperative cardiovascular algorithm and selectively underwent coronary angiography following non-invasive testing. All the patients in the other arm of the study had preoperative coronary angiography.[14] While the groups were clinically similar, the myocardial revascularization

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