Perioperative cardiovascular evaluation: heads or tails?

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Summary

When dealing with surgical patients, a perioperative evaluation is essential to anticipate complications and institute measures to reduce the risks. Several algorithms and exams have been used to identify postoperative cardiovascular events, which account for more than 50% of perioperative mortality. However, they are far from ideal. Some of these algorithms and exams were proposed before important advances in cardiology, at a time when pharmacological risk reduction strategies for surgical patients were not available. New biomarkers and exams, such as C-reactive protein, brain natriuretic peptide, and multislice computed tomography have been used in cardiology and have provided important prognostic information. The ankle-brachial index is another significant marker of atherosclerosis. However, specific information regarding the perioperative context of all these methods is still needed. The objective of this article is to evaluate cardiovascular risk prediction models after noncardiac surgery.

Keywords: Perioperative care; general surgery; brain natriuretic peptide; general anesthesia; cardiovascular risk; ankle-brachial index.

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Introduction

Perioperative evaluation is an important step before referring a patient to surgery. The purpose is not just clearance for surgery, but to perform an overall evaluation of the clinical status, make recommendations, deal with cardiovascular risk factors or cardiac problems, and estimate the procedure's risk. Thereupon the medical team and patient can decide the best way to minimize complications, or even to postpone the operation[1]. In addition to clinical experience and common sense, algorithms for perioperative evaluation have been proposed, tested, and validated to contribute to this decision. In general, sensitivity and specificity are quite similar among algorithms; however, they are unfortunately only somewhat better than a coin toss. In addition, most of the assessments have been based upon clinical characteristics of patients submitted to surgery over ten years prior. More recent perioperative evaluation guidelines include flowcharts suggesting tests or pharmacological interventions that may be a rather frustrating support for the algorithms, although much more acceptable to attending physicians.

On the other hand, population growth, developing countries' welfare, technological improvement, new surgical techniques allied to new materials and devices, and faster non-invasive strategies have led to an increase in the number of surgeries[2,3]. Indeed, patients previously considered non-candidates for surgery may now have renewed hope. Consequently, a larger number of patients older than 75 years are being referred to surgery involving multiple cardiovascular risk factors bringing about increased postoperative mortality and duration of hospitalization[4]. Recent predictions estimate that, from 2010 to 2040, the aging population in the United States will increase the incidence of coronary heart disease by approximately 26%, as well as the costs related to care by 41%[5]. It is estimated that more than 40 million surgeries are performed annually in Europe[6], and 240 million around the world[7]. In developing countries, the same scenario is observed. From 1997 to 2007, an increase of 20.42% was observed in the number of surgical procedures in Brazil[2]. In the last few years, however, the same authors observed a 30% increase in the number of case-fatalities[2]. Whether coincident or related events, both findings represent important challenges: how to anticipate and prevent the increase in perioperative complications in this apparently higher risk population without imposing a great economic burden?

Cardiovascular complications and perioperative algorithms

Cardiovascular complications are of special concern when dealing with surgical patients, since approximately 1% of them present with acute myocardial infarction (AMI) after the procedure. Generally it is associated with other noncardiac events with an odds ratio > 6, significantly increasing duration of hospitalization[8]. Related cardiovascular mortality reaches 0.3% (1.2 million patients in Europe alone), accounting for more than 50% of postoperative deaths after vascular surgeries[6,9].

Perioperative cardiovascular risk can be estimated by assessing clinical status, functional capacity and intrinsic risk of the surgery[3]. However, sometimes it may be very difficult to estimate this risk in patients with subclinical presentation of diseases.

Methods and algorithms were developed some time ago, and are being used in clinical practice with a high frequency[10-12]. However, some of these algorithms were proposed prior to the development of important advances in cardiology such as the use of aspirin and statins for coronary artery disease and acute coronary syndromes[13-19]. They were also developed before important pharmacological risk reduction strategies were available for surgical patients, such as beta-blockers and statins[20-22]. Despite having been cautiously validated in the past, it remains to be investigated whether these algorithms are still applicable in different populations submitted to different treatments. Do they continue to merit confidence? Do they predict cardiovascular events or are they little better than as tossing a coin?

The American Society of Anesthesiologists (ASA) classification was first described in 1941[23] and revised in 1963 (Box 1). It was the first attempt to predict surgical complications and is still, by far, the most often used by anesthesiologists. No other preoperative index has achieved the same widespread use. It was first designed to estimate the physiological status with no need for clinical resources and, although it can predict postoperative complications, it has a limited capability to predict cardiovascular complications. Moreover, there is a major problem related to poor reproducibility even among anesthesiologists[24].

The Detsky Index[11] is a modified version of the original risk index[10]. In his study, Detsky showed that the accuracy of the original method proposed by Goldman et al. had dropped from 81% to 69%. After inclusion of angina pectoris severity, previous myocardial infarction, critical aortic stenosis, and alveolar pulmonary edema, the accuracy of the new index increased to 75%. Conversely, the authors observed many events in patients with low-risk scores (false negative) and a limited discrimination power in patients referred for vascular or other major surgery. Based upon the findings of Eagle et al.[9] and Vanzetto et al.,[25] the American College of Physicians (ACP) published a guideline for assessment and management of perioperative risk, suggesting the Modified Cardiac Index for stratification of all patients prior to surgery (Box 1)[26,27]. To minimize the limitations of this method, they recommended the use of a non-invasive cardiac ischemic test for individuals with a

Box 1 – Perioperative risk indexes

American Society of Anesthesiologists Score (ASA Grade)[23]	Revised Cardiac Risk Index (Lee et al., 1999)[12]
I – Normal health patient II – Patient with mild systemic disease III – Patient with severe systemic disease IV – Patient with severe systemic disease that is a constant threat to life V – A moribund patient who is not expected to survive without the operation	1 – High risk type of surgery (intraperitoneal, intrathoracic, or suprainguinal vascular procedures) 2 – Ischemic heart disease (includes any of the following: history of myocardial infarction, history of positive exercise test, current complaint of chest pain, i.e., considered to be secondary to myocardial ischemia, use of nitrate therapy, or electrocardiography with pathologic Q waves) 3 – Congestive heart failure 4 – History of cerebrovascular disease 5 – Preoperative treatment with insulin 6 – Preoperative serum creatinine > 2.0 mg/dL
Modified Cardiac Risk Index Index[a,11]	
Prior myocardial infarction • Last infarction within 6 months: 10 points • Last infarction more than 6 months ago: 5 points Angina pectoris • Canadian Angina Class 3: 10 points • Canadian Angina Class 4: 20 points	Arrhythmia • Rhythm other than sinus or sinus with PACs: 5 points • More than five premature ventricular beats: 5 points Poor general medical status: 5 points • pO_2 < 60 mm Hg, pCO_2 > 50 mmHg, K < 3 mmol/L, blood urea nitrogen level > 50 mmol/L, creatinine 3mg/dL, bedridden
Alveolar pulmonary edema • Pulmonary edema within one week: 10 points • Pulmonary edema at any time: 5 points	Age > 70 years: 5 points
Suspected critical aortic stenosis: 20 points	Emergency surgery: 10 points
Eagle and Vanzetto variables (low risk variables)[b,9,25]	
Age > 70 years	History of myocardial infarction
History of angina	ST-segment ischemic abnormalities during resting electrocardiography
Diabetes mellitus	Hypertension with severe left ventricular hypertrophy
Q waves on electrocardiogram	History of congestive heart failure
History of ventricular ectopy	

[a]Class I: 0 to 15 points (< 3% perioperative cardiac events); class II 20 to 30 points (3 to 15% perioperative cardiac events); class III: more than 30 points (> 15% perioperative cardiac events). [b]Class I patients still do not reliably identify low risk patients for perioperative cardiac events. For these patients, when two or more low risk variables are present, consider referring for noninvasive testing. PAC**,** premature atrial complex.

low-risk of cardiovascular complications who were to undergo vascular surgery and had more than two low-risk variables (Box 1). Although recommended by the ACP, the Detsky Index did not show any improvement in the prediction of cardiac risk when compared to other methods such as the Goldman, the ASA, or the New York Heart Association classification of angina[28]. Thus, despite the increased number of variables collected (and more complicated to use), the ACP algorithm does not offer clear advantages over simpler methods for patient evaluation prior to noncardiac surgeries.

Comparing a new algorithm proposal with Detsky's and Goldman's, Lee et al. found even lower areas under the ROC curve for these two methods, and demonstrated a good accuracy for the prediction of cardiovascular events with a different system (Table 1)[12]. This approach is recommended by the new guidelines of the American College of Cardiology, American Heart Association, and European Society of Cardiology[1,29]. Although very simple to use, this new index, called the Revised Cardiac Risk Index (RCRI – Box 1), did not perform well for patients undergoing abdominal aortic aneurism (AAA) repair. A later validation of the RCRI showed limited value for the prediction of cardiovascular mortality[30].

Indeed, Bertges et al. found that the RCRI did not perform well for vascular surgery patients, consistently underestimating the composite cardiac complications across all risk groups. Therefore, the authors suggested

Table 1 – Area under the ROC curve for the perioperative cardiac indices (Based on Lee et al., 1999)[12]

Index	Derivation Cohort (ROC area)	Validation Cohort (ROC area)
Original Cardiac Risk Index	0.606	0.701
Modified Cardiac Risk Index	0.545	0.582
Revised Cardiac Risk Index	0.759	0.806

a new method (Vascular Study Group of New England Cardiac Risk Index – VSG CRI) to predict cardiovascular complications. They added older age, chronic obstructive pulmonary disease, smoking, and long term β-blocker use as clinical variables[31]. This last method seems to reflect a higher risk population instead of merely reflecting the effect of the drug. With these modifications, the sensitivity, specificity, positive predictive value, and negative predictive value were 68%, 62%, 11%, and 97%, respectively. In another study, the RCRI was inferior to the new proposed score (Myocardial Infarction and Cardiac Arrest Score – MICA) across all studied patients, including AAA surgery[32].

In a systematic review evaluating the ability to predict cardiac complications and mortality after major noncardiac surgery, the RCRI was only moderately good at discriminating between low-risk versus high-risk patients for cardiac events[33]. The index was not adequate to predict cardiac events after vascular noncardiac surgery or to predict all-cause mortality[33].

Moreover, the RCRI does not take age into account as a risk factor, although the same group of researchers later showed that age > 70 confers a higher risk for perioperative cardiac and noncardiac complications[4].

In summary, there are several algorithms for perioperative risk estimation, with a wide variation of accuracy for the prediction of cardiovascular complications. The most important are shown in Table 2.

Image methods

Echocardiography is the cornerstone of complementary cardiological evaluation and the most prescribed preoperative noninvasive test[34]. It is readily available, with no contraindications and does not require intravenous injection, radioactive isotopes, or exposure to radiation. It provides information about cardiac dimensions, valve areas and function, abnormal communications between the left and right side, and calculation of cardiac output and ejection fraction. Despite all these advantages, the request of routine echocardiogram does not seem to improve survival or detection of cardiac complications[35], and may increase length of hospitalization after major elective noncardiac surgery[36].

Coronary angiography (CA) is a well-established method for detecting coronary artery disease (CAD). It is invasive, but widely available, even in small hospitals. Although there are no data regarding its use in the perioperative period, its indications, as well as revascularization, are similar to angiography indications in nonsurgical settings[1,29].

Cardiac stress tests are unequivocally the most often performed exams in patients referred to surgeries for detection of CAD. In general, their use before elective major surgery is associated with improved survival in intermediate and high risk patients. This is probably due to the identification of those who could benefit from the introduction of perioperative drug therapy such as β-blockers[37]. They have been used since the late 1980's after the study by Eagle et al. demonstrated the benefit of dipyridamole-thallium image scans for patients undergoing vascular operations[9]. Their ability to predict cardiovascular complications is similar to that of clinical variables alone. However, when used together, thallium redistribution can separate intermediate risk patients into low- and high- risk groups with postoperative cardiac ischemic events rates of 3.2% and 29.6%, respectively[9]. These findings were confirmed by another study, which also found that the larger the ischemic area, the higher the probability of major cardiovascular events[25]. Dobutamine-atropine echocardiography is a safe exam and lower in cost than scintigraphy. A positive result greatly increases the likelihood ratio (LR) of a perioperative cardiac event and, above all, it effectively identifies a low-risk group with a very low incidence of complications[38]. Meta-analysis of published data also showed a better diagnostic performance of stress echocardiography in comparison to myocardial perfusion scintigraphy, with a negative LR of 0.23 *vs.* 0.44 and a positive LR of 4.09 *vs.* 1.83 for detection of myocardial infarction or death, respectively[39,40].

Recently, multislice computed tomography (MSCT) was shown to be useful in the screening for CAD with a high sensitivity and negative predictive value[41]. There is only one study evaluating the role of MSCT in patients referred for surgery and, although it is a retrospective study with serious limitations, it increased the capability of detecting CAD when used together with scintigraphy. Furthermore, when compared to CA, MSCT may identify patients at high-risk of cardiovascular events with the same rate, however at a lower cost[42].

Reactive hyperemia is a vasodilatation of arterial vessels that occurs after a period of tissue ischemia and depends on local production of vasodilators. It is related to traditional cardiovascular risk factors and markers of inflammation[43,44].

Table 2 – Algorithms for perioperative risk evaluation

Score	Year	Advantages	Disadvantages
ASA[23]	1963	Very simple to use	Poor reproducibility, not developed for cardiovascular complications and does not take into account age and complexity of the operation
Goldman[10]	1977	Simple to use	Developed before important advances in cardiology care
Detsky[11]	1986	Simple to use and well validated in other studies	Poor discriminative power for patients classified as intermediate risk. Developed before important advances in medicine
Charlson[45,46]	1987	Takes into account several risk factors not considered in other scores such as cancer, AIDS and liver disease. Validated in several populations	Originally used to predict mortality in general population. Used a high risk population admitted in a hospital. It was not validated in a large general population referred for noncardiac surgery
RCRI[15]	1999	Simple to use. Well validated in other populations	Poor performance for vascular surgeries (especially AAA repair) and for mortality prediction
Fleisher-Eagle[47]	2001	Simple to use. Similar to RCRI without history of cerebrovascular disease	The algorithm is a theoretical approach and was not validated in any population
EMAPO[48]	2007	Considers diseases not mentioned in previous guidelines and modern treatment options. Stratifies patients into five levels with a narrower interval of complications in each category	Complex execution due to the large number of items to consider. It was not validated in other studies and didn't show any improvement compared to Detsky's model
POSSUM[49]	1991	Allows comparative audit between different populations	Not validated specifically for risk stratification. Seems to over predict death by a factor greater than two[50]
VSG-CRI[31]	2010	Developed specifically for patients undergoing vascular surgeries with a better performance than the RCRI	Not validated in other populations
MICA[32]	2011	Performed better than RCRI for myocardial infarction and cardiac arrest. Takes into account the type of surgery	Developed from a surgical database without active search for cardiac complications. Not validated in other populations

AAA, aortic aneurism repair; AIDS, acquired immune deficiency syndrome; ASA, American Society of Anesthesiologists; EMAPO, multicenter study of perioperative evaluation; MICA, myocardial infarction or cardiac arrest score; POSSUM, physiological and operative severity score for enumeration of mortality and morbidity; VSG-CRI, vascular study group of New England cardiac risk index; RCRI, Revised Cardiac Risk Index.

There are few studies on this technique for perioperative evaluation and results are controversial[51,52]. More research is needed to define its role in this field.

Biomarkers

In perioperative evaluation, new advances have recently been made, especially regarding biomarkers. Brain natriuretic peptide (BNP) and N-terminal pro-BNP (NT-proBNP) are produced by myocytes in response to stress and are important prognostic indicators of heart failure. They can identify patients with high-risk of cardiovascular complications after noncardiac surgery despite the absence of inducible ischemia and low left ventricular ejection fraction[53-55], and they seem to be useful even in emergency noncardiac surgery[56]. Cuthbertson et al. demonstrated that a BNP > 40 $pg.mL^{-1}$ has a sensitivity of 75% and a specificity of 70% for predicting perioperative death or myocardial injury, and also performed better than the RCRI[57]. When meta-analyzed, elevated BNP or NT-proBNP were predictors of adverse cardiovascular outcomes at 30 and 90 days and at over six months[58-60]. However, they are most useful to identify event-free survival and may not accurately identify mortality with a high degree of certainty – high negative predictive value and low positive predictive value[59].

Inflammatory markers such as C-reactive protein (CRP), which is related to atherogenesis and atherosclerotic plaque instability, may identify patients with elevated coronary risk. However, their use in perioperative evaluation has not been completely defined. In 2010, Choi et al. demonstrated that higher levels of CRP are associated with an increased risk of AMI, pulmonary edema, and cardiovascular death after major noncardiac surgery[61]. Yet, when associated with NT-proBNP, it increased the relative risk by threefold compared to classical algorithms for clinical events[61]. High-sensitivity CRP and fibrinogen were also recently studied, and at elevated levels they seem to independently predict cerebral ischemic events after carotid endarterectomy in patients, whether symptomatic or not[62].

Ankle brachial index

The ankle brachial index (ABI) is valuable for cardiovascular risk quantification and is perhaps the most promising source of information in the perioperative period, especially when compared to intima media thickness, coronary calcium score, and coronary and carotid atherosclerotic plaques[63,64]. In comparison with these methods, it is less expensive, faster, and feasible in office care, with a good acceptance by patients and little intra- and inter-observer variability[65-67]. The procedure is simple and can be carried out by a trained nurse or other health care professional[64]. It is easily done by measuring the systolic blood pressure (BP) with a portable Doppler ultrasound machine on each arm and on the dorsalis pedis and posterior tibial arteries of each ankle. The highest of the two arm pressures is selected, as is the highest of the two pressures of each ankle. The ABI is obtained by dividing the highest ankle BP in each leg by the highest arm pressure. The lowest value between the two indices (one for each leg) defines the risk of the patient. Normally, the BP is higher in the legs than in the arms[68,69]. Thus, it is expected that a normal ABI would be > 0.9 and ≤ 1.3. Values > 1.3 suggest a non- compressible calcified artery in the ankle, thus the ABI is not reliable in this situation, because of unreliable BP measurements[68,69]. Values between 0.41 and 0.9 are associated with peripheral arterial disease (PAD) and severe PAD when ≤ 0.4[69]. Asymptomatic patients with abnormal ABI and no prior cardiovascular disease, older than 70 years, or older than 50 years with an additional cardiac risk factor, should be treated as a patient with established PAD[70]. Furthermore, an abnormal ABI and PAD are associated with atherosclerosis in coronary and cerebral arteries and a higher incidence of AMI, stroke, and cardiovascular and all-cause mortality[63,70-72].

Although there is a close relationship between abnormal ABI and atherosclerosis, including in coronary arteries, the association of ABI with other cardiovascular scores has been poorly studied; however, it appears to be useful. In a recent meta-analysis the ABI has proven to be an independent cardiovascular risk factor, and when associated with the Framingham risk score (FRS), an abnormal result doubled all-cause mortality, cardiovascular mortality and major coronary events in all groups of the FRS[64]. Further, after inclusion of the ABI, 20% of men and 33% of women had their Framingham risk category changed. In women, this effect was mainly a change from low-risk to a high-risk category. In another study, the addition of ABI to traditional cardiovascular risk factors such as diabetes, hypertension, smoking, and hypercholesterolemia improved the sensitivity, specificity, and predictive values for a future cardiovascular event[72].

Flu et al., recently demonstrated that an asymptomatic low ABI (< 0.9) increases the risk of perioperative myocardial damage over twofold in patients undergoing AAA or carotid artery stenosis repair, even after adjusting for other cardiovascular risk factors[73]. Unfortunately, there are no data about the use of ABI in other patients referred for nonvascular surgery, which comprises the majority of surgeries performed worldwide. Such use could add extensive information about this population, especially if associated with well-validated perioperative cardiovascular risk scores.

Conclusions

With such conflicting information regarding the perioperative evaluation and its algorithms and exams, a cautious and accurate clinical evaluation of the patient's cardiac risk is critical. The accuracy of methods available for predicting postoperative complications is better than random, but their performance is not ideal. Thus, measures and approaches that are widely available and easy to perform for the accurate prediction of postoperative cardiovascular events are urgently needed.

The ideal risk prediction model would be one that is simple, reproducible, accurate, objective, and available to all patients[74]. Coronary calcium score, intima media thickness, pulse wave velocity, and ABI, which can predict a higher cardiovascular risk in the general population, appear to be promising for perioperative evaluation, adding important information to current guidelines and algorithms. The ABI, an easy to perform and widely available exam in office practice and points of care, appears to be the best approach and the most promising method, but evidence to support its use in the perioperative context, especially for patients undergoing non-vascular surgeries is still needed.

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