Evaluating Cardiac Risk in Noncardiac Surgery

Víctor G. Dávila-Román

Core Laboratory, and the Cardiovascular Division, Cardiovascular Imaging and Clinical Research,
Washington University School of Medicine, St Louis, Missouri, USA

In the United States, more than 33 million patients undergo noncardiac surgery each year, at a cost of 450 000 million dollars per year. Approximately 4% of these patients present perioperative complications, at an additional cost of 25 000 million dollars per year.[1] The number of cardiovascular complications arising from non-cardiac surgery exceeds 1 million patients worldwide.[2] Due to the increasing size of the elderly population (defined as people over 65 years old) in most of the developed world, it is predicted that during the coming decades the number of surgical operations will increase by 25%, surgery-related costs by 50%, and perioperative complications by 100%.[3] Given that more than 60% of patients with vascular disease also have coronary heart disease, the preoperative assessment of patients undergoing noncardiac surgery is a public health priority.[4]

Randomized clinical trials have been employed to design evidence-based strategies which can help to identify the people at greater risk of perioperative cardiac complications and to reduce risk.

These recommendations have been summarized and published in the AHA/ACC guideline update.[5]

The AHA/ACC guidelines address 3 main issues. First, to identify cardiac risk in patients based on a background of cardiovascular disease and easily obtainable laboratory tests; second, to evaluate the patient's functional capacity; and third, to define the level of risk according to the type of surgery involved. This staged approach to assessing risk is illustrated in Figure 1 of the AHA/ACC guideline.[5] The main clinical variables with predictive value are recent acute coronary syndrome (that is, an acute myocardial infarction [AMI] 7 days prior to surgery), recent AMI (between 7 days and 1 month before surgery), unstable angina, large areas of ischemic myocardium detected in non-invasive tests, decompensated congestive heart failure, serious arrhythmias, and severe valvular heart disease. The variables predictive of low or medium cardiac risk were also defined. In addition, the AHA/ACC guidelines take into account functional capacity and define a cut-off value of <4 METS as an indicator of greater risk. Furthermore, specific risks associated with the type of surgery employed may lead to it being defined as high risk: aortic and major vascular surgery, any serious emergent intervention, peripheral vascular surgery or any surgical procedure of extended duration, large fluid replacement, or substantial blood loss. Medium-risk surgical procedures include intraperitoneal and intrathoracic surgery and carotid endarterectomy. Low-risk surgical procedures include superficial and endoscopic surgery.

In addition to these clinical parameters, the additional stratification of preoperative cardiac risk is recommended by use of the risk assessment strategies defined above. Coronary angiography is recommended for people at high risk, stress testing for those at medium risk, and no additional assessment for those at low risk. Due to the high prevalence of concomitant vascular and cardiac atherosclerosis, a large number of patients are categorized as being at medium-risk. Non-invasive stress testing (stress echocardiography or myocardial perfusion imaging [MPI]) is indicated for these patients to evaluate myocardial ischemia and its severity and both global and regional left ventricular function. Significant or extensive myocardial ischemia in the stress test is usually defined by the presence of at least 5 ischemic regions (using a 17-region model under stress echocardiography) or at least 3 ischemic walls (using a 6-wall model under MPI). Patients with extensive ischemia should then undergo invasive coronary angiography followed by coronary artery bypass

Correspondence: Dr. V.G. Dávila-Román,
Professor of Medicine, Anesthesiology and Radiology, Medical Director,
Cardiovascular Imaging and Clinical Research Core Laboratory,
Cardiovascular Division,
Box 8086, Washington University School of Medicine, 660 South Euclid
Ave, Saint Louis, MO 63110, USA
E-mail: vdavila@wustl.edu

graft surgery or percutaneous coronary intervention (PCI), with the theoretical aim of reducing the postoperative complications of noncardiac surgery.[6-9] Recent studies have suggested changing the emphasis from myocardial revascularization in the preoperative period to optimizing medical treatment during the perioperative period, mainly through the use of beta-blockers.[10]

Several recent landmark studies have contributed arguments toward de-emphasizing preoperative myocardial revascularization prior to noncardiac surgery. Lindenauer et al[11] used propensity-score matching to study the relationship between the perioperative use of beta-blockers and in-hospital mortality in a retrospective cohort study of 122 338 patients over 18 years who received beta-blockers 2 days before undergoing major non-cardiac surgery (compared to 541 297 patients who did not receive them). The patients were grouped according to their scores using the Revised Cardiac Risk Index (RCRI). This index stratifies the perioperative risk of cardiac events according to the type of surgery and risk factors, including cardiovascular factors (presence or absence of a background of ischemic heart disease, congestive heart failure, and cerebrovascular disease) and renal factors (serum creatinine concentrations >2 mg/dL), or diabetes mellitus (preoperative insulin therapy).

The scores range from 0 to 5, with a higher probability of serious perioperative complications as the scores increase. They observed a direct relationship between perioperative beta-blocker therapy and risk of death which varied directly with the cardiac risk score: among the patients with an RCRI score of 0 and 1 (low-risk group), treatment involved "no benefit and possible harm" (with a 13%-43% increase in the risk of death), whereas for those with an RCRI score from 2 to 5 (medium- and high-risk groups), perioperative beta-blocker therapy was associated with a lower risk of in-hospital death (with a 10%-43% decrease in the risk of death).

In short, the study indicated that beta-blockers could be detrimental to low-risk patients and possibly beneficial for high-risk patients.

The CARP (Coronary Artery Revascularization Prophylaxis) study randomly assigned patients at greater risk of perioperative cardiac complications and clinically significant coronary disease to myocardial revascularization or no myocardial revascularization before elective major vascular surgery.

All patients received optimal medical treatment and the primary endpoint was long-term mortality.[12] Of the patients assigned to preoperative coronary revascularization, percutaneous coronary intervention was performed in 59% and coronary artery bypass graft surgery in the remaining 41%. The 30-day AMI rate was similar in both groups (12% vs 14% in the 2 groups, respectively; P=.37). At a median follow-up of 2.7 years, mortality was also similar in both groups (22% vs 23%; P=.92). Thus, the CARP trial demonstrated that in patients with stable cardiac symptoms, the short- and long-term outcomes of preoperative coronary revascularization are similar to those of optimal medical treatment. A possible shortcoming of the CARP study is that the results may not be applicable to patients at higher risk—such as those presenting significant left main coronary artery stenosis, severe left ventricular disease (LEVF <20%) or severe aortic stenosis—given that most of the patients presented stable 1- or 2-vessel coronary disease.

To address this issue in high-risk patients, Poldermans et al[13] published the results of the DECREASE-V (Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo Study Group V) study. This randomized pilot study was designed to test the efficacy and safety of preoperative coronary revascularization in high-risk patients undergoing elective major vascular surgery. It included 430 high-risk patients who underwent stress testing (dobutamine echocardiography or MPI); 101 (23%) presented extensive ischemia and were randomly assigned to myocardial revascularization (n=49) or to no revascularization. All patients received beta-blockers during the perioperative period to obtain a target heart rate of 60-65 beats/min and antiplatelet therapy was continued during surgery. The endpoints were the composite of all-cause death or AMI at 30 days and during 1-year follow-up. Coronary angiography demonstrated 2-vessel disease in 12 (24%) patients, 3-vessel disease in 33 (67%), and left main coronary artery disease in 4 (8%). Myocardial revascularization did not improve 30-day clinical outcome; the incidence of the main composite endpoint was 43% versus 33% (P=.30). No benefit was observed at 1-year follow-up following coronary revascularization (composite endpoint 49% and 44% in patients undergoing revascularization or no revascularization, respectively; P=.48). Furthermore, 2 patients died because of a ruptured aneurysm after myocardial revascularization while awaiting surgery. Thus, this randomized pilot study of high-risk patients (43% presented decreased ventricular function and 73%, left main coronary artery disease or 3-vessel disease) awaiting elective vascular surgery provides additional evidence supporting the use of beta-blockers in the perioperative period. Furthermore, it raises serious doubts about the short- and long-term benefits of myocardial revascularization before noncardiac surgery. In this

issue of *Revista Española de Cardiología*, in the update entitled "Coronary Risk Assessment in the Management of Patients Undergoing Noncardiac Vascular Surgery," Schouten et al[14] meticulously analyze the preoperative assessment of patients undergoing non-cardiac vascular surgery and reiterate the importance of placing greater emphasis on guaranteeing optimal perioperative medical treatment. They address the issue of clinical cardiac risk scores that identify the patients at greater risk during the perioperative period. The use of laboratory tests is addressed and how they should be used to indicate additional non-invasive cardiac tests and establish treatment.

The perioperative period is characterized by a series of hemodynamic, hemostatic, and proinflammatory changes that can aggravate stable coronary disease. An increase in sympathetic tone gives rise to hypertension and tachycardia, which increases shear stress on arterial plaque; the stress of surgery can cause platelet activation, with vasoconstriction and platelet aggregation, or initiate the coagulation cascade as well as the onset of hypercoagulation characterized by an increase of procoagulant factors and a decrease of fibrinolytic factors; finally, proinflammatory mediators are increased by surgical stress and can promote plaque rupture and thrombosis. A study investigating the pathology of fatal AMI in the perioperative period found that this is similar to that of AMI in other settings in relation to coronary plaque rupture and thrombus formation.[15] The use of beta-blockers during the perioperative period is reasonable during this period given their beneficial effect on such complications. The mechanism of action of beta-blockers includes reducing blood pressure and heart rate, and thus they improve the balance between myocardial oxygen supply and demand. In addition to their antiarrhythmic properties, beta-blockers also improve diastolic function by increasing filling time. Beta-blocker therapy is currently indicated for hypertension, coronary heart disease (including AMI), and stable heart failure. Their perioperative use in medium- and high-risk cardiac patients is another indication that is becoming increasingly established. However, this issue is not free from controversy, and a recent clinical trial and several metaanalyses[16,17] have raised questions concerning their benefits during the perioperative period.

Given the results of these clinical trials, the AHA/ACC guidelines have been updated.[10] The class I recommendation (conditions for which there are signs that treatment is beneficial) is to continue with beta-blocker therapy in patients undergoing noncardiac surgery who were taking them previously for any ACC/AHA class I indication (for example,

heart failure), rather than only in the case of angina, symptomatic arrhythmias, or hypertension. Beta-blockers are indicated in patients undergoing vascular surgery when the preoperative tests demonstrate ischemia, which remains a class I recommendation. The class IIa recommendation (conflicting evidence with the weight of evidence in favor of its efficacy) is to use beta-blockers in the perioperative period, and these are now "probably recommended" when preoperative assessment identifies high cardiac risk. The class IIb recommendation (conflicting evidence, with less well-established efficacy) is that perioperative beta-blockers "can be considered" in the patients presenting a single risk factor undergoing medium- or high-risk procedures, and also in patients undergoing vascular surgery with low cardiac risk. The class III recommendation (evidence that treatment is not effective) remains unchanged, that is, beta-blockers should not be given to patients who have absolute contraindications. Finally, it is important to emphasize that intensive preoperative assessment with coronary angiography combined with myocardial revascularization remains the best approach to treatment in patients with symptomatic coronary disease, such as those with unstable angina.

A special situation among cardiac patients undergoing noncardiac coronary surgery is presented by those undergoing PCI with stenting.

These patients require antiplatelet therapy combined with acetylsalicylic acid for life and clopidogrel for 1-6 months (depending on the type of stent). The risk of early stent thrombosis increases in patients presenting with acute coronary syndrome, diabetes, kidney failure, or long or bifurcation lesions who have ceased antiplatelet therapy; acute coronary syndrome and diabetes should be highlighted as being among the predictors of late stent thrombosis.[18,19] Although the incidence of early thrombosis (≤30 days after implantation) is 1.1% when drug-eluting stents are employed, late incidence (30 days after implantation) is 0.6%/year and remains so for at least 3 years more.[20] Among these patients, noncardiac surgery involves a high risk of stent thrombosis and major adverse cardiac events, especially if this is performed early after PCI and antiplatelet therapy is interrupted.[20] Although it seems prudent to delay noncardiac surgery for at least 2-4 weeks after stent implantation, as recommended in the ACC/AHA guidelines, the optimal time of surgery and the best anticoagulant regime for these patients remains uncertain.

The recommended management strategies for patients with coronary stents undergoing noncardiac surgery have recently been revised.[21]

Despite the importance of all of these studies on how to improve the assessment and perioperative management of patients undergoing noncardiac surgery, many issues remain pending. First, as the authors of the DECREASE-V study point out, in order to establish the role of coronary revascularization before noncardiac surgery, any such study would have to screen 9000 patients, of whom 2000 would have to have 3 or more cardiac risk factors. Second, the rates of short- and long-term cardiovascular complications remain very high, regardless of the treatment group, and thus new medical or surgical strategies are needed to improve the clinical outcome. Third, it has yet to be established which beta-blocker (short-acting or long-acting) is optimal, the best time to initiate treatment, the optimal form of administration (intravenous or oral), and the ideal target heart rate. Fourth, it is not clear if the perioperative use of beta-blockers would be beneficial or detrimental to low-risk patients. Fifth, there is a lack of controlled randomized studies which could help to identify the best anticoagulant regimen for patients with coronary stents undergoing non-cardiac surgery.

In summary, when assessing a patient before noncardiac surgery, we should take advantage of the opportunity to identify the cardiac risk factors and the best treatment modality that will benefit the patient, not only during the perioperative period, but also during long-term follow-up.

Even when myocardial revascularization is not performed before noncardiac surgery, patients at medium or high risk require continuous supervision and intensive treatment to reduce this risk, given that they have a high incidence of long-term cardiovascular events.

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