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REVIEW ARTICLE

Preoperative evaluation of patients with, or at risk of, coronary artery disease undergoing non-cardiac surgery

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The increasing number of patients with coronary artery disease undergoing major non-cardiac surgery justifies guidelines concerning preoperative evaluation, stress testing, coronary angiography, and revascularization. A review of the recent literature shows that stress testing should be limited to patients with suspicion of a myocardium at risk of ischaemia, and coronary angiography to situations where revascularization can improve long-term survival. Recent data have shown that any event in the coronary circulation, be it new ischaemia, infarction, or revascularization, induces a high-risk period of 6 weeks, and an intermediate-risk period of 3 months. A 3-month minimum delay is therefore indicated before performing non-cardiac surgery after myocardial infarction or revascularization. However, this delay may be too long if an urgent surgical procedure is requested, as for instance with rapidly spreading tumours, impending aneurysm rupture, infections requiring drainage, or bone fractures. It is then appropriate to use perioperative beta-block, which reduces the cardiac complication rate in patients with, or at risk of, coronary artery disease. The objective of this review is to offer a comprehensive algorithm to help clinicians in the preoperative assessment of patients undergoing non-cardiac surgery.

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Contemporary medicine shows a trend towards more aggressive surgery in sicker patients, among whom the prevalence of ischaemic heart disease is increasing. This tendency creates a requirement for guidance in the preoperative evaluation of patients known to have, or at risk of, coronary artery disease. There is an abundance of studies on this subject, but the way to evaluate these patients is still the object of considerable debate. Much of the controversy is because of the obvious difficulties of conducting large randomized controlled clinical trials on this topic, and to the relatively low incidence of perioperative cardiac events (<10%). The rate of postoperative myocardial infarction is 0.7% after general surgery in a male population over 50 yr old, but increases to 3.1% after vascular surgery where the prevalence of asymptomatic coronary artery disease is particularly high.[3 53 61] Because of this prevalence, most of the studies have focused on vascular patients, who represent less than 10% of the adult surgical population. This fact may introduce a bias when the results are extrapolated to other surgical cohorts.

The purpose of preoperative evaluation is to lower perioperative morbidity and mortality with minimal expense from preoperative testing, and to concentrate economic investment on high-risk patients where specialized tests might modify perioperative management and improve long-term benefit. Testing a low-risk population not only increases costs unnecessarily, but may increase morbidity and causes harm by delaying a non-cardiac operation. The main question to be answered is: does the patient need cardiological testing? When coronary artery disease is present, three other questions arise: may the patient benefit from coronary revascularization? Is non-cardiac surgery so imperative that it should be carried out rapidly despite the risk? Is it possible to decrease this risk?

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As the workload resulting from perioperative ischaemic cardiac evaluation is significant, clinicians need practical guidelines for their daily practice. This review aims to offer them an update on the literature on preoperative assessment of patients known to have, or at risk of, coronary artery disease undergoing non-cardiac surgery. It also presents an evaluation algorithm used in our institution. The level of evidence in the studies cited in the text is mentioned in the references.

Clinical predictors

Despite sophisticated technologies, history and physical examination of the patient remain the key elements of preoperative risk assessment. Risk stratification of patients with known, or at risk of, coronary artery disease is usually based on three elements:[115] (i) the patient risk factors; (ii) functional capacity of the patient; and (iii) the risk factors of surgery.[20] The vast majority of the studies has been performed in North America and among Veterans Administration Hospitals, the population of which consists mainly of elderly white male patients. However, the prevalence of coronary artery disease and its morbidity varies considerably in different countries. For example, the incidence of infarction among patients with abdominal aortic aneurysm is 16% in France, but 50% in Sweden.[4 55] Similarly, there are ethnic differences in the response to treatment between white and non-white populations.[24 124] Thus, it may be inaccurate to transpose the results of one population to another. On the other hand, the risk of surgery is highly dependent on surgical skills, anaesthetic care, and nursing quality. Each institution should therefore establish its own audit in order to take appropriate decisions when choices have to be made between different treatment modalities.

Risk factors of the patients

Risk factors of the patients are usually subdivided into three categories: major, intermediate, and minor (Table 1). Major predictors are markers of unstable coronary disease and include: recent myocardial infarction (<6 weeks), unstable or severe angina (class III–IV), ongoing ischaemia after myocardial infarction, ischaemia and congestive heart failure, or malignant arrhythmias. New or changing symptoms suggest atheromatous plaque rupture and should be presumed to be infarction unless proven otherwise. A 6-week period is necessary for the myocardium to heal after an infarction and for the thrombosis to resolve.[116] Patients with coronary revascularization done within the preceding 40 days should also be classified as high-risk patients.[79] Because of sympathetic stimulation and hypercoagulability during and after surgery, patients with major predictors have a five times greater perioperative risk.[20 84] Only vital or emergency surgical procedures should therefore be considered for these patients. All elective operations should be postponed and the patients properly investigated and treated.

Table 1 Classification of cardiac risk factors linked to patient status modified from references.[20 22 64 69 83 92 114] CABG=coronary artery bypass graft

Major factors (markers of unstable coronary artery disease)
Myocardial infarction <6 weeks
Angina class III–IV
Residual ischaemia after myocardial infarction
Clinical ischaemia and congestive heart failure
Clinical ischaemia and malignant arrhythmias
CABG or PTCA <6 weeks
Intermediate factors (markers of stable coronary disease)
Prior myocardial infarction >6 weeks and <3 months (>3 months if complicated) by clinical history or ECG abnormalities
Angina class I–II
Asymptomatic patient post infarction with maximal therapy
Documented previous perioperative ischaemia
Silent ischaemia (Holter monitoring)
Post CABG or PTCA >6 weeks and <3 months, or >6 yr, or with anti-anginal therapy
Ventricular arrhythmia
Diabetes mellitus
Age (physiological) >70 yr
Compensated or prior heart failure, ejection fraction <0.35
Minor factors (increased probability of coronary artery disease)
Familial history of coronary artery disease
Polyvascular status
Uncontrolled systemic hypertension
Hypercholesterolaemia
Smoking
ECG abnormalities (arrhythmia, LVH, bundle branch block)
Post infarction (>3 months), asymptomatic without treatment
Post CABG or PTCA >3 months and <6 yr, and no symptoms of angina nor anti-anginal therapy

Intermediate-risk factors, such as previous myocardial infarction (>6 weeks and <3 months) without sequelae or threatened myocardium, stable angina (class I–II) with optimal medical treatment, or documented previous perioperative ischaemic events, are independent predictors for perioperative cardiac complications; they are proof of well established but controlled coronary artery disease. Diabetes mellitus is included in this category because it is frequently associated with silent ischaemia, and represents an independent risk factor for perioperative mortality, as do low ejection fraction (EF <0.35) and compensated heart failure.[20 65] The relevance of advanced age (>70 yr), hypertension and left ventricular hypertrophy (LVH) to the intermediate or minor risk category is still controversial. American guidelines tend to consider age as a minor factor but, if it is estimated by physiological age and not chronological age, it should belong to the intermediate category.[20 22 50 65 93 101] The presence of hypertension among intermediate or minor risk categories depends probably on the population studied, as it is an easily controllable factor in the perioperative period.[57] LVH has been considered as an independent marker of ischaemic disease and cardiac complications, but recent recommendations tend to consider it a minor factor.[17 33 37 65 76] Risk

Table 2 MET in increasing order (Duke Activity Status Index) (adapted from Hlatky, 1989[54])

1–4 MET	Standard light home activities
	Walk around the house
	Walk 1–2 blocks on level ground at 3–5 km h^{-1}
5–9 MET	Climb a flight of stairs, walk up a hill
	Walk on level ground at >6 km h^{-1}
	Run a short distance
	Moderate activities (golf, dancing, mountain walk)
>10 MET	Strenuous sports (swimming, tennis, bicycle)
	Heavy professional work

factors are additive: complication rates increase with their number, as does the necessity to investigate the patients.[65 76]

Minor risk factors are markers of an increased probability of coronary artery disease, but not of an increased perioperative risk; they are mentioned in Table 1.[2] In patients asymptomatic within 6 yr after coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA), evidence suggests that the risk of subsequent non-cardiac surgery is the same as in non-coronary patients, as long as the delay of 3 months is respected after revascularization, and the stress tests are negative within the previous 2 yr.[21 22 26 37 85 111]

Functional capacity

Exercise tolerance is a major determinant of perioperative risk.[20 22 42 81] It is usually evaluated by the estimated energy requirement for various activities, and graded in metabolic equivalents (MET) on a scale defined by the Duke Activity Status Index (Table 2).[54] One MET represents the oxygen consumption of a resting adult (3.5 ml kg^{-1} min^{-1}). Ergometric measurements on a treadmill inducing ischaemia at low-level exercise (<5 MET or heart rate <100 min^{-1}) identifies a high-risk group, whereas the achievement of more than 7 MET (or heart rate >130 min^{-1}) without ischaemia identifies a low-risk group.[122] Vascular patients who are able to exercise to 85% of their maximal heart rate have a low risk of a perioperative cardiac event.[78] More simply, the inability to climb two flights of stairs is associated with a positive predictive value of 89% for cardiopulmonary complications.[42] In the absence of valve pathology, the ejection fraction of the left ventricle can be considered as an adequate measurement of the myocardial functional reserve.[100] Patients with good functional capacity and no symptoms can be considered free of any severe coronary artery disease.[86] Despite its predictive value in the perioperative setting, the Duke Activity Status Index has never been specifically tested for ischaemic patients.[84]

Risk factors associated with surgery

Surgical procedures can be stratified into three categories, according to their level of perioperative physiological stress (Table 3).[20 22] When estimating the risk of an operation, one must also take into consideration the risk of not operating on the patient. This evaluation is particularly important for oncological or limb salvaging procedures. It is unethical to reject a patient when their survival is threatened by the disease—as with rapidly spreading tumours, impending aneurysm rupture, infections requiring surgery, or disabling bone fractures. In order to balance the risks, it might be necessary to limit the extent of the planned procedure, or to plan repeated operations. Risk reduction strategies must also be applied, such as maintaining normothermia, avoiding extreme anaemia, controlling postoperative pain, and prescribing perioperative beta-block.[76 107 127] The performance of the individual institution must be taken into account, as it is a determinant factor in the success of particular procedures.

Table 3 Cardiac risk classification of non-cardiac surgical procedures adapted from ACA/AHA guidelines for perioperative cardiovascular evaluation for non-cardiac surgery[20 22]

Minor procedures (cardiac complication rate <1%)
Endoscopic procedures
Ambulatory surgery
Breast and superficial procedures
Eye surgery
Plastic and reconstructive surgery
Intermediate procedures (cardiac complication rate 1–5%)
Minor vascular surgery, including carotid endarterectomy
Abdominal and thoracic procedures
Neurosurgery
ENT procedures
Orthopaedic surgery
Prostatectomy
Major procedures (cardiac complication rate >5%)
Emergency intermediate and major procedures
Aortic and major vascular surgery
Prolonged surgical procedures, large fluid shifts or blood loss
Unstable haemodynamic situations

Previous ischaemia

During the 1980s, the rule prevailed to wait 6 months after a myocardial infarction before embarking on non-cardiac surgery.[97 109 114] Since then, the cardiological management and the functional assessment of patients have evolved significantly. It appears now that the risk after a previous infarction is related less to the age of the infarction than to the functional status of the ventricles and to the amount of myocardium at risk from further ischaemia, as evaluated during convalescence.[22 104 105] A small infarction without residual angina in the context of a good functional status allows essential non-cardiac surgery as soon as 6 weeks after the ischaemic episode.[115] On the contrary, a patient with a large infarct, residual symptoms and ejection fraction below 0.35 has a high probability of a further cardiac event, even 6 months after the infarction. Usual practice guidelines consider the period within 6 weeks of infarction as a time of high risk for a perioperative cardiac event, because it is the

mean healing time of the infarct-related lesion.[22 80 116] The period from 6 weeks to 3 months is of intermediate risk; this period is extended beyond 3 months in cases with complications such as arrhythmias, ventricular dysfunction, or continued medical therapy.[1] In uncomplicated cases, no benefit can be demonstrated for delaying surgery more than 3 months after an ischaemic accident.[115]

Previous coronary revascularization

Patients who do well after CABG have an attenuated risk of cardiac events during subsequent non-cardiac surgery. Retrospective studies have disclosed a significant improvement in survival of revascularized patients, particularly those with triple-vessel coronary artery disease and depressed ventricular function, when they undergo subsequent non-cardiac vascular surgery.[85 98 110] In the Coronary Artery Surgery Study (CASS) experience, these patients have a mortality of 0.9%, instead of 2.4% for those who have not been revascularized;[37] recent data show the same trend.[51] However, when the complication and mortality rates of CABG are taken into account, the combined mortality of cardiac and non-cardiac procedures is not different from the mortality of non-cardiac surgery when ischaemic heart disease has been managed by medical treatment only.[37] A patient might therefore benefit from preoperative coronary revascularization if the CABG procedure presents a low risk and will improve long-term survival, and if the planned non-cardiac procedure is high risk but can wait for at least 3 months.

The short-term effect of prophylactic CABG among vascular patients has been addressed in two decisional analyses; both showed it was safer to proceed directly with a non-cardiac operation and close monitoring before coronary revascularization.[31 75] The benefit of coronary revascularization might be even lower among patients undergoing non-vascular surgery, as they have already a lower probability of perioperative cardiac events.[3 84] Obviously, there is no indication to advise prophylactic revascularization in order to protect the ischaemic myocardium from the effects of a subsequent non-cardiac operation. The indications for coronary revascularization are aimed at reducing long-term mortality and prolonging survival.[33 36 75] They are the same in patients being evaluated for a non-cardiac operation as for non-surgical population and include: unstable angina, left main coronary artery disease, three-vessel disease, proximal left anterior descending artery disease, and decreased ventricular function.

Asymptomatic, functionally active patients with previous successful coronary revascularization within the last 6 yr are in a low-risk category and should not be investigated further for a non-cardiac operation; this cut-off point is based on a slight but non-significant increase in postoperative infarction rate among patients 6 yr after CABG surgery.[21] Patients having a negative stress test or satisfactory angiography in the last 2 yr can be cleared for non-cardiac surgery without further testing, if the symptomatology and treatment have not changed since the examination.[20 22]

In the 1990s, it seemed that PTCA had a significant protective effect on the ischaemic complications of subsequent non-cardiac surgery. In two studies from the Mayo Clinic, major vascular surgery was performed on average 11 days after PTCA;[27 58] overall mortality of surgery was halved and infarction rate five times less in the groups having previous PTCA compared with non-revascularized patients. Such results with dilatative angioplasty have been repeated, showing improvement in vascular surgery outcome for patients having undergone PTCA 11 days to 18 months earlier.[45] However, with the advent of stenting during PTCA, recent studies have heralded fundamentally different results. In one study, there were eight deaths and seven myocardial infarctions among 40 patients who underwent coronary stent placement less than 2 weeks before non-cardiac surgery.[60] In addition, patients undergoing non-cardiac surgery within 40 days of PTCA are nearly three times more likely to have an adverse cardiac event than normal controls, and are no less likely to have a poor cardiac outcome than non-revascularized patients until 90 days after PTCA.[92] Any surgery performed within 6 weeks of PTCA presents an excessive risk of stent thrombosis and infarction if the antiplatelet medication is stopped, or of major bleeding if the treatment is maintained throughout the operation.[22 79 119] This is a period of major risk: most of the re-stenoses requiring repeat PTCA occur during the first months after stenting, and documented stent thrombosis is associated with a mortality rate of 7%.[15 17] The optimal timing for surgery is therefore a delay of 3 months after PTCA and stenting. Compared with PTCA, CABG with internal mammary grafting has a better long-term protective effect, particularly in diabetic patients;[38] the rate of late cardiac events (>3 yr) is halved in surgically revascularized patients.[27 35]

Preoperative testing

Preoperative testing is aimed at answering precise questions raised by clinical history and examination. No cardiovascular test should be performed if the results will not change perioperative management. The therapeutic impact may differ according to the situation: medical treatment may be optimized, surgical procedure modified, anaesthetic management adjusted, or the risk/benefit ratio of a surgical procedure evaluated differently. These complex decisions can be taken more objectively when the actual risk can be quantified by appropriate screening tests.[70] However, no magic test will ever exist to fully stratify all risks, because perioperative cardiac events are multifactorial.[84]

The indication for preoperative tests is based on Bayes' theorem, which specifies that the predictive value of testing is optimized when it is applied to an intermediate-risk population (Table 1), as the incidence of false negatives and false positives is inversely proportional to disease

Table 4 Comparison of three preoperative stress tests. *Relative risk is the probability of a cardiac event when a test result is positive divided by the probability of that event when the test result is negative (modified from Mantha[73]). **Cost at the University Hospital of Lausanne (CHUV), Switzerland

Test	Median relative risk*	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Cost** (€)
Ambulatory ECG (Holter)	2.7	68	66	25	190
Exercise ECG		69	73	20	220
Dipyridamole-thallium	4.6	85	80	23	410
DSE 6.2	80	90	30	570	

prevalence. The probability of a complication is a function of the probability of the disease in the category to which the patient belongs. In such a Bayesian model using clinical predictors and results of dipyridamole-thallium scintigraphy (DTS), it appears that modifications are introduced by the test only in the intermediate-risk patient category.[66] Without symptoms of angina, previous infarction or heart failure, the probability of suffering from coronary artery disease is 6%; if diabetes is also excluded, the probability falls to 4%;[86] further testing of such a patient has an extremely low impact on complication rate. Similarly, the outcome of a patient with a clear history of active coronary artery disease will not be modified by screening tests.

Stress tests (exercise ECG, DTS, or dobutamine echocardiography) are dynamic investigations, which demonstrate the ischaemic threshold, the maximal tolerated heart rate, the localization, and the amount of threatened myocardium. An interruption of the test before reaching the maximal theoretical heart rate identifies an increased risk of perioperative ischaemic events.[70] The positive predictive value of all stress tests is modest (20–30%), whereas their negative predictive value is excellent (95–100%); this should not be surprising, as the incidence of perioperative cardiac complications is low (<10%) and more than 90% of patients have a straightforward perioperative course.[10] In a meta-analysis of the predictive value of four preoperative tests (DTS, ejection fraction estimated by radionuclide ventriculography, ambulatory electrocardiography, and dobutamine stress echocardiography (DSE)), DSE appears more discriminating, but the data do not allow selection of an optimal test because of overlapping confidence intervals (Table 4).[73] DSE seems particularly informative because it investigates the segmental coronary blood supply and allows simultaneous quantification of ventricular function.

The pertinence of tests is increased for multi-vessel disease, but diminished in cases of isolated single-vessel stenosis.[41] Beside the specificities of each test, it is the expertise of its medical interpretation and the characteristics of the population in which it is applied which alters its impact. Such differences may introduce significant bias when comparing the efficiency of these tests in predicting outcomes. The comparison of various studies is further confounded because some are based on consecutive case recruitment, whereas others analyse selective testing of classes of patients.[33]

Electrocardiography (24 h Holter monitoring)

Preoperative ambulatory ECG (Holter monitoring) is relatively inexpensive but may be difficult to analyse because of electrocardiographic abnormalities precluding adequate interpretation in up to 50% of patients.[95] One highly powered study demonstrated that the detection of silent preoperative ischaemia has a positive predictive value of 38% for postoperative cardiac events, whereas its absence precludes perioperative problems in non-vascular surgery in 99% of patients and in vascular surgery in 86%.[30] When electrocardiographic criteria of LVH were added to ST segment depression, the preoperative Holter ECG became significantly predictive of postoperative events.[62] However, other studies show less clear-cut data, and results are not unanimous in non-cardiac surgery, probably because postoperative ischaemia is primarily a result of ischaemic events occurring during surgery.[67 69 95] Perioperative stress and techniques of patient management are probably more determinant features than the presence of preoperative electrocardiographic signs of ischaemia.

Exercise ECG

The exercise ECG is a widely available and inexpensive method of screening for coronary artery disease but depends on the exercising ability of the patient and the legibility of the ECG. Often, vascular patients do not reach the target heart rates because of limb claudication, and therefore have an inadequate examination. In patients who can perform the test, studies conducted in vascular and non-vascular patients are not conclusive for its ability to predict perioperative cardiac complications.[32 41 59 113] However, a recent prospective study on intermediate-risk patients confirmed that a ST-segment depression of 0.1 mV or more during exercise is an independent predictor of perioperative ischaemic events.[39] Because of its availability and low cost, the exercise ECG should be considered as the first screening step in stress testing for non-vascular patients with a normal ECG and good mobility.[20]

Dipyridamole-thallium scintigraphy

When myocardial perfusion is increased by vasodilation with dipyridamole, infarcted areas appear as fixed defects, whereas ischaemic myocardium appears as defects, which

are reversible when reperfused on later images. There is an incremental increase in the probability of postoperative cardiac events with increasing size and number of these defects.[12 14] Reversible defects are efficient markers of the myocardium at risk, and are clearly associated with an adverse cardiac event.[19] Quantification of their delayed redistribution at 4–24 h is more predictive of cardiac death or myocardial infarction than simple dichotomous interpretation in positive/negative results.[32 108 118] There is strong evidence that DTS has a good predictive value for determining a low or high operative risk when applied to a selected population of clinical intermediate-risk, vascular patients.[66 118] However, it has no real screening value, when applied to a large unselected vascular or non-vascular population, or among patients already classified clinically as low- or high-risk candidates for surgery.[4 68]

Left ventricular ejection fraction

There is strong evidence that simple assessment of the resting ejection fraction by transthoracic echocardiography alone does not improve prediction of ischaemic complications in cardiac patients, although it is useful for evaluating outcome in current or poorly controlled heart failure.[22 49 77] A depressed ejection fraction predicts only postoperative left ventricular dysfunction and correlates better with late than early postoperative cardiac events.[83 102] Technetium-99 radionuclide angiography offers a more precise and more reproducible measurement, but is not a better predictor of ischaemic events.[117]

Dobutamine stress echocardiography

An increase in oxygen demand following dobutamine perfusion (40 μg kg^{-1} min^{-1}) is more discriminative, as it can induce wall motion abnormalities pathognomonic of ischaemic myocardium. According to most meta-analyses, it offers the best prediction for perioperative events, with a negative predictive value close to 100% and a positive predictive value up to 38% among intermediate- or high-risk patients (Table 4), even if it does not add discriminative power in patients with no clinical markers of coronary artery disease.[11 23 74 84 88 108] Patients demonstrating extensive ischaemia under dobutamine stimulation (>5/16 left ventricular segments involved), experience 10 times more cardiac events than patients with limited stress-induced ischaemia (<4 segments involved).[11] Based on a Dutch study of 1351 consecutive patients undergoing major vascular surgery, DSE can be considered as an effective test for identifying the small group (2%) of patients at high ischaemic risk who should undergo coronary angiogram and possible revascularization. In contrast, patients with moderate risk (<4 segments involved) could undergo surgery directly under beta-block protection.[11]

Coronary angiography

Coronary angiography is an invasive procedure, which carries mortality of 0.01–0.05%, and a morbidity of 0.03–0.25%.[75] It is indicated only in cases of unstable coronary syndromes, of uncertain stress tests in high-risk patients undergoing major surgery, or when there is a possible indication for coronary revascularization.[22] When the coronary artery disease is diffuse in small vessels, as in subendocardial ischaemia without wall motion abnormalities, or when the patient is not a candidate for revascularization because of comorbid states, coronary angiography has little impact, as the probability of the results leading to PTCA or CABG is very low.[104] Coronary angiography should therefore be performed before a non-cardiac operation only in high-risk patients who warrant coronary revascularization for medical reasons, irrespective of the preoperative context.

Test limitations

Predictions are only probabilities of events: a negative preoperative test in a particular patient, although reassuring for the anaesthetist, does not mean that cardiac complications are excluded. Independent of its prognostic capacity, each test has its own advantages and contraindications (Table 5). More importantly, the primary factor for deciding the most efficient test is institution-specific: the best prediction will be provided by the most qualified department, whether it is cardiology, nuclear medicine, or the echo laboratory.

The concept that postoperative ischaemia and infarction are related to perioperative excess oxygen demand is supported by the fact that ischaemic events peak at the second and third postoperative day, whereas tachycardia is maximum during days 1 and 2.[69] Patients with higher maximum heart rates after surgery have more ischaemic episodes and a longer cumulative duration of ischaemia.[96] There is a strong correlation between immediate postoperative ischaemia (ST-segment depression) and cardiac events supervening after surgery.[67] Nowadays, stress echocardiography is the closest replication of an equivalent increase in myocardial oxygen consumption. Nevertheless, there is no test that adequately mimics the physiological stress response to surgery, with prolonged sympathetic stimulation and tachycardia, increased coronary vasomotor tone, hypercoagulability, potential atheromatous plaque rupture leading to thrombus formation, hypothermia, and blood loss.[28 33 107] Moreover, the culprit lesion causing myocardial infarction often occurs in a insignificantly stenosed coronary vessel.[26 43] Although DTS and DSE have good predictive accuracy in patients undergoing vascular surgery,[87 88] they seem not as efficient in patients undergoing non-vascular operations.[63 125] Without prospective studies on selected populations, it is not yet

Table 5 Advantages and disadvantages of preoperative tests

Test	Advantages	Disadvantages
Tests for myocardial perfusion		
Ambulatory ECG (Holter)	Simple, non-invasive	Baseline ECG abnormalities restrict diagnostic possibilities, poor predictive ability
Exercise ECG	Simple, non-invasive	Relies on patient mobility, baseline ECG abnormalities restrict diagnostic possibilities, poor predictability in vascular patients
DTS	Sensitivity 85%, specificity 80%	Contraindicated in unstable angina and asthma, delayed images at 4 to 24 h use of radioactive material, requires overnight fasting
DSE	Sensitivity 80%, specificity 90%, ventricular function detects dynamic ischaemia	Depends on transthoracic echogenicity, operator-dependent
Tests for myocardial function		
Transthoracic echo	Simple, rapidly available	Diagnostic only in case of transmural ischaemia, no predictability for ischaemia
Technetium-99 scanning	No interobserver variability, high reproductibility	Expensive, less availability

possible to define the real impact of stress tests on outcome in general surgery.

Patients receiving effective chronic beta-block are difficult to evaluate with stress tests because they have a limited increase in heart rate and cardiac output on exercise. The sensitivity of stress tests for diagnosing a coronary lesion is significantly lowered under these circumstances.[29 123] However, as a preoperative prognostic tool, these tests retain their full value, as they demonstrate which level of stress these patients can endure before showing myocardial ischaemia under the protection of beta-adrenergic antagonism. The decreased incidence of ischaemic modifications with beta-block is a diagnostic drawback, but is nevertheless a demonstration of the level of protection reached with this medication.

Testing takes time and money. Only intermediate-risk (Table 1), and low-functional status (Table 2) patients, undergoing major or vascular surgery (Table 3) benefit from stress testing. High-risk patients should undergo coronary angiography. In a theoretical model of decision analysis, using as an end-point mortality rates for abdominal aortic aneurysm resection and CABG, Glance[44] suggests that preoperative screening, in which high-risk patients proceed directly to angiography and possible CABG, intermediate-risk patients are first screened with DTS, and low-risk patients undergo no testing before vascular surgery, may improve 5-yr survival from 77 to 86%. In this model, routine testing of all patients is of no benefit compared with selective testing of the intermediate-risk category, and is more expensive. Some patients have an obvious indication for urgent surgery and yet have a clinical coronary status, which would require investigation because of the possible need for revascularization. Testing and treating them would impose an unacceptable delay in the surgical treatment of the life-threatening primary disease. In such a case, it is not indicated to thoroughly investigate the patient, as the decision to operate with the shortest delay is made whatever the results. Based on recent data on risk stratification, it can be asserted that these emergency operations can be performed as soon as possible, but should be accompanied by perioperative treatment with beta-blockers.[11 90 127]

Diabetes mellitus

In diabetic patients, the risk of coronary artery disease is two to four times higher than in the corresponding general population.[2] Moreover, diabetes is frequently associated with silent ischaemia; if detected by Holter monitoring, it has a positive predictive value of 35% for postoperative cardiac events.[30] Asymptomatic diabetic patients have an incidence of ischaemic events similar to patients with stable coronary artery disease.[48] Clinicians should have a low threshold for cardiac testing in diabetics, as the following factors must be added to the usual minor clinical predictors (Table 1): obesity, physical inactivity, albuminuria, dyslipidaemia, and age more than 55 yr.[103] Chronically elevated glucose (>11 mmol litre^{-1}) and glycosylated haemoglobin levels greater than 7% are better predictors of cardiac events than the simple presence of diabetes.[16 47 103] Diabetics with proven coronary artery disease (intermediate-risk predictors) have a much poorer long-term outcome after vascular surgery, with an increased probability of cardiac death or myocardial infarction compared with non-diabetics with equivalent coronary artery disease.[12 14]

Asymptomatic diabetic patients with two or more risk factors should be investigated by stress testing if they have a low-functional capacity (Table 2), or if they are to undergo major or vascular surgery. Only individuals with good functional capacity undergoing minor or intermediate surgery (Table 3) can proceed directly to surgery. This is a more aggressive attitude than for the general population. The modification of hypoglycaemic symptoms with beta-

blockers does not preclude their use in diabetics, as they offer a perioperative protection against ischaemia.[47 127]

Vascular surgery

Preoperative evaluation for coronary ischaemia most frequently involves vascular surgical patients, even if they are asymptomatic because of limitations in physical activity: 37% of surgical vascular patients without symptoms of myocardial ischaemia have significant coronary disease at angiography, and 15% have disease that warrants intervention.[1 52 53] The perioperative infarction rate in vascular surgery is three times higher than in non-vascular surgery.[61] The mortality rate for non-cardiac vascular surgery in patients with coronary artery disease is 5–9%, whereas it is only 1–2% in patients free of coronary disease, or in patients who have had previous CABG.[37 40 53] The incidence of perioperative non-fatal myocardial infarction in vascular surgery is 8.5% when the patients have proven coronary artery disease, but only 1.6% in patients with no risk factors, and 1.9% if the patient has had a CABG;[21 118] the latter results are obtained in patients who survived at least 6 months after their cardiac operation.

The data might seem to support prophylactic CABG. However, the mortality/morbidity of coronary revascularization, of a non-cardiac procedure and of postponement of vascular surgery must be added.[28 31] The mortality of vascular patients in cardiac surgery (6.5%) is much higher than the mortality of patients without vascular disease (0.5–2%).[8 31 50 82 98 99] Prior CABG offers no short-term benefit to these patients. In a decision analysis study comparing the strategy of prior coronary revascularization *vs* proceeding directly to vascular surgery, Mason and colleagues found poorer overall short-term outcomes with the combined procedures for the four end points of non-fatal myocardial infarction, stroke, cost, and mortality.[75] The indication for revascularization is the potential long-term benefit of an increased survival, independent of non-cardiac operative events. Routine coronary angiography in vascular patients does not provide short-term perioperative benefit.[44]

In a retrospective study on 6895 US Medicare patients, it appears that coronary revascularization has a protective effect on cases undergoing abdominal aortic surgery (fall in mortality from 4.1 to 2.8%), but not on those who underwent infra-inguinal vascular surgery.[35] In older patients (>70 yr), the benefit of previous coronary revascularization is probably non-existent, as mortality correlated to CABG or PTCA increases with age and the potential life-prolonging effect decreases. Finally, the benefit from CABG or PTCA may vary considerably between different institutions or different surgeons: when the perioperative mortality of abdominal aortic surgery is low (<3%), preoperative testing for coronary artery disease becomes insignificant in modifying the clinical outcome, and previous revascularization is no longer necessary in all but highly symptomatic patients.[106]

Pharmacological pretreatment

Is any pharmacological perioperative treatment protective against ischaemia? In the past, controlled studies with nitrates, calcium-channel blockers, clonidine, or digoxin have all produced negative answers.[7 13 18 25 94] More recent prospective randomized studies have focused on the use of beta-blockers with favourable results.[127] In both vascular and general surgery, the cardiac perioperative mortality is reduced by 8% and the ischaemic complication rate by 15% in patients treated with atenolol.[71] Among vascular patients with abnormal DSE, cardiac mortality, and morbidity are lowered from 34% in a control group to 3.4% in a group treated with bisoprolol.[90] Perioperative beta-block reduces the mortality of vascular patients in all risk categories except in patients with unstable coronary syndromes needing revascularization, as indicated by extensive ischaemia induced at DSE.[11] The treatment is started a few days before surgery, and continued during the first postoperative week. The dose is titrated to achieve a resting heart rate between 50 and 60 beats min^{-1}.[22] Older age is not a contraindication.[126] If preoperative administration is not possible, i.v. beta-block at the start of anaesthesia, followed by continuous postoperative treatment, is also efficient.[120] During a 3-yr follow-up, continuous administration of bisoprolol also protects from late ischaemic cardiac events after vascular surgery.[89 91] As sympathetic stimulation and tachycardia are among the most important factors in the development of perioperative myocardial ischaemia, and as ischaemia might appear in an insignificantly stenosed coronary artery, it is not surprising that sympathetic block is an effective method of preventing cardiac morbidity and mortality in non-cardiac surgery, as it is in non-surgical patients after myocardial infarction.[26 43 46 69] There might be non-responders, as recent investigations have disclosed less effect of beta-block in American black individuals than in the white population.[24 124]

As a consequence, in patients with known, or at risk of coronary artery disease, $beta_1$-selective antagonists should be considered in the perioperative period when these patients are to undergo major or vascular surgery. Despite the concern of many anaesthetists, the benefits of fewer cardiac complications in patients with coronary artery disease outweigh the risks of adverse effects in stage IV peripheral arterial disease, diabetes, and obstructive lung disease.[11 34 112 121 127] In most cases, the risk of non-cardiac surgery alone with prophylactic $beta_1$-block is lower than the cumulative risk of coronary angiography, a revascularization procedure and a non-cardiac vascular operation.[10 64]

Nevertheless, the recent trend towards $beta_1$-antagonism is essentially based on six publications summing up a total of 502 patients receiving perioperative beta-block.[11 71 90 91 120 126] Only three of them are randomized (total, 201 beta-block patients),[71 90 126] and only two are outcome studies (158 beta-block patients *vs* 154 controls, short- and long-term follow-up).[71 90 91 120] Obviously, more

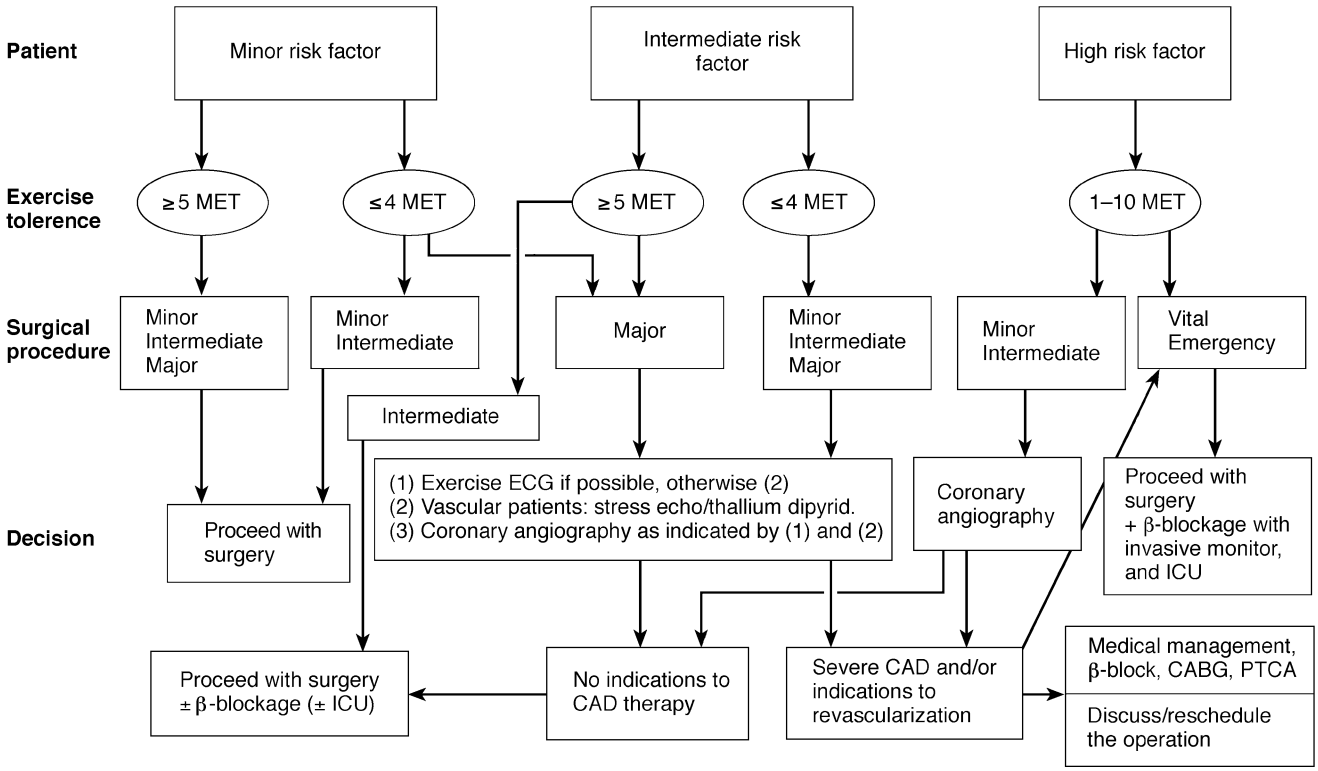

Fig 1 Algorithm for evaluating patients suffering from, or at risk of, myocardial ischaemia.

studies are needed before this therapy can be presented as state-of-the-art management.

Algorithm

The American College of Cardiology/American Heart Association Guidelines for Perioperative Cardiovascular Evaluation for Noncardiac Surgery have promoted recommendations based on evidence and expert opinions, and summarized them in a decisional algorithm which has proven efficient and cost-effective when tested on clinical patients for vascular surgery.[5 20 22] The American College of Physicians has adopted a position based on a meta-analysis of studies considered of strong, fair, or weak quality, and proposed an algorithm based on a modified cardiac risk index;[1 84] vascular and non-vascular surgery are separated. Other workers have published their own views on preoperative cardiac assessment, and have suggested useful paradigms.[36 56 72 74 115]

In our proposition (Fig. 1), the algorithm starts with a stratification of patients in three categories on the basis of clinical predictors (Table 1): low-risk (increased probability of coronary artery disease), intermediate-risk (stable coronary artery disease), and high-risk (unstable coronary syndrome). It proceeds through two evaluation steps: the exercise tolerance of the patient (cut-off point between 4 and 5 MET, Table 2) and the importance of the surgical procedure (minor, intermediate, or major, Table 3). Stress tests are performed only in the intermediate-risk category. Coronary angiography is considered in patients with unstable coronary syndromes or with stress tests revealing large areas of myocardium at risk. High-risk patients should undergo only mandatory or emergency procedures; anaesthesia should then be provided by an experienced anaesthetist using invasive monitoring and aggressive treatment of haemodynamic or ischaemic abnormalities. The choice of anaesthesia technique, like use of epidural analgesia, might be of significance in cardiac morbidity and mortality, but this is outside the scope of this review.[6 9]

Conclusions

Several studies have addressed the problem of preoperative evaluation of patients known to have, or at risk of, coronary artery disease. Nevertheless, in the absence of large, randomized, multicentre studies with clear-cut results, we have to rely on evidence-based medicine and Bayesian analysis for choosing preoperative strategies. The proposed framework suggests a rather conservative approach, limiting stress testing to intermediate-risk patients with suspicion of a myocardium at risk of ischaemia, and coronary angiography to situations where revascularization can improve long-term survival. A specialized and costly test is indicated only when the additional information provided has a positive impact on patient outcome.

Recent publications tend to show an increased risk of proceeding with non-cardiac surgery less than 3 months after coronary revascularization, which has been demonstrated to have no place in preventing the ischaemic complications of non-cardiac operations. Moreover, it is frequently impossible to wait to treat myocardial ischaemia when the patient requires a life-saving operation. In these situations, recent studies, although scarce, have demonstrated a marked benefit of operating under the protection of $beta_1$-adrenergic antagonism. As postoperative infarction has a better correlation with peri- and postoperative ischaemic events than with preoperative ischaemia, it seems logical to be aggressive in the prevention and treatment of perioperative events. Finally, it appears that the best strategy is very institution-specific. Every institution should construct its own guidelines, based on local performances and results.

To help clarifying the comparison between different publications with dissimilar methodologies, the references are annotated into levels of evidence according to the guidelines of evidence-based medicine. Level I of evidence contains large studies with prospective, randomized selection of patients, blinding, and clear-cut results. Level II contains small, randomized trials with uncertain results. Level III comprises non-randomized studies with contemporaneous controls. Level IV corresponds to non-randomized studies with historical controls. Level V includes uncontrolled case series and expert opinions. Theoretical models, meta-analyses, and guidelines are not coded.

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