Approximately 100 million people undergo non-cardiac surgery annually worldwide. It is estimated that around 3% of patients undergoing non-cardiac surgery experience a major adverse cardiac event. Although cardiac events, like myocardial infarction, are major cause of perioperative morbidity or mortality, its true incidence is difficult to assess. The risk of perioperative cardiac complications depends mainly on two conditions: 1) identified risk factors, and 2) the type of the surgical procedure. On that basis, different scoring systems have been developed in order to accurately assess the perioperative cardiac risk and to improve the patient management. Importantly, patients with estimated high risk should be tested preoperatively by non-invasive cardiac imaging modalities. According to test results, they can proceed directly to planned surgery with the use of cardioprotective drugs (β-blockers, statins, aspirin), or to myocardial revascularization prior to non-cardiac surgery. In this review, we discuss the role of clinical cardiac risk factors, laboratory measurements, additional non-invasive cardiac testing, and consequent strategies in perioperative management of patients undergoing non-cardiac surgery.

Key words: non-cardiac surgery, perioperative cardiac risk, management strategies

INTRODUCTION

Early or late perioperative cardiovascular morbidity and mortality are among the major problems in patients undergoing non-cardiac surgery. It is estimated that of almost 40 million annually performed surgical procedures in Europe, cardiovascular mortality occurs in 0.3%, and postoperative myocardial infarction (MI) in 1%. In a pooled analysis of unselected non-cardiac surgery patients over the age of 40 years, a 30-day incidence of postoperative cardiac events (MI and cardiac death) was 2.5%. The rate of these events is even higher in vascular surgery patients (6.2%). The true event rate of postoperative cardiac complications can be even higher, since most of them occurs asymptotically, and depends on the type of postoperative surveillance (Figure 1). The majority of postoperative cardiac complications are caused by sudden or prolonged myocardial ischemia due to a primary coronary event (such as plaque erosion and/or rupture, fissuring, or dissection) or due to either increased oxygen demand or decreased supply (such as coronary artery spasm, coronary embolism, anaemia, arrhythmias, hypertension, or hypotension). Other major determinants of adverse postoperative outcome are aortic stenosis and left ventricular dysfunction. The pathophysiology of cardiac events in those two conditions is related to an interaction of developing hypotension and low cardiac output during surgery, and possible underlying coronary artery disease (CAD).

To reduce postoperative cardiac morbidity and mortality, preoperative screening is of paramount importance. This screening involves identification of potential risk factors, as well as different noninvasive imaging modalities. In this review, we will describe the current status of preoperative risk stratification for patients undergoing non-cardiac surgery.

ESTIMATION OF CARDIAC RISK

Identification of clinical risk factors, which can predict postoperative cardiac complications, was of a great interest for the past 30 years. For that purpose, several risk indices were developed, such as Goldman cardiac risk index, the Detsky modified multifactorial risk index, Eagle’s risk score, American Society of Anesthesiologist index, and Canadian Cardiovascular Society index. However, no index was significantly superior to the other. The recently published revision of the Goldman’s risk index by Lee et al., named Revised Cardiac Risk Index, substan-
tially improved its predictive value. By identifying 6 predictors of major postoperative cardiac complications (ischemic heart disease, congestive heart failure, cerebrovascular disease, diabetes mellitus treated with insulin, renal failure, and high risk surgery), this risk index stratifies patients in 4 categories: with 0, 1, 2, and >3 risk factors. The estimated rates for postoperative major cardiac complications in each group are 0.4%, 0.9%, 7%, and 11%, respectively. Boersma et al. validated the Lee risk index in a large cohort of 108,593 patients who underwent all types of non-cardiac surgical procedures, including vascular surgical procedures, and demonstrated a substantial improvement by adding the surgical risk of the various procedures, age, and ECG findings (Figure 2). These data suggest that the Revised Cardiac Risk Index by Lee et al is probably suboptimal for identifying patients with greater cardiac risk, perhaps because it excluded emergency operations and perhaps because the type of surgery, which is one of the main determinants of adverse cardiovascular outcome, was considered in only 2 subtypes: high risk, including intraperitoneal, intrathoracic, and suprainguinal vascular procedures; and all remaining nonlaparascopic procedures, mainly including orthopedic, abdominal, and other vascular procedures.

The European Society of Cardiology (ESC) guidelines on perioperative cardiovascular evaluation and care for non-cardiac surgery provide the stepwise algorithm to preoperative cardiac assessment. This algorithm uses the urgency of non-cardiac surgery, clinical risk factors, and patients’ functional capacity in prediction of postoperative cardiac events. (Table 1) The first step in this algorithm is to determine the urgency of non-cardiac surgery. Patients needing emergency non-cardiac surgery should proceed to surgery without the delay of additional cardiac evaluation, with the instructions for postoperative surveillance and risk factor management. The next steps refer to the patients considered for elective non-cardiac surgery:

- a) In the presence of unstable (active) cardiac conditions the surgery should be canceled or delayed until the cardiac problem has been clarified and treated appropriately. (Table 2)
- b) Patients scheduled for the low risk surgery (reported cardiac risk generally <1%) and good functional capacity, or diminished functional capacity but no risk factors, should proceed with planned surgery.
- c) Patients scheduled for intermediate risk surgery (reported cardiac risk generally 1-5%) or high risk surgery (reported cardiac risk generally >5%), with poor or unknown functional capacity and 1-2 clinical risk factors, should proceed with the planned surgery with tight heart rate control using beta-blockers, or to preoperative testing if that will change management; the same refer to the patients scheduled for intermediate risk surgery, poor or unknown functional capacity, and >3 risk factors.
- d) Patients scheduled for high risk surgery (reported cardiac risk generally >5%), poor or unknown functional capacity, and >3 risk factors should be considered for preoperative testing if it will change the management.

**LAPAROSCOPIC SURGERY - MORE ELEGANT, BUT NOT LESS RISKY**

Quick recovery and reduced duration of short-term disability are the main advantages of laparoscopic over open non-cardiac surgery. On the other hand, it may be associated with considerable cardiovascular, neuroendocrine, and renal changes induced by iatrogenic pneumoperitoneum needed to create the workspace. All these changes together produce a state physiologically similar to chronic heart failure. The main haemodynamic changes consist of increase in systemic and pulmonary vascular resistances (increase in afterload), and decrease in cardiac output. Haemodynamic changes are influenced also by the patient’s posture - head-down position causes the afterload to return to normal while increasing the preload, whereas it is opposite with head-up position. However, the pa-

**TABLE 1**

**SHORT-TERM RISK OF MAJOR ADVERSE CARDIAC EVENTS FOR DIFFERENT TYPES OF SURGERY**

<table>
<thead>
<tr>
<th></th>
<th>Low (&lt;1%)</th>
<th>Intermediate (1-5%)</th>
<th>High (&gt;5%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental</td>
<td>Carotid</td>
<td></td>
<td>Aortic</td>
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<tr>
<td>Breast</td>
<td>Head and neck</td>
<td></td>
<td>Peripheral vascular</td>
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<tr>
<td>Eye</td>
<td>Neurological/Orthopaedic major (spine and hip)</td>
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</tr>
<tr>
<td>Endocrine</td>
<td>Pulmonary, renal/liver transplant</td>
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<tr>
<td>Gynaecological</td>
<td>Urological major</td>
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<tr>
<td>Reconstructive</td>
<td>Abdominal</td>
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<tr>
<td>Orthopaedic minor (knee surgery)</td>
<td>Peripheral arterial angioplasty</td>
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<tr>
<td>Urological minor</td>
<td>Endovascular aneurism repair</td>
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tient’s posture is based on surgeons’ rather than cardiovascular requirements. Pneumoperitoneum induced distension of the abdomen can provoke bradycardia or atrioventricular block by stimulation of the vagus. Sometimes that can be beneficial, mimicking ß-blocker effect as it will be discussed later. Neuroendocrine changes consist of plasma renin and aldosterone increase, as well as increase in adrenalin, noradrenalin and vasopressin.16,17 Renal function impairment is caused by decrease in renal blood flow and glomerular filtration rate, and may result in fall in urine output.18

In conclusion, described physiological changes induced by laparoscopic technique could be linked with serious perioperative adverse cardiac events, especially in patients with known cardiac disease. This is recognized by recently published ESC guidelines, which recommends that patients before laparoscopic interventions should be screened in the same manner as for open surgical procedures.

**ADDITIONAL LABORATORY MEASUREMENTS - B-TYPE NATRIURETIC PEPTIDE AND C-REACTIVE PROTEIN**

Apart from the measurements indicating clinical risk factors (i.e. serum creatinine for renal failure, fasting glucose for diabetes mellitus, etc.), B-type natriuretic peptide (BNP) and N-terminal part of its precursor (NT-proBNP), as well as C-reactive protein, have been recently identified as predictors of perioperative adverse cardiac events.

In a prospective study of 182 vascular surgery patients, Feringa et al. evaluated association of preoperative NT-proBNP levels with myocardial ischemia and troponin T release.19 Myocardial ischemia was detected in 21% and troponin T release in 17% of patients. After adjustment for clinical risk factors and stress echocardiography results, higher NT-proBNP levels were associated with higher incidence of myocardial ischemia and troponin T release. The optimal cutoff value of NT-proBNP to predict ischemia and/or troponin T release was 270 ng/l. Higher baseline NT-proBNP levels were also associated with a larger ischemic burden at electrocardiographic monitoring.

Two recently published studies showed that both NT-proBNP and CRP predicts perioperative adverse cardiac events better than Lee’s Revised Cardiac Risc Index.20, 21 Moreover, the predictive power of that risk index could be improved significantly by addition of CRP and NT-proBNP. Taking into account objectiveness, relatively low cost and availability of these two biomarkers, establishing of their universal cut-off values through the future studies can make them a first-line tool in preoperative risk assessment.

**ADDITIONAL NON-INVASIVE TESTING**

Further cardiac testing is warranted only if the test results will change perioperative management. Beside that preoperative noninvasive testing increases cost of treatment of non-cardiac surgery patients, it also might delay surgery and increase operative risk. Although there is no doubt that high-risk patients (>3 risk factors and poor functional capacity) should be further evaluated by noninvasive testing, the question whether or not it can be omitted in intermediate-risk patients (1 or 2 risk factors) remains open. Recently published Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echo II (DECRAE II) study tried to resolve this dilemma.3 Of 1,476 screened vascular surgery patients treated with beta-blockers, 770 were identified to be of intermediate-risk for postoperative major cardiac events. These patients were randomly assigned to cardiac stress-testing (n=386) or no testing. Test results were used to optimize perioperative cardiac care, including optimal heart rate (HR) control in patients with ischemia below the ischemic HR threshold, and coronary revascularization was considered in those with extensive ischemia on test (>5 left ventricular segments). All patients proceeded to planned vascular surgery with ß-blocker therapy aiming at a HR of 60 to 65 beats per minute. Study results showed that patients assigned for no testing had the same incidence of primary end-
points (cardiac death or nonfatal MI) as those assigned for testing (1.8% vs. 2.3%; P=0.62), and they waited for the vascular surgery intervention almost 3 weeks less.

Several non-invasive imaging modalities can be used for the additional preoperative testing, such as resting transthoracic echocardiography (TTE), dobutamine stress echocardiography (DSE), myocardial perfusion scintigraphy (MPS), cardiac computed tomography (CCT), and cardiac magnetic resonance (CMR).

**RESTING TRANSTHORACIC ECHOCARDIOGRAPHY**

This is the most widely available, simple, and inexpensive mode of cardiac imaging, but as all other non-invasive imaging modalities it is not performed on routine basis. It is accurate in evaluation of ventricular and valvular function and morphology. Since impaired left ventricular function is recognized as a significant predictor of perioperative adverse cardiac events, it is important to evaluate its nature and degree preoperatively by TTE. Information regarding resting left ventricular function may be important in decision making regarding perioperative beta blocker therapy. TTE is also recommended for the estimation of severity of valvular stenosis or insufficiency (i.e. significant aortic stenosis is associated with the 5-fold increase of perioperative cardiac events).22

**DOBUTAMINE STRESS ECHOCARDIOGRAPHY**

This diagnostic method is based on the enhancement of myocardial oxygen demand and subsequent ischemia by infusion of incremental doses of dobutamine, which increases myocardial contractility and heart rate. Contractile dysfunction in ischemic myocardial segments is assessed by echocardiography as wall motion abnormalities. Numerous studies showed DSE as predictive for short- and long-term perioperative cardiac events, with a high negative and moderate positive predictive value.23-26 The most useful prognostic data obtained during DSE are ischemic threshold (i.e., the cardiac workload necessary to induce myocardial ischemia), extent and severity of wall motion abnormalities. The test results are limited in patients on β-blocker therapy (diminished HR response), and in those with bad image quality.

**MYOCARDIAL PERFUSION SCINTIGRAPHY**

Diminished blood flow through the stenotic coronary arteries can be diagnosed using of small amounts of intravenously administered radioactive tracers such as thallium-201 or technetium 99m. Perfusion defects are more obvious if recorded during exercise or pharmacologic stress, and can be classified as reversible (ischemia) or fixed (scar). This diagnostic technique has been extensively studied in the setting of preoperative risk assessment, showing its high sensitivity but low specificity in predicting postoperative cardiac complications.27,28 The likelihood
of perioperative complications is higher with reversible perfusion defects, and increases with its extent.29

CARDIAC COMPUTED TOMOGRAPHY

In the past decade, cardiac computed tomography (CCT) emerged as reliable diagnostic method for the assessment of CAD, coronary artery anatomy, and cardiac function. Constant technological improvements in the field of CCT (introduction of dual-source and 256-slice CTs) impose it as an excellent alternative to standard coronary angiography in selected group of patients. Studies investigating the accuracy of CCT in detection of obstructive CAD report its sensitivity, specificity, positive and negative predictive value to be 94-99%, 95-97%, 76-97%, and 93-99%, respectively.30,31 In regard to high specificity of CCT reported, it appears as an excellent diagnostic modality for excluding CAD. In difference to conventional coronary angiography, CCT allows the assessing of atherosclerotic plaque morphology and identifying unstable plaques.32,33 The assessment of plaque morphology may have an important role in identifying patients who are at greater perioperative risk for adverse cardiac events. Cardiac computed tomography also showed high accuracy in assessing coronary artery bypass graft and stent patency.34-36 Nevertheless, there are certain limitations to the use of CCT in those settings which can lead to the diminished quality of the images of the grafts and implanted stents (i.e., presence of surgical clips, calcifications, and metallic artifacts). Although two-dimensional echocardiography will remain the preferred tool in preoperative assessment of global left ventricular function and wall motion, CCT has been shown as accurate tool for these purposes.37

There are certain limitations of CCT that cannot be ignored. Image acquisition is highly dependent on heart rhythm and rate (motion artifacts), amount of coronary calcification, and it requires exposing of patients to relatively high radiation dose. Above all, the cost of the CCT equipment is higher in comparison to other widely available noninvasive imaging modalities, i.e. echocardiography. In the light of these limitations remains the question who is the candidate for preoperative testing with CCT. To our opinion, it appears reasonable to use CCT in further defining of perioperative risk in patients who have equivocal noninvasive cardiac stress tests, i.e. DSE or MPS.

CARDIAC MAGNETIC RESONANCE

The particular interest for cardiac magnetic resonance (CMR) in the settings of preoperative risk stratification is based on its excellent abilities in assessment of ventricular function, myocardial perfusion, and coronary artery anatomy.38-40 In patients who are not suitable for DSE (i.e., bad images because of suboptimal acoustic window),
stress. CMR using dobutamine appears as a good alternative. The protocol for administration of dobutamine and image analysis in stress CMR is similar to DSE. Studies have shown high accuracy and reproducibility of dobutamine stress CMR in detection of wall motion abnormalities. In the study of Hundley et al., dobutamine stress CMR showed excellent performance in predicting of future cardiac events in patients with inducible ischemia (hazard ratio 3.3, CI 1.1 to 9.7). The same group analyzed the accuracy of dobutamine stress CMR for preoperative risk assessment. Of the 102 patients referred for non-cardiac surgery (29 vascular, and 73 nonvascular), myocardial ischemia occurred in 25 patients during dobutamine stress CMR.

Postoperative cardiac events (death, nonfatal MI, and congestive heart failure) developed in 5 of those patients, presenting a sensitivity and specificity of the test in predicting of perioperative cardiac complications of 84% and 78%, respectively. Because of its noninvasive nature, superb image quality, absence of radiation and application of contrast media, CMR appears to be excellent cardiovascular imaging modality. The main limitations are complexity of the technique, low availability, cost, and high dependency on the operator expertise.

**HOW THE TEST RESULTS CAN INFLUENCE THE MANAGEMENT?**

Patients with estimated intermediate- or high-risk for perioperative cardiac complications, with normal tests and no stress-induced myocardial ischemia should proceed with the planned surgery under optimal medical therapy. The situation is more complex if the test results are positive and final decision whether to operate with the use of optimal cardioprotective therapy or to perform preoperative myocardial revascularization depends mainly on the extent and severity of stress-induced myocardial ischemia.

**CARDIOPROTECTIVE MEDICAL THERAPY - ß-BLOCKERS AND STATINS**

Cardioprotective effect of ß-blockers is based on the fact that they can diminish the effects of increased sympathetic activity in surgical patients.

In DECREASE I trial, 112 selected vascular surgery patients with evidence of myocardial ischemia on preoperative DSE were randomized to receive placebo or bisoprolol (5-10 mg). Treatment with bisoprolol was started at least 7 days before surgery. Perioperative bisoprolol use resulted in 10-fold reduction in the incidence of cardiac death and myocardial infarction (3.4% vs. 34%; P<0.001).

Importantly, maximum benefit of ß-blocker therapy in vascular surgery patients with CAD can be achieved only if a tight HR control is established. That was proved in a recently published study on 272 vascular surgery patients on chronic ß-blocker therapy. Higher doses of ß-blockers and lower HR were associated with reduced perioperative ischemia detected on ECG Holter monitoring (hazard ratio: 2.49; 95% confidence interval (CI): 1.79-3.48) and troponine T release (hazard ratio:1.53;95% CI:1.16-2.03).

The beneficial cardioprotective effect of ß-blockers in non-cardiac surgery was questioned by the recently published PeriOperative ISchematic Evaluation (POISE) trial. In the trial, 8,351 patients were randomly assigned to either controlled-release oral metoprolol-succinate or placebo. Fewer patients in the metoprolol group than in the placebo group had a myocardial infarction (4.2% vs. 5.7% patients; hazard ratio 0.73; CI=0.60-0.89; p=0.0017). Nevertheless, the incidence of deaths and stroke in the metoprolol group was higher than in the placebo group (3.1% vs. 2.3% patients; hazard ratio 1.33; CI=1.03-1.74; p=0.0317 for all-cause mortality; 1.0% vs. 0.5% patients; hazard ratio 2.17, CI=1.26-3.74; p=0.0053 for stroke). The different outcomes in the POISE trail in comparison to those previously mentioned can be explained by strikingly different ß-blockers dosing regimes. Unusually high starting dose of metoprolol-succinate in the POISE trial, as well as short initiation time of therapy before surgery, might have caused an unfavorable hemodynamic condition that ultimately resulted in hypotension, higher incidence of stroke and all-cause mortality.

Thus, regardless to the POISE trial results, current ESC guidelines recommend the use of perioperative ß-blocker therapy, preferably long-acting agents started days to weeks before elective surgery, and aiming tight HR control.

Cardioprotective effect of statins is based on their so-called "pleiotropic" properties (i.e., improving endothelial function, enhancing the stability of atherosclerotic plaques, decreasing oxidative stress and inflammation, and inhibiting thrombogenic response).

To evaluate the association between statin use and perioperative mortality, Poldermans et al. performed a case-controlled study among patients who underwent major vascular surgery. A cardiovascular complication during the perioperative phase was the primary cause of death in 104 (65%) case subjects. Statin therapy was significantly less common in cases than in controls (8% vs 25%; P=0.001). The risk of perioperative mortality among statin users was reduced 4.5 times compared with nonusers (adjusted odds ratio for perioperative mortality among statin users as compared with nonusers was 0.22 (95% CI: 0.1 to 0.47).

Prospective, double-blinded placebo-controlled trial by Durazzo et al., randomized 100 patients referred for vascular surgery to either 20 mg atorvastatin or placebo for 45 days. After 6 months of follow-up, the incidence of cardiovascular events (death, nonfatal MI, stroke, or unstable angina pectoris) was 3 times lower with atorvastatin than with placebo (8% vs. 26%; p=0.031).

**MYOCARDIAL REvascularization PRIOR TO NON-CARDIAC SURGERY**

Both percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) are evaluated in purpose of risk reduction in non-cardiac surgery patients.

Recently published prospective randomized Coronary Artery Revascularization Prophylaxis (CARP) trial comprised 510 patients who were scheduled for elective major surgery.
vascular surgery, and were selected for preoperative coronary angiography if a cardiology consultant considered that there was an increased risk for perioperative cardiac complications. Patients with at least 70% stenosis of one or more major coronary arteries were randomized to receive either preoperative myocardial revascularization (PCI: n=141; CABG: n=99) plus medical management, or medical management alone in conjunction with their elective vascular procedure. The study did not find the difference in 30-days mortality rate between patients who had myocardial revascularization prior to vascular surgery and those who were treated medically (3.1% vs. 3.4%; p=0.87). The rate of perioperative nonfatal myocardial infarction as detected by troponin elevation also did not differ in preoperatively revascularized patients and patients treated medically (11.6% vs 14.3%; p=0.37). Additionally, the late survival rates at median follow-up of 2.7 years did not differ significantly between preoperatively revascularized patients and those who were not (78% vs 77%). Furthermore, the results of this trial also indicated that myocardial revascularization prior to vascular surgery was associated with delay or cancellation of the required vascular operation.

However, CARP trial findings may be explained by the fact that the vast majority of included patients had single-or two-vessel disease with a preserved left ventricular function, and sufficient cardio-protection by medical therapy (β-blockers in 85% of all patients, aspirin in 72%, and statins in 53%). Hence, if a beneficial effect of the invasive strategy of prophylactic revascularization is to be expected, then patients with extensive CAD are those who should benefit from this strategy. This hypothesis was evaluated in recently published DECREASE-V Pilot study. The total of 101 patients scheduled for elective vascular surgery, with extensive stress-induced ischemia on DSE (≥5 ischemic of 17 segments) or MPS (≥3 ischemic walls), were randomized either to prophylactic myocardial revascularization (49 patients) or medical therapy (52 patients). A reduced left ventricular ejection fraction (<35%) was observed in 43 (43%) patients. Among the patients allocated to preoperative myocardial revascularization, three-vessel disease had 33 (67%), and left main disease had 8 (8%) patients.

A PCI was performed in 32 patients and CABG in 17. The 30-day outcome was not improved by myocardial revascularization; the incidence of all-cause mortality or nonfatal MI for patients with preoperative revascularization or medical treatment only was 43% vs. 33%, respectively (p=0.3). The same was observed for the incidence of one-year composite end points (revascularization group: 49% vs. medical therapy group: 44%; p=0.48).

The results of study by Marco et al. were in line with the DECREASE-V Pilot regarding in-hospital major adverse cardiac events, but at almost 8 years of follow-up revascularized patients showed significantly lower incidence of major adverse cardiac events (relative risk reduction of 54%) In the era of coronary stents, PCI became an attractive alternative to CABG in the management of non-cardiac surgery patients. The current ESC guidelines have recommended postponing non-cardiac surgery for ≥6 weeks after bare metal stent (BMS) placement and for ≥1 year after drug-eluting stent (DES) placement. However, much debate has ensued about these intervals. In a study of 550 non-cardiac surgery patients with previous stent placement (376 with a DES and 174 with a BMS), Van Kuijk et al. attempted to assess the influence of different intervals between stenting and non-cardiac surgery, and the use of dual antiplatelet therapy on the occurrence of perioperative major adverse cardiac events (death, myocardial infarction, and repeated revascularization). In the PCI-BMS group, the rate of MACEs during the intervals of <30 days, 30 days to 3 months, and >3 months was 50%, 14%, and 4%, respectively (overall p<0.001). In the PCI-DES group, the rate of major adverse cardiac events changed significantly with the interval after PCI (35%, 13%, 15%, 6%, and 9% for patients undergoing non-cardiac surgery <30 days, 30 days to 3 months, 3 to 6 months, 6 to 12 months, and >12 months, respectively, overall p<0.001). Of the patients who experienced a MACE, 45% and 55% were receiving single and dual antiplatelet therapy at non-cardiac surgery, respectively (p=0.92); the risk of severe bleeding in patients with single and dual antiplatelet therapy was 4% and 21%, respectively (p<0.001).

The authors concluded that there is an inverse relation between the interval from PCI to noncardiac surgery and perioperative major adverse cardiac events. Also, continuation of dual antiplatelet therapy until noncardiac surgery did not provide complete protection against major adverse cardiac events.

Potentially harmful effect of myocardial revascularization in high-risk non-cardiac surgery patients might arise from two reasons: a) the delaying of planned non-cardiac surgery, and b) higher cumulative risk of both coronary revascularization and non-cardiac surgery then non-cardiac surgery alone. Current ESC guidelines recommend that prophylactic myocardial revascularization should be considered in non-cardiac surgery patients with cardiac unstable conditions only (Table 2).

**ANTIPLATELET DRUGS WITHDRAWAL - WHEN THE RISK OVERWELMS THE BENEFIT**

Within the first year after stenting, approximately 5% of patients who have undergone PCI will be operated for conditions that require non-cardiac surgery. When patients undergo surgery early after stenting, the rate of MI and mortality (average, 30% and 20-40%, respectively) is 5- to 10-fold higher than in matched patients undergoing the same operation after appropriate delay or under maximal medical therapy. The risk of coronary thrombosis is maximal during the period of ongoing re-endothelialization, and it increases when antiplatelet medications are suddenly discontinued. In addition to coronary stenting, antiplatelet agents are widely prescribed for primary and secondary prevention of cerebrovascular and CAD in patients with: stable/unstable angina, MI, TIA/stroke, severe
carotid artery stenosis/stenting, peripheral vascular disease. Moreover, antiplatelet therapy is prescribed as primary prevention for high-risk patients with multiple cardiovascular risk factors (diabetes mellitus, cigarette smoking, hypercholesterolemia, hypertension). 37, 58

The fear for excessive bleeding, especially by surgeons and anesthesiologists, often leads to inappropriate or prolonged discontinuation of antiplatelet therapy before surgery, sometimes substituted by empirically administered heparin. Unfortunately, most of the information so far available on the risk of early antiplatelet discontinuation and on the most appropriate timing and duration of interruption of the treatment before surgery comes from retrospective studies or meta-analyses of small observational studies, with no direct evidence coming from prospective studies. 39 While it is important to recommend not to inappropriately discontinue antiplatelet therapy in patients at high cardiovascular risk, it must be considered that major bleeding can also jeopardize postoperative course in patients at high risk of cardiovascular events. 60, 61 Of particular interest are patients scheduled for high bleeding risk surgery, where the occurrence of bleeding is associated with serious morbidity/mortality (intracranial, intraspinial, intracranial), and where antiplatelet therapy must be stopped and the operation postponed 5-10 days (Figure 4). 62, 63 However, in patients undergoing other types of high bleeding risk operations (i.e. abdominal, general, hip etc.) anticipated blood loss (transfusions) should not be the main reason for discontinuation of antiplatelet therapy. We proposed algorithm how to manage those patients in different clinical situations (Figure 5).

Thus, it seems rational to withdraw antiplatelet therapy before planned surgery when bleeding risk clearly overwhelms the estimated risk of atherothrombotic events, or in patients undergoing surgery associated with high bleeding-associated morbidity/mortality.

CONCLUSION

Clinical cardiac risk markers, together with the type and urgency of planned non-cardiac surgery, can truly stratify patients in intermediate- and high-risk population. Intermediate-risk patients can likely be operated without any additional noninvasive screening, and should be treated with β-blockers (aiming HR 60-65/min) and statins. In addition to intensive medical therapy with β-blockers and statins, high-risk patients should be screened noninvasively for the extent of underlying CAD if that will change treatment management. The choice of the test should be based on the local experience and short-term availability. Although preoperative myocardial revascularization did not show significant advantages compared to the medical therapy in high-risk patients with stable CAD, it has to be considered in patients with unstable CAD. In patients in whom myocardial revascularization was done by PCI with stents, antiplatelet therapy should only be discontinued perioperatively if bleeding risks with increased mortality or sequelae are comparable or higher than observed cardiovascular risks after its withdrawal.

SUMMARY

PREOPERATIVNA PROCENA SRČANOG RIZIKA

Svake godine, priблиžno 100 miliona ljudi širom sveta podvrge se nekoj od nesrečanih hirurških intervencija. Procjenjuje se da oko 3% bolesnika nakon nesrečane hirurške doživi ozbiljan, neželjeni kardiošloški događaj. Iako su kardiošloški događaji, kao što je infarkt srca, glavni uzrok perioperativnog morbiditya i mortaliteta, pravu inciden ciju tih događaja teško je proceniti. Rizik od nesrezanih perioperativnih kardiošloških komplikacija zavisi od svojstava patološke baze, operativne intervencije i statusa bolesnika. Bolesnici sa visokim rizikom perioperativnog rizika imaju visoku smrtnost u periodu od 30 dana posle operacije.

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