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### Pre-operative cardiovascular assessment in non-cardiac surgery: an update

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#### Introduction

Cardiac complications are a major cause of peri-operative morbidity and mortality. In particular, vascular surgery patients are at increased risk with reported mortality rates of 1.5-2% for endovascular and 3-4% for open procedures [1, 2]. Mortality is mainly caused by peri-operative myocardial infarction (accounting for 10-40% of postoperative deaths), in addition non-fatal peri-operative myocardial infarction may compromise long-term outcome since it is associated with an increased risk of late mortality [3-5].

Peri-operative cardiac complications are either caused by myocardial ischaemia or by acute coronary thrombosis. Myocardial ischaemia may result from an increase in myocardial oxygen demand (tachycardia, hypertension, pain) or decreased supply (hypotension, vasospasm, tachycardia, hypoxia, anaemia). Coronary plaque rupture may be caused by factors that increase intra-coronary wall stress and the presence of a hypercoagulable state, leucocyte activation, and activation of the inflammatory response may contribute to the pathophysiology of coronary artery occlusion.

The ultimate goal of pre-operative assessment is to collect information on the extent and the stability of the cardiovascular disease in order to predict the patient's cardiac risk and to develop pre- and intra-operative strategies that may help to decrease this risk and improve short- and long-term outcome.

#### Prediction of cardiac risk

Risk stratification is aimed at identifying the different peri-operative variables that might influence the risk of each patient suffering an adverse outcome. Ultimately, such risk stratification will help to guide medical decisions and to determine optimal therapy for those patients at risk.

Over the years, different risk models have been proposed based on risk factors that had been identified by multivariate analysis. Initially, such scoring systems assigned a different weight to different risk factors, in order to arrive at a composite risk [6]. More recently, Lee et al derived and validated a simpler index for the prediction of cardiac risk for stable patients undergoing non-urgent non-cardiac surgery [7]. This Revised Cardiac Risk Index (RCRI) assigns one point for the presence of one of the following six risk factors: high risk surgical procedure, history of ischaemic heart disease, history of congestive heart failure, history of cerebrovascular accident, pre-operative treatment with insulin, or a serum creatinine greater than 177  $\mu\text{mol.l}$ . The estimated risks of major cardiac complications for indices 0, 1, 2, and 3 or more are 0.4 (0.1-0.8) %, 1.0 (0.5-1.4) %, 2.4 (1.3-3.5) % and 5.4 (2.8-7.9) %, respectively. This index provides an easy way for identifying patients who are at increased risk and has become one of the most widely used risk indices.

#### Pre-operative assessment

Cardiac indices are used to assess the prior probability of peri-operative cardiac risk in a given patient. This information may help in the decision whether or not to develop further strategies for diagnosis and peri-operative management. However, a simple estimate of risk as such does not allow the practitioner to clearly define the specific needs of each individual patient with regard to further testing and peri-operative strategies. This necessitates information on the extent and stability of the patient's individual cardiovascular disease. Such information is usually obtained from clinical assessment and, potentially, from additional technical testing.

## Clinical assessment

There are a number of active cardiac conditions that are considered to indicate a major clinical risk for peri-operative complications. According to the ACC/AHA 2007 guidelines [8], the presence of one or more of these conditions necessitates further evaluation and adapted management which may result in delay of surgery unless the surgery is urgent (Class I recommendation, level of evidence (LOE) B (Figure 1)). These major risk factors are summarised in Table 1 and include unstable coronary syndromes, decompensated heart failure, significant arrhythmias and severe valvular disease.

Figure 1

Overview of the classification of recommendations and levels of evidence. Both the size of the treatment effect (classes) and an estimate of the certainty of a treatment effect (levels) on a particular variable is taken into account.

	class I benefit >>> risk	class IIa benefit >> risk	class IIb benefit ≥ risk	class III risk ≥ benefit
	treatment / action SHOULD be performed	IT IS REASONABLE to perform treatment / action	treatment / action MAY BE CONSIDERED	treatment / action SHOULD NOT be performed
LEVEL A	<ul style="list-style-type: none"> <li>treatment / action is effective / useful</li> <li>sufficient evidence from multiple RCTs or meta-analyses</li> </ul>	<ul style="list-style-type: none"> <li>in favor of: treatment / action is effective / useful</li> <li>some conflicting evidence from multiple RCTs or meta-analyses</li> </ul>	<ul style="list-style-type: none"> <li>effectiveness / usefulness of treatment / action is less well established</li> <li>greater conflicting evidence from multiple RCTs or meta-analyses</li> </ul>	<ul style="list-style-type: none"> <li>treatment / action is NOT effective / useful or even harmful</li> <li>sufficient evidence from multiple RCTs or meta-analyses</li> </ul>
LEVEL B	<ul style="list-style-type: none"> <li>treatment / action is effective / useful</li> <li>limited evidence from single RCT or non-randomized studies</li> </ul>	<ul style="list-style-type: none"> <li>in favor of: treatment / action is effective / useful</li> <li>some conflicting evidence from single RCT or non-randomized studies</li> </ul>	<ul style="list-style-type: none"> <li>effectiveness / usefulness of treatment / action is less well established</li> <li>greater conflicting evidence from single RCT or non-randomized studies</li> </ul>	<ul style="list-style-type: none"> <li>treatment / action is NOT effective / useful or even harmful</li> <li>limited evidence from single RCT or non-randomized studies</li> </ul>
LEVEL C	<ul style="list-style-type: none"> <li>treatment / action is effective / useful</li> <li>only expert opinion, case studies, or standard of care</li> </ul>	<ul style="list-style-type: none"> <li>in favor of: treatment / action is effective / useful</li> <li>only expert opinion, case studies, or standard of care</li> </ul>	<ul style="list-style-type: none"> <li>effectiveness / usefulness of treatment / action is less well established</li> <li>only expert opinion, case studies, or standard of care</li> </ul>	<ul style="list-style-type: none"> <li>treatment / action is NOT effective / useful or even harmful</li> <li>only expert opinion, case studies, or standard of care</li> </ul>

Table 1

Active cardiac conditions that necessitate further evaluation and treatment before non-cardiac surgery

<b>Unstable coronary syndromes</b>
<ul style="list-style-type: none"> <li>unstable or severe angina</li> <li>recent myocardial infarction (within 30 days)</li> </ul>
<b>Decompensated heart failure</b>
<b>Significant arrhythmias</b>
<ul style="list-style-type: none"> <li>high-grade atrioventricular block</li> <li>symptomatic ventricular arrhythmias</li> <li>supraventricular arrhythmias with uncontrolled ventricular rate (&gt; 100 bpm at rest)</li> <li>symptomatic bradycardia</li> <li>newly diagnosed ventricular tachycardia</li> </ul>
<b>Severe valvular disease</b>
<ul style="list-style-type: none"> <li>severe aortic stenosis (mean pressure gradient &gt; 40 mm Hg, area &lt; 1 cm<sup>2</sup> or symptomatic)</li> <li>symptomatic mitral stenosis</li> </ul>

The recent ACC/AHA guidelines [8] have proposed a step-wise approach for peri-operative cardiac assessment and management of cardiac patients scheduled for non-cardiac surgery. The first step determines the urgency of the operation. In some cases, the necessity for immediate surgery is such that no time is left for further cardiac assessment and/or treatment. In such instances, adequate measures for peri-operative surveillance and treatment should be anticipated while further risk stratification and risk factor management will be planned during the postoperative period.

If there is no need for emergency surgery, the second step is to screen the patients for the presence of active cardiac conditions. These include a history of ischaemic heart disease, history of compensated or prior heart failure, history of cerebrovascular disease, diabetes mellitus, and renal insufficiency (creatinine level > 177 µmol/l). If one of these conditions is present, they should be further evaluated and, when necessary, treated. For all these conditions, the potential benefits of delaying surgery to optimize the effects of treatment must be weighed against the risk of delaying the surgical procedure. With respect to a previous recent myocardial infarction, it is recommended to wait 4-6 weeks before performing elective surgery, even if there are no adequate clinical trials on the subject. If no active cardiac conditions are present, the third step is to assess the risk of surgery (Table 2). Many surgical procedures are associated with a low risk of peri-operative complications even in high-risk patients. In such cases it is recommended to proceed with planned surgery. In the case of intermediate or high risk surgery, further assessment of the patient's physical status is indicated. The fourth step evaluates whether the patient can sustain a functional capacity equal or greater than 4 metabolic equivalents (METs) without symptoms. If so, the recommendation is to proceed with surgery. If, however, the patient is symptomatic or the functional capacity of the patient is unknown, further assessment is necessary.

**Table 2**

The risk of cardiac death and non-fatal myocardial infarction for non-cardiac operations

<b>High risk (cardiac risk &gt; 5%)</b>
<ul style="list-style-type: none"> <li>• aortic surgery</li> <li>• major vascular surgery</li> <li>• peripheral vascular surgery</li> </ul>
<b>Intermediate risk (cardiac risk 1- 5%)</b>
<ul style="list-style-type: none"> <li>• intraperitoneal and intrathoracic surgery</li> <li>• carotid endarterectomy</li> <li>• head and neck surgery</li> <li>• orthopedic surgery</li> <li>• prostate surgery</li> </ul>
<b>Low risk (cardiac risk &lt; 1%)</b>
<ul style="list-style-type: none"> <li>• endoscopic procedures</li> <li>• superficial procedures</li> <li>• cataract surgery</li> <li>• breast surgery</li> <li>• ambulatory surgery</li> </ul>

The fifth step will determine the need for further evaluation and potential treatment prior to surgery based on the presence of a number of clinical risk factors. These include a history of ischaemic heart disease, history of congestive heart failure, history of cerebrovascular disease, diabetes mellitus and a pre-operative creatinine level > 177 µmol/l. If there are no clinical risk factors, surgery can be planned. If the patient has one or two risk factors then the recommendation is to proceed to planned surgery but with adequate heart rate control. Alternatively, further assessment of the cardiac status by non-invasive testing can be considered, but only if it will change management. In high risk surgery patients with three or more risk factors, it is suggested that testing should only be considered if the results of such tests will change management. For intermediate risk surgery patients, there is insufficient data to determine the best strategy (proceed to surgery with heart rate control or perform further testing).

## Non-invasive testing

The ultimate aim of additional pre-operative testing is to provide an objective measure of functional capacity, and to identify the importance of pre-operative myocardial ischaemia and rhythm disturbances. Several non-invasive tests have been suggested to answer these questions.

### Resting 12-lead electrocardiogram

A pre-operative resting 12-lead electrocardiogram is recommended for patients with at least one clinical risk factor who will undergo vascular surgical procedures (class I, LOE:B) and for patients with known coronary heart disease, peripheral arterial disease, or cerebrovascular disease who are undergoing intermediate-risk surgical procedures (class I, LOE:C). It is considered reasonable to perform a 12-lead electrocardiogram in patients with no clinical risk factors undergoing vascular surgical procedures (class IIa, LOE: B) and in patients with at least one risk factor (class IIb, LOE:B). Pre- and postoperative resting 12-lead electrocardiograms are not indicated in asymptomatic patients undergoing low-risk surgery (class III, LOE:B).

### Non-invasive evaluation of left ventricular function

Pre-operative resting left ventricular function can be evaluated by echocardiography, radionuclide angiography or contrast ventriculography. It is reasonable to perform a pre-operative evaluation of left ventricular function in patients with dyspnoea of unknown origin, with current or prior heart failure, and in patients with worsening dyspnoea or other change in clinical status (class IIa, LOE: C). Routine peri-operative evaluation of left ventricular function is not recommended (class III, LOE: B).

### Stress testing

Pre-operative stress testing is recommended in patients with active cardiac conditions in whom non-cardiac surgery is planned and who should be evaluated and treated before surgery (class I, LOE:B) and in patients with three or more clinical risk factors and a poor functional capacity (< 4 METs) who require vascular surgery but only if it will change management (class IIa, LOE: B). It may be considered in patients with at least one to two clinical risk factors and poor functional capacity who require intermediate-risk or vascular surgery, but only if it will change management (class IIb, LOE: B). Finally, pre-operative stress testing is not considered useful in patients undergoing low-risk surgery and for patients with no clinical risk factors undergoing intermediate-risk surgery (class III, LOE: C).

In patients who can not exercise, two alternative techniques can be used to assess the importance of the coronary artery disease. One is to increase myocardial oxygen demand by increasing heart rate (with pacing or dobutamine), the other is to induce a hyperaemic response with pharmacological vasodilators such as dipyridamole or adenosine. The most commonly used imaging techniques include echocardiography and radionuclide myocardial perfusion imaging methods. While most currently applied tests have a satisfactory sensitivity and specificity, a recent meta-analysis indicated that dobutamine stress echocardiography seemed to have a positive trend towards better diagnostic performance, especially where there is valvular or left ventricular dysfunction [9]. Another application of these techniques is to evaluate in coronary artery disease patients the extent of viable myocardium, hence to identify those patients that may benefit from revascularization [10].

## **Pre-operative treatment**

### Revascularisation

The potential benefits of pre-operative coronary revascularisation remain a point of debate. Recent studies indicate that only a selected patient population may benefit from such intervention [11, 12]. The prevailing evidence suggests that the indications for pre-operative coronary revascularisation are, in fact, identical to those in the non-operative setting. The recommendations of the ACC/AHA 2007 guidelines on this issue are as follows. Coronary revascularisation is considered useful in patients with stable angina who have significant left main coronary artery disease, three-vessel disease, or two-vessel disease with a significant stenosis of the proximal left anterior descending coronary artery AND either an ejection fraction < 50% or demonstrable ischaemia on non-invasive testing (class I, LOE: A). It is also recommended in patients with unstable angina, non-ST-segment elevation myocardial infarction and those with acute ST-segment elevation myocardial infarction (class I, LOE: A). The usefulness of pre-operative coronary revascularisation is

not well established in high-risk ischaemic patients (such as in the presence of an abnormal stress echocardiograph with at least five-segments of regional wall motion abnormalities) (class IIb, LOE: C) and for low-risk ischaemic patients with an abnormal dobutamine stress echocardiography (1-4 segments) (class IIb, LOE: B). Finally, prophylactic coronary revascularisation is not recommended in patients with stable coronary artery disease (class III, LOE: B).

Once the decision for pre-operative coronary revascularisation has been taken, a choice should be made between surgery and percutaneous coronary intervention (PCI). A recent study in patients undergoing multi-vessel coronary artery revascularisation as prophylaxis for elective vascular surgery indicated that patients having coronary surgery had fewer myocardial infarctions after the vascular surgery than those having had PCI. This difference between groups was attributed to a more complete revascularisation [13].

Percutaneous coronary revascularisation with the use of stents presents another issue. Stents have been introduced to reduce the incidence of re-stenosis. To prevent early in-stent thrombosis all patients receiving a coronary stent are prescribed dual anti-platelet therapy, the duration of which depends on the type of stent used. Recently, data has indicated that with drug-eluting stents, late in-stent thrombosis may occur related to the interruption of anti-platelet therapy [14]. Approximately 5% of patients who had coronary stenting require some form of non-cardiac surgery within 1 year [15]. Since anti-platelet therapy may increase the risk of peri-operative bleeding, these drugs are usually discontinued at the time of surgery. It has been recognised that such action may have disastrous consequences for the surgical patient [16] and, therefore, specific guidelines have been developed for the management of such patients [17, 18]. With respect to potential pre-operative revascularisation by percutaneous coronary angioplasty, a strategy of balloon angioplasty or bare-metal stent placement followed by 4-6 weeks of dual anti-platelet therapy is recommended (class IIa, LOE: B). In patients who have received drug-eluting coronary stents and who need an urgent surgical procedure, necessitating the discontinuation of thienopyridine therapy, it is suggested that aspirin is continued and to restart the thienopyridine as soon as possible (class IIa, LOE: C). Elective non-cardiac surgery is not recommended within 4-6 weeks of bare-metal coronary stent implantation or within 12 months of drug-eluting coronary stent implantation in patients in whom thienopyridine therapy, or the dual therapy of aspirin and thienopyridine will need to be discontinued peri-operatively (class III, LOE: B). Finally, elective non-cardiac surgery is also not recommended within 4 weeks of balloon angioplasty (class III, LOE: B).

#### Valve repair

With regard to the indications for valvular repair before non-cardiac surgery, only limited data is available and do not allow the production of recommendations. Based on clinical experience it seems logical that in those patients with valvular disease that is severe enough to constitute an indication for surgical correction should undergo such surgery before the non-cardiac surgery. It has been suggested that a less invasive approach using balloon valvuloplasty might constitute an intermediate step in reducing the operative risk of non-cardiac surgery in these patients [19] but there are no controlled studies on this subject at present.

### **Peri-operative management**

#### Medical therapy

In recent years, a growing number of studies have indicated that optimisation of peri-operative medical therapy may result in an improved postoperative outcome. The most efficient drugs in this regard are the  $\beta$ -blocking agents and the statins.

#### $\beta$ -blockers

While numerous studies have demonstrated an improved outcome in patients receiving peri-operative  $\beta$ -blocker therapy, this has not consistently been confirmed in other studies (reviewed in ref. 20). Poldermans et al demonstrated that further cardiac testing could safely be omitted in intermediate-risk patients, as long as  $\beta$ -blockers were prescribed and titrated to achieve tight heart rate control [21]. The safety of peri-operative  $\beta$ -blockade has recently been questioned with the publication of the results of the POISE trial [22]. This study showed a beneficial effect of high-dose controlled-release metoprolol therapy on the risk of peri-operative myocardial infarction, but at the cost of an increased risk of stroke and overall mortality. It seems, however, that the time of initiation and dose of  $\beta$ -blocker therapy, dose adjustments for tight heart rate control, and correct estimation of the underlying cardiac risk of the individual patient are important factors in determining the effectiveness of the therapy [23, 24].

The ACC/AHA 2007 guidelines recommend continuing  $\beta$ -blocker therapy in patients who are already on such medication (class I, LOE: C).  $\beta$ -blockers should also be given to patients undergoing vascular surgery who are at high cardiac risk because of the presence of ischaemia on pre-operative testing (class I, LOE: B).  $\beta$ -blockers are probably recommended for vascular surgery patients in whom pre-operative assessment has indicated the presence of coronary heart disease, and for patients undergoing intermediate or high risk surgery in the presence of high cardiac risk ( $> 1$  clinical risk factor) (class IIa, LOE: B). The benefit of  $\beta$ -blocker therapy is uncertain in patients with only a single risk factor undergoing intermediate- or high risk surgery (class IIB, LOE: C) and in high risk surgery patients with no clinical risk factors and not on  $\beta$ -blocker therapy (class IIb, LOE: C). Finally,  $\beta$ -blockers should not be given in patients with absolute contra-indications to their use.

### Statins

Statins were initially prescribed because their lipid-lowering properties which seem highly effective in the secondary prevention of cardiac events [25]. However, statins have other beneficial properties on atherosclerotic vascular disease, which are known as its pleiotropic effects [26]. These include plaque stabilization, oxidative stress reduction and decreased vascular inflammation. Trials in coronary artery disease patients have shown a beneficial effect of statin therapy on outcome (reviewed in refs. 20 and 24). More recently, these positive effects have also been observed in patients undergoing major non-cardiac surgery with a significant reduction in postoperative cardiovascular morbidity and mortality [27-32].

The ACC/AHA guidelines recommend statins be continued for all patients scheduled for non-cardiac surgery and currently taking this medication (class I, LOE: B). For patients with or without clinical risk factors undergoing vascular surgery, statins are considered reasonable (class IIa, LOE: B). For patients with at least one clinical risk factor scheduled for intermediate-risk surgery, statin therapy can be considered (class IIb, LOE: C).

### Others

Aspirin (acetylsalicylic acid) has a key role in the primary and secondary prevention of cardiovascular disease and it is commonly used, in association with clopidogrel, for the prevention of coronary stent thrombosis. Its potential beneficial effect in the peri-operative period of non-cardiac surgery is less well established. Concerns with regard to peri-operative bleeding have been a frequent reason to interrupt this therapy. In a recent meta-analysis it was shown that although aspirin increased the risk of bleeding complications, this did not lead to a greater severity of bleeding [33]. It was suggested that aspirin should only be discontinued if it may cause bleeding risks associated increased mortality or if the sequelae are similar in magnitude to the expected cardiovascular risks of aspirin withdrawal. A recent meta-analysis on the hazards of discontinuing or not adhering to aspirin among 50 279 patients at risk for coronary artery disease demonstrated that non-adherence or withdrawal was associated with a three-fold greater risk of major cardiac events [34].

$\alpha_2$ -agonists have been shown to reduce peri-operative mortality and myocardial infarction during vascular and other major non-cardiac surgery [35, 36]. It is recommended that use of  $\alpha_2$ -agonists for peri-operative control of hypertension may be considered for surgical patients with known coronary artery disease or at least one clinical risk factor (class IIb, LOE: B). They should not be given to patients with contra-indications to this medication (class III, LOE: C).

The potential beneficial effects of peri-operative calcium channel blocker therapy remain to be established. A meta-analysis of 11 studies involving 1007 patients showed a reduction in myocardial ischaemia and supraventricular tachycardia with calcium channel blockers and a trend towards reduced death and myocardial infarction. These effects were mainly observed with diltiazem, whereas dihydropyridines and verapamil did not decrease the incidence of myocardial ischemia [37].

### Peri-operative monitoring

#### ST-segment monitoring

The presence of perioperative ST-segment changes has been associated with cardiac morbidity and mortality in patients undergoing non-cardiac surgery. Intra- and postoperative ST-segment monitoring with computerised ST-segment analysis is useful for patients with known coronary artery disease or those undergoing vascular surgery (class IIa, LOE: B). It may also be used in patients with one or more risk factors for coronary artery disease (class IIb, LOE: B).

### Pulmonary artery catheter

Peri-operative use of a pulmonary artery catheter (PAC) remains a controversial issue. While significant information can be obtained from its use, no differences have been observed in survival or cardiovascular morbidity compared with standard care in patients undergoing major non-cardiac surgery [38]. Use of PACs is reasonable in patients at risk for major haemodynamic disturbances. However, the decision to use a PAC must be based on careful assessment of the patient's disease, the surgical risk and the practitioner's experience in use of this modality (class IIb, LOE: B). The decision should take in to account the potential complications associated with their use [39].

### Trans-oesophageal echocardiography

The use of trans-oesophageal echocardiography (TOE) is widely accepted in cardiac surgery. However, to date there is insufficient evidence to support its routine use as a diagnostic monitor or to guide therapy during non-cardiac surgery. The emergency use of intra-operative or perioperative TOE, however, is considered reasonable in order to determine the cause of an acute life-threatening haemodynamic abnormality (class IIa, LOE: C).

### Blood glucose concentration

The impact of tight control of blood glucose concentration on peri-operative morbidity and mortality has been the subject of several recent studies. It has been suggested that control of blood glucose concentrations to < 8 mmol.l in the peri-operative period may improve outcome and minimise the risk of severe hypoglycaemia in anaesthetised patients [40, 41]. The American College of Endocrinology recommends that preprandial glucose should be less than 6 mmol.l, maximal glucose should not exceed 10 mmol.l and in the intensive care unit, blood glucose concentration should be controlled to less than 6 mmol.l. [42].

The ACC/AHA guidelines recommend peri-operative control of blood glucose concentrations in patients with diabetes mellitus or acute hyperglycaemia who are at high risk for myocardial ischaemia or who are undergoing vascular and major non-cardiac surgery with planned admission to the ICU (class IIa, LOE: B). However, the usefulness of strict peri-operative blood glucose control is uncertain in patients with diabetes mellitus or acute hyperglycaemia undergoing non-cardiac surgery but without planned admission to the ICU (class IIb, LOE: C).

### Anaesthetic management

Neuraxial anaesthetic techniques can result in sympathetic blockade and cause a decrease in preload and afterload. Although initially some randomised controlled trials suggested that the use of a neuraxial technique might have beneficial effects on outcome, this data has not been unequivocally confirmed in more recent studies on larger patient populations. The use of thoracic epidural analgesia in coronary artery bypass surgery was associated with less pulmonary complications but did not decrease the incidence of myocardial infarction or overall mortality [43]. A randomised trial in 1021 patients compared the impact on outcome of general anaesthesia with opioid analgesia and combined general-epidural anaesthesia and analgesia in intra-abdominal aortic, gastric, biliary, and colonic surgery. There were no overall differences in death or major complications. However, in a subgroup of patients undergoing aortic surgery, the incidence of myocardial infarction was lower [44]. The Multicenter Australian Study of Epidural Anesthesia randomised 915 patients undergoing major intra-abdominal surgery to either general anaesthesia or combined general and epidural anaesthesia and analgesia. Although, there was a modestly improved pulmonary outcome in the patients allocated to the epidural group, no differences were observed in the incidence of death or cardiovascular events between both groups, even in patients who underwent aortic surgery [45]. In a recent meta-analysis which included a large number of non-cardiac surgery patients, Liu et al concluded that, to date, there is insufficient evidence to confirm (or deny) that postoperative analgesic techniques affect major post-operative morbidity and mortality. [46].

In recent years, increasing evidence has indicated that volatile anaesthetic agents may have cardioprotective properties. In the setting of coronary artery surgery, the use of these drugs has been shown to be associated with a better preservation of postoperative myocardial function and less evidence of postoperative myocardial damage (reviewed in ref. 47). As far as non-cardiac surgery is concerned, there are no randomised trials that have compared the effects of different anaesthetic agents on outcome. Recently, a retrospective analysis was performed on data of a phase II study that compared the Na<sup>+</sup>/H<sup>+</sup> exchanger type I inhibitor, zonisipride with placebo on the incidence of cardiac events in 784 high-risk patients scheduled for urgent or elective major arterial vascular surgery.

The type of anaesthesia was retrospectively retrieved from the database and patients were subdivided in two groups: inhalational vs. non-inhalational anaesthetic regimen. The incidence of postoperative cardiac events was no different between the two groups and maximum postoperative troponin I levels were similar in both groups in the total population and in the patients undergoing peripheral arterial surgery. In patients undergoing aortic surgery the incidence of elevated troponin levels greater than 1.5 and 4 ng.ml<sup>-1</sup> tended to be lower in the inhalational vs. the non-inhalational group in the aortic surgery (28 % vs. 18 % and 30% vs. 20 %, respectively) but this difference did not reach statistical significance. The authors suggested that potential beneficial effects on the extent of postoperative myocardial damage in high risk patients undergoing arterial surgery will probably be more apparent in abdominal aortic surgery than in peripheral vascular surgery and that further sufficiently powered studies using a standardised protocol were necessary to definitively address this question [48]. The ACC/AHA guidelines give a class IIa, LOE: B recommendation for the use of volatile anaesthetic agents during non-cardiac surgery in haemodynamically stable patients at risk for myocardial ischaemia.

Other measures used in the peri-operative period that may help to improve outcome include maintenance of normothermia [49] and adequate peri-operative pain management.

### Postoperative surveillance

Postoperative myocardial ischaemia is a strong predictor of peri-operative cardiac morbidity. Since its occurrence is not necessarily accompanied by pain, it may remain untreated until overt symptoms of cardiac failure occur. A peri-operative myocardial infarction is associated with a 30-50% peri-operative mortality and reduced long-term survival [50, 51]. Therefore, accurate diagnosis is essential.

Peri-operative myocardial infarction can be documented by assessing clinical symptoms, serial electrocardiograms, cardiac-specific biomarkers, comparative ventriculographic studies, and radioisotopic or magnetic resonance studies. Measurements of troponin T or I have been shown to indicate myocardial damage with smaller degrees of injury [52]. However, studies on the predictive value of elevated cardiac troponin levels for long-term outcome show variable results with some studies indicating a close association with intermediate and long-term cardiovascular morbidity and mortality [53-55], whereas other are less clear cut [56].

Currently, there seem to be no standard criteria for the diagnosis of peri-operative myocardial infarction in patients undergoing non-cardiac surgery. Although the use of sets of criteria [57], reflecting the unique features of peri-operative myocardial infarction, may improve the diagnosis, a routine cardiac specific troponin measurement is not recommended. The 2007 ACC/AHA guidelines recommend postoperative troponin measurement in patients with ECG changes or chest pain typical of the acute coronary syndrome (class I, LOE: C). However, its measurement is not well established in patients who are clinically stable and have undergone vascular and intermediate-risk surgery (class IIb, LOE: C) and is not recommended in asymptomatic stable patients who have undergone low-risk surgery (class III, LOE: C). Recently, assessment of pro-B-type natriuretic peptide is gaining interest as a predictor of adverse events and outcome after non-cardiac surgery [58, 59].

### **Conclusions**

Patients undergoing non-cardiac surgery are at risk of major peri-operative cardiac events. Recognition of this risk may greatly influence outcome after such surgery and over the years guidelines have been developed in order to help for better care of these patients. However, adherence to such guidelines may critically depend on the convenience of its use in clinical practice. Recently, Hoeks et al [60] determined the adherence to the 2002 ACC/AHA guidelines [61] and reported disappointing results. There seemed to be poor agreement between these guidelines and daily clinical practice. Only 21% of patients underwent non-invasive testing when recommended. In addition, patients who did not have additional testing despite recommendations received as little cardiac management as did those patients in the low-risk population. This implies that despite the existence of well-defined guidelines, high-risk patients do not get the peri-operative management they need. This study poses a number of interesting questions. Are the guidelines too complex to be followed or are patients treated with  $\beta$ -blockers, statins, and anti-platelet drugs considered to be maximally protected already, so that further testing is not considered necessary [62]? While this remains an open question, it has to be acknowledged that the 2007 ACC/AHA guidelines on peri-operative cardiovascular evaluation and care for non-cardiac surgery are substantially simpler with less intermediate steps in the decision tree than the 2002 guidelines.

In general, pre-operative testing should allow optimal preparation of the patient for the period of surgery in order to improve the peri-operative outcome. However, it must be remembered that the use of non-invasive and certainly invasive additional testing should be limited to those instances in which the results of these tests will indeed change patient management.

### Key Learning Points

- A structured five step approach allows the identification of those patients who necessitate further cardiac assessment before non-cardiac surgery
- The prevailing evidence suggests that the indications for pre-operative revascularisation are the same as those in the non-operative setting
- Current  $\beta$ -blocker and statin therapy should be continued during the peri-operative period
- To date there is no hard evidence that the choice for a particular anaesthetic technique affects outcome after surgery, provided stable haemodynamics are preserved

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