Chapter 1

Ischaemic Heart Disease

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Key Points

- Perioperative risk is determined predominantly by patient-specific factors. The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) model or the Revised Cardiac Risk Index (RCRI) are recommended for cardiac perioperative risk stratification.
- Patients who cannot perform >4 metabolic equivalents (METs) of work during activities of daily living have an increased risk.
- A resting electrocardiogram should be performed in symptomatic patients with (CAD) coronary artery disease and in asymptomatic CAD patients who require intermediate- or high-risk surgery.
- Stress testing for myocardial ischaemia and assessment of left ventricular function should be considered for patients with stable CAD, requiring non-emergency surgery, who have low functional capacity and intermediate or high risk for perioperative events.
- Preoperative angiography and coronary revascularisation are recommended in stable patients with extensive myocardial ischaemia and/or severe angina despite adequate medical therapy.
- The primary aim of coronary revascularisation is to relieve symptoms and improve long-term prognosis rather than perioperative risk.
- In the absence of a coronary stent, routine perioperative aspirin therapy is not indicated, but continuation may be reasonable in patients with CAD or cerebrovascular disease when the risk of perioperative bleeding is not high.
- In general, elective non-cardiac surgery should not be performed within 4 weeks after bare metal stent implantation or within 12 months after drug-eluting stent implantation in patients in whom dual antiplatelet will need to be discontinued perioperatively. With contemporary stents, the risk of stent thrombosis during non-cardiac surgery appears to be low beyond 6 months from implant.
- Routine use of perioperative beta-blockers for all CAD patients is not indicated.

Coronary artery disease (CAD) is an important determinant of perioperative mortality and morbidity related to non-cardiac surgery. There is no widely accepted definition of post-operative cardiac morbidity, and hence event rates, to a large extent, depend on the definition used in any given dataset. In an international prospective study in 15,133 patients aged 45 years or older, requiring at least an overnight hospital admission after non-cardiac surgery, cardiac troponin T (TnT) levels were measured 6 to 12 hours after surgery and on days 1, 2 and 3. Isolated troponin elevation (>0.02 ng/mL) was present in 11.6 per cent of patients. The 30-day mortality rate was 1.9 per cent (95% CI, 1.7%–2.1%). Multivariable analysis demonstrated that peak TnT values were associated with higher 30-day mortality compared with those without an elevation in TnT (Devereaux et al., 2012).

Risk Prediction

Age is an important determinant of perioperative risk due, in part, to the increased prevalence of CAD and cardiovascular risk factors, especially diabetes mellitus. In addition, frailty, a measure of cognitive and functional status in the elderly, has been associated with adverse post-operative outcomes (Dasgupta et al., 2009). In a study of 125 patients at least 70 years of age undergoing non-cardiac (82% had orthopaedic procedures) surgery, increasing frailty was associated with post-operative complications, increased length of hospitalisation and inability to be discharged home, independent of age. Please see also Chapter 14.

Patients with unstable angina and a history of a recent myocardial infarction (MI) have a high

perioperative risk (Shah et al., 1990). The risk decreases over time and is modified by the coronary revascularisation. The data suggest that a gap of ≥8 weeks is required after an MI before non-cardiac surgery risk is minimised, especially if coronary revascularisation is not performed (Livhits et al., 2011b).

The impact of prior coronary artery bypass grafting (CABG) on outcomes over a 10-year follow-up period has been retrospectively analysed in 3368 patients undergoing non-cardiac surgery in the Coronary Artery Surgery Study (CASS) database (Eagle et al., 1997). Abdominal, vascular, thoracic and head and neck surgery had a combined MI/death rate among patients with non-revascularised coronary disease of greater than 4 per cent. Among 1961 patients undergoing higher-risk surgery, prior CABG was associated with fewer post-operative deaths (1.7% versus 3.3%, p = 0.03) and MI (0.8% versus 2.7%, p = 0.002) compared with medically managed CAD. In contrast, 1297 patients undergoing urologic, orthopaedic, breast and skin operations had mortality of less than 1 per cent regardless of prior coronary treatment. Prior CABG was most protective in patients with advanced angina and/or multi-vessel coronary artery, depressed left ventricular function, as well as in those undergoing high-risk surgery, and the benefit lasted for at least 6 years. These data must be interpreted in light of the fact that they are more than 2 decades old and are not reflective of contemporary medical therapy for CAD. Nonetheless, one interpretation of the data is that stable and asymptomatic patients who have had CABG within the prior 6 years are relatively protected and may proceed with their operation without routine preoperative stress testing. However, this cannot be extrapolated to patients with significantly impaired cardiac function post CABG.

Patients with a prior history of percutaneous coronary intervention (PCI) represent an important group that requires detailed preoperative assessment as they may be at increased perioperative risk, especially in cases of unplanned or urgent surgery following coronary stenting. It has been generally recommended that elective surgery be deferred for 12 months after drug-eluting stent implantation in order to allow adequate stent endothelialisation (Assali et al., 2009). Recent data from studies of patients who have second-generation drug-eluting stents, which have improved biological properties, suggest that the risk of stent thrombosis may be low beyond 6 months following implantation (Feres et al., 2013; Hawn et al., 2013; Wijeysundera et al., 2012). In patients with bare metal stents, it is recommended that elective procedures should be deferred for at least 4 weeks, and ideally 3 months following the PCI. For the occasional patient who has had recent balloon angioplasty without a stent, the operation should be delayed for at least 2 weeks after the PCI.

Although patient-specific factors are more important than surgery-specific factors in predicting cardiac risk, the type of surgery is an important consideration. Surgical procedures can be divided into low, intermediate and high risk with estimated 30-day cardiac event rates (cardiac death and MI) of <1 per cent, 1–5 per cent and >5 per cent, respectively (Table 1.1).

Table 1.1 Surgical risk estimate according to type of surgery or intervention. Kristensen et al. *Eur Heart J* 2014;35:2383–2431. Reprinted with permission from Oxford University Press.

Low-risk: <1%	Intermediate-risk: 1–5%	High-risk: >5%
• Superficial surgery • Breast • Dental • Endocrine: thyroid • Eye • Reconstructive • Carotid asymptomatic (CEA or CAS) • Gynaecology: minor • Orthopaedic: minor (meniscectomy) • Urological: minor (transurethral resection of the prostate)	• Intraperitoneal: splenectomy, hiatal hernia repair, cholecystectomy • Carotid symptomatic (CEA or CAS) • Peripheral arterial angioplasty • Endovascular aneurysm repair • Head and neck surgery • Neurological or orthopaedic: major (hip and spine surgery) • Urological or gynaecological: major • Renal transplant • Intra-thoracic: non-major	• Aortic and major vascular surgery • Open lower limb revascularisation or amputation or thromboembolectomy • Duodeno-pancreatic surgery • Liver resection, bile duct surgery • Oesophagectomy • Repair of perforated bowel • Adrenal resection • Total cystectomy • Pneumonectomy • Pulmonary or liver transplant

Legend: CEA = carotid endarterectomy, CAS=carotid artery stenting, %=per cent

Operations without significant fluid shifts or physical stress have the lowest risk. These estimates do not take into account the patient's co-morbidities. Emergency and urgent operations carry a greater risk compared to elective procedures. In emergency procedure (e.g. major trauma, ruptured abdominal aortic aneurysm, perforated viscus), cardiac evaluation will not change the need for surgical intervention, but may modify immediate perioperative management. In urgent surgical procedures (e.g. critical limb ischaemia or bowel obstruction), the benefits of surgery outweigh the cardiac risk, and in these cases, cardiac assessment may again influence the perioperative management. Occasionally, high cardiac risk may influence the choice of intervention and lead to a percutaneous/less-invasive procedure (e.g. peripheral arterial angioplasty instead of infra-inguinal bypass). In non-emergency surgical procedures, the cardiac evaluation assists in the decision between intervention (e.g. for carotid endarterectomy or abdominal aneurysm repair) or conservative management.

The clinical history, physical examination and 12-lead electrocardiogram identifies the majority of patient-specific clinical risk factors which, combined with the inherent risk associated with the surgical procedure, can be used to estimate the perioperative risk of adverse cardiac events. A validated risk-prediction tool, of which there are several, can be helpful in preoperative risk stratification. Older risk assessment models such as the original Goldman cardiac risk index (Goldman et al., 1977), the Detsky modified risk index (Detsky et al., 1986) or the Eagle criteria (Eagle et al., 1989) are no longer recommended as they do not reflect contemporary practice.

The Revised Cardiac Risk Index (RCRI), based on six criteria (Table 1.2), is an easy-to-use and widely accepted tool to assess perioperative risk of major cardiac complications such as MI, pulmonary oedema, ventricular fibrillation or cardiac arrest and complete heart block (Lee et al., 1999). Patient with 0 or 1 risk factor have a low risk of major adverse cardiovascular events (MACE), such as myocardial infarction and death, while those with ≥2 have an increased risk. The RCRI performs reasonably well in all types of non-cardiac surgery, but is less accurate in patients undergoing vascular surgery. RCRI also appears not to be accurate for predicting all-cause mortality, likely due to the fact that it does not include risk factors for non-cardiac causes of perioperative mortality (Ford, Beattie and Wijeysundera, 2010).

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) Myocardial Infarction or Cardiac Arrest (MICA) risk-prediction model has been devised more recently and appears to have superior discrimination compared to the RCRI, especially in patients requiring vascular surgery (Bilimoria et al., 2013; Gupta et al., 2011). Using inguinal hernia surgery as the reference, the risk tool provides adjusted odds ratio for MI or cardiac arrest for a variety of surgical procedures. The risk of these complications in the derivation cohort of more than 200,000 patients undergoing surgery was 0.65 per cent. Independent predictors of adverse event were age, abnormal creatinine, dependent functional status, American Society of Anesthesiologists' (ASA) physical status and the type of surgery. An online calculator is available at www.surgicalriskcalculator.com/miorcardiacarrest.

This risk calculator is a tool consisting of 20 patient factors plus the surgical procedure. Although the ACS NSQIP is more comprehensive than the other risk calculators, it is more complex, which may limit its use. The calculator has not yet been externally validated. Despite this, the NSQIP model or the RCRI is recommended for cardiac perioperative risk stratification.

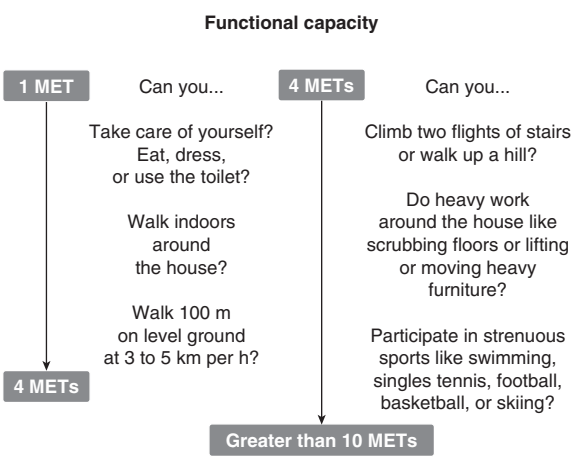
Table 1.2 Clinical risk factors according to the revised cardiac risk index. (Lee et al. Circulation 1999;100:1043–9)

Ischaemic heart disease (angina pectoris and/or previous myocardial infarction)
Heart failure
Stroke or transient ischaemic attack
Renal dysfunction (serum creatinine >170 umol/L or 2 mg/dL or a creatinine clearance of <60 mL /min/ 1.73 m^2)
Diabetes mellitus requiring insulin therapy
Undergoing suprainguinal vascular, intraperitoneal or intrathoracic surgery

Legend: umol/L =micromole per litre, mg/dL =milligram per decilitre, mL/min/ 1.73 m^2 = millilitre per minute per 1.73 square metre
umol = micromole, L= litre, mg=milligram, dL=decilitre, mL=millilitre, min=minute, m^2= metre square

Functional Status and Perioperative Risk

A patient's capacity for physical activity is a good risk marker for adverse cardiac events. Patients with good preoperative functional status are at lower risk while those with diminished functional status are at increased risk. In general, highly functional asymptomatic patients can proceed with surgery without cardiovascular testing. Activities of daily living can provide a reasonable estimate of functional status, and can be measured in terms of metabolic equivalents (METs) (Figure 1.1). Basal resting oxygen consumption is 1 MET for a 40–year-old, 70-kg man. A widely accepted grading for functional capacity is excellent (>10 METs), good (7–10 METs), moderate (4–6 METs), poor (<4 METs) or unknown. Patients who cannot perform more than 4 METs of work during activities of daily living have an increased risk. Examples of activities associated with >4 METs are climbing a flight of stairs, walking on level ground at 4 mph, walking up a hill and performing heavy work around the house. More formal assessment may be performed using the Duke Activity Status Index (Hlatky et al., 1989) and the Specific Activity Scale (Goldman et al., 1981). In a study of 600 consecutive patients undergoing non-cardiac surgery, poor functional status (defined as the inability to walk four blocks or climb two flights of stairs) was associated with perioperative myocardial ischaemia and cardiovascular events, even after adjustment for other risk factors (Reilly et al., 1999). The probability of a serious complication was inversely related to the functional capacity. More recent data from the NSQIP database have demonstrated that dependent functional status, defined as the need for assistance with activities of daily living, is also associated with an increased risk of perioperative morbidity and mortality (Tsiouris et al., 2012).

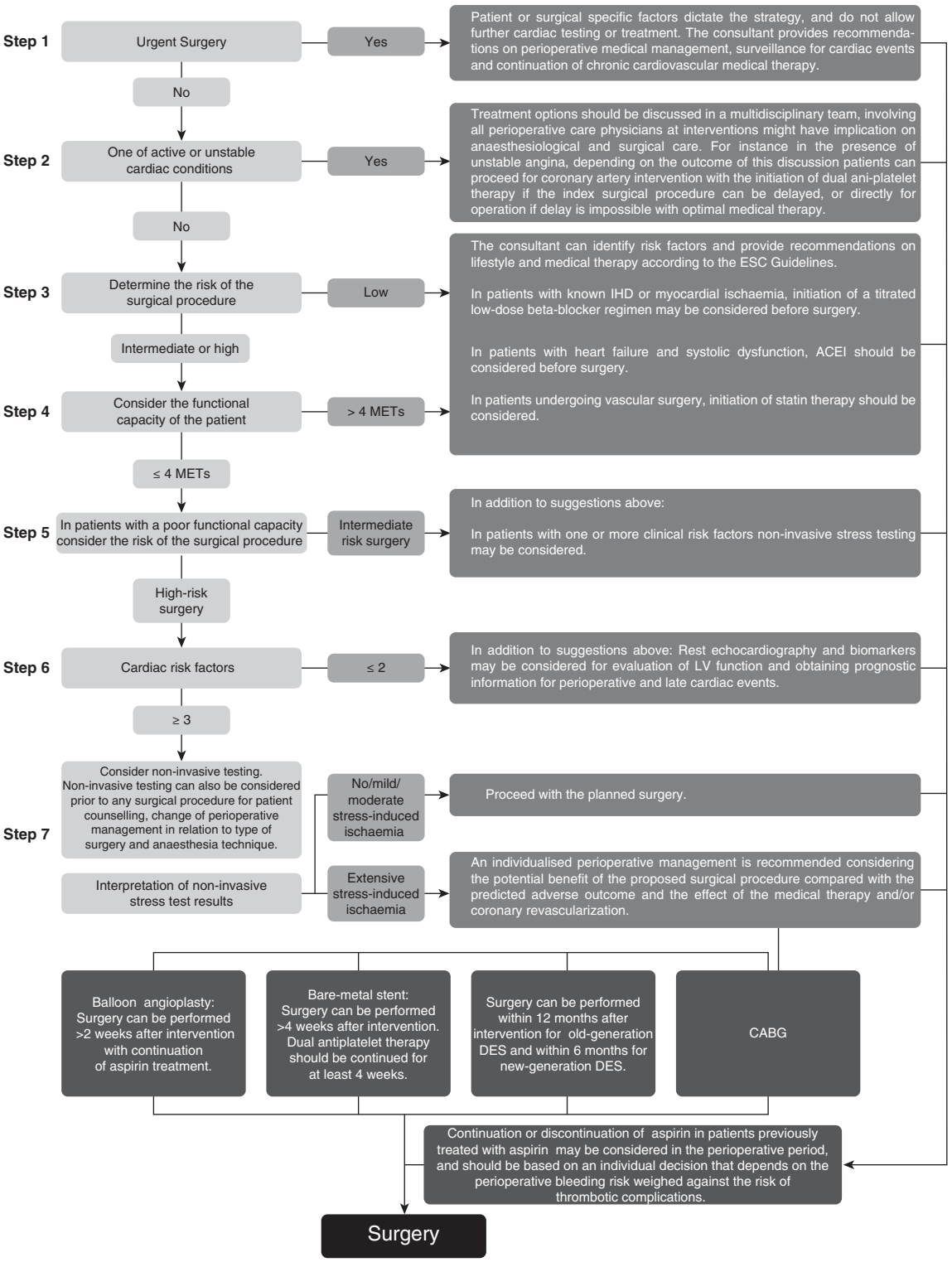


Legend : METs = metabolic equivalent, m = metre, km = kilometre, h = hour

Figure 1.1 Estimated functional capacity and energy requirements of daily activities. Kristensen et al. Eur Heart J 2014;35:2383–2431. Reprinted with permission from Oxford University Press.

Stepwise Approach to Perioperative Cardiac Assessment in Coronary Artery Disease

The European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA) guidelines have outlined a stepwise approach to perioperative cardiac assessment (Kristensen et al., 2014) (Figure 1.2). A similar approach has been recommended by the joint task force of the American College of Cardiology (ACC) and the American Heart Association (AHA) (Fleisher et al., 2014). The following recommendations broadly follow this general approach. In patients with risk factors for or known CAD, *step one* is to establish the urgency of the operation. In an emergency, the procedure cannot be deferred, and hence the surgical team must determine the clinical risk factors that potentially may influence perioperative management, and surgery is undertaken with appropriate monitoring and management to mitigate the risk. *Step two and subsequent steps* relate to non-emergency operations, and at this stage it is important to establish whether the CAD is stable, based on the history, ECG and biomarkers. Cardiology assessment and management are required if an acute coronary syndrome is present. *Step three* is to risk-stratify stable patients using a validated risk-scoring system, as described earlier, that combines patient and surgical variables to estimate the likelihood of perioperative MACE. The aim of risk stratification is to identify patients with low cardiac risk who can be operated on safely without further assessment since it is unlikely that risk-reduction strategies will reduce the perioperative risk further. Moreover, risk reduction with pharmacological treatment is most cost-effective in patients with increased cardiac risk. Patients with a low risk of MACE (<1%) may proceed to surgery without further testing. For patients with an elevated risk of MACE, *step four*



Legend : ESC = European Society of Cardiology, ACEI = angiotensin converting enzyme inhibitor, LV = left ventricle, DES = drug eluting stent, CABG = coronary artery bypass graft, MET= metabolic equivalent

Figure 1.2 Summary of perioperative cardiac risk evaluation and management. Kristensen et al. *Eur Heart* J 2014;35:2383–2431. Reprinted with permission from Oxford University Press.

involves an objective assessment of the patients' functional capacity using a scale (Figure 1.1). For patients with a functional capacity of >4 METs, it is reasonable to proceed with surgery without further evaluation. *Step five* relates to patients who have a low (<4 METs) or unknown functional capacity. In these patients, a decision needs to be reached as to whether further testing will impact management (e.g. decision to perform the non-cardiac surgery or willingness to undergo coronary revascularisation, depending on the results of the test) or perioperative care. If yes, then stress testing may be considered. Often, this would be a pharmacological stress test, but in patients with unknown functional capacity, exercise stress testing may be reasonable to perform. Stress testing is particularly indicated in patients with three or more risk factors (see Table 1.2). If stress testing is unlikely to change management, then the patient may proceed directly to surgery or a discussion regarding alternative strategies, such as non-invasive treatments or palliation, may be appropriate. Coronary angiography and revascularisation should be considered if the stress test is abnormal, especially if there is extensive inducible ischaemia.

Preoperative Investigations for Coronary Artery Disease

The presence of left ventricular dysfunction and myocardial ischaemia are the major cardiac determinants of risk in patients with CAD. Non-invasive testing is performed to detect these abnormalities in patients who are stable and require non-emergency operations in order to guide management (e.g. appropriate surgical and anaesthetic techniques, patient counselling), and determining long-term prognosis. A risk-based approach is required since routine assessment for the presence of left ventricular dysfunction and myocardial ischaemia is not indicated before non-cardiac surgery.

A 12-lead electrocardiogram is frequently performed as part of preoperative cardiovascular risk assessment. Abnormalities on the electrocardiogram are predictive of outcomes, independent of clinical findings and perioperative ischaemia (Jeger et al., 2006). However, the resting electrocardiogram has limited sensitivity to detect obstructive CAD. The predictive value increases with the patient's age and with the presence of risk factors for CAD. However, a standard age or risk factor burden cut-off for recommending a preoperative electrocardiogram has not been established. Obtaining a recording in symptomatic patients with CAD is within standard practice. In asymptomatic individuals, an electrocardiogram is recommended for those with an established diagnosis of CAD or one or more CAD risk factors who require intermediate- or high-risk surgery. The optimal time interval between obtaining the electrocardiogram and the operation is unknown, but there is some agreement that an interval of 1 to 3 months is adequate for stable patients.

Routine assessment of left ventricular function is not recommended due to its limited incremental predictive value for detecting severe CAD and perioperative risk, over and above clinical risk factors (Halm et al., 1996). However, it may be performed, usually by echocardiography, in patients with symptoms of myocardial dysfunction, and asymptomatic patients with high surgical risk.

Stress tests are helpful in non-invasively diagnosing and risk-stratifying CAD. There is a correlation between the extent of inducible ischaemia and perioperative outcome such that those who have a positive stress test at low exercise workloads have significantly increased risk of perioperative and long-term cardiac events. Conversely, onset of myocardial ischaemia at high workloads is associated with only a small increase in risk, compared to a normal test. Although exercise stress is generally preferred, since it facilitates estimation of functional capacity, most patients in whom preoperative stress testing is indicated cannot exercise adequately to achieve a target heart rate. Many have abnormal resting electrocardiograms such that pre-existing ST-segment abnormalities at rest may preclude analysis of the stress electrocardiogram. Thus, a pharmacological (e.g. adenosine, dobutamine etc.) stress test with cardiac imaging (e.g. echocardiogram, nuclear perfusion imaging) is recommended in patients with limited exercise tolerance or abnormal resting electrocardiograms. These studies can detect the presence and severity of inducible ischaemia as well as prior myocardial infarction. The incremental value of dobutamine stress echocardiography in the assessment of cardiac risk prior to non-vascular surgery has been reported in a study of 530 patients (Das et al., 2000). An ischaemic threshold of <60 per cent of the age-predicted maximal heart rate was found to be an independent predictor of adverse post-operative cardiac events. A negative stress echocardiogram is associated with a low incidence of cardiac events post-operatively; however, in current practice, the

positive predictive value for events following surgery is relatively low. In a meta-analysis of 10 studies investigating dipyridamole thallium-201 imaging prior to vascular surgery, the 30-day cardiac death or non-fatal myocardial infarction rates were 7 per cent in patients with fixed defects, 9 per cent in patients with inducible ischaemia compared to 1 per cent in patients with a normal stress test imaging. There was a higher incidence of cardiac events in patients with two or more reversible defects (Shaw et al., 1996). As with stress echocardiography, the negative predictive value of a normal perfusion stress test is high, but the positive predictive value of a reversible perfusion defect is relatively low. The aforementioned meta-analysis also compared dipyridamole thallium-201 imaging and dobutamine stress echocardiography for risk stratification in patients requiring vascular surgery. The prognostic value for perioperative ischaemic events of both modalities was found to be similar (Shaw et al., 1996). In general, diagnostic accuracy of these tests is reduced if the test is used in patients with low pre-test probability of CAD and high in those with a high pre-test probability. Thus, selective use of stress tests is advocated in scenarios where the findings may influence perioperative management. It is recommended for high- and intermediate-risk surgery in patients with poor functional capacity (<4 METs), especially in the presence of more than two of the clinical risk factors (see Table 1.2). The finding of extensive stress-induced ischaemia represents a high-risk group who should be considered for angiography.

Few patients require coronary angiography and revascularisation prior to non-cardiac surgery. There is a paucity of data from randomised clinical trials on its usefulness in patients scheduled for non-cardiac surgery. Caution must be exercised given the inherent risks of invasive procedures, and the potential for unwarranted delay in the operation. Preoperative angiography is recommended in stable patients with extensive myocardial ischaemia and/or severe angina (Canadian Cardiovascular Society Class III–IV), despite adequate medical therapy requiring non-emergency, non-cardiac surgery. Prompt coronary angiography is also recommended for patients with non-ST-elevation acute coronary syndromes requiring non-emergency operations, other than those with a low-cardiac-risk profile. The decreased risk of coronary computerised tomography angiography compared with invasive angiography seems attractive; however, data are limited on this imaging modality for preoperative risk stratification, and its role remains uncertain (Ahn et al., 2013). For details of coronary computerised tomography angiography please refer to Chapter 5 D and E.

Preoperative Coronary Revascularisation

The majority of fatal perioperative myocardial infarctions occurs in patients with significant three vessel and/or left main disease (Dawood et al., 1996). The presence of one or more of the following features of plaque instability, rupture, plaque haemorrhage or intraluminal thrombus, is detected in approximately half the cases. Thus, the pathophysiology of fatal perioperative myocardial infarctions is similar to that occurring in the absence of non-cardiac surgery. A combination of low flow and high demand leads to ischaemia in the presence of obstructive CAD, which, together with plaque instability, likely contributes to the underlying substrate.

Current guidelines recommend that the decision to perform myocardial revascularisation should be based on standard management of CAD (Table 1.3). The timing of revascularisation depends on whether CAD is stable or unstable, and whether PCI versus CABG is required depending on the severity of CAD, as well as the technical feasibility of the two types of revascularisation. The primary aim of revascularisation is to relieve symptoms and improve long-term prognosis in patients with obstructive CAD rather than perioperative risk.

Limited data are available on the efficacy of revascularisation prior to non-cardiac surgery, but a few trials provide useful insights. In the Coronary Artery Revascularisation Prophylaxis (CARP) trial, patients with stable CAD requiring elective major vascular surgery were randomised to either optimal medical therapy or revascularisation (CABG or PCI) (McFalls et al., 2004). The study was conducted in 18 Veterans' Affairs medical centres from which 510 (9%) of 5859 patients scheduled for vascular operations were enrolled. The indications for a vascular operation were an expanding abdominal aortic aneurysm (33%) or occlusive arterial disease of the legs (67%). Coronary angiography was recommended for eligible patients if a cardiology consultant considered the patient at increased risk for a perioperative cardiac complication. Guidelines for coronary angiography were provided for each site on the basis of combined

Table 1.3 Indications for revascularisation in patients with stable angina or silent ischaemia. Windecker et al. *Eur Heart J* 2014;35:2541–2619. Reprinted with permission from Oxford University Press.

Extent of CAD (anatomical and/or functional)		Class[b]	Level[c]
For prognosis	Left main disease with stenosis >50%[a]	I	A
	Any proximal LAD stenosis >50%[a]	I	A
	Two-vessel or three-vessel disease with stenosis >50%[a] with impaired LV function (LVEF <40%)[a]	I	A
	Large area of ischaemia (>10% LV)	I	B
	Single remaining patent coronary artery with stenosis >50%[a]	I	C
For symptoms	Any coronary stenosis >50%[a] in the presence of limiting angina or angina equivalent, unresponsive to medical therapy	I	A

[a] With documented ischaemia or FFR ≤0.80 for diameter stenosis < 90%.

[b] Class of recommendation.

[c] Level of evidence.

Legend: CAD=coronary artery disease, FFR = fractional flow reserve, LAD = left anterior descending coronary artery, LV = left ventricle, LVEF = left ventricular ejection fraction.

clinical risk factors and the presence or absence of ischaemia on a non-invasive stress imaging study. Nuclear stress imaging was performed in 316 (62%) of the patients. The size of the reversible defect relative to total myocardial perfusion was determined at each site and graded semi-quantitatively, and was graded as moderate or large in 226 patients. Seventy-four per cent of the patients were at least intermediate risk because of either clinical criteria or results from non-invasive imaging test findings. On the basis of the coronary angiogram, a patient was eligible for the study if one or more major coronary arteries had a stenosis of ≥70% per cent and were suitable for revascularisation. The choice of PCI versus CABG was at the discretion of the local investigators. PCI was performed in 59 per cent and CABG in 41 per cent of the revascularisation arm. Thirty-three per cent of the patients had three-vessel disease. The median time from randomisation to vascular surgery was 54 days in the revascularisation group and 18 days in the group not undergoing revascularisation. At 2.7 years after randomisation, mortality in the revascularisation group was 22 per cent versus 23 per cent (p = 0.92) in the medical therapy group. At 30 days after the vascular operation, post-operative MI rates, defined as an elevation in troponin levels, occurred in 12 per cent versus 14 per cent (p = 0.37), respectively. Thus, the study indicated that systematic prophylactic coronary revascularisation before elective vascular surgery does not alter outcomes in stable patients. In a subsequent analysis of the CARP database, it was reported that outcomes for multivessel disease were better in those who underwent CABG compared with those who had PCI (Ward et al., 2006). In another post hoc analysis of the database of patients who underwent coronary angiography, in both the randomised and registry of the CARP trial, only the subset of patients with unprotected left main disease appeared to benefit from prophylactic revascularisation (Garcia et al., 2008).

Monaco and colleagues have investigated 208 consecutive elective major vascular surgery patients who had a revised cardiac risk index of 2 or more. The subjects were randomised to either selective strategy, in whom coronary angiography was performed based on the results of non-invasive tests, or to routine preoperative coronary angiography (Monaco et al., 2009). As expected, the revascularisation rate in the latter group was higher (40.1% versus 58.1%, p = 0.01); however, in-hospital MACE rates were not significantly different. Survival and freedom from death/cardiovascular events, at a mean follow-up of approximately 6 years, were significantly better in those who had routine angiography. Thus, this study with a smaller sample size, compared to the CARP trial, indicated that a strategy of routine coronary angiography improved long-term outcomes of peripheral arterial disease surgical patients who were at medium-to-high perioperative risk.

The utility of systematic coronary angiography, and revascularisation if needed, on the incidence of cardiac ischaemic events after carotid endarterectomy

has been evaluated in another study of 426 patients (Illuminati et al., 2010). These patients had no history of CAD and a normal echocardiogram and electrocardiogram. Subjects were randomised to either routine pre-procedural coronary angiography or routine care. In the coronary angiography group, 66 of 216 patients had PCI and 2 had CABG before CEA. Carotid endarterectomy was performed at a median duration of 4 days following PCI. There was no difference in the rates of post-operative mortality or stroke between the two study groups. There were no post-operative cardiac events in the coronary angiography group, whereas there were nine ischaemic events in the control group (p = 0.01). There were no complications related to coronary angiography, and no cervical haematomas occurred in patients undergoing surgery with dual antiplatelet therapy. Thus, this trial suggests that systematic preoperative coronary angiography, with PCI, significantly reduces the incidence of post-operative myocardial events after carotid endarterectomy in patients without clinical evidence of CAD.

While these recent trials have suggested that there may be a benefit from routine coronary angiography and revascularisation in higher-risk stable patients undergoing vascular surgery, more studies are needed in order to change clinical practice. Based on current evidence, prophylactic myocardial revascularisation before high-risk surgery may be considered in the presence of moderate-to-large areas of ischaemia on a stress test. However, routine revascularisation before low- and intermediate-risk surgery in patients with known stable CAD is not recommended.

There has not been a prospective clinical trial conducted, and there is unlikely to be one, investigating the role of prophylactic revascularisation in patients with a recent acute coronary syndrome requiring non-cardiac surgery given the relatively uncommon occurrence, and evidence for cardiac benefit from revascularisation in unstable CAD. In general, for acute coronary syndrome patients needing revascularisation prior to the non-cardiac operation, PCI rather than CABG is performed, especially if surgery is urgent. CABG may be more appropriate in cases of complex multi-vessel disease where the non-cardiac surgery can be deferred to allow for recovery from CABG. In a retrospective study of 16,478 patients from an administrative database, patients with an MI within 3 years of undergoing an operation (hip surgery, cholecystectomy, bowel resection, elective abdominal aortic aneurysm repair or lower extremity amputation) were evaluated. Post-operative 30-day and 1-year outcomes were compared between those who did and those who did not have preoperative revascularisation (Livhits et al., 2011). Patients who were revascularised prior to their operation had lower rates of reinfarction (5.1% versus 10.0%; p <0.001) as well as 30-day (5.2% versus 11.3%; p <0.001) and 1-year (18.3% versus 35.8%; p <0.001) mortality. The data suggest that patients with an MI within 3 years of a non-cardiac operation may benefit from preoperative revascularisation, but the retrospective design, many differences in baseline patient characteristics of those who did and did not undergo revascularisation and other confounding factors limit the clinical applicability of the study.

In general, PCI may be appropriate prior to non-cardiac surgery to manage an acute coronary syndrome, high-risk coronary anatomy or life-threatening arrhythmias due to myocardial ischaemia. Factors that require consideration prior to PCI are the risk of bleeding and ischaemic events associated with the surgery in a patient taking dual antiplatelet therapy and the urgency of the operation. Drug-eluting stents are appropriate for patients at low risk of bleeding and if the non-cardiac surgery can be deferred for at least 12 months. Recent data suggest that the risk of stent thrombosis is low after 6 months using second-generation drug-eluting stents, and that non-cardiac surgery may be performed after this period (Hawn et al., 2013; Wijeysundera et al., 2012). If elective surgery is required sooner than 12 months, then bare metal stent implantation and dual antiplatelet therapy for 4 to 6 weeks with continuation of aspirin perioperatively may be an appropriate option. CABG should be favoured over bare metal stents in patients with a high risk of restenosis (small diameter vessel, long lesions, multiple stents required, left-main trunk lesions). If the non-cardiac surgery is needed in a shorter time frame, or the risk of bleeding with dual antiplatelet therapy is high, then consideration should be given to balloon angioplasty with provisional bare metal stenting.

The indications for preoperative CABG are the same as for those for CAD in general (Windecker et al., 2014). If preoperative evaluation indicates that CABG is indicated, this should be done prior to non-cardiac surgeries that are not low risk. The need to recommend CABG prior to non-cardiac operations is fortunately infrequent, and must be made with

consideration of the cumulative mortality and morbidity risks of both the coronary and non-cardiac surgeries in the context of the patient's co-morbidities, functional status and overall prognosis.

Pharmacological Therapy

Antiplatelet Therapy

The role of aspirin in patients with CAD requiring non-cardiac surgery who have not had prior PCI with a stent is unclear. Analysis of retrospective studies suggests that preoperative withdrawal of aspirin increases thrombotic complications (Burger et al., 2005). The Pulmonary Embolism Prevention trial randomised 13,356 patients undergoing hip surgery to 160 mg aspirin or placebo. While aspirin therapy reduced the risk of deep vein thrombosis (the primary goal of the study), it did not demonstrate a benefit for the occurrence of perioperative MI or vascular deaths (PEP Collaborative Group, 2000). In the POISE 2 trial, 10,010 patients requiring non-cardiac surgery and at risk for vascular complications were randomised to aspirin or placebo (Devereaux et al., 2014). Patients were stratified according to whether they had not been taking aspirin before the study (initiation stratum, with 5628 patients), or they were already on an aspirin regimen (continuation stratum, with 4382 patients). Aspirin, 200 mg daily or placebo was initiated before surgery and continued daily (at a dose of 100 mg) for 30 days in the initiation stratum and for 7 days in the continuation stratum, after which patients resumed their regular aspirin regimen. The primary outcome of death or non-fatal MI at 30 days occurred in 7.0 per cent in the aspirin group and 7.1 per cent in the placebo group. Major bleeding was more common in the aspirin group than in the placebo group (4.6% vs. 3.8%, $p = 0.04$). The primary and secondary outcome results were similar in the two aspirin strata. Patients within 6 weeks of placement of a bare metal stent or within 1 year of drug-eluting stent deployment were excluded from the trial, and the number of patients with PCI outside of this time window was too few to derive any conclusion. Only 23 per cent of the study population had known prior CAD, and the population excluded patients undergoing carotid endarterectomy surgery. Thus, the use of aspirin needs to be individualised, weighing the risk and benefits. Routine perioperative use of aspirin in all patients is not indicated, but continuation may be reasonable in patients with CAD or cerebrovascular disease when the risk of perioperative bleeding is not high.

It is estimated that between 5–25 per cent of patients with coronary stents require non-cardiac surgery within 5 years after stent implantation (Kristensen et al., 2014). Stent thrombosis risk in the perioperative period for both bare metal and drug-eluting stents is greatest in the first 4 to 6 weeks following PCI (Berger et al., 2010; Cruden et al., 2010; Grines et al., 2007; Hawn et al., 2013; Kaluza et al., 2000; Nuttall et al., 2008; Van Kuijk et al., 2009; Wijeysundera et al., 2012; Wilson et al., 2003). The prognosis of stent thrombosis appears to be worse than for de novo coronary occlusion. Interruption of dual antiplatelet therapy during this early period is a strong risk factor for stent thrombosis (Iakovou et al., 2005; Van Werkum et al., 2009). The decision to continue dual antiplatelet therapy during this period for urgent or emergency non-cardiac surgery should be individualised, with the risk of perioperative bleeding weighed against the benefits of continuing therapy. The risk of drug-eluting stent thrombosis during non-cardiac surgery appears to be low after 6 months with contemporary stents (Hawn et al., 2013; Wijeysundera et al., 2012). The management of antiplatelet therapy in patients who have had PCI with a stent should be discussed by the surgeon and the cardiologist, so that the balance between the potential risks of surgical bleeding on antiplatelet therapy and stent thrombosis off dual antiplatelet therapy is carefully considered. It is recommended that aspirin and a P2Y12 inhibitor (clopidogrel, ticagrelor, prasugrel) be continued for 4 weeks after bare metal stents and for 12 months after drug-eluting stents, followed by aspirin alone unless the risk of life-threatening surgical bleeding on aspirin is unacceptably high. Elective non-cardiac surgery after drug-eluting stents may be considered after 6 months, if the risk of further delay is greater than the expected risks of ischaemia and stent thrombosis. Elective non-cardiac surgery should not be performed within 4 weeks after bare metal stent implantation or within 12 months after drug-eluting stent implantation in patients in whom dual antiplatelet will need to be discontinued perioperatively. In patients with stents undergoing surgery that requires discontinuation of the P2Y12 inhibitors within the previously stated time periods, aspirin should be continued perioperatively and the P2Y12 receptor-inhibitor should be resumed as soon as possible (preferably within 48 hours) after surgery. In