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Managing perioperative risk in patients undergoing elective non-cardiac surgery

Rupert M Pearse,[1] Peter J E Holt,[2] Michael P W Grocott[3 4]

[1]Barts and The London School of Medicine and Dentistry, Queen Mary's University of London EC1M 6BQ, UK
[2]Department of Outcomes Research, Vascular Institute, St George's Hospital, London, UK
[3]University of Southampton, Southampton SO17 1BJ, UK
[4]Surgical Outcomes Research Centre, UCLH/UCL Comprehensive Biomedical Research Centre, London

Correspondence to: R Pearse, Intensive Care Unit, Royal London Hospital, London E1 1BB
r.pearse@qmul.ac.uk

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The perioperative care of patients undergoing major surgery is increasingly recognised as an area that substantially affects public health and for which needs are poorly met. Around 15% of people who undergo inpatient surgery are at high risk of complications, such as pneumonia or myocardial infarction, because of age, comorbid disease, or the complexity of the surgical procedure.[1 2] High risk surgical patients account for 80% of all perioperative deaths. Non-cardiac surgery is an important cause of death and disability, owing to the high volume of procedures and related adverse outcomes.[1-6] Around 250 million major surgical procedures are performed worldwide each year.[3] This number is increasing as gross domestic product rises in poorer countries.[3] Assuming a hospital mortality rate of 1%, non-cardiac surgery will be associated with 2.5 million deaths worldwide each year and complication rates at least five times this figure.[1-6] Patients who survive postoperative complications commonly experience functional limitations and reduced long term survival.[4-6]

Varying mortality rates between hospitals indicate the potential and the need to improve survival after surgery.[7] However, the reasons for the variation in mortality are not fully understood, making effective planning more difficult. We review evidence from clinical studies, systematic reviews, and practice guidelines that influence the current and future components of optimal perioperative medicine for patients undergoing major surgery.

SUMMARY POINTS

Non-cardiac surgery has a low overall mortality but is associated with a large number of deaths because so many procedures are performed

Most deaths occur in a group of patients who are at high risk because of advanced age, comorbid disease, or major surgery (hospital mortality rate 12%)

More effective systems can improve quality of perioperative care and may improve survival while reducing healthcare costs

Further research is needed to identify the most effective approaches to perioperative medicine for high risk patients

Routine audit of outcomes after all non-cardiac surgery is urgently needed

SOURCES AND SELECTION CRITERIA

Perioperative medicine is an emerging healthcare concept, and because of inconsistent use of search terms, research articles in this field are not easily identified by systematic literature review. This article is not intended to provide an exhaustive account of work in this field but to explain the importance of the topic and highlight the most promising developments. The authors consulted a number of UK and international experts in formulating the contents of this review. We also consulted clinicians in hospital and community settings to prioritise the topics presented. In addition, we searched various databases including Clinical Evidence and the Cochrane Collaboration.

Why do patients develop postoperative complications?

Adverse events caused by failures in surgical or anaesthetic technique have received much attention and study but are infrequent relative to the number of procedures performed. However, most patients develop some degree of postoperative morbidity as a result of physiological, endocrine, and inflammatory changes associated with the tissue injury of surgery. Relatively minor consequences, such as temporary pain and immobility, are common, but serious or fatal complications can also develop (box). The magnitude, duration, and consequences of postoperative morbidity are determined by complex interplay between the indication for surgery, the resulting tissue injury, and patient factors—such as age and co-morbid disease. Chronic conditions that often affect postoperative

Common preventable complications after non-cardiac surgery that may be prevented by enhanced perioperative care

Pneumonia
Superficial and deep wound infection
Myocardial infarction
Arrhythmias
Severe pain
Pulmonary embolism
Acute kidney injury
Stroke
Respiratory failure
Acute confusion or delirium
Cardiac arrest

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outcomes include diabetes, heart failure, chronic obstructive pulmonary disease, and poor nutritional status.[8-10] In some patients, the burden of postoperative morbidity will result in a recognised diagnosis, such as pneumonia or myocardial infarction. Many patients will also experience non-specific injury to one or more organ system. Perioperative organ injury may be associated with reduced long term survival even if it is not severe enough to satisfy accepted definitions of a complication or to require treatment in a critical care unit.

How can we predict which patients will develop complications?

Epidemiological evidence suggests that clinicians often fail to identify patients at high risk of complications and allocate the appropriate level of perioperative care (as defined by guidelines).[1 2] Large epidemiological studies have shown that in the UK, less than a third of high risk patients are admitted to critical care after surgery.[1 2] Because most deaths occur in the high risk group, better preoperative identification of these patients may improve the quality of perioperative care. Offering patients clearer information about risk might alter their decision or the surgeon's recommendation to undergo surgery.

The simplest method of perioperative risk assessment is to identify factors such as age over 65 years, comorbid disease, and major surgery.[1 2 9 10] In the UK, overall hospital mortality after inpatient non-cardiac surgery is 1.9%, but for patients older than 65 years this increases to 3.8%.[1 2] Comorbidities such as heart failure and diabetes are associated with an increase in mortality of threefold to fivefold.[1 2 9]

However, screening patients for known risk factors does not necessarily result in appropriate perioperative care, as defined by expert opinion and practice guidelines, for high risk patients. The American College of Cardiology/American Heart Association guidelines stratify patients according to exercise capacity, to focus use of preoperative investigations on those who will benefit most.[11] However, it remains unclear which investigations are beneficial, since the evidence base for preoperative testing consists mainly of small studies with methodological limitations.

The findings of a large retrospective study suggested that preoperative risk assessment by non-invasive cardiac stress testing, such as cardio-pulmonary exercise testing (CPET) or dobutamine stress echocardiography, is associated with improved one year survival after high risk non-cardiac surgery—presumably because the test results led to an increased level of care.[12] There is particular interest in the use of CPET, which involves exercise on a cycle ergometer with simultaneous spirometry to provide indices of cardiorespiratory function (fig 1). Poor exercise capacity determined by CPET is associated with increased rates of postoperative complications and death.[13] A systematic review of small studies supports the rationale for CPET, but large blinded studies of the predictive accuracy of this test have not been performed.[13] As a result, the optimal thresholds between risk categories and the overall clinical effectiveness of the test remain unclear.

At present, few hospitals have adequate resources to offer CPET or other cardiac stress tests to every eligible patient. An alternative approach would be to first offer simple objective tests to all patients, to identify those who need more detailed investigation. An emerging technology is the use of preoperative blood sampling to measure biomarkers in plasma. Together with clinical data, this allows a basic assessment of perioperative risk category (low, intermediate, or high). This information could then guide the use of more detailed clinical evaluation and diagnostic tests. Promising candidate markers include B-type natriuretic peptide, glomerular filtration rate estimated from serum creatinine, and cardiac troponins. These biomarkers reflect levels of pre-existing organ dysfunction that predispose to postoperative complications. The findings of a systematic review confirm the potential of B-type natriuretic peptide to predict short and medium term postoperative outcomes.[14] However, most of the evidence supporting biomarker based risk assessment is derived from single centre studies, and clinical implementation is currently limited. Uncertainties again include the predictive accuracy and optimal thresholds between risk categories.

Fig 1 | Patient undergoing CPET to assess perioperative risk before major elective surgery

Large international trials are planned and under way to define the best approach to perioperative risk assessment. Such assessment will allow all patients to be offered initial preoperative screening based on simple factors such as age, type of surgery, plasma biomarkers, and clinical risk scores. Patients at low risk could be offered early surgery following assessment in the community, while complex patients would be offered more sophisticated tests and detailed assessment by a perioperative physician. This

QUESTIONS FOR ONGOING AND FUTURE RESEARCH

Epidemiology

How many patients undergo non-cardiac surgery and what care do they receive?

What is the incidence of complications and death after non-cardiac surgery?

Risk assessment

How should we define the high risk surgical patient?

Can plasma biomarkers, exercise testing, or other methods accurately identify high risk patients before surgery?

How important is recent myocardial infarction as a risk factor?

Can plasma biomarkers help early identification of critically ill patients after surgery?

Interventions

Does focused postoperative critical care improve outcomes for high risk patients?

Does the use of cardiac output monitoring to guide fluid and inotropic therapy improve outcomes?

Can different approaches to perioperative respiratory support improve patient outcomes?

Does the use of perioperative anticoagulant therapy improve patient outcome?

Does cessation of smoking before surgery improve postoperative outcomes?

would improve patient choice and allow treatment plans tailored for the individual, with best use of postoperative critical care resources.

Which interventions can prevent postoperative complications?

Recent developments in perioperative medicine have focused on service delivery and organisation as well as specific medical interventions to reduce postoperative complications. For example, the World Health Organisation operating theatre checklist has been widely implemented as part of the patient safety agenda, following a recent cohort study suggesting improved outcomes after checklist introduction.[15]

Perioperative β-adrenoceptor antagonist therapy

Small randomised trials and some larger cohort studies have suggested benefit from β-adrenoceptor antagonist therapy in the perioperative period. Standard doses of atenolol or metoprolol, when started up to four weeks before surgery, may reduce the incidence of perioperative myocardial injury, especially for patients with ischaemic heart disease.[16] Subsequently, a large randomised trial found a reduction in major adverse cardiac events from 6.9% in the placebo group to 5.8% in the group assigned to perioperative metoprolol, but with a disappointing increase in 30 day mortality from 2.3% to 3.1%.[17] Although we do not recommend starting perioperative β-adrenoceptor antagonist therapy in unselected surgical patients, there may be a role in patients at high risk of myocardial ischaemia on the basis of clinical history and cardiac stress testing.[18] Careful planning is required for all patients receiving oral cardiovascular drug treatments during the perioperative period. This requires effective communication between hospital and community care teams.

Optimisation of perioperative intravenous fluid and inotropic therapy

Recent guidelines on the perioperative use of fluid have helped to establish consistency in clinical practice, although controversy about best practice remains. In particular, it is uncertain whether the dose of fluid is best determined by a formula based on body mass, the response of physiological variables (for example, cardiac output) to a fluid challenge, or a combination of the two.[19] Small single centre trials with inconsistent findings form the main evidence base for perioperative fluid management. An increase in the availability of less invasive monitoring equipment, including oesophageal Doppler and arterial waveform analysis,[20] has facilitated the widespread use of cardiac output monitoring. This has been used to guide treatment algorithms for fluid and inotropic treatment, primarily in patients undergoing abdominal surgery or proximal femoral fracture repair. The findings of systematic reviews suggest that this approach is associated with a mortality reduction of 37% and a two to three day reduction in length of hospital stay.[21 22] The National Institute for Health and Clinical Excellence (NICE) has endorsed the use of perioperative cardiac output monitoring (oesophageal Doppler) while acknowledging the need for further research.[23] However, the technology has only partly been adopted into clinical practice and we await the outcomes of large clinical trials with interest.

There is some confusion about the rationale for fluid and inotropic treatments, which increase cardiac output, while β-adrenoceptor antagonists decrease it. At present, cardiac output guided fluid therapy is recommended for most patients undergoing abdominal surgery and proximal femoral fracture repair. The addition of low dose inotropic therapy may also be considered for high risk patients in these categories. The evidence base for the use of β-adrenoceptor antagonists is less clear and should be restricted to patients in whom increased perioperative heart rate is likely to result in myocardial ischaemia.

Perioperative respiratory therapy

Both surgery and anaesthesia result in impaired respiratory function. Around 1.5% of patients develop pneumonia after surgery, with a 30 day mortality rate over 20%.[24] Respiratory complications are a particular problem after abdominal surgery. Although accepted in practice, the benefit of chest physiotherapy after abdominal surgery remains uncertain and systematic reviews do not support its routine use.[24 25] Early use of postoperative continuous positive airway pressure with a facemask seems to be beneficial. A recent systematic review of small and medium size trials found that this treatment reduced the incidence of pulmonary complications after major abdominal surgery (relative risk 0.66; 95% CI 0.52 to 0.85).[26] An alternative is to allow high risk patients around four to six hours of invasive ventilation after abdominal surgery, to ensure that endotracheal extubation occurs only once patients are fully awake, with adequate cardiorespiratory function and complete reversal of muscle relaxant drugs.

ADDITIONAL EDUCATIONAL RESOURCES

Royal College of Anaesthetists (www.rcoa.ac.uk)—detailed information on what anaesthesia involves with resources for patients and healthcare professionals

Royal College of Surgeons of England (www.rcseng.ac.uk)—patient information on many different types of surgery as well as resources for healthcare professionals

Patient safety first (www.patientsafetyfirst.nhs.uk)—guidance for healthcare professionals on how to improve patient safety during the perioperative period

UK Department of Health (www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_115155)—published guidelines on Enhanced Recovery After Surgery (ERAS) programmes

TIPS FOR THE NON-SPECIALIST

- Don't underestimate the short and medium term risks of major non-cardiac surgery, especially for older patients and those with comorbid disease
- Objective tests may help to identify high risk patients but will only improve outcome if additional perioperative care can be provided
- Complications often develop several days after major surgery and sometimes after the patient leaves hospital
- Effective engagement between community and hospital teams may improve perioperative care planning and follow-up for complex cases

Smoking cessation may reduce the incidence of pneumonia, but only in patients who stop at least two months before surgery.[24] High concentrations of inspired oxygen were associated with a reduced incidence of wound infection in early trials, but a subsequent large trial did not confirm this benefit.[27] The benefits of perioperative epidural anaesthesia and analgesia after surgery may be subtle. However, there is evidence from randomised trials and systematic reviews that routine perioperative pain control via the epidural route may lead to fewer respiratory complications and perhaps improved survival for patients who undergo major abdominal and orthopaedic surgery (RR 0.89; 95% CI 0.81 to 0.98).[24 28 29]

Postoperative critical care

Epidemiological studies have found that mortality rates after elective gut and vascular surgery are two to four times greater than those for cardiac surgery in patients aged over 65 years.[1 2] This partly reflects differences between underlying disease processes, but also highlights inequitable provision of care between patients with different clinical conditions. Postoperative critical care is routine after cardiac surgery but unusual for non-cardiac surgery. Most clinicians believe high risk patients undergoing major non-cardiac surgery would benefit from postoperative admission to critical care. However, evidence to support its routine use is limited. The findings of systematic reviews suggest that nurse led protocols allow efficient provision of good quality critical care after cardiac surgery.[30] Many hospitals now take a similar approach to care for non-cardiac surgical patients with the aim of reducing respiratory failure that follows surgery owing to partial reversal of muscle relaxants, pain, agitation, hypothermia, and impaired respiratory mechanics.

Postoperative critical care units need not offer all the advanced treatments available in an intensive care unit (such as renal replacement therapy). The primary objective is to provide up to 24 hours of postoperative critical care, with short term invasive ventilation and cardiovascular support that is nurse led and protocol driven. At the end of this period most patients will be suitable for standard ward care, while a smaller number will require admission to intensive care. We suggest that increased use of routine postoperative admission to critical care may result in more effective resource use than the current approach, in which patients go to a surgical ward immediately after major surgery with subsequent escalation to critical care only when complications develop. The use of early warning scores derived from nursing observations is now well established in identifying ward patients in whom care should be escalated. Depending on the findings of ongoing research, in the future this approach may be supplemented by measurement of plasma biomarkers.

Enhanced recovery after surgery

A specific multimodal approach to elective perioperative care, known as enhanced recovery after surgery (ERAS) is increasingly used to accelerate recovery after major surgery. It was originally proposed for colorectal cancer surgery but is now used for other purposes, including urology, gynaecology, and major joint replacements. The four key elements of this approach are: comprehensive preoperative evaluation and preparation of the patient; optimal anaesthesia and minimally invasive surgery to reduce the patient's stress response to surgery; appropriate postoperative management of symptoms such as pain with early mobilisation; and early resumption of normal diet. Preoperative management of patients' expectations about the postoperative period is particularly emphasised, along with empowering patients to be involved in their own recovery. Some components of the ERAS package are evidence based (such as cardiac output guided fluid therapy, epidural analgesia, and early enteral nutrition), while others are included on the basis of expert opinion (for example, early mobilisation). Systematic reviews of randomised trials and case control studies of the ERAS package reported a consistent reduction in hospital stay and a possible reduction in postoperative morbidity for patients who were managed with this approach, although postoperative survival did not improve and there was a trend towards increased hospital readmission rates.[31-33] Adoption of ERAS in the UK has been associated with reduced use of hospital beds without any evidence of adverse clinical consequences.[34]

Could systems of perioperative care be better designed?

Healthcare systems design has a substantial effect on the detection and management of postoperative adverse events, and hence on clinical outcomes. Outcome measures are increasingly used to underpin qual-

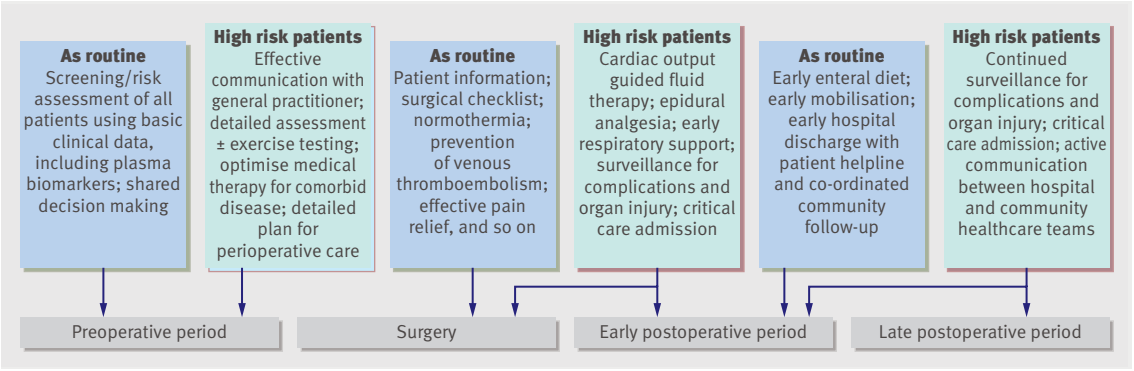

Fig 2 | **Care pathway for routine and high risk patients undergoing major non-cardiac surgery, with selected examples of assessments and interventions for each. The key components are effective planning and communication between hospital and community healthcare teams**

ity improvement frameworks and inform purchasing or commissioning of healthcare services. The focus on reducing the incidence of postoperative complications is predicated on the assumption that this will lead to global improvements in quality and patient experience. Postoperative complications are expensive to treat and improved quality of care may decrease overall healthcare costs.

Various targets in the care pathway have been identified for patient safety and quality improvement initiatives (fig 2). Many of these have been described in this review, including preoperative risk assessment and multidisciplinary clinics involving surgeons, anaesthetists, and physicians, which allow for more effective decision making and better communication with community healthcare teams. Systems to facilitate effective treatment plans for patients with delayed recovery after hospital discharge should also be set up to allow those with suspected complications to return promptly to hospital for review by the surgical team. When planning services many factors need to be considered, including the availability of critical care beds, numbers of specialised nursing staff, and working patterns. Well-planned systems of perioperative care exist more commonly in centres that treat high volumes of patients, and there is a clear association between hospital volume and clinical outcomes for many complex surgical procedures.[35]

Although not all the components of quality improvement frameworks are supported by high grade evidence, and some aspects remain controversial, the broader objectives of the quality improvement movement are increasingly shared by stakeholders. Effective clinical governance is a key feature of hospitals that deliver high quality care. This includes accurate collection of outcome data, internal audit, benchmarking against defined quality standards, and transparent publication of results. Programmes like the Veterans Administration National Surgical Quality Improvement Program initiative show how effectively accurate data can be used to improve quality.[6 7] However, in the UK and many other countries, effective audit of perioperative care is only performed for a minority of procedures.

Further research is required to confirm how promising developments in perioperative medicine can be implemented to maximise patient benefit. Implementation would be led most effectively by perioperative physicians from a range of clinical backgrounds, to ensure a high standard of assessment and care from the decision to operate through to the first few months after surgery, and allowing effective engagement with community healthcare.

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STATISTICAL QUESTION

Case-control studies: sources of bias

Answers *c* and *d* are true, while *a* and *b* are false.

PICTURE QUIZ A man with intra-abdominal calcification

1 The abdominal radiograph shows a soft tissue density in the right upper quadrant with thin curvilinear calcification outlining the wall. The diagnosis is a porcelain gallbladder.
2 The plain abdominal radiograph is highly suggestive of the condition but the definitive diagnosis is made by computed tomography. Ultrasound can also be used to localise the abnormality to the gallbladder.
3 Porcelain gallbladder is associated with gallstones and has traditionally been associated with adenocarcinoma of the gallbladder, although recent reviews suggest that this may not be the case. Cholecystectomy is the mainstay of management.

CASE REPORT

Persistent fever and rash in a young child

1 Kawasaki disease.
2 There is no definitive diagnostic test for Kawasaki disease. Kawasaki disease can be diagnosed when a child has been febrile for five or more days together with four or more of these findings:
   - Polymorphous exanthema
   - Bilateral non-exudative conjunctival injection
   - Changes in the lips and oral cavity
   - Changes in the extremities
   - Cervical lymphadenopathy.
3 The treatment is intravenous immunoglobulin (2 g/kg body weight as a single infusion) and aspirin.
4 Coronary artery aneurysms are the most important cardiovascular complication.