The use of early intervention to prevent postoperative complications

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Purpose of review

The incidence of complications following major surgery is surprisingly high. Patients who develop complications suffer a reduction in long-term survival. This review aims to explore recent advances in the management of surgical patients aimed at preventing postoperative complications.

Recent findings

Identifying patients prior to surgery who are at risk of a poor outcome remains challenging. There are a number of scoring systems to assist clinical risk assessment. Recent work has investigated the use of plasma biomarkers for perioperative risk prediction. Therapies aimed at reducing complication rates by attempting to improve tissue oxygen delivery include goal-directed haemodynamic therapy and postoperative noninvasive ventilation. The role of perioperative β-adrenoceptor antagonists remains unclear. Other important measures include the use of a surgical safety checklist and thromboprophylaxis.

Summary

Current systems for the identification and treatment of high-risk surgical patients are inadequate. Further research is required to establish the optimal approach to the identification and management of the high-risk surgical patient.

Keywords

oxygen delivery, perioperative care, surgery

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Introduction

Recent estimates suggest that 234 million major surgical procedures are performed worldwide each year [1••]. In the overall population, the incidence of postoperative complications and death is low. However, a readily identified high-risk subgroup accounts for over 80% of postoperative deaths but less than 15% of in-patient procedures [2,3]. This pattern of poor outcomes following major surgery can be readily identified worldwide [4,5]. Patients who develop complications but survive will still suffer reductions in functional independence and in the long-term, a substantially reduced life expectancy [5]. It is essential, therefore, that we continue to improve outcomes following major surgery. The systematic assessment of patients will allow identification of those at greatest risk and hence individualized care to ensure the best possible outcome. The aim of this article is to describe our current understanding of why postoperative complications occur and how these concepts are being applied to improve outcomes.

Identifying patients at risk of complications

A key component of the high complication rates after surgery is the failure to identify the patients at greatest risk so that appropriate perioperative interventions can be provided [2,3]. For example, in the UK less than 30% of high-risk patients are admitted to critical care after surgery [2,3]. As most postoperative deaths occur in the high-risk population, better identification of these patients would lead to substantial improvements in outcome through targeted use of resources and specific interventions. The typical high-risk case is an elderly patient, with comorbid disease, undergoing major or complex surgery, often as an emergency. A variety of scoring systems have been developed to facilitate clinical risk assessment [6]; however, they lack diagnostic precision and there is some doubt as to whether they may be safely applied in the assessment of individual patients. Submaximal cardiopulmonary exercise testing (CPET) is now increasingly used to provide a more objective assessment of perioperative risk [7]. Poor functional capacity and, in particular, low anaerobic threshold are associated with a high risk of postoperative complications and death [7]. However, CPET is time-consuming and costly to perform and is not an option for patients undergoing emergency surgery. One alternative may be the use of biomarkers to evaluate operative risk. Preoperative measurement of plasma B type natriuretic

peptide concentrations may allow the prediction of complications following both cardiac and noncardiac surgery [8,9]. Other candidate biomarkers include C-reactive protein and serum creatinine/estimated glomerular filtration rate [10,11]. Further research is needed to identify the optimal approach to risk assessment using biomarkers.

Pathophysiology: why do patients develop postoperative complications?

Happily, relatively few patients develop complications as a result of a specific failure of anaesthetic or surgical technique. However, a large number of patients will develop complications that relate to the interplay between the tissue injury-induced inflammatory response and the preexisting disease state. In noncardiac surgical patients, the majority of postoperative complications result either from infection or thrombosis.

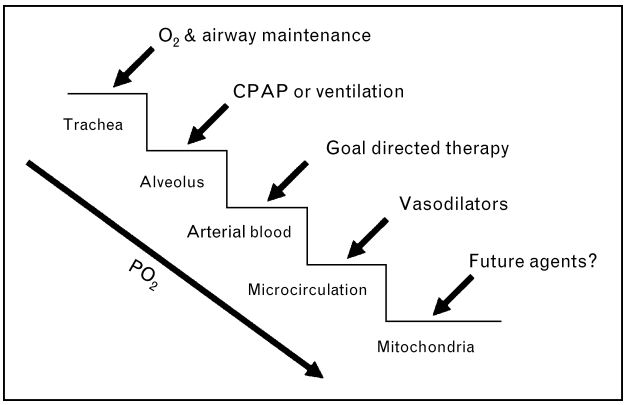
Tissue oxygen delivery and consumption

It is well established that high-risk surgical patients who fail to mount an adequate global oxygen delivery will more frequently develop postoperative complications, which are often fatal [12–14]. The importance of adequate perioperative global oxygen delivery (DO_2) may relate in part to adverse events, which result in excessive oxygen consumption (VO_2). Considerable changes in oxygen consumption occur in the perioperative period. Although anaesthesia and invasive ventilation may reduce oxygen consumption [15], pathological abnormalities, including shivering [16], pain and agitation will result in significant increases in VO_2. Imbalance between global oxygen delivery and consumption is particularly common during the first few hours after major surgery. The importance of the balance between oxygen supply and demand is illustrated by studies describing significant reductions in central venous oxygen saturation ($ScvO_2$) following major noncardiac surgery [17,18]. It has been suggested that poor global oxygen delivery is associated with reduced tissue perfusion and oxygenation and hence postoperative complications, although this has yet to be demonstrated. There is some evidence to suggest that surgical wound infections are associated with reductions in tissue PO_2 [19]. The findings of several studies suggest that reductions in microvascular blood flow during gastrointestinal surgery may be associated with an increased incidence of complications [20–22]. In a recent investigation by our group, sublingual microvascular flow was impaired in patients who developed postoperative complications even prior to elective surgery [20]. Figure 1 highlights the role of current and potential future therapies aimed at improving tissue oxygen delivery.

Myocardial injury

Perioperative myocardial ischaemia differs from the classical pattern. A greater proportion of patients who develop perioperative myocardial ischaemia present with an acute coronary syndrome as opposed to classic ST-segment elevation [23]. Perioperative increases in heart rate and arterial pressure appear to result in an imbalance of myocardial oxygen supply and demand, which, when coupled with systemic inflammation and the procoagulant state, may result in myocardial injury in patients with preexisting coronary artery disease [23].

Figure 1 The perioperative oxygen cascade indicating the role of current and potential future therapies to prevent postoperative complications



CPAP, continuous positive airways pressure.

Venous thromboembolism

The high-risk surgical patient will typically have a number of important risk factors for venous thromboembolism (VTE), including advanced age, heart failure, malignancy, chemotherapy, previous stroke, immobility and, of course, major surgery itself [24]. Most of these factors result in endothelial damage, blood stasis or hypercoagulability, the key aetiological factors first described by Virchow.

Respiratory management

The importance of perioperative respiratory management is well recognized. Interventions as simple as the use of supplemental inspired oxygen may improve the incidence of wound infections [25]. Postoperative pulmonary complications appear to be related to local changes in lung mechanics associated with anaesthesia as well as the inflammatory effects of major surgery and mechanical ventilation [26]. Atelectasis occurs rapidly after the induction of anaesthesia and may persist for many days resulting in hypoxaemia in up to 50% of patients undergoing abdominal surgery [27]. A number of strategies have been shown to reduce atelectasis formation during surgery, including positive end expiratory pressure and recruitment manoeuvres [28]. However, improvements in pulmonary function are often temporary [29]. Postoperative physiotherapy may improve lung

volumes and oxygenation but the outcome benefits remain unclear [30]. The findings of a recent systematic review and meta-analysis suggest that the use of continuous positive airways pressure (CPAP) after abdominal surgery may reduce the incidence of postoperative respiratory complications [31]. Interestingly, there is some evidence to suggest significant beneficial effects of CPAP and noninvasive ventilation even following gastric tube reconstruction [32]. These may include a reduced incidence of acute lung injury, reintubation and anastomotic leak [32]. The use of low tidal volume mechanical ventilation is now routine in critical care practice [33]. There is some evidence that this approach may improve surrogate markers of respiratory function and inflammation in surgical patients [34], although there is, as yet, no evidence of improved clinical outcome.

For the majority of patients undergoing surgery with general anaesthesia, endotracheal extubation is performed immediately after surgery. In a small proportion of patients, extubation is performed after a short period of invasive ventilation in intensive care. Delayed extubation may minimize periods of high oxygen consumption due to pain, agitation, hypothermia and increased work of breathing. This approach is routine following cardiac surgery. Systematic reviews in this area are inconclusive [35,36]. However, the benefits of short periods of invasive ventilation following major abdominal surgery require further investigation.

Cardiovascular management

There are a number of strategies relating to the cardiovascular management of the surgical patient of which we will focus on three.

Perioperative use of β-adrenoceptor antagonists

A number of small early studies [37,38] suggested a beneficial effect of β-adrenoceptor antagonist therapy on the incidence of perioperative myocardial injury. Although previous systematic reviews have supported this conclusion [39], the evidence base remains problematic. The findings of a recently completed large international randomized controlled trial [PeriOperative ISchemic Evaluation (POISE) trial] [40••] suggest the indications for such treatment may not be as clear as previously thought. Patients enrolled in POISE were randomized to perioperative metoprolol or placebo. Metoprolol was associated with a reduction in the composite end-point of myocardial infarction, cardiac arrest and cardiovascular death but disappointingly, an increase in overall mortality. Although there has been some suggestion that this outcome was the result of excessive doses of β-antagonists, this does not appear to be the case [41]. However, the findings may be the result of the use of β-antagonists in unselected patients, not all of whom stood to benefit from this therapy. This trial strongly emphasizes the importance of tailoring perioperative care to the individual patient. Expert opinion currently advises the continued use of perioperative β-adrenoceptor antagonists but with careful consideration of the indications and optimal dose in individual patients [41].

Perioperative goal-directed haemodynamic therapy

Goal-directed haemodynamic therapy (GDHT) is a term that describes the protocolized use of cardiac output and related parameters as end-points for the administration of fluid and/or inotropic therapies. Although in early studies cardiac output was measured using the pulmonary artery catheter, there are now a number of less invasive methods available [42]. The group of Shoemaker *et al.* [43] were the first to perform an interventional trial of perioperative GDHT, the findings of which suggested this treatment was associated with a significant reduction in mortality. However, that study was criticized for several important methodological flaws, including poorly defined control and intervention group care and a lack of clear randomization procedures. A number of further trials were performed suggesting reductions in morbidity [44,45] and mortality [46,47]. Others, however, failed to show any benefit, particularly in the case of vascular surgery [48,49]. This may relate to harmful effects, in particular myocardial ischaemia, when inotropic therapy is administered in high doses. However, more recent GDHT protocols, using only low-dose inotropic therapy, do not appear to be associated with myocardial ischaemia [50]. The importance of the dose of inotropic agents has also been highlighted by the findings of a recent meta-regression analysis of five published clinical trials of perioperative dopexamine infusion. These suggest that in low doses (≤ 1 μg/kg/min), dopexamine is associated with a reduction in 28-day mortality [low-dose dopexamine 6.3% versus control 12.3%; odds ratio 0.50 (0.28–0.88); $P = 0.016$] [51•]. There appears to be no survival benefit associated with high-dose dopexamine. It is worth noting, however, that not all trials included in this analysis demonstrated a benefit with dopexamine infusion [52].

Restrictive versus liberal approach to perioperative fluid therapy

There have been a number of clinical trials comparing 'liberal' and 'restrictive' protocols for perioperative intravenous fluid prescription according to body mass [53–55]. The findings of these trials have led to a certain amount of confusion regarding the optimal fluid management during the perioperative period. Given that the stress response to surgery will induce fluid and salt retention, it seems logical to prescribe maintenance fluids at a reduced rate in the postoperative period [56,57•]. However, it should be noted firstly that although maintenance fluid can and should be prescribed according to body

mass, this is not a rational method of estimating fluid losses and the need for resuscitation. Furthermore, in many of these trials, the protocol termed 'restrictive' most closely reflects routine clinical care, whereas the 'liberal' protocol would often result in excessive fluid administration. Nonetheless, the findings of these trials have proved inconsistent. It is clear that those patients who develop oedema are more likely to develop postoperative complications [58]. However, this may relate as much to the patient and the nature of the surgical procedure as to the fluid strategy [58]. Intravenous fluid resuscitation should be prescribed according to logical physiological end-points. The administration of excessive maintenance fluids is no more or less preferable than the failure to resuscitate a hypovolaemic patient.

Other

There are a number of general aspects of perioperative care which are likely to offer significant outcome benefits. Clearly, the use of thromboprophylaxis is of particular importance [59]. The findings of a recent case series suggest that the use of a safety checklist for patients undergoing noncardiac surgery may also improve outcomes [4]. Other interventions that should be routinely considered include the use of warming blankets to prevent perioperative hypothermia [60]. This approach may reduce the incidence of wound infection, suggesting a pathophysiological process related to tissue perfusion. The benefits of epidural analgesia/anaesthesia remain unproven [61]; however, a recent meta-analysis of clinical trials involving almost 6000 patients suggested a reduction in the incidence of pneumonia associated with epidural analgesia for thoracic and abdominal surgery [62]. Nutritional support is another important aspect of perioperative care that seems likely to be of great importance. The effects of major surgery include catabolism, insulin resistance and impaired peripheral glucose utilization. However, the optimal approach to nutritional support before and after surgery requires further clarification. There are several promising lines of research into other methods of improving postoperative outcome. Of particular interest is the use of volatile anaesthetics to prevent ischaemia–reperfusion injury and the pleiotropic, anti-inflammatory and antithrombotic effects of statins.

Conclusion

The high-risk surgical population is larger than generally realized. These patients account for over 80% of postoperative deaths but less than 15% of in-patient procedures [2,3]. Current systems for the identification and treatment of high-risk surgical patients are inadequate. Postoperative complications generally result from the interplay between the tissue injury-induced inflammatory response and preexisting disease states. In noncardiac surgical patients, the majority of postoperative complications are either infectious or thrombotic in nature. A great deal of further research is required to clarify various key aspects of care of the high-risk surgical patient. Areas of particular importance include the role of plasma biomarkers in risk assessment, the efficacy of GDHT and the optimal approach to perioperative respiratory care.

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R.P. and S.J. are named inventors on a patent application related to dopexamine and have a related intellectual property agreement with Circassia Holdings.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

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- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 374–375).

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