Preoperative optimization of the high-risk surgical patient

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After major surgery there is a significant risk of major complications and even death, particularly in the elderly and patients with significant cardiorespiratory disease. In the UK, recent large audits have shown a 30-day mortality rate of 5.6% for elective colorectal cancer surgery,52 19.3% for emergency colorectal surgery,62 7.3% for elective infrarenal aortic aneurysm and aortal-iliac occlusive disease surgery,4 9–15% for oesophagectomy and 13–15% for elective gastrectomy.34

Major surgery generates a strong systemic inflammatory response that in turn leads to an increase in oxygen requirement from an average of 110 ml min⁻¹ m⁻² at rest to an average of 170 ml min⁻¹ m⁻² in the postoperative period.43 55 This substantial increase in oxygen demand is normally met by increases in cardiac output and tissue oxygen extraction. Most patients can meet the increased oxygen demand by increasing cardiac output and will usually do well after surgery. However, there remains a group who may not have the physiological reserve to increase cardiac output to the required level and this group of patients is at higher risk of complications after surgery. Trials have identified high-risk patients and implemented strategies before surgery to increase oxygen delivery (Do₂) to the levels that major surgery demands.15 30 55 67 Although some of these trials have demonstrated an improvement in outcome, the strategy remains controversial.

The exact mechanisms that lead to postoperative complications are not completely understood, but an understanding of the existing knowledge on the pathogenesis of postoperative morbidity and mortality will help the clinician understand the rationale for increasing Do₂ and tissue perfusion in the high-risk surgical patient.

In this paper we review the role of inadequate tissue perfusion and Do₂ in the development of complications after major surgery, the results of trials of preoperative interventions that aim to improve cardiac function and hence Do₂, developments in the identification of patients who are most likely to benefit from these interventions and the role of fluids and inotropes in optimization strategies.

Why do patients get major complications after major surgery?

In patients undergoing major surgery, commonly monitored physiological variables such as heart rate, arterial pressure, central venous pressure (CVP), temperature and haemoglobin concentration are poor predictors of complications after surgery. Less commonly measured variables such as cardiac index (CI), Do₂, gastric intramucosal pH (pHi) and stroke volume have been shown to be better predictors of postoperative outcome.12 38 46 56 58 Survivors of major surgery and critical illness tend to have a higher CI, Do₂ and oxygen consumption (Vo₂) than non-survivors.9 10 13 15 21 28 30 48 54 55 57 67 68 Moreover, normal values for these variables are not necessarily predictive of survival: in one series, 76% of patients who died after critical illness had achieved normal values.11

The presence of an oxygen debt can be demonstrated despite normal haemodynamic and oxygen transport variables in both postoperative and critically ill patients. An observational study by Bland and colleagues13 showed that increases in cardiac output leading to a 'supra-normal' Do₂ of greater than 600 ml min⁻¹ m⁻² was associated with greater survival than those whose postoperative Do₂ was less than 600 ml min⁻¹ m⁻², but still within an acceptable range. In a series of 253 high-risk surgical patients, Shoemaker and colleagues54 demonstrated the importance of maintaining adequate Do₂ throughout the perioperative course. Patients were classified retrospectively as survivors without complications, survivors with complications or non-survivors. Vo₂ was measured at frequent intervals before, during and after the surgical procedure, and oxygen debt

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was calculated using the patients resting operative control values. Before surgery there were no differences in CI, \(D_O_2\), or \(V_O_2\) between the different outcome groups. In the 63 patients who died, mean cumulative intra-operative oxygen deficit was 12.0 litre m\(^{-2}\) and maximum debt was 33.2 litre m\(^{-2}\) at 17.8 h after surgery. This was in contrast to the 158 survivors with no organ failure whose intraoperative oxygen deficit was 5.7 litre m\(^{-2}\), with a maximum debt of 9.2 litre m\(^{-2}\) at 4.1 h after surgery. Essentially, the magnitude and duration of oxygen deficit was greatest in the non-survivors, slightly less in the survivors with organ failure and least in the survivors without organ failure. In a side arm of this study, 56 patients were randomized to a control group that was maintained at normal haemodynamic and oxygen transport values, and a protocol group that was maintained at so-called ‘supra-normal’ values of CI greater than 4.5 litre min\(^{-1}\) m\(^{-2}\), \(D_O_2\) greater than 600 ml min\(^{-1}\) m\(^{-2}\) and \(V_O_2\) greater than 170 ml min\(^{-1}\) m\(^{-2}\). The control group, who had normal values as their targets, averaged a maximal oxygen debt of 17.3 litre m\(^{-2}\) at 31 h after surgery, lasting for more than 48 h, whilst the protocol group with ‘supra-normal’ values had a maximal oxygen debt of 7.6 litre m\(^{-2}\) at 3 h after surgery, lasting an average of 13 h. Mortality in the control group was 34% with 31 organ failures, compared with a mortality of 4% in the protocol group and one organ failure. The magnitude and duration of oxygen debt correlated with the incidence of postoperative organ failure and death; minimization of these debts by augmenting CI, \(D_O_2\) and \(V_O_2\) to supra-normal levels led to a reduction in morbidity and mortality.

\(D_O_2\) is dependent on oxygen content of the arterial blood, and cardiac output. Timmins and colleagues\(^{63}\) observed the response of cardiac performance in terms of CI, left ventricular stroke work index (LVSWI), and cardiac power output (CPO) after administration of fluid and inotropes in critically ill patients and then looked for patterns in survivors and non-survivors. LVSWI and CPO were significantly higher in survivors on admission, and all three variables were significantly higher after maximal resuscitation in the surviving group. Poeze and colleagues\(^{46}\) showed that patients with lower stroke volumes after cardiac surgery, as measured by oesophageal Doppler, were more likely to have complications. The reduced cardiac performance seen in non-survivors suggests that the ability to increase cardiac work, and hence \(D_O_2\), sufficiently to meet the increased metabolic need of the postoperative phase is associated with increased survival.

In recent years, much interest has been directed towards the role of the gut in the pathogenesis of postoperative morbidity and mortality. Low gastric pH and increased gastric luminal carbon dioxide tension are highly predictive of postoperative complications.\(^7\) It can be shown that with increasing global oxygen delivery, splanchnic oxygen delivery increases and a parallel change is seen in splanchnic oxygen consumption, suggesting that improved systemic oxygen delivery improves splanchnic oxygen delivery and hence gastric pH.\(^{50-51,64}\) Gastric pH has been shown to be a good predictor of outcome after major surgery\(^{33,38,45,47}\) and in critically ill patients.\(^{26}\) Optimizing stroke volume using oesophageal Doppler monitoring during cardiac surgery to guide fluid therapy improved gastric pH, reduced complications and shortened time in the intensive care unit (ICU) and hospital stay.\(^{38}\)

In compensated shock that appears clinically normal, any inadequacy of \(D_O_2\) is concentrated to the gut.\(^{25}\) The splanchnic circulation is sensitive to hypoperfusion and in low flow states, splanchnic blood flow decreases out of proportion to the overall decreases in cardiac output, and recovers last.\(^{1,35}\) It has been suggested that in non-occlusive intestinal ischaemia the enteric mucosal barrier is disrupted and translocation of endotoxin (lipopolysaccharide) and microorganisms occurs into the circulation.\(^{32,41}\) Translocation initiates the cytokine pathway\(^{20}\) (see review by Galley and Webster in this issue for further details), rendering the individual at an increased risk of sepsis and multiple organ failure; patients with proven translocation have significantly more postoperative septic complications.\(^{16,40,53}\) The incidence of translocation increases with age, the urgency of the surgery and the presence of distal bowel obstruction.\(^{40}\) Endotoxin is known to be a potent activator of the pathways involved in the inflammatory response,\(^{36,37,66}\) and depressed or falling levels of circulating antibodies to endotoxin (EndoCAb) can be interpreted as exposure to endotoxin. In cardiac surgery, low levels of IgM EndoCAb are associated with poor postoperative outcome, supporting the concept that endo-toxaemia has an important role in the pathogenesis of postoperative morbidity.\(^{8,27}\)

Bacteria and endotoxin induce cytokine secretion by tissue macrophages, stimulate neutrophil migration, activate the complement and coagulation cascades and generally induce a pro-inflammatory state. The cytokines secreted by endotoxin-activated macrophages include interleukin (IL)-1, IL-6 and tumour necrosis factor (TNF), and these can impair oxygen delivery to the gut through their actions on the microcirculation, potentiating the further translocation of endotoxin and bacteria, and also activation of the inflammatory system.

TNF is a polypeptide that reacts with a specific receptor on a diverse number of cell types. Its primary role is as an inflammatory cytokine that recruits polymorphic nucleocytes to areas of infection and trauma, and provides the major physiological stimulus for production of IL-1 and IL-6. IL-1 acts as a pyrogen, stimulates hypothalamic production of prostaglandins and stimulates the inflammatory cascade. IL-6 production is stimulated by IL-1 and TNF, and there is a correlation between plasma concentrations of endotoxin and IL-6.\(^{14}\) Prolonged elevated plasma concentration of IL-6 in trauma, burns and elective surgical patients is associated with increased morbidity and mortality.\(^{2,19,49}\) The high concentrations of IL-6 seen in blood from the mesenteric veins of resected colonic segments compared
with systemic levels indicates that the bowel is the source of the IL-6 response to surgical trauma in colorectal surgery.60

In summary it can be seen that poor outcome from major surgery is associated with a number of physiological factors including poor cardiac function and hence reduced \(\text{DO}_2\), reduced gut perfusion and a strong systemic inflammatory response. In theory, strategies that aim to improve these variables by optimizing haemodynamic function may improve outcome from surgery.

Preoperative haemodynamic optimization of high-risk surgical patients

Studies that have investigated optimization of surgical patients have varied in their approaches to both the timing of interventions, and the goals they have aimed to achieve. This article focuses on studies that have applied interventions in the preoperative phase, and are grouped according to the variables targeted by the interventions.

Preoperative optimization of oxygen delivery

The strategy of preoperative optimization of \(\text{DO}_2\) developed from the observational work of Bland and Shoemaker,13 as previously discussed. In a prospective randomized controlled trial, 88 elective and emergency patients were preoperatively randomized to one of three groups.55 A CVP-control group \((n=30)\) had a central venous catheter placed and were managed using the standard clinical values available by CVP measurement as therapeutic goals. The pulmonary artery flotation catheter (PAFC)-control group \((n=30)\) had a PAFC placed, and were managed to achieve haemodynamic and oxygen transport variables within normal ranges. The PAFC-protocol group had a PAFC placed in order to manipulate haemodynamic and oxygen transport values to supra-normal levels of CI greater than 4.5 litre min \(^{-1}\) \(\cdot\) \(\text{m}^2\), \(\text{DO}_2\) greater than 600 ml min \(^{-1}\) \(\cdot\) \(\text{m}^2\), pulmonary artery occlusion pressure (PAOP) below 18 mm Hg, CVP below 15 mm Hg, systemic vascular resistance (SVR) above 1450 dyne s cm \(^{-5}\) and \(\text{VO}_2\) above 170 ml min \(^{-1}\) \(\cdot\) \(\text{m}^2\). Patients were admitted to the ICU before surgery, and therapeutic ‘goals’ were achieved using infusions of crystalloid and colloid solutions, packed red blood cells and various inotropes and vasodilators. In the PAFC-protocol group, target \(\text{DO}_2\) was achieved in two-thirds of patients using fluid administration alone.

Before therapy was initiated, haemodynamic and oxygen transport values were comparable for the PAFC-control and PAFC-protocol groups. After surgery the study design ensured significant increases in CI, \(\text{DO}_2\) and \(\text{VO}_2\) in the PAFC-protocol group compared with the PAFC-control group. Mortality was 4% in the PAFC-protocol group, 23% in the CVP-control group and 33% in the PAFC-control group \( (P<0.02)\). In the PAFC-protocol group there was also a significant reduction in the incidence of major complications and in the length of stay in the ICU. CI, \(\text{DO}_2\) and \(\text{VO}_2\) were within standard normal values in the PAFC-control group, suggesting that the reduction in mortality in the PAFC-protocol group was a result of a deliberate elevation of \(\text{DO}_2\) to supra-normal levels using fluid and inotropes.

Boyd and colleagues15 studied a similar high-risk population in a randomized controlled trial of 107 patients (elective and emergency), enrolled and randomized into protocol and control groups. All patients had a PAFC inserted and were then resuscitated to a PAOP of 12–14 mm Hg, a mean arterial pressure (MAP) of 80–110 mm Hg, oxygen saturation above 94% and urine output greater than 0.5 ml kg \(^{-1}\) \(\cdot\) h \(^{-1}\). The only difference between the two groups was a therapeutic target for the protocol group of \(\text{DO}_2\) greater than 600 ml min \(^{-1}\) \(\cdot\) \(\text{m}^2\), aided if required by the administration of dopexamine, a dopaminergic and beta-2 adrenergic agonist. There were no differences between the groups in baseline characteristics or baseline haemodynamic and oxygen transport variables before resuscitation and administration of dopexamine. CI and \(\text{DO}_2\) were significantly increased in the treatment group before surgery as a result of the protocol. On admission to the ICU after surgery, all patients were resuscitated back to their previous goals, and in the protocol group \(\text{DO}_2\) was maintained above 600 ml min \(^{-1}\) \(\cdot\) \(\text{m}^2\) by further titration of dopexamine, which was continued until two consecutive plasma lactate levels were below 1.5 mmol litre \(^{-1}\). Mortality was reduced from 22.2% in the control group to 5.7% in the treatment group \((P=0.015)\), and there was a reduction in the mean number of complications per patient from 1.35 in the control group to 0.68 in the treatment group \((P=0.008)\). Although the majority of patients did not reach their target \(\text{DO}_2\), the strategy of deliberately aiming to increase \(\text{DO}_2\) to supra-normal levels reduced mortality and complications. Twenty-six patients out of the 107 were admitted to the trial during or after surgery; however, of the 81 patients admitted to the trial before surgery (43 protocol and 38 control), survival was 7.0% vs 23.7% \((P=0.04)\) in favour of the protocol group, and complication rates were similar, with 0.70 complications per patient in the protocol group and 1.45 in the control group \((P=0.009)\).

Wilson and Woods67 conducted a prospective randomized controlled trial with double blinding of the protocol groups in a series of 138 patients undergoing elective high-risk aortic, thoraco-abdominal or abdominal surgery. Patients were identified as high risk through a combination of surgical and medical factors, and were assigned to one of three groups of 46: control, or preoptimized with either dopexamine or epinephrine (adrenaline). The control group remained on the general surgical ward with no preoperative fluid protocol. The protocol groups were admitted to the ICU for a minimum of 4 h before surgery, and had full monitoring instigated, including insertion of a PAFC. Both groups were initially fluid optimized with colloid until a
PAOP of 12 mm Hg was reached (blood products were used if the haemoglobin concentration was less than 110 g litre \(^{-1}\)). Patients then received either epinephrine 0.025 µg kg \(^{-1}\) min \(^{-1}\) or dopexamine 0.125 µg kg \(^{-1}\) min \(^{-1}\) by double-blind infusion; these were increased by single multiples of the baseline until the target \(D_O2\) of greater than 600 ml min \(^{-1}\) m \(^{-2}\) was achieved. The infusion was continued for 12–24 h after surgery, and all patients received at least the baseline dose of inotrope even if their target \(D_O2\) had been achieved during the fluid administration phase. Hospital mortality in the protocol groups was 3%, compared with 17% in the control (\(P=0.007\)), and morbidity and hospital length of stay were significantly reduced in the group receiving dopexamine.

Lobo and colleagues\(^{30}\) conducted a prospective randomized controlled trial of 37 high-risk patients undergoing major elective surgery. Patients had common goals in terms of MAP, PAOP, haematocrit and arterial oxygen saturation, but were allocated to a control group in which the target \(D_O2\) was 520–600 ml min \(^{-1}\) m \(^{-2}\), or the protocol group in which \(D_O2\) was driven to supra-normal levels of greater than 600 ml min \(^{-1}\) m \(^{-2}\). All patients followed the same protocol pathway and dobutamine was used as the primary inotrope in both groups to achieve the desired targets. Mortality was reduced from 50% in the control group to 15.7% in the protocol group (\(P<0.05\)).

Sandham and colleagues\(^{52}\) conducted a multicentre, prospective, randomized controlled trial over a 9-yr period involving 1994 patients over the age of 60 yr and of ASA grade III or IV who were due to undergo major elective or urgent surgery. Patients were allocated to either a standard care group, who received conventional therapy, or a catheter group, who received goal-directed therapy via the aid of a PAFC in order to achieve \(D_O2\) of 550–600 ml min \(^{-1}\) m \(^{-2}\) or CI of 3.5–4.5 litre min \(^{-1}\) m \(^{-2}\). Twenty-one percent of patients in the catheter group reached the \(D_O2\) target before surgery, rising to 63% after surgery. CVP catheters were placed in 77% of the non-PAFC group and mean CVP measures were identical between groups at all perioperative stages. Hospital mortality was 7.7% in the standard care group and 7.8% in the catheter group (\(P=0.004\)). In both groups, the actual mortality was half of the expected control mortality of 15% used in the sample size calculation. There are several possible reasons for this. The majority of patients (87%) were ASA III, and with relatively good cardiac function (87% were NYHA I or II). The goal set for \(D_O2\) was 550–600 ml min \(^{-1}\) m \(^{-2}\), compared with greater than 600 ml min \(^{-1}\) m \(^{-2}\) in the previous trials described, and only a minority of patients (21%) achieved this target before surgery. Although the PAFC patients received more inotropes, colloid and blood products than control patients, the identical CVP measures suggest that the fluid and inotrope therapy in the control group resulted in similar haemodynamic end-points. Finally, this trial took 9 yr to complete, during which there may well have been significant improvements in surgical technique and perioperative care.

**Other preoperative haemodynamic optimization strategies**

Other preoptimization strategies have been employed that target end-points other than \(D_O2\), such as CI or mixed venous saturation.

Berlauk and colleagues\(^{9}\) investigated the role and timing of preoperative optimization of haemodynamic status in 89 patients undergoing peripheral vascular surgery. The patients were randomized to receive a PAFC either 12 h (group 1) or 3 h (group 2) before the operation (group 1) or no PAFC (group 3). Those that received the PAFC were fluid resuscitated and given vasoactive and inotropic agents to achieve end-points of CI greater than 2.8 litre min \(^{-1}\) m \(^{-2}\), SVR below 1100 dyne s cm \(^{-5}\) and PAOP of 8–15 mm Hg. Those who did not meet these criteria were excluded from the study. The groups were well matched in most criteria, but 80% of the patients with angina were randomized to group 1. The mortality in the PAFC groups was 1.5%, compared with 9.5% in the control group (\(P=0.08\)). Those patients that were particularly high risk (e.g. recent myocardial infarction, severe heart failure or valvular heart disease) were excluded as it was deemed that there was evidence that this group would benefit from PAFC placement. Patients in the PAFC groups had fewer adverse intra-operative events (hypotension, tachycardia, arrhythmia) (\(P<0.05\)), and lower postoperative cardiovascular mortality when compared with the control group (\(P<0.05\)). Although the protocol group did receive transdermal glyceryl trinitrate, which may help account for this.

Valentine and colleagues\(^{65}\) applied the same ‘tune up’ criteria to 120 patients scheduled for aortic reconstructive surgery and failed to show any benefit. The protocol group had PAFC placement at least 14 h before surgery and were treated to the same protocol as that applied in Berlauk’s study, whilst the control group had no preoperative interventions. Overall mortality was 5% in the protocol group and 1% in the control group, with more intra-operative complications in the PAFC group (18% vs 5%, \(P=0.02\)). All patients underwent adenosine thallium scintigraphy before surgery, and those with a reversible perfusion defect were excluded. In addition, any patient with unstable angina, recent changes in anginal symptoms, cardiac failure, severe valvular heart disease or chronic renal failure were excluded. Therapeutic targets in the PAFC group did not guarantee a \(D_O2\) of 600 ml min \(^{-1}\) m \(^{-2}\).
Ziegler and colleagues studied 72 patients undergoing aortic and limb salvage surgery. This study compared different methods of using a PAFC for managing surgical patients. All 72 patients had a PAFC inserted without complication, and patients in the protocol group were optimized with fluids, inotropes and vasodilators to achieve PAOP above 12 mm Hg, Hb above 100 g litre\(^{-1}\), and a mixed venous oxygen saturation above 65%. In the control group the PAFC was available for intra-operative and post-operative fluid management, but no specific preoperative therapy was initiated. There was no difference in mortality (9% vs 5%) or morbidity between the two groups. The physiological goals, in particular the mixed venous oxygen saturation, are relatively low.

Bender and colleagues studied a similar group to Berlauk and randomized 103 patients undergoing elective infrarenal aneurysm and lower limb revascularization surgery to receive a PAFC before surgery and to be optimized to a CI above 2.8 litre min\(^{-1}\) m\(^{-2}\), PAOP of 8–15 mm Hg and SVR below 1100 dyne s cm\(^{-5}\), or to receive standard care (n=53). In the protocol group, a combination of crystalloid solutions, dopamine and sodium nitroprusside was used to obtain the desired targets. Mortality was 2% in the protocol group (1/51) and 1.9% in the control group (1/53), and there was no difference in morbidity between the two groups. This low mortality, coupled with only 35% of the protocol group needing haemodynamic manipulation after PAFC insertion (compared with more than 60% in the Berlauk trial), suggests that the study population was not particularly high risk.

A degree of preoperative optimization of haemodynamic variables was used in a multicentre trial examining the effects of dopexamine on outcome after major elective or emergency abdominal surgery. A total of 412 patients defined as high risk were admitted to ICUs before surgery and had PAFCs inserted. Fluid, blood products and oxygen were then given to achieve CI above 2.5 litre min\(^{-1}\) m\(^{-2}\), PAOP of 10 mm Hg, haemoglobin concentration greater than 100 g litre\(^{-1}\), arterial oxygen saturation above 94% and MAP of 70 mm Hg. Obtaining the minimum of all these targets would allow a patient to be considered optimized with a \(D_0_2\) of 320 ml min\(^{-1}\) m\(^{-2}\). After reaching baseline targets, patients were randomly allocated to receive placebo or dopexamine 0.5 or 2.0 \(\mu\)g kg\(^{-1}\) min\(^{-1}\). Infusions were maintained for 24 h after surgery. There was no overall difference in mortality or morbidity. A post-hoc subgroup analysis of 51 patients who required urgent surgery revealed that mortality at 28 days was 29% in the placebo group, 11% in the group receiving dopexamine 2.0 \(\mu\)g kg\(^{-1}\) min\(^{-1}\) and 0% in patients receiving dopexamine 0.5 \(\mu\)g kg\(^{-1}\) min\(^{-1}\).

In summary, studies of preoperative haemodynamic intervention that do not target supra-normal values of \(D_0_2\), or that do not study the highest risk groups of patients, do not show clear benefit in outcome. In patients who are at high risk of complications or death, a deliberate attempt to elevate \(D_0_2\) to supra-normal levels (>600 ml min\(^{-1}\) m\(^{-2}\)) has led to reductions in mortality and morbidity. These studies have been relatively small in size, but do show a consistent outcome benefit.

### Identifying patients likely to benefit from preoperative optimization of oxygen delivery

The principle of preoperative investigations is to gain information about patients that leads to modification of their perioperative management, and to improve the outcome from major surgery. Shoemaker and colleagues published criteria for high-risk patients that encompassed a mixture of patient and laboratory factors, but these do not quantify the degree of cardiorespiratory disease an individual has, or stratify the risk.

As mentioned previously, if a patient is unable to elevate cardiac output and \(D_0_2\) to the required levels, they are more likely to have a poor outcome after major surgery. To identify the high-risk surgical patient, objective information on dynamic cardiorespiratory function is needed in order to assess perioperative needs and to provide accurate information on the risks and benefits of the procedure to the patient. Functional activity can be graded in terms of metabolic equivalents (METs) by the Duke Activity Status Index. One MET represents the resting oxygen consumption of an adult (approximately 3.5 ml kg\(^{-1}\) min\(^{-1}\)), and grading of a person’s ability to perform various levels of exertion provides a rough subjective surrogate for the maximal \(V_0_2\), one of the best indices of cardiorespiratory fitness. The subjective measurement of exercise tolerance provides good positive prediction of complications, in that if an individual is unable to climb two flights of stairs then they have an 89% chance of postoperative cardiorespiratory complications, but the actual risk of an adverse outcome is not stratified.

Stress tests such as dobutamine stress echocardiography, exercise ECG and dipyridamole thallium scintigraphy have been used to identify high-risk patients and quantify risk. The positive prediction value of these tests for postoperative ischaemic events is poor at 20–30%, although the negative prediction value is much higher at 95–100%. These tests evaluate the presence of myocardial ischaemia and the limitations on heart rate, but do not give information on the extent of cardiac failure and the limitations on \(D_0_2\).

Cardiopulmonary exercise testing (CPX testing) examines the ability of the cardiorespiratory systems to deliver oxygen to tissues under stress, in this case the exercising limb muscles. As the work rate increases, in order to generate adequate levels of ATP, the oxygen demands of the exercising muscle increase, leading to an increase in cardiac output. Eventually the energy demands outstrip the supply of oxygen and aerobic metabolism is supplemented by anaerobic metabolism, with the consequent generation of lactate. The oxygen consumption at which this occurs is known as the anaerobic threshold (AT), and can be identified easily in most individuals. Older and
Role of fluids and inotropes

Although some patients will achieve target $D_O^2$ with volume resuscitation alone, it seems that a variable but significant proportion of the population will require inotropic support to obtain predefined haemodynamic goals. The use of inotropes is not without consequence, as they may alter regional blood flow and cause tissue hypoxia, and myocardial oxygen supply and demand requirements can be mismatched, with the potential to cause myocardial ischaemia, and increased systemic VO$_2$ can occur. There appears to be a difference in outcome when different inotropes are used. In the study of Wilson and colleagues, mortality was reduced in both groups that received fluid and an inotrope (dopexamine or epinephrine) but there was a marked reduction in complications and length of hospital stay only in the dopexamine group.

The role of inotropes in optimization of high-risk surgical patients may encompass other factors apart from an increase in oxygen transport variables. Catecholamines inhibit TNF secretion and alter the IL-6 to IL-10 ratio (a measure of the balance of pro- and anti-inflammatory cytokines), and this modulation of the cytokine response may be a mechanism that influences the decreased morbidity and mortality seen in the optimization trials.

As discussed above, one of the major causes of postoperative morbidity is impairment of the function of the gastrointestinal barrier. Dopexamine has been shown to preserve gut barrier function, being significantly less likely to cause gastrointestinal paralysis in animal models compared with epinephrine and norepinephrine (noradrenaline), improves gastric pHi and therefore by inference, splanchnic oxygen delivery, and reduces inflammatory changes in the gastrointestinal mucosa after major abdominal surgery.

Conclusion

Major body cavity surgery causes a strong inflammatory response, which in turn causes a marked increase in oxygen requirements. To match the demand, a patient will have to be able to elevate their cardiac output accordingly. The high-risk patient is one who can’t spontaneously elevate their cardiac output to the required level, and for elective cases we may be able to identify these patients through CPX testing.

To successfully manage a high-risk patient it is appropriate to monitor stroke volume and CI, and to use these variables to ensure that the patient’s circulation is optimally filled. Once optimal filling has been achieved, it is logical to measure indices of tissue perfusion and oxygen demand, such as base deficit, lactate levels, mixed venous oxygen saturation or gastric pHi. If these variables indicate persistent tissue hypoperfusion, it is likely that the CI and $D_O^2$ at the point of optimal filling is still inadequate and will need to be improved with inotropic support.

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