Chapter 24

Gastrointestinal surgery

S. Patel

This chapter will discuss several topics of relevance to anesthesia for gastrointestinal (GI) surgery, with especial reference to colorectal surgery.

Colorectal surgery

Colorectal surgery secondary to colorectal cancer, diverticular disease, inflammatory bowel disease and (less commonly) trauma, ischemic colitis, volvulus, and iatrogenic perforation is performed commonly in both an elective and emergency setting.

- Typical mortality following colorectal surgery in western countries is around 5% – higher than adult cardiac surgery.
- The incidence of complications after colorectal surgery varies from 13% to 37% in most studies [1]. In a recent retrospective study, the risk for incurring at least one postoperative complication was 24.0% in non-emergency and 48.2% in emergency patients [2].
- The 30-day in-hospital mortality during emergency surgery is three to four times higher in comparison to elective surgery [3]. The overall morbidity (medical or surgical complications) after emergency colorectal surgery is 3 to 10 times higher than morbidity after elective surgery.
- Several factors influence morbidity and mortality, such as functional status, nutrition, American Society of Anesthesiologists (ASA) grade, and perioperative optimization of physiology and clinical care.

Anesthesia for colorectal surgery is often poorly represented in major anesthesia textbooks. Indeed, publications related to enhanced recovery protocols and perioperative fluid therapy are frequently found in non-anesthesia journals.

Aspiration, rapid sequence induction, and cricoid pressure

In the U.K., a national audit of "Major complications of airway management" (NAP4) [4] has highlighted aspiration of stomach contents as a major contributory factor for anesthesia-related morbidity and mortality. In this audit, 55 serious airway-related incidents during general anesthesia were reported. Of these, 26 involved aspiration, and of all the anesthetic-related deaths reported to NAP4, 50% were due to aspiration.

Anesthesia and Perioperative Care of the High-Risk Patient, *Third edition*, ed. Ian McConachie.
Published by Cambridge University Press.

Risk factors

In the NAP4 audit [4], risk factors were present in 90% of 23 cases in whom aspiration was the primary event. During the preoperative period, assessment of risk factors and of their modification are fundamental aspects for prevention of aspiration. This is particularly important for urgent or emergency surgery. However, failure to assess/recognize risk factors for aspiration and to adjust the anesthetic technique accordingly were strikingly evident in the NAP4 audit and other large studies. Factors which predispose patients to aspiration include:

- Stomach and lower GI: feeding or lack of adequate fasting and delayed gastric emptying due to structural or functional causes such as pain, trauma, pyloric stenosis, intestinal obstruction, diabetes mellitus, and chronic renal failure.
- Esophagus: reduced lower esophageal tone, reflux, hiatus hernia, motility disorders, and previous surgery.
- Impaired reflexes: head injury, stroke, loss or impaired consciousness due to drugs or diseases, and neuromuscular diseases such as myasthenia gravies and Guillain Barré syndrome.
- Other factors: emergency surgery, pregnancy of >20 weeks, obesity, raised intra-abdominal pressure (e.g., abdominal laparoscopic surgery), multiple laryngoscopy, difficult intubation, and the lithotomy position.
- Supraglottic airway devices (SGDs), such as the laryngeal mask airway (LMA), may also be a risk factor, although when aspiration occurs with the use of an SGD, other risk factors for aspiration are almost always present. In one case series, identified risk factors were present in 19 of 20 patients who aspirated while an LMA was in place [5]. Second generation devices (e.g., proseal LMA or igel), with a channel for the passage of regurgitated material, may be helpful. Other practical points to consider with the use of an SGD are careful selection of cases, assurance of proper placement, avoidance of high inflation pressures and a lighter plane of anesthesia during the maintenance phase, and adequate reversal if paralytic agents were used.

Prevention

- Use of regional anesthesia, fasting as per standard guidelines, premedication in indicated cases with prokinetics drugs, antacids, H2-blockers, and proton pump inhibitors for high-risk cases, and rapid sequence induction and intubation (RSII) may prevent aspiration or minimize consequences [6]. In selected cases, insertion of a nasogastric tube and drainage of stomach contents should be done, as with intestinal obstruction or a paralytic ileus.
- Awareness, education, and training of staff are also important to reduce the incidence of aspiration [7].

Diagnosis

- Presence of gastric contents in endotracheal tube, LMA, or suction catheter should raise suspicion of aspiration. Symptoms vary depending on the nature of aspirated material (volume, particles, and pH), its sterility, and whether the patient is awake or anesthetised. Hypoxia and airway obstruction may be mild to severe. Fever, coughing, tachypnea, presence of wheeze, and crepitations on auscultation are also common features. Aspiration should be included in the differential diagnosis of airway obstruction, laryngospasm, bronchospasm, cyanosis, and pulmonary edema during the perioperative period.

Management

- Depending on the urgency and patient's clinical condition, surgery may proceed. In one study, 42 (64%) patients who aspirated but did not develop a cough, wheeze, decrease in arterial hemoglobin oxygen saturation while breathing room air of >10% less than the preoperative value, or radiographic abnormalities within two hours of aspiration had no further respiratory sequelae [8].
- Management depends on severity and may include chest physical therapy, bronchodilators, intubation and mechanical ventilation, and antibiotics.

Rapid sequence induction and intubation

RSII is performed to minimize the time interval between loss of protective airway reflexes and tracheal intubation with a cuffed endotracheal tube to prevent the risk of aspiration in at-risk patients. NAP4 [4] has identified several cases where the omission of RSII, although there were strong indications for its use, was followed by patient harm or death from aspiration. RSII has evolved and it consists of: optimal positioning of the patient, pre-oxygenation, injection of an opioid and a hypnotic intravenous (IV) injection of a fast-acting neuromuscular blocking agent, cricoid pressure (CP), and tracheal intubation. However, most of these components have not been standardized to form a universal protocol [9]. Induction and neuromuscular blocking drugs, timing of their administration, position of the patient during RSII, whether to do manual positive pressure mask ventilation, suppression of the intubation response, and application of CP during RSII are all debatable issues. The use of CP is probably the most debated aspect of RSII.

Cricoid pressure

To apply CP or not has remained controversial five decades since its introduction in clinical practice by Sellick in 1961. There are arguments for and against its use, which are outlined in Table 24.1 [10]. Despite lack of strong supporting evidence, CP is still considered an integral part of RSII.

For its optimal use, knowledge of anatomy, training, and use of the correct force with correct timing at the correct site are all important. The technique is as follows:

- After identifying the cricoid cartilage, pressure of 10 to 20 N for an adult patient (1 N equals approximately 10 kg) should be applied while the patient is awake before induction.
- Force should be increased to 30 to 40 N when the patient is unconscious.
- Excessive or lighter force is often applied by anesthesiologists and other healthcare professionals.
- CP should be released if the glottic view is obscured.

Simulated demonstration and application, use of mechanical devices or models to "feel" the correct force, and frequent retraining are some of the measures to increase its successful use. In pediatric populations, CP is used less frequently. Smaller anatomical structures,

Table 24.1. Pros and cons of cricoid pressure

	Arguments in favor	Arguments against
Evidence	Time-tested technique and has been a standard component of rapid sequence induction to prevent aspiration in at-risk patients. In the U.K., it is standard	Level D evidence No RCTs are available Evidence is from study on cadavers
Benefits	Prevents aspiration of gastric contents in high-risk cases at induction	Regurgitation of esophageal contents and aspiration can occur at the time of extubation
Technical aspects	Simple procedure and easy to learn Easy to teach and apply in clinical circumstances Devices can be used to teach and monitor force applied	Knowledge of CP and force necessary among clinicians is poor Difficult to judge how much force is applied Usually variable force is applied and there is no monitoring It is difficult to sustain force if intubation takes time
Efficacy	If correctly applied, prevents aspiration	Regurgitation and aspiration has been reported despite applying CP
Anatomical basis	CP substitutes for the loss of tone in the cricopharyngeus, which forms the upper esophageal sphincter Cricoid ring is a complete cartilage and effectively occludes esophagus to prevent regurgitated material to enter into the trachea Esophagus position is irrelevant as CP occludes hypopharynx with which it constitutes an anatomical unit	Reduces the lower esophageal sphincter tone up to 50% depending on the degree of the force applied Esophagus is not in the central position in nearly 50% of patients. CP may further displace esophagus laterally and does not occlude it in all cases CP flexes the neck and head, which may cause a suboptimal intubating position
Risks	Safe to apply and has been used in millions of patients No difference in visualization of larynx and does not increase the risk of difficult intubation There is no evidence that CP leads to failed intubation Airway risks are because of lack of training in use of CP	Interferes with mask ventilation, changes laryngoscopy grade, and may increase the intubation time or make it difficult, particularly if excessive force is applied. The incidence of these risks varies depending on the degree of force, and may occur in 50% of cases with recommended 30–40 N force Make insertion of LMA and intubation via LMA difficult Glotic view with fiberoptic endoscope, and other video laryngoscopes may also be impeded Esophageal rupture if vomiting occurs while CP is applied

Table 24.1. *(cont.)*

	Arguments in favor	Arguments against
Other	Prevents gastric insufflation during mask ventilation, which can be beneficial particularly in pediatric patients Effective in the presence of nasogastric tube	Causes patient discomfort and may provoke retching and vomiting

unknown effective force, and practical difficulty in application with an adult hand are some limiting factors to the use of CP in these cases. The force required may be as low as 5 N in infants and up to between 15 and 25 N in teenagers [11].

Fluid therapy

There is evidence that the type of fluid, its volume and timing of administration, and the patient's baseline physiology and response to fluid therapy influence GI functional recovery and complications (Figure 24.1). Many colorectal surgical patients have cardiorespiratory, renal, and endocrine problems. This high-risk group of patients may be more at risk for fluid overload.

Intestinal fluid dynamics

- Intestinal capillaries are fenestrated. The intestines have a large extracellular compartment and are more susceptible to edema formation in comparison to lung tissue. Alterations in microvascular permeability, portal venous pressure, plasma albumin level, and intestinal lymphatic function or flow result in imbalance of intestinal capillary Starling forces.
- Diseases (e.g., inflammatory bowel, peritonitis, bowel obstruction), technical factors (e.g., bowel preparation, bowel exposure and manipulation), and luminal factors (e.g., nutrients, toxins) are some of the potential factors that interfere with GI fluid balance.
- Systemic hypovolemia or hypervolemia may lead to intestinal edema, ischemia, hypoxia, acidosis, impaired healing, reduced nutrient delivery, and bacterial translocation. Clinical GI complications, like delayed oral intake, anastomosis leak, and delayed hospital discharge, may develop if fluid therapy is not optimal.

Choice of fluid: crystalloid or colloid

The crystalloid/colloid debate has existed since the 1980s. The debate shall be summarized with special relevance to GI surgery.

Experimental studies

- Goal-directed (GD) colloid therapy is associated with a significant increase in microcirculatory blood flow and oxygen tension in the small intestine, and in healthy and perianastomotic colonic tissue [12].
- GD crystalloid therapy, although increasing cardiac index and mean blood pressure (BP) by 15%, did not improve intestinal macro- and microcirculatory blood flow and oxygenation.

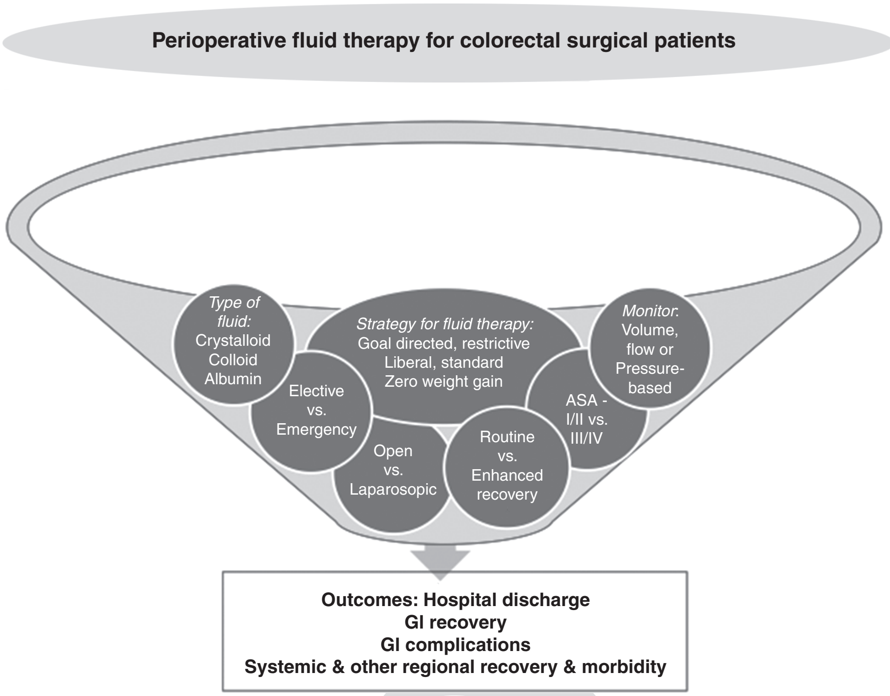

Figure 24.1. Influences of fluid therapy.

- Liberal crystalloid administration, even in large amounts (20 mL/kg), did not improve oxygen pressure in the small and the large intestine [13]. In fact, large-volume crystalloid therapy has been found to decrease bursting pressure, and also impaired healing at the anastomotic site with increased weight gain in experimental animals [14].
- In various septic models, colloids have been reported to have positive microcirculatory effects in the intestines, such as improved microcirculatory flow, decreased inflammatory markers, increased perfused capillary density, blockage of capillary leakage, reduced leukocyte adherence to endothelium, inhibition of platelet and erythrocyte aggregation.

Clinical crystalloid studies

- In a study by Prien et al. [15], colloid osmotic pressure decreased by 25% and water content in the jejunum increased significantly in patients receiving Ringer's lactate during Whipple's procedure. In contrast, both these parameters remained unchanged in the 10% hydroxyethyl starch group.
- In a retrospective review by Schnüriger et al. [16], high volume crystalloid resuscitation was found to be an independent risk factor for anastomotic leak (AL) following repair of traumatic colon injuries. The authors found a five-fold increased risk of anastomotic breakdown if the volume of crystalloid was more than 10.5 L in the first three postoperative days.

Clinical colloid Studies

- Recent large randomized controlled trials (RCTs) have raised concerns for the use of hydroxyethyl starch in severely septic patients, mainly because of increased renal complications, and recent guidelines recommend avoiding hetastarches [17]. Such clinical circumstances may arise in complicated colorectal surgical patients undergoing emergency surgery for severe peritonitis or a major AL, and in patients with abdominal sepsis.
- However, during elective abdominal surgery and in trauma patients, use of tetrastarches, particularly waxy maize-derived hydroxyethyl starch (130/0.4) is not associated with an adverse outcome [18,19]. There was no increased incidence of renal impairment or failure, or blood loss.

Recently, Chappell et al. [20] suggested the use of crystalloid to replace urinary loss and insensible loss via perspiration while iso-oncotic colloid should be used to replace plasma loss from the circulation due to pathological fluid shift and acute blood loss of up to a liter. They questioned the existence of a fluid-consuming "third space" whereby fluids are sequestered in the tissues.

Type of fluid therapy

Standard (routine), restrictive (low-volume), liberal (high-volume), goal-directed (targeted), and zero-weight gain are fluid management strategies studied in colorectal surgical patients. There is a lack of uniform definitions of the terms standard, restrictive, and liberal fluid administration [21].

- Standard (routine) fluid therapy is based on a fixed mL/kg/h calculation, which counts the period of perioperative fasting, maintenance, and replacement requirements. This approach may lead to fluid deficit or excess.
- Unmonitored restrictive (low-volume) and liberal (high-volume) fluid administration may also lead to hypovolemia or hypervolemia, respectively.
- There is evidence that liberal fluid therapy has been associated with weight gain, splanchnic edema, and pulmonary complications.
- In an RCT, Brandstrup et al. [22] reported a reduction in the rate of complications in a group of patients whose fluid therapy was designed to maintain unchanged body weight compared to a group receiving more liberal intravenous fluids.
- Restrictive fluid therapy may lead to increased sympathetic activation and may cause systemic hypotension, leading to increased use of vasopressors.

Restrictive fluid therapy

- In one RCT, intraoperative fluid restriction was associated with reduced perioperative central venous blood oxygen saturation ($ScvO_2$), even when using goal-directed boluses to correct hypovolemia [23]. The authors observed associations between reduced $ScvO_2$, hypovolemia, and postoperative complications in fluid restricted patients.
- Hubner et al. [24] studied restricted fluid therapy in patients undergoing fast-track open abdominal surgery in the presence of epidural analgesia. There was increased use of colloid boluses and vasopressors (to achieve a mean arterial pressure [MAP] of >60 mmHg and urine output of >0.5 mL/h) in fast-track patients, although this did not

reach statistical significance. The use of vasopressors during restrictive fluid therapy may raise concerns about intestinal oxygenation and metabolic function.

- Wenkui et al. [25] suggested monitoring serum lactate in fluid-restricted patients during fast-track surgery. In this study, colloid fluid boluses were needed in 25% of patients during the postoperative period to maintain the serum lactate level at the preoperative level.

Balanced fluid therapy

- Varadhan and Lobo [26] have analyzed studies using "fixed"-fluid volume therapy during major open abdominal surgery. Patients were considered in "fluid balance" if they received 1.75–2.75 L/d during the intraoperative and postoperative period. If patients received $<$1.75 L/d (restrictive) or $>$2.75 L/d (liberal), they were considered in "fluid imbalance" status. There was a 59% reduction in risk of developing complications and significant reduction in hospital stay in the fluid-balance group.

Goal-directed fluid therapy

- Stroke volume (SV) optimization is the common goal targeted in several studies. Fluid boluses are repeated until the increase in SV is less than 10% following the bolus. Colloids are frequently used to achieve a sustainable fluid bolus response.
- Other specific hemodynamic goals, such as SV variation or data derived from arterial pressure waveform analysis (stroke volume variation and pulse pressure variation) and central venous saturation, have also been used.
- Choice of the specific monitoring modality is still debated and there is no overwhelming evidence supporting the use of any particular tool.
- In the U.K., use of esophageal Doppler ultrasound has been recommended. However, it has generated controversy and it has been pointed out that initial clinical benefits with Doppler-guided fluid therapy might not be evident when compared with laparoscopic surgery together with enhanced recovery protocols [27].
- Early GI functional recovery and shorter hospital stay (average, two days) are frequently reported positive outcomes with GD fluid therapy [28]. This meta-analysis also reported a 30% reduction in the incidence of pneumonia and renal complications in a mixed surgical population.

Specific clinical circumstances (Figure 24.1)

Emergency surgery

- Emergency-complicated colorectal surgical patients are often fasted for days, poorly monitored for fluid balance, and have large concealed or revealed fluid losses.
- Inadequate resuscitation-associated systemic consequences and pre-existing medical problems makes fluid therapy more complex and challenging.
- Aggressive fluid therapy may be required to achieve optimal systemic perfusion.

Enhanced recovery protocols

- Patients on fast-track enhanced recovery protocols are expected to have no mechanical bowel preparation (except in left colon or rectal surgery), a short fasting period, oral

carbohydrate drink, no nasogastric tube, early postoperative oral intake, and reduced stress response (see later).
- As a result, fluid shift and duration of intravenous fluid therapy are likely to be small and short, respectively. Therefore, liberal use of fluid may not be justified. However, GD fluid therapy and fluid restriction are also controversial for patients on enhanced recovery protocols.

Laparoscopic surgery

- Bowel exposure and handling is minimal and recovery faster for patients undergoing laparoscopic colon surgery.
- Using transesophageal echocardiography, Concha et al. [29] found that patients undergoing laparoscopic colon surgery required 50% less crystalloid to maintain baseline left ventricular end-diastolic volume index and cardiac index when compared with open surgery: 3 mL/kg/h compared to 6 mL/kg/h.

In summary, a standard or formulaic approach is not possible because of the dynamic nature of the fluid shift and various fluid compartments. Frequent careful evaluations of the clinical condition and clinical contexts, and a review of fluid loss are essential and should not be overlooked because of overemphasis on technology and the search for optimized "numbers."

Anesthesia and the intestinal circulation

- The intestinal circulation is important for absorption of nutrients, formation and excretion of feces, and preservation of peristalsis. Protection of gut mucosal barrier function is pivotal during the perioperative period and certain critical conditions such as hemorrhage and sepsis.
- Normal superior and inferior mesenteric arterial blood flow is approximately 700 and 500 mL/min. There is an extensive collateral circulation. However, in some areas of the colon it is sparse, leading to a susceptibility to ischemia. The mucosa and submucosa receive 75% of the blood supply. A unique microcirculation permits transmural redistribution of blood flow. The mucosa is susceptible to hypoxia and hypoperfusion because of the counter current flow arrangement of the arteriole and venule in a villus.
- Several intrinsic (myogenic, metabolic, endothelium-derived factors, GI hormones, etc.) and extrinsic (sympathetic activity, circulatory vasoactive substances, systemic hemodynamic status) factors control intestinal blood flow [30].

Effects of anesthetic agents and techniques

Inhalational anesthetic agents may change intestinal blood flow (IBF) by direct cardiovascular effects like BP, cardiac output, redistribution of blood flow, or direct effects on mesenteric vascular smooth muscle. Effects on circulatory catecholamines, central sympathetic discharge, and splanchnic nerve activity influence mesenteric vascular resistance.

- In a human study [31], isoflurane increased PO_2 in the near resection and anastomotic site in comparison to desflurane. The authors suggested isoflurane preserved reactive hyperemia better following local tissue injury or manipulation.

- In another human study [32], use of one minimum alveolar concentration (MAC) desflurane increased jejunal blood flow compared to 1 MAC isoflurane, without significant changes in systemic hemodynamics.
- Thus, local mechanisms can play a crucial role during inhalational anesthesia. Isoflurane and sevoflurane also reduce mesenteric vascular resistance. The use of inhalational anesthetics may blunt the stress-induced increase in splanchnic vascular resistance.
- In addition, Kim et al. [33] recently demonstrated multiple protective effects of isoflurane postconditioning against intestinal ischemia–reperfusion injury.
- Propofol decreases mesenteric vascular resistance and increases IBF in a dose-dependant manner despite a decrease in MAP [34]. The increase in IBF is more in the small intestine than colon.
- Ketamine maintains capillary circulation and reduces leak following hemorrhagic shock and resuscitation [35].

Epidural analgesia

The level of epidural block (e.g., number of segments and region of block), baseline sympathetic activity in mesenteric and systemic blood vessels, volume status, and concentration of local anesthetic are important determining factors for intestinal circulatory effects of epidural anesthesia/analgesia. Theoretically, if the block is limited to mesenteric sympathetic activity (T8-L1), arteriolar dilation and venodilation would increase both macro- and microcirculation.

- Johannson et al. [36] observed an increase in intestinal microcirculatory blood flow despite a decrease in systolic BP in patients undergoing colon resection. Authors attributed this effect to decreased mean venous resistance.
- In contrast, Gould et al. [37] found a reduction in inferior mesenteric artery flow by 20% and colon serosal flow by 35% – both strongly correlated with reduction in MAP. In this study, blood flow was not related to cardiac output and did not respond to fluid alone but required vasopressor to restore MAP, inferior mesenteric artery flow, and colon serosal blood flow. The authors suggested maintaining the MAP with vasopressor during the perioperative period, in the presence of epidural block.
- In both these studies, 0.5% bupivacaine bolus was used during the intraoperative study period. Continuous infusion of lower concentrations of local anesthetic might have produced different results.

Recently, there has been interest in intestinal circulatory effects of epidural anesthesia during critical conditions such as sepsis and hemorrhage. There is a potential for redistribution of IBF to other organs or away from the ischemic or anastomotic site to normal intestine (longitudinal steal), or from mucosa to the muscularis region (horizontal steal). These effects are not well researched.

IBF in critical conditions

Hemorrhage

- The effect of angiotensin II and vasopressin on mesenteric vascular resistance may increase systemic vascular resistance significantly during shock [38].

- However, autoregulation of mucosa is better preserved in hemorrhagic shock in comparison to septic shock.
- Restoration of IBF and oxygenation, with fluid and blood resuscitation, usually lags behind improvements in systemic hemodyamic parameters [39].

Sepsis

- Stage of sepsis (early or late), volume status, and systemic hypotension are important clinical factors that determine the magnitude of intestinal circulatory and oxygenation disturbances.
- Redistribution of blood flow from muscularis to mucosa tends to maintain mucosal blood flow [40].
- However, in advanced septic shock, microcirulatory blood flow may be reduced by 50% due to endothelial swelling and microvascular thrombosis.

Increased intra-abdominal pressure (IAP)

- Direct effects lead to increased local vascular resistance.
- Mucosal perfusion is affected at lower pressures, but at higher pressures (>20 mmHg) mesenteric artery flow is also reduced [41].
- Persistent IAP causes intestinal hypoperfusion despite normal systemic BP. Decreased cardiac output and hypovolemia further exaggerate the effects. Bacterial translocation, intestinal edema, impaired intestinal motility, and breakdown of the anastomosis are serious consequences of moderate to severe IAP [42].

Effect of therapeutic strategies

Nutrition

With enteral feeding, macro- and micro-IBF is increased two to three times. Lipids followed by glucose are mostly responsible for the increase in blood flow. In contrast, total parenteral nutrition decreases intestinal blood flow [43].

Fluid therapy

Experimental studies suggest that goal-directed fluid therapy improves the small and large intestine macro- and microcirculation.

Vasopressorsinotropes

Effects of inotropes/vasopressors on the intestinal circulation are complex and may not follow systemic changes. Several reviews have addressed this subject [44,45].

- Norepinehrine (NE) may be the first choice for patients with septic shock who have received fluid resuscitation.
- NE may also be safe to use in fluid restricted patients undergoing abdominal surgery. Administration of 0.12±0.05 μg/kg/min NE was required to reach the target BP of 75 mmHg in fluid restricted (3 mL/kg/h) animals [46]. There were no adverse effects on the small intestine or colon blood flow and oxygenation.
- Anesthetic agents may modulate effects of vasopressors and inotropes. Dose-dependant increases in gastric mucosal oxygen saturation were observed with NE in the presence of sevoflurane [47]. Neither NE nor epinephrine changed gastric mucosal oxygen

saturation in the presence of propofol anesthesia despite doubling systemic oxygen delivery in the case of epinephrine.

In summary, the intestinal circulation is not well studied during the perioperative period in humans. There is very little information about the effects of anesthetic agents and techniques on intestinal macro- and microcirculation, or how anesthesia interacts with vasopressors or may modify the intestinal circulation in the presence of sepsis, hemorrhage, or other ischemic conditions.

Anesthesia and the anastomosis

AL is a major complication following GI surgery. AL occurs more frequently following esophagectomy and low rectal resection. For colorectal surgery, the incidence ranges from 2% to 4% for intraperitoneal and 6% to 12% for extraperitoneal anastomosis. It may lead to abdominal and systemic sepsis and increases the risk of mortality two to five times. The diagnosis is mainly clinical and/or radiological.

Risk factors

Risk factors have not been consistent in the various studies [48] because of heterogeneity of data (e.g., diagnosis, site of anastomosis, exclusion criteria) and different definitions used [49]. AL could occur due to patient, operative, or technical factors.

- Malnutrition (hypoalbuminemia and anemia), smoking, use of steroids, and an American Society of Anesthesiologists (ASA) score of >3 are frequently reported patient-related risk factors.
- Infraperitoneal anastomosis, prolonged surgery (>4 hours), amount of blood loss (>300 mL), blood transfusion, and intraoperative septic conditions may also predispose to AL.
- Male gender, obesity, location of tumor within 12 cm from anal verge, use of abdominal drains, and emergency surgery are also implicated in some studies.
- Mechanical bowel preparation, laparosopic surgery, surgical technique for anastomosis (e.g., hand sewn or stapled), and intraoperative testing of anastomosis does not seem to influence AL incidence.

Systemic and intestinal oxygenation

Tissue oxygenation

The oxygen supply to intestinal and abdominal wounds is critical for prevention of infection and promotion of healing at both ends of the anastomosis.

- In an experimental model, all intestinal anastomoses developed a major leak below a critical perianastomotic level of 25 mmHg pO_2 [50].
- In a human study [51], low tissue pO_2 levels were found to be of value in the prediction of an AL.
- However, Schietroma et al. [52] reported 46% lower anastomosis leak in an 80% inspired oxygen concentration [FiO_2] group (relative ratio [RR], 0.63; 95% confidence interval [CI_{95}], 0.42–0.98) compared to a 30% FiO_2 group, and suggested that 80% FiO_2 should be administered routinely during surgery and for up to six hours in the postoperative period.

Hemodynamic optimization

The blood supply at the anastomotic site may depend on blood volume status, cardiac output and its distribution, local capillary perfusion, and several pathological and technical factors (e.g., mobilization of tissue and suture tension). GD fluid therapy or GD hemodynamic management (fluids and or inotropes) have been suggested to reduce major GI complications including AL [53]. However, caution is necessary with regards to the use of vasopressors.

- Zakiroson et al. [54] found intraoperative use of intermittent boluses of vasopressors (phenylephrine and ephedrine) was not associated with increased AL. In contrast, NE infusion in an intensive care setting during the postoperative period increases the risk of AL three(times. The authors suggested that it could be due to hypovolemia during the use of the vasopressor infusion.

Non-steroidal anti-inflammatory drugs (NSAIDs)

Inhibition of cyclooxygenase (COX) enzymes by NSAIDs affects leukocyte function, induces apoptosis, and decreases crypt survival. It also reduces production of vascular endothelial growth factor and angiogenesis, and interferes with collagen formation and cross-linking.

- Klein et al. [55] reported higher AL patients treated with diclofenac in comparison to ibuprofen and controls ($P<0.001$ for diclofenac versus controls; $P=0.004$ for ibuprofen versus controls). After multivariate logistic regression analysis, only diclofenac treatment was a risk factor for leakage (odds ratio [OR] 7.2, CI_{95} 3.8–13.4, $P<0.001$).
- There are contradictory reports with regard to selective Cox-2 inhibitors. In one recent retrospective study [56], increased AL was found with the use of mainly non-selective NSAIDs such as diclofenac but not with selective Cox-2 inhibitors such as meloxicam and celecoxib.

Large RCTs are needed to resolve the controversy surrounding NSAIDs and AL.

Neostigmine

- Neostigmine increases intraluminal pressure and colonic and rectal motor activity which, in theory, may cause excessive traction on anastomotic suture lines, resulting in leakage.
- However, animal studies do not suggest an increased incidence of AL associated with the use of neostigmine, but clinical evidence for such an effect is lacking.

N_2O

N_2O causes bowel distension. However, there are no reports of increased incidence of AL with its use.

Epidural analgesia

Epidural anesthesia increases intestinal motility and tone by interrupting nociceptive pain afferents and blockade of thoracolumbar sympathetic efferents. This could lead to anastomosis dehiscence. However, epidural analgesia may improve intestinal blood flow directly by mesenteric vasodilation.

- Holte and Kehlet [57] analyzed RCTs and concluded that there was no statistical difference in AL between:
  - epidural analgesia versus systemic opioid
  - epidural opioid versus systemic opioid
  - epidural analgesia -opioid mixture versus systemic opioid
  - epidural opioid versus systemic opioid
- Thus epidural analgesia does not seem to have harmful effects on intestinal anastomosis and this has been confirmed by a recent large study [58].

Oxygen and surgical site infection (SSI)

SSI is one of the most common causes of hospital-acquired infection in surgical patients. The incidence of wound infection following colorectal surgery varies from 5% to 25% in different studies. Surgical (e.g., open versus laparoscopic, elective versus emergency, technique, duration, blood transfusion, etc.), host (e.g., nutritional immune status, obesity), clinical practice (e.g., administration of antibiotics, temperature, glycemic control, hand hygiene), and environmental (e.g., clean air, local infection control policy) factors may all influence the rate of SSI.

Rationale for perioperative hyperoxia

- Hyperoxia increases the rate of local phagocytosis and decreases systemic inflammatory mediators such as tumor necrosis factor (TNF)-α. Reactive oxygen species (ROS) are critical mediators required for oxidative intracellular killing of micro-organisms by leukocytes and macrophages.
- Wound hypoxia is common in the early postoperative period due to local tissue trauma leading to vasoconstriction, thrombosis and edema, and increased oxygen demand by defensive immune cells and healing tissue. Higher FiO_2 has been demonstrated to increase the pO_2in subcutaneous tissue and the colon [59].
- The differing effects of moderate hyperoxia (e.g., FiO_2 40%–60%) or higher FiO_2 for long postoperative periods on SSI are not known.

Perioperative studies:

- Most studies have compared 30% with 80% FiO_2 during the intraoperative period and for a brief time in the immediate postoperative period. Both the concentration and duration of oxygen administration studied are arbitrary choices.
- In the first major study to examine this issue, Greif et al. [59] reported a 50% reduction in SSI with the use of 80% FiO_2 in elective colorectal surgical patients.
- Other studies have been performed, which vary in their methodology, exclusion criteria, definition of SSI, type of surgery, duration of surgery, bowel preparation, and fluid and pain management.
- Seven meta-analyses have examined the effectiveness of hyperoxia on SSI, the most recent being published in 2013 [60].
- For colorectal surgery, high FiO_2 reduced the risk of SSI (RR 0.78, CI_{95} 0.6–1.02). They found no increased risk of postoperative atelectasis and a reduction in postoperative nausea and vomiting in patients receiving inhalational anesthesia without prophylactic antiemetics [60].

In summary, hyperoxia may have a modest benefit in reduction of SSI in patients undergoing elective colorectal surgery. It is included in some institutions' "colorectal care bundle" to reduce SSI.

Enhanced recovery protocols

- Major surgical trauma disturbs homeostatic function and may result in organ dysfunction. In addition, several factors exaggerate the stress response or delay the return of normal physiological functions. These include inadequate nutrition, fluid and temperature imbalance, and pain.
- Kehlet and Wilmore [61] suggested that early recovery and hospital discharge could be achieved by adopting a multidisciplinary "bundle of care" protocol to achieve enhanced recovery after surgery (ERAS).
- Much of the focus has been on colorectal surgery.
- Each part of the protocol is potentially beneficial but the best results should be obtained by combining them into an overall package of care.
- The concept of fast-track surgery continues to evolve and is now well established in many countries to accelerate physiological and functional recovery following colorectal surgery.

Aims of the ERAS approach

Enhanced recovery protocols (ERP) incorporate and deliver evidence-based elements of clinical care in an integrated pathway (Figure 24.2). The aims of ERP for colorectal surgery are:

- to maintain or achieve early return of systemic and gastrointestinal functions
- to accomplish stress (e.g., hemodynamic, metabolic, inflammatory, and immune) and pain free surgery
- to rehabilitate patients from associated pathophysiological changes toward independence

Advantages

Length of stay

Length of the stay in hospital has been the primary outcome of many studies evaluating the usefulness of ERPs. Most RCTs and meta-analyses have demonstrated significant reduction of hospital stay by two to three days [62,63], when compared to conventional care after open colorectal surgery. However, there was significant heterogeneity among the RCTs for the effect of ERP on the length of hospital stay.

- In a Cochrane review [64] of four RCTs (119 ERAS patients versus118 conventional recovery patients) including at least seven items in the ERAS group and no more than two in the conventional arm found that length of stay was significantly reduced in the ERAS group (mean difference, −2.94 d; CI_{95}, −3.69 to −2.19), and readmission rates were equal in both groups (Cochrane). However, the quality of RCTs was low.

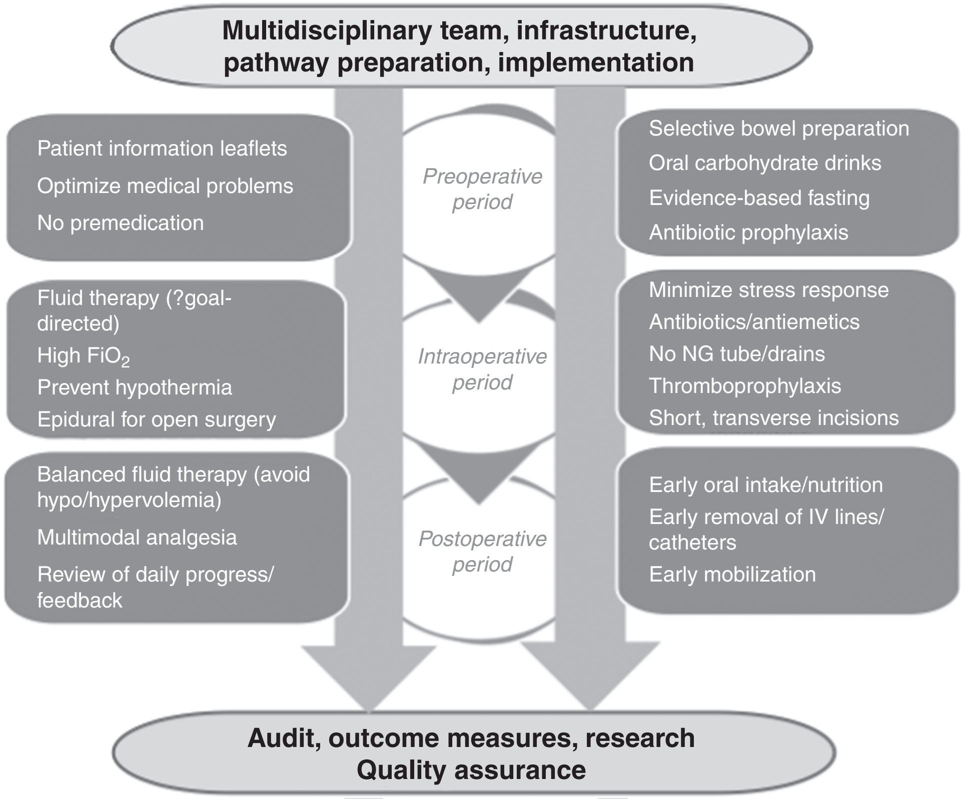

Figure 24.2. Enhanced recovery after surgery pathways.

Furthermore, hospital discharge criteria are not uniform.

- Massen et al. [65] suggested to use functional outcomes (first day tolerance of food, good pain control on oral analgesics, defecation, and independence in activities of daily living to preoperative care level) to judge the success of ERP.

Note: ERP may not reduce length of stay for patients undergoing laparoscopic surgery.

Effect on morbidity

In a meta-analysis of 453 patients (226 in the ERAS group and 226 in the traditional care group) from six RCTs, Vadradan et al. [63] found a 50% reduction in complication rates in the ERAS group after open surgery. However, the method of reporting complications and their severity was not uniform among studies.

Stress response

Ren et al. [66] reported lower insulin resistance, cortisol, and cytokine levels, and negative nitrogen balance and higher albumin in the ERP group compared to standard care. They suggested that lower stress and inflammatory responses and better metabolic and nutritive indices are responsible for the lower morbidity and early recovery with ERP.

Postoperative ileus

- Tolerance of a normal diet and time of first bowel movement were decreased by >1 day in all randomized trials.
- Elements of ERP such as avoidance of nasogastric (NG) tubes, optimal fluid therapy, use of epidural analgesia for open surgery, and emphasis on opiate-free analgesia are beneficial for early GI function recovery.
- Laparoscopic surgery may add advantage to ER protocols in minimizing postoperative paralytic ileus.

Safety

Most studies have found that ERP is safe and does not lead to increased rate of readmissions. It does not increase the rate of either medical or surgical complications. However, there is no difference in mortality compared to standard care.

Implementation

- Multidisciplinary teams, which include surgeons, anesthetists, nursing staff, pain team, physical therapists, and nutrition experts, are essential for implementing ERP. Patient education and counseling is also important. Depending on local structure, managerial or community support may be required.
- Acceptance of protocols, organization of structured perioperative care (e.g., to facilitate nutrition, mobilization, and other nursing care), training and retraining of staff (e.g., new junior doctors and other staff), and monitoring of protocol compliance are important for successful implementation.

ERP components and its compliance, deviation, and failure

Compliance

Comprehensive compliance for all components may not be possible and always practical. Even partial compliance is found to be beneficial but improving compliance results in more benefits.

- Gustafsson et al. [67] studied over 900 patients between 2002 and 2004, and 2005 and 2007. The adherence to ERP was 43% and 74%, respectively. Overall, moving from 50% to 90% compliance with ERP led to improvement in outcomes such as reduced complications, fewer symptoms causing delayed discharge, and shorter length of stay.
- In a systematic review, Ahmed et al. [68] found that compliance of ERP in the postoperative period was the most problematic. This may be due to multiple individuals being involved in care, lack of motivation to accept changes, and unawareness of ERP elements among staff.

Importance of individual components

- Recent guidelines have reviewed the evidence for each component [69].
- The influence of individual components of ERP on outcome is difficult to judge.
- The numbers of components used are variable in studies evaluating ERP and ranged from 4 to 12.
- Preoperative counseling, avoidance of NG tubes, postoperative enforced enteral nutrition, and early mobilization were included in all studies. Preoperative carbohydrate

loading, no mechanical bowel preparation, epidural analgesia, no abdominal drains, and morphine-sparing analgesia were also employed in most of the RCTs.
- Vlug et al. [70] found that two postoperative phase elements (normal diet and enforced mobilization in the first three postoperative days) were independent predictors for early discharge from hospital.

Deviation and failure

- In a retrospective study [71] of 385 patients who underwent laparoscopic colorectal surgery, the compliance rate was 85% for pre- and intraoperative elements; 41% deviated from one or two postoperative elements. In a univariate analysis, delayed discharge (31%) was associated strongly with deviation of all five postoperative elements – continued IV fluids after day 1, lack of functioning epidural analgesia, failure to mobilize on day 1, insertion of the NG tube for vomiting, and reinsertion of the urinary catheter.
- Intraoperative complications and failure to mobilize are important causes of deviation [72]. It has been suggested that failure to mobilize should be considered as a red flag sign following laparoscopic colorectal surgery and should be investigated. Failure to mobilize may occur due to postoperative complications (e.g., gut dysfunction), poor pain relief, or orthostatic hypotension due to various causes.
- ERP can be modified as per local need and if a complication occurs.
- ERP also depends on the individual surgery. For example, rectal surgery/pelvic surgery may require mechanical bowel preparation, stoma formation, longer urinary catheterization, etc.
- ERP may also be influenced by the patient's choice. For example, failure to consent for epidural analgesia.

Therefore, although the principles of ERP are generalized, an individualized approach is desirable.

References

1. Alves A, Panis Y, Mathieu P, et al. Association Française de Chirurgie: Postoperative mortality and morbidity in French patients undergoing colorectal surgery: results of a prospective multicenter study. *Arch Surg* 2005; **140**: 278–83.
2. Ingraham AM, Cohen ME, Bilimoria KY, et al. Comparison of hospital performance in nonemergency versus emergency colorectal operations at 142 hospitals. *J Am Coll Surg* 2010; **210**: 155–65.
3. Sjo OH, Larsen S, Lunde OC, et al. Short term outcome after emergency and elective surgery for colon cancer. *Colorectal Dis* 2009; **11**: 733–9.
4. Cook TM, Woodall N, Frerk C. Major complications of airway management in the UK: results of the 4th National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society. Part 1: Anaesthesia. *Br J Anaesth* 2011; **106**: 617–31.
5. Keller C, Brimacome J, Bittersohl J, et al. Aspiration and the laryngeal mask airway: three cases and a review of the literature. *Br J Anaesth* 2004; **93**: 579–82.
6. Ng A, Smith G. Gastresophageal reflux and aspiration of gastric contents in anesthetic practice. *Anesth Analg* 2001; **93**: 494–513.
7. Kluger MT, Short TG. Aspiration during anaesthesia: a review of 133 cases from the Australian Anaesthetic Incident Monitoring Study (AIMS). *Anaesthesia* 1999; **54**: 19–26.
8. Warner MA, Warner ME, Weber JG. Clinical significance of pulmonary

aspiration during the perioperative period. *Anesthesiology* 1993; **78**: 56–62.

9. Neilipovitz DT, Crosby ET. No evidence for decreased incidence of aspiration after rapid sequence induction. *Can J Anaesth* 2007; **54**: 748–64.

10. El-Orbany M, Connolly L. Rapid sequence induction and intubation: current controversy. *Anesth Analg* 2010; **110**: 1318–25.

11. Walker RWM, Ravi R, Haylett K. Effect of cricoid force on airway calibre in children: a bronchoscopic assessment. *Br J Anaesth* 2010; **104**: 71–4.

12. Kimberger O, Arnberger M, Brandt S, et al. Goal-directed colloid administration improves the microcirculation of healthy and perianastomotic colon. *Anesthesiology* 2009; **110**: 496–504.

13. Hiltebrand LB, Pestel G, Hager H, et al. Perioperative fluid management: comparison of high, medium and low fluid volume on tissue oxygen pressure in the small bowel and colon. *Eur J Anesthesiol* 2007; **24**: 927–33.

14. Marjanovic G, Villain C, Juettner E, et al. Impact of different crystalloid volume regimes on intestinal anastomotic stability. *Ann Surg* 2009; **249**: 181–5.

15. Prien T, Backhaus N, Pelster F, et al. Effect of intraoperative fluid administration and colloid osmotic pressure on the formation of intestinal edema during gastrointestinal surgery. *J Clin Anesth* 1990; **2**: 317–23.

16. Schnüriger B, Inaba K, Wu T, et al. Crystalloids after primary colon resection and anastomosis at initial trauma laparotomy: excessive volumes are associated with anastomotic leakage. *J Trauma* 2011; **70**: 603–10.

17. Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med* 2013; **41**: 580–637.

18. Martin C, Jacob M, Vicaut E, et al. Effect of waxy maize-derived hydroxyethyl starch 130/0.4 on renal function in surgical patients. *Anesthesiology* 2013; **118**: 387–94.

19. Van Der Linden P, James M, Mythen M, et al. Review article: safety of modern starches used during surgery. *Anesth Analg* 2013; **116**: 35–48.

20. Chappell D, Jacob M, Hofmann-Kiefer K, et al. A rational approach to perioperative fluid management. *Anesthesiology* 2008; **109**: 723–40.

21. Rahbari NN, Zimmermann JB, Schmidt T, et al. Meta-analysis of standard, restrictive and supplemental fluid administration in colorectal surgery. *Br J Surg* 2009; **96**: 331–41.

22. Brandstrup B, Tønnesen H, Beier-Holgersen R, et al. Effects of intravenous fluid restriction on postoperative complications: comparison of two perioperative fluid regimens: a randomized assessor-blinded multicentre trial. *Ann Surg* 2003; **238**: 641–8.

23. Futier E, Constantin JM, Petit A, et al. Conservative vs restrictive individualized goal-directed fluid replacement strategy in major abdominal surgery: a prospective randomized trial. *Arch Surg* 2010; **145**: 1193–200.

24. Hubner M, Schafer M, Demartines N, et al. Impact of restrictive intravenous fluid replacement and combined epidural analgesia on perioperative volume balance and renal function within a fast track program. *J Surg Res* 2012; **173**: 68–74.

25. Wenkui Y, Ning L, Jianfeng G, et al. Restricted perioperative fluid administration adjusted by serum lactate level improved outcome after major elective surgery for gastrointestinal malignancy. *Surgery* 2010; **147**: 542–52.

26. Varadhan KK, Lobo DN. A meta-analysis of randomised controlled trials of intravenous fluid therapy in major elective open abdominal surgery: getting the balance right. *Proc Nutr Soc* 2010; **69**: 488–98.

27. Srinivasa S, Taylor MH, Sammour T, et al. Esophageal Doppler-guided fluid administration in colorectal surgery: critical appraisal of published clinical trials. *Acta Anesthesiol Scand* 2011; **55**: 4–13.

28. Corcoran T, Rhodes JE, Clarke S, et al. Perioperative fluid management strategies in major surgery: a stratified meta-analysis. *Anesth Analg* 2012; **114**: 640–51.

29. Concha MR, Mertz VF, Cortinez LI, et al. Pulse contour analysis and transesophageal echocardiography: a comparison of measurements of cardiac output during laparoscopic colon surgery. *Anesth Analg* 2009; **109**: 114–18.

30. Matheson PJ, Wilson MA, Garrison RN. Regulation of intestinal blood flow. *J Surgi Res* 2000; **93**: 182–96.

31. Müller M, Schindler E, Roth S, et al. Effects of desflurane and isoflurane on intestinal tissue oxygen pressure during colorectal surgery. *Anaesthesia* 2002; **57**: 110–15.

32. O'Riordan J, O'Beirne HA, Young Y, et al. Effects of desflurane and isoflurane on splanchnic microcirculation during major surgery. *Brit J Anaesth* 1997; **78**: 95–6.

33. Kim M, Park SW, Kim M, et al. Isoflurane postconditioning protects against intestinal ischemia-reperfusion injury and multi-organ dysfunction via transforming growth factor-beta1 generation. *Ann Surg* 2012; **255**: 492–503.

34. Carmichael FJ, Crawford W, Khayyam N, et al. Effect of propofol infusion on splanchnic hemodynamics and liver oxygen consumption in the rat: a dose-response study. *Anesthesiology* 1993; **79**: 1051–60.

35. Brookes Z, Brown L, Reilly C. Differential effects of intravenous anaesthetic agents on the response of rat mesenteric microcirculation in vivo after haemorrhage. *Brit J Anaesth* 2002; **88**: 255–63.

36. Johansson K, Ahn H, Lindhagen J, et al. Effect of epidural anaesthesia on intestinal blood flow. *Br J Surg* 1988; **75**: 73–6.

37. Gould TH, Grace K, Thome G, et al. Effect of thoracic epidural anaesthesia on colonic blood flow. *Brit J Anaesth* 2002; **89**: 446–51.

38. Reilly PM, Wilkins KB, Fuh KC, et al. The mesenteric hemodynamic response to circulatory shock: an overview. *Shock* 2001; **15**: 329–43.

39. Knotzer H, Pajk W, Maier S, et al. Comparison of lactated Ringer's, gelatine and blood resuscitation on intestinal oxygen supply and mucosal tissue oxygen tension in haemorrhagic shock. *Brit J Anaesth* 2006; **97**: 509–16.

40. Hiltebrand LB, Krejci V, Banic A, et al. Redistribution of microcirculatory blood flow within the intestinal wall during sepsis and general anesthesia. *Anesthesiology* 2003; **98**: 658–69.

41. Olofsson PH, Berg S, Ahn HC, et al. Gastrointestinal microcirculation and cardiopulmonary function during experimentally increased intra-abdominal pressure *Crit Care Med* 2009;, **37**: 230–9.

42. Faisal AM, Abell LM, Chawla LS. Understanding intra-abdominal hypertension from the bench to the bedside. *J Intensive Care Med* 2012; **27**: 145–60.

43. Marcel G, Macfie J, Anderson A, et al. Changes in superior mesenteric artery blood flow after oral, enteral, and parenteral feeding in humans. *Crit Care Med* **37**: 171–6.

44. Boerma EC, Ince C. The role of vasoactive agents in the resuscitation of microvascular perfusion and tissue oxygenation in critically ill patients. *Intensive Care Med* 2010, **36**: 2004–18.

45. Gelman S, Mushlin PS. Catecholamine-induced changes in the splanchnic circulation affecting systemic hemodynamics. *Anesthesiology* 2004; **100**: 434–9.

46. Hiltebrand LB, Koepfli E, Kimberger O, et al. Hypotension during fluid-restricted abdominal surgery: effects of norepinephrine treatment on regional and microcirculatory blood flow in the intestinal tract. *Anesthesiology* 2011; **114**: 557–64.

47. Schwarte LA, Schwartges I, Schober P, et al. Sevoflurane and propofol anesthesia differentially modulate the effects of epinephrine and norepinephrine on microcirculatory gastric mucosal oxygenation. *Br J Anesth* 2010; **105**: 421–8.

48. Kingham TP, Pachter HL. Colonic anastomotic leak: risk factors, diagnosis, and treatment. *J Am Coll Surg* 2009; **208**: 269–78.

49. Bruce J, Krukowski ZH, Al-khairy G, et al. Systematic review of the definition and measurement of anastomotic leak after gastrointestinal surgery. *Br J Surg* 2001; **88**: 1157–68.

50. Sheridan WG, Lowndes RH, Young HL. Tissue oxygen tension as a predictor of colonic anastomotic healing. *Dis Colon Rectum* 1987; **30**: 867–71.

51. Karliczek A, Benaron DA, Baas PC, et al. Intraoperative assessment of microperfusion with visible light spectroscopy for prediction of anastomotic leakage in colorectal anastomoses. *Colorectal Dis* 2010; **10**: 1018–25.

52. Schietroma M, Carlei F, Cecilia E, et al. Colorectal infraperitoneal anastomosis: the effects of perioperative supplemental oxygen administration on the anastomotic dehiscence. *J Gastrointest Surg* 2012; **16**: 427–34.

53. Giglio MT, Marucci M, Testini M, et al. Goal-directed haemodynamic therapy and gastrointestinal complications in major surgery: a metaanalysis of randomized controlled trials. *Br J Anaesth* 2009; **103**: 637–46.

54. Zakrison T, Nascimento BA Jr, Tremblay LN, et al. Perioperative vasopressors are associated with an increased risk of gastrointestinal anastomotic leakage. *World J Surg* 2007; **31**: 1627–34.

55. Klein M, Gogenur I, Rosenberg J. Postoperative use of non-steroidal anti-inflammatory drugs in patients with anastomotic leakage requiring reoperation after colorectal resection: *cohort study based on prospective data. BMJ* 2012; **345**: e6166.

56. Gorissen KJ, Benning D, Berghmans T, et al. Risk of anastomotic leakage with non-steroidal anti-inflammatory drugs in colorectal surgery. *Br J Surg* 2012; **99**: 721–7.

57. Holte K, Kehlet H. Epidural analgesia and risk of anastomotic leakage. *Reg Anesth Pain Med* 2001; **26**: 111–17.

58. Halabi WJ, Jafari MD, Nguven VQ, et al. A nationwide analysis of the use and outcomes of epidural analgesia in open colorectal surgery. *J Gastrointest Surg* 2013; **13**: 1130–7.

59. Greif R, Akca O, Horn EP, et al. Supplemental perioperative oxygen to reduce the incidence of surgical-wound infection. *N Engl J Med*. 2000; **342**: 161–7.

60. Hovaguimian F, Lysakowski C, Elia N, et al. Effect of intraoperative high inspired oxygen fraction on surgical site infection, postoperative nausea and vomiting, and pulmonary function: systematic review and meta-analysis of randomized controlled trials. *Anesthesiology* 2013; **119**: 303–16.

61. Kehlet H, Wilmore DW. Multimodal strategies to improve surgical outcome. *Am J Surg* 2002; **183**: 630–41.

62. Gouvas N, Tan E, Windsor A, et al. Fast-track vs. standard care in colorectal surgery: a meta-analysis update. *Int J Colorectal Dis* 2009; **24**: 1119–31.

63. Varadhan KK, Neal KR, Dejong CH, et al. The enhanced recovery after surgery (ERAS) pathway for patients undergoing major elective open colorectal: a meta-analysis of randomized controlled trials. *Clin Nutr* 2010; **29**: 434–40.

64. Spanjersberg WR, Reurings J, Keus F, et al. Fast track surgery versus conventional recovery strategies for colorectal surgery. *Cochrane Database Syst Rev* 2011; **2**: CD007635.

65. Maessen JMC, Dejong CHC, Kessels AGH, et al. Length of stay: an inappropriate readout of the success of enhanced recovery programs. *World J Surg* 2008; **32**: 971–5.

66. Ren L, Zhu D, Wei Y, et al. Enhanced Recovery After Surgery (ERAS) Program attenuates stress and accelerates recovery in patients after radical resection for colorectal cancer: a prospective randomized controlled trial. *World J Surg* 2012; **36**: 407–14.

67. Gustafsson UO, Hausel J, Thorell A, et al. Adherence to the Enhanced Recovery After Surgery Protocol and outcomes after colorectal cancer surgery. *Arch Surg* 2011; **146**: 571–7.

68. Ahmed J, Khan S, Lim M, et al. Enhanced Recovery after Surgery Protocols: compliance and variations in practice

during routine colorectal surgery. *Colorectal Dis* 2012; **14**: 1045–51.

69. Gustafsson U, Scott MJ, Schwenk W, et al. Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS) society recommendations. *World J Surg* 2013; **37**: 259–84.

70. Vlug MS, Bartels SA, Wind J, et al. Which fast track elements predict early recovery after colon cancer surgery? *Colorectal Dis* 2012; **14**: 1001–8.

71. Smart NJ, White P, Allison AS, et al. Deviation and failure of enhanced recovery after surgery following laparoscopic colorectal surgery: early prediction model. *Colorectal Dis* 2012; **14**: e727–34.

72. Boulind CE, Yeo M, Burkill C, et al. Factors predicting deviation from an enhanced recovery programme and delayed discharge after laparoscopic colorectal surgery. *Colorectal Dis* 2012; **14**: e103–10.