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Guidelines for Perioperative Care in Elective Colonic Surgery: Enhanced Recovery After Surgery (ERAS®) Society Recommendations

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Abstract

Background This review aims to present a consensus for optimal perioperative care in colonic surgery and to provide graded recommendations for items for an evidenced-based enhanced perioperative protocol.

Methods Studies were selected with particular attention paid to meta-analyses, randomised controlled trials and large prospective cohorts. For each item of the perioperative treatment pathway, available English-language literature was examined, reviewed and graded. A consensus recommendation was reached after critical appraisal of the literature by the group.

Results For most of the protocol items, recommendations are based on good-quality trials or meta-analyses of good-quality trials (quality of evidence and recommendations according to the GRADE system).

Conclusions Based on the evidence available for each item of the multimodal perioperative care pathway, the Enhanced Recovery After Surgery (ERAS) Society, International Association for Surgical Metabolism and Nutrition (IASMEN) and European Society for Clinical Nutrition and Metabolism (ESPEN) present a comprehensive evidence-based consensus review of perioperative care for colonic surgery.

This study was conducted on behalf of the ERAS® Society, the European Society for Clinical Nutrition and Metabolism and the International Association for Surgical Nutrition and Metabolism

The guidelines are published as a joint effort between the Enhanced Recovery After Surgery (ERAS) Society, for Perioperative Care, The European Society for Clinical Nutrition and Metabolism (ESPEN) and The International Association for Surgical Metabolism and Nutrition (IASMEN) and copyrights for this publication is shared between the three societies. The guidelines are published jointly in World Journal of Surgery (IASMEN) and Clinical Nutrition (ESPEN), and will also be available on the ESPEN (http://www.espen.org), IASMEN (http://www.iasmen.org) and ERAS Society website (http://www.erassociety.org).

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Introduction

The delay until full recovery after major abdominal surgery has been greatly improved by the introduction of a series of

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evidence-based treatments covering the entire perioperative period and formulated into a standardised protocol. Compared with traditional management, Enhanced Recovery After Surgery (ERAS®) represents a fundamental shift in perioperative care [1–4]. The ERAS care pathways reduce surgical stress, maintain postoperative physiological function, and enhance mobilisation after surgery. This has resulted in reduced rates of morbidity, faster recovery and shorter length of stay in hospital (LOSH) in case series from dedicated centres [1–4] and in randomised trials [5, 6].

Several versions of Enhanced Recovery Programmes have been published over the years [7–9].

This article represents the joint efforts of the ERAS Society (www.erassociety.org), International Association for Surgical Metabolism and Nutrition (IASMEN; www.iasmen.org) and the European Society for Clinical Nutrition and Metabolism (ESPEN) to present an updated and expanded consensus review of perioperative care for colonic surgery based on current evidence.

Methods

Literature search

The authors met in April 2011 and the topics for inclusion were agreed and allocated. The principal literature search utilised MEDLINE, Embase and Cochrane databases to identify relevant contributions published between January 1966 and January 2012. Medical Subject Headings terms were used, as were accompanying entry terms for the patient group, interventions and outcomes. Key words included "colon", "enhanced recovery" and "fast track". Reference lists of all eligible articles were checked for other relevant studies. Conference proceedings were not searched. Expert contributions came from within the ERAS Society Working Party on Systematic Reviews.

Study selection

Titles and abstracts were screened by individual reviewers to identify potentially relevant articles. Discrepancies in judgement were resolved by the senior author and during committee meetings of the ERAS Society Working Party on Systematic Reviews. Reviews, case series, non-randomised studies, randomised control studies, meta-analyses and systematic reviews were considered for each individual topic.

Quality assessment and data analyses

The methodological quality of the included studies was assessed using the Cochrane checklist [10]. The strength of evidence and conclusions were assessed and agreed by all authors in May 2012. Quality of evidence and recommendations were evaluated according to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system [11–13]. Quoting from the GRADE guidelines [13], the recommendations are given as follows: "Strong recommendations indicate that the panel is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects". "Weak recommendations indicate that the desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but the panel is less confident". Recommendations are based on quality of evidence ("high", "moderate", "low" and "very low") but also on the balance between desirable and undesirable effects; and on values and preferences [13]. The latter implies that, in some cases,

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strong recommendations may be reached from low-quality data and vice versa.

Evidence base and recommendations

ERAS items

Preadmission information, education and counseling

Detailed information given to patients before the procedure about surgical and anaesthetic procedures may diminish fear and anxiety and enhance postoperative recovery and quicken hospital discharge [14, 15]. A preoperative psychological intervention, aimed at decreasing patient anxiety, may also improve wound healing and recovery after laparoscopic surgery [16, 17]. Personal counseling, leaflets or multimedia information containing explanations of the procedure along with tasks that the patient should be encouraged to fulfil may improve perioperative feeding, early postoperative mobilisation, pain control, and respiratory physiotherapy; and hence reduce the prevalence of complications [18–20]. Ideally, the patient and a relative/care provider should meet with surgeon, anaesthetist and nurse.

Summary and recommendation:

Patients should routinely receive dedicated preoperative counseling (can only be beneficial and not harmful)

Evidence level:

Low (study quality, uncertain endpoints)

Recommendation grade:

Strong

Preoperative optimisation

Eight randomised controlled trials (RCTs) have been undertaken in various settings investigating the role of preoperative physical conditioning (Prehab) on surgical outcomes [21–27]. The surgical settings were general abdominal surgery, cardiothoracic surgery and orthopaedic surgery. Although there were varying degrees of improvement in physiological function and surgical recovery, only 1 study found improvement in physiological function that correlated with improved surgical recovery [25]. These results may have been influenced by: a lack of appropriate physiological endpoints; studies being conducted within elderly cohorts; excessively intensive exercise regimens; and lack of adherence to the designated programmes. Further research is needed by investigating Prehab in younger patient populations. There is also a need for further research into methods that can improve adherence to Prehab.

It is generally accepted that preoperative medical optimisation is necessary before surgery. Alcohol abusers have a two-to-threefold increase in postoperative morbidity, the most frequent complications being bleeding, wound and cardiopulmonary complications. One month of preoperative abstinence reduces postoperative morbidity by improving organ function [28, 29]. Smoking is another patient factor that has a negative influence on recovery. Current smokers have an increased risk for postoperative pulmonary and wound complications [30]. One month of abstinence from smoking is required to reduce the incidence of complications [30–33].

Summary and recommendation:

Increasing exercise preoperatively may be of benefit. Smoking should be stopped 4 weeks before surgery and alcohol abusers should stop all alcohol consumption 4 weeks before surgery (can only be beneficial and not harmful).

Evidence level:

Prehab: Very low (inconsistency)
Alcohol: Low (only one high-quality RCT)
Smoking: High

Recommendation grade:

Prehab: No
Alcohol: Strong
Smoking: Strong

Preoperative bowel preparation

Mechanical bowel preparation (MBP) has adverse physiologic effects attributed to dehydration [34], is distressing for the patient, and is associated with prolonged ileus after colonic surgery [35]. Moreover, it has been shown that patients receiving MBP have a tendency towards a higher incidence of spillage of bowel contents, which might increase the rate of postoperative complications [36]. Thus, the "dogma" of MBP before elective abdominal surgery has been strongly challenged. The last Cochrane review of 2011 (which included 18 RCTs with 5,805 patients undergoing elective colorectal surgery) could not find statistically significant differences between patients with MBP versus no MBP, or with MBP versus rectal enema alone, in terms of anastomotic leakage, mortality rates, need for reoperation and wound infections [37].

Most of the RCTs on MBP have included patients undergoing open colorectal surgery, and the extrapolation to laparoscopic surgery might be questionable. Some surgeons argue that MBP makes laparoscopic surgery technically easier. It has been shown that laparoscopic colectomy might be undertaken safely without preoperative MBP [38]. Nonetheless, precisely localising small tumours is more difficult by laparoscopy due to loss of palpation, thus requiring intraoperative colonoscopy with preoperative MBP. However, preoperative tattoo would obviate such a need.

Summary and recommendation:

MBP should not be used routinely in colonic surgery.

Evidence level:

High

Recommendation grade:

Strong

Preoperative fasting and carbohydrate treatment

Fasting from midnight has been standard practice in the belief that this secures an empty stomach and thereby reduces the risk of pulmonary aspiration in elective surgery. There has never been any scientific evidence behind this dogma. A meta-analyses including a Cochrane review of 22 RCTs showed that fasting from midnight does not reduce gastric content nor raises the pH of gastric fluid compared with patients allowed free intake of clear fluids until 2 h before anaesthesia for surgery [39, 40]. Equally, intake of clear fluids $\leq$2 h before surgery does not increase the prevalence of complications. National and European Anaesthesia Societies now recommend intake of clear fluids until 2 h before the induction of anaesthesia as well as a 6-h fast for solid food [41–44]. Obese (and even morbidly obese) patients have been reported to have the same gastric-emptying characteristics as lean patients [45, 46]. Diabetic patients with neuropathy may have delayed gastric emptying for solids, thereby possibly increasing the risk of regurgitation and aspiration [47]. There are no conclusive data showing delayed emptying for fluids. Patients with uncomplicated type-2 diabetes mellitus have been reported to have normal gastric emptying [48]. When given along with normal diabetic medication, gastric emptying of a carbohydrate drink was shown to be normal [49]. The clinical effectiveness of preoperative carbohydrate treatment has yet to be established in diabetic subjects. By providing a clear fluid containing a relatively high concentration of complex carbohydrates 2–3 h before anaesthesia, patients can undergo surgery in a metabolically fed state. Four-hundred millilitres of a 12.5 % drink of mainly maltodextrins has been shown to reduce preoperative thirst, hunger, and anxiety [40, 50] as well as postoperative insulin resistance [51]. Carbohydrate treatment results in less postoperative losses of nitrogen and protein [52, 53] as well as better-maintained lean body mass [54] and muscle strength [55, 56]. Data from RCTs indicate accelerated recovery, and preliminary data from a meta-analysis show a one day-shorter stay in hospital for patients receiving preoperative carbohydrate loading in major abdominal surgery [57, 58].

Summary and recommendation:

Clear fluids should be allowed up to 2 h and solids up to 6 hrs prior to induction of anaesthesia. In those patients were gastric emptying may be delayed (duodenal obstruction etc.) specific safety measures should at the induction of anaesthesia. Preoperative oral carbohydrate treatment should be used routinely. In diabetic patients carbohydrate treatment can be given along with the diabetic medication.

Evidence level:

Solids and fluids (overall); Moderate (study quality)
Diabetic patients: Low (inconsistency)
Carbohydrate loading (overall): Low (inconsistency, study quality)
Diabetic patients: Very low (few studies, low quality)

Recommendation grade:

Fasting guidelines: Strong
Preoperative carbohydrate drinks: Strong
Preoperative carbohydrate drinks, diabetic patients: Weak

Preanaesthetic medication

Preoperative education can reduce patient anxiety to an acceptable level without the need for anxiolytic medication. Avoiding prolonged starvation times and adhering to the ERAS guidance on carbohydrate loading is also beneficial [50]. Long-acting sedative premedication should be avoided within 12 h of surgery because it affects immediate postoperative recovery by impairing mobility and oral intake. In 2009, a Cochrane review on premedication for anxiolysis for adult day surgery concluded that patients receiving oral anxiolytics were discharged from hospital successfully but that some of the studies showed an impairment in psychomotor function 4 h postoperatively, which reduces the patient's ability to mobilise, eat and drink [59]. Administration of sedatives for anxiolysis (particularly by the oral route) can be unpredictable, and is difficult to facilitate effectively for patients being admitted on the day of surgery, so is best avoided. If necessary, short-acting anaesthetic drugs (e.g., fentanyl combined with small incremental doses of midazolam or propofol) can be administered under monitoring to facilitate regional anaesthetic procedures such as spinal anaesthesia or thoracic epidural placement before the induction of anaesthesia with minimal residual effect at the end of surgery.

Summary and recommendation:

Patients should not routinely receive long- or short-acting sedative medication before surgery because it delays immediate postoperative recovery. If necessary, short-acting intravenous drugs can be titrated carefully by the anaesthetist to facilitate the safe administration of epidural or spinal analgesia because these do not significantly affect recovery.

Evidence level:

Sedative medication: High

Recommendation grade:

Strong

Prophylaxis against thromboembolism

The incidence of asymptomatic deep vein thrombosis (DVT) in colorectal surgical patients without thromboprophylaxis is ≈30 %, with fatal pulmonary embolus (PE) occurring in 1 % of subjects. Patients with malignant disease, previous pelvic surgery, taking corticosteroids preoperatively, extensive comorbidity and hypercoaguable states are at increased risk [60]. All colorectal patients should receive mechanical thromboprophylaxis with well-fitted compression stockings because these have been shown to significantly reduce the prevalence of DVT in hospitalised patients [61]. The addition of intermittent pneumatic compression should also be considered, particularly in patients with malignant disease or who have undergone pelvic surgery [62]. There is extensive evidence supporting the use of pharmacological thromboprophylaxis with low-molecular-weight-heparin (LMWH) or unfractionated heparin. A recent study of 4,195 colorectal patients demonstrated that pharmacological prophylaxis reduced the prevalence of symptomatic venous thromboembolism (VTE) from 1.8 to 1.1 % and also reduced overall colorectal cancer mortality [63]. Once-daily LMWH is as effective as twice-daily administration [64]. The risks of postoperative haemorrhage, heparin-induced thrombocytopaenia and epidural haematoma with permanent injury are rare (best/worst case scenario, 1 in 54,000/1 in 24,000) [65]. It is recommended that epidural catheters are not placed or removed within 12 h of heparin administration [66–68].

The use of VTE-prophylaxis for surgical inpatients is well established, but the benefit of extended prophylaxis for 28 days after discharge is controversial. A recent Cochrane meta-analysis of four RCTs demonstrated a significant reduction in the prevalence of symptomatic DVT in patients with extended prophylaxis from 1.7 to 0.2 % (confidence interval (CI) 0.06–0.80; $P = 0.02$; number needed to treat = 66) [69]. In an American audit of 52,555 patients entered into the National Surgical Quality Improvement Database from 2005 to 2008, the prevalence of early post-discharge symptomatic VTE was lower at 0.67 %. This would suggest that >200 patients would have to receive thromboprophylaxis to prevent one symptomatic VTE event [60]. A cost analysis of pronged prophylaxis undertaken by the UK National Institute of Health and Clinical Excellent demonstrated that it was cost-effective for cancer surgery patients, but this evidence was based only on 3 RCTs [62]. A universal policy of protracted thromboprophylaxis may not be appropriate in all colorectal patients, particularly in patients having minimally invasive or laparoscopic surgery, where the VTE risk may be even lower [70]. Current international guidelines, however, advocate its use in patients who have had major cancer surgery in the abdomen or pelvis [62, 71].

Summary and recommendation:

Patients should wear well-fitting compression stockings, have intermittent pneumatic compression, and receive pharmacological prophylaxis with LMWH. Extended prophylaxis for 28 days should be given to patients with colorectal cancer.

Evidence level:

Stockings, compression, LMVH, extended prophylaxis: High

Recommendation grade:

Strong

Antimicrobial prophylaxis and skin preparation

In a Cochrane review on antimicrobial prophylaxis in colorectal surgery [72], the authors concluded that the use of antibiotic prophylaxis for patients undergoing colorectal surgery is imperative to reduce the risk of surgical-site infections. For intravenous antibiotics, it is accepted that the best time for administration is 30–60 min before the incision is made [73]. Repeated doses during prolonged procedures may be beneficial [74]. The timing of oral administration of antibiotics is much less certain, especially in the light of current recommendations against mechanical colon cleansing before surgery [75], because oral antibiotics have not been studied in the uncleansed colon. Antibiotics to be given should include cover against aerobic and anaerobic bacteria.

A study comparing different types of skin cleansing showed that the overall prevalence of surgical-site infection was 40 % lower in a concentration chlorhexidine-alcohol group than in a povidone-iodine group [76]. However, there is a risk of fire-based injuries and burn injuries if diathermy is used in the presence of alcohol-based skin solutions [77]. Hair clipping is associated with fewer surgical-site infections than shaving with razors if hair removal is necessary before surgery, although the timing of hair removal does not seem to affect the outcome [78].

Summary and recommendation:

Routine prophylaxis with intravenous antibiotics should be given 30–60 min before initiating colorectal surgery. Additional doses should be given during prolonged procedures according to the half-life of the drug used.

Evidence level:

Antibiotic prophylaxis, chlorhexidine-alcohol preparation: High

Recommendation grade:

Strong

Standard anaesthetic protocol

There are no RCTs comparing general anaesthetic techniques for colorectal surgery. It makes good sense to use short-acting induction agents such as propofol combined with a short-acting opioid like fentanyl, alfentanil or a remifentanil infusion. Short-acting muscle relaxants can be titrated using neuromuscular monitoring. Maintaining a deep neuromuscular block during surgery helps facilitate vision and surgical access. Anaesthesia can be maintained using short-acting inhalational anaesthetics such as sevoflurane or desflurane in oxygen-enriched air. Alternatively, total intravenous anaesthesia (TIVA) using target-controlled infusion pumps can be utilised, and may be beneficial in patients with susceptibility to postoperative nausea and vomiting (PONV).

In the elderly population, there is increasing evidence that too deep an anaesthetic can be harmful and can increase the risk of postoperative confusion. Using a bi-spectral index (BIS) monitor may help to titrate the depth of anaesthesia to a minimum in this group of patients [79].

The anaesthetist is responsible for three key elements in affecting outcome after surgery: stress reactions to the surgery, fluid therapy, and analgesia. Recognition of the importance of these ERAS components has led to the description of a "trimodal approach" for optimising outcomes in laparoscopic surgery for anaesthetists [80]. A regional anaesthetic block used in addition to general anaesthesia during surgery can minimise the need for postoperative intravenous opiates, thereby allowing rapid awakening from anaesthesia which can facilitate early enteral intake and mobilisation on the day of surgery. In open surgery, the use of epidural analgesia has proven to be superior to opioid-based alternatives for several important outcomes [81], including pain [82], PONV [83] and complications [84]. In laparoscopic surgery, emerging data indicate that alternative methods such as spinal anaesthesia, intravenous lidocain and patient-controlled anaesthesia (PCA) may be equally effective [80]. A regional block can also reduce the stress response [85]. This includes reducing insulin resistance (the main mechanism behind hyperglycaemia). Glucose monitoring is important [86] because hyperglycaemia can lead to an increased prevalence of postoperative complications [87], although the use of an intensive insulin regimen must be balanced against the risk of hypoglycaemia [88]. During surgery, fluid delivery should be targeted against physiological measures [89] and mean arterial pressure maintained using vasopressors once normovolaemia has been established so that overload of salt and water is avoided [90]. This is particularly important if using epidural anaesthesia to maintain blood flow to the gut [91]. Minimal invasive monitoring of cardiac output is being increasingly used to target fluid therapy. Rockall et al. have shown consistently low LOSH using oesophageal Doppler monitoring to direct fluid on an individual basis in patients receiving morphine (2.8 days), epidural (3.7 days) and spinal (2.7 days) anaesthesia [92]. Ultra-short LOSH (<23 h) was achieved by the same research team by combining spinal analgesia and goal-directed fluids [93].

Attention to airway management and ventilation is important to reduce the risk of postoperative chest infection and lung injury (a major cause of morbidity after major surgery). Micro-aspiration during anaesthesia may be a risk factor and can be reduced by using correctly sized endotracheal tubes with cuff-pressure control. Levy et al. showed that pulmonary function after laparoscopic surgery was not significantly affected by the analgesic regimen (thoracic epidural analgesia, spinal or morphine). Early mobilisation has an important part to play in pulmonary function [80].

Summary and recommendation:

A standard anaesthetic protocol allowing rapid awakening should be given. The anaesthetist should control fluid therapy, analgesia and haemodynamic changes to reduce the metabolic stress response. Mid-thoracic epidural blocks using local anaesthetics and low-dose opioids should be considered for open surgery. In laparoscopic surgery, spinal analgesia or morphine PCA is an alternative to epidural anaesthesia. If intravenous opioids are to be used the dose should be titrated to minimise the risk of unwanted effects.

Evidence level:

Rapid awakening: Low (lack of data),
Reduce stress response: Moderate (extrapolated data)
Open surgery: High
Laparoscopic surgery: Moderate (study quality)

Recommendation grade:

Strong

PONV

PONV affects 25–35 % of all surgical patients and is a leading cause of patient dissatisfaction and delayed discharge from hospital. The aetiology of PONV is multifactorial and can be classified into three factors: patient, anaesthetic and surgical. Female patients, non-smokers and those with a history of motion sickness are at particular risk. The use of volatile anaesthetic agents, nitrous oxide and parenteral opiates increase the risk significantly. Major abdominal surgery for colorectal disease is associated with a high prevalence of PONV, reaching 70 % in some trials [94]. There are numerous national and international guidelines relating to the use of prophylactic antiemetics, which can reduce PONV by $\leq$40 % [95]. Many of these guidelines advocate the use of PONV scoring systems (e.g., Apfel score), which stratify patients into low-to-high risk groups and dictates antiemetic prophylaxis based on the perceived preoperative risk [96]. These scoring systems have been proven to reduce PONV significantly in RCTs but have not been widely implemented into routine clinical practice. An alternative strategy not yet studied may be to administer antiemetic prophylaxis to all patients who are having inhalational anaesthesia, opiates or major abdominal surgery. This approach is gaining popularity among the anaesthetists given that the cost and side-effect profile of commonly used antiemetic drugs is small [97].

In recent years, the concept of a multimodal approach to PONV has gained momentum. This combines non-pharmacological and pharmacological antiemetic techniques in addition to ERAS programmes [98]. Non-pharmacological techniques include the avoidance of emetogenic stimuli such as inhalational anaesthetics, and the increased use of propofol for the induction and maintenance of anaesthesia. Minimal preoperative fasting, carbohydrate loading and adequate hydration of patients can also have a beneficial effect. The use of high inspired oxygen concentrations during anaesthesia has been implicated in a reduced prevalence of PONV, although a recent meta-analysis has cast some doubt on its efficiency [99, 100]. Regional anaesthetic techniques such as epidurals and transversus abdominal plane (TAP) blocks, have been proven to reduce postoperative opiate use, which may in turn influence the prevalence of PONV [101]. The use of non-steroidal anti-inflammatory drugs (NSAIDS) as an alternative to opiate analgesia is well established.

Antiemetics can be classified into four main pharmacological subtypes depending on the receptor system they act upon: cholinergic, dopaminergic (D2), serotonergic (5-hydroxytryptamine type 3 (5-HT3)) and histaminergic (H1). Each of the classes is superior to placebo in reducing the risk of PONV [102]. There is also extensive evidence for the use of dexamethasone, which is postulated to act via central and peripheral mechanisms [103]. The potency of the antiemetic effect is enhanced if $\geq$2 antiemetics are used in combination: the serotonin analogues ondansetron or droperidol [104]. Dexamethasone has also been shown to have positive effects on reducing the prevalence of PONV, but its immunosuppressive effects on long-term oncological outcomes are unknown. Newer antiemetic drugs such as neurokinin-1 (NK_1) receptor antagonists have been developed, and initial trial results have been encouraging [105].

If, despite prophylaxis, PONV is present postoperatively, the additional agents not used for prophylaxis can be added to maximise the potency of the multimodal approach.

Summary and recommendation:

A multimodal approach to PONV prophylaxis should be adopted in all patients with $\geq$2 risk factors undergoing major colorectal surgery. If PONV is present, treatment should be given using a multimodal approach.

Evidence level:

Low (multiple interventions)

Recommendation grade:

Strong

Laparoscopy and modifications of surgical access

Laparoscopy in colonic resection improves recovery if judged by the prevalence of postoperative complications, pain and hospital stay [106–111]. It may also reduce the prevalence of postoperative immunosuppression [111] while providing equivalence in cancer outcomes [112–116]. The debate during the last 5 years has centred around whether open surgery undertaken within an ERAS programme can match laparoscopic resection which is similarly optimised. Two small blinded randomised studies reported conflicting results, with one showing no difference in hospital stay between laparoscopic and open surgery [117] whereas the other non-blinded study reported a 2.5-day in hospital stay reduction after laparoscopic surgery [118]. Readmission rates of >20 % were high in both arms of the first trial and in the open group of the second trial, but acceptable at 5 % in the laparoscopic arm of the latter trial.

Recently, the Laparoscopy and/or Fast-track Multimodal Management Versus Standard Care (LAFA) study reported the results from its multicentre RCT which randomised between laparoscopic and open segmental colectomy within 9 Dutch centres [111]. The median primary and total stay in hospital was 2-days shorter after laparoscopic resection. Regression analysis showed that laparoscopic surgery was the only predictive factor to reduce hospital stay and morbidity. A detailed analysis has suggested that laparoscopy has the potential to be used in >90 % of patients undergoing elective surgery for colorectal cancer, and that a conversion rate of <10 % is achievable [119].

Other methods that one might consider to add value in colonic resection would include the use of robotic-assisted surgery, single incision laparoscopic surgery (SILS) and hand-assisted laparoscopic surgery (HALS). The advantages of robotic surgery include seven degrees of movement, three-dimensional (3D) views, tremor filtration, motion scaling, and improved ergonomics. Whether this will translate into substantial improvement in clinical outcomes remains to be seen, and research is in progress in rectal surgery [120]. The use of SILS has increased recently but as yet there are no robust data to justify its advantage over conventional laparoscopy [121]. HALS is more widespread in certain parts of the world, but no clear evidence exists demonstrating clinical improvements in recovery when compared with conventional multiport laparoscopic surgery [122]. There are data demonstrating that recovery is influenced by wound length [123] and that rates of incisional hernia are proportional to it [124]. Also, there is debate regarding whether transverse incisions have an advantage over longitudinal ones [8] but robust data are not available.

Summary and recommendation:

Laparoscopic surgery for colonic resections is recommended if the expertise is available.

Evidence level:

Oncology: High.
Morbidity: Low (inconsistency).
Recovery/LOSH: Moderate (inconsistency).

Recommendation grade:

Strong

Nasogastric intubation

A meta-analysis in 1995 showed that routine nasogastric decompression should be avoided after colorectal surgery because fever, atelectasis, and pneumonia are reduced in patients without a nasogastric tube [125]. A meta-analysis of 28 RCTs on the use of nasogastric decompression after abdominal surgery included 4,195 patients [126]. Surgery included colorectal resection (7 RCTs), gastroduodenal sugery (7 RCTs), biliary and gynaecological surgery (2 (RCTs each), vascular and trauma surgery (1 RCTs each) and mixed surgical populations (7 RCTs). Eight RCTs with 862 patients showed a reduction of the time interval from surgery to the first passage of flatus by half a day if nasogastric intubation was avoided. Pulmonary complications tended to be less common and, in a subgroup analysis of only patients undergoing colorectal surgery, the incidence of pulmonary complications wound infection, ventral hernia or anastomotic leak was no different. LOSH and gastric discomfort showed data in favour of no nasogastric decompression in most of the RCTs. Similar results were confirmed in a published meta-analysis in 2011 [127]. There is no *rationale* for routine insertion of a nasogastric tube during elective colorectal surgery except to evacuate air that may have entered the stomach during ventilation by using a facial mask before endotracheal intubation.

Summary and recommendation:

Postoperative nasogastric tubes should not be used routinely. Nasogastric tubes inserted during surgery should be removed before reversal of anaesthesia.

Evidence level:

High

Recommendation grade:

Strong

Preventing intraoperative hypothermia

Maintaining normothermia is important to maintain normal body homeostasis. Patients becoming hypothermic (definition: <36 °C) have been shown to have higher rates of wound infection [128, 129], and earlier studies reported morbid cardiac events [130] and bleeding [131]. In recovery, there is a higher risk of shivering in patients who are hypothermic, which increases oxygen consumption at a critical time [132]. Pain scores are also better in patients who are not hypothermic. It is imperative to maintain the patient's temperature, rather than allowing it to drop and then trying to restore it. Pre-warming patients with a warm air blanket before coming to the operating theatre has been shown to improve core temperature before surgery [133, 134]. This may be more important for patients who are exposed while having prolonged anaesthetic procedures (e.g., monitoring catheters and epidural insertion).

Maintaining temperature during the procedure can be achieved by using forced-air warming blankets, heating mattresses under the patient, or circulating-water garment systems [135]. All have been shown to be effective at maintaining normothermia during surgery. Active warming should be continued into the postoperative period until the patient's temperature is ≥36 °C [136]. In addition, intravenous fluids should be warmed from the start of administration [132]. The patient's temperature should be monitored to enable warming to be adjusted and to avoid hyperpyrexia which otherwise may occur in prolonged procedures if patients develop a systemic inflammatory response syndrome (SIRS).

A Cochrane review in January 2011 reached the conclusion that heating or humidifying the carbon dioxide gas used for insufflation does not improve the patient's temperature or pain scores after surgery [137].

Summary and recommendation:

Intraoperative maintenance of normothermia with a suitable warming device (such as forced-air heating blankets, a warming mattress or circulating-water garment systems) and warmed intravenous fluids should be used routinely to keep body temperature >36°C. Temperature monitoring is essential to titrate warming devices and to avoid hyperpyrexia.

Evidence level:

Maintenance of normothermia: High.
Temperature monitoring: Moderate (extrapolated data).

Recommendation grade:

Strong

Perioperative fluid management

Fluid therapy plays a vital part in achieving optimal outcomes after surgery but continues to be one of the most controversial aspects of perioperative care. Intravascular volume is one of the key determinants of cardiac output and therefore oxygen delivery to the tissues. Intravascular hypovolaemia at a particular time can lead to hypoperfusion of vital organs and the bowel, which can lead to complications. However, administering too much fluid can lead to bowel oedema and increased interstitial lung water, which can also lead to complications [138]. If the patient is normovolaemic, blood pressure should be maintained using vasopressors to avoid fluid overload.

It is apparent that fluid requirements in patients undergoing surgery by a laparotomy is different to laparoscopic surgery due to increased fluid shifts, bowel handling and an increased SIRS. The patient is also more likely to have thoracic epidural analgesia (TEA), which also changes vascular tone and venous capacitance, and further complicates fluid therapy. Laparoscopic surgery, therefore, would appear to offer the potential to simplify the way fluid is administered and reduce fluid requirements, but there is evidence that cardiac output is reduced by the physiological consequences of the head-down position and pneumoperitoneum. Therefore, it is important to target fluid and oxygen delivery appropriately in this group of patients [139].

Fluid shifts should be minimised if possible. That is, avoiding bowel preparation, maintaining hydration by giving oral preload up to 2 h before surgery, as well as minimising bowel handling and exteriorisation of the bowel outside the abdominal cavity and avoiding blood loss.

Studies have tried to determine whether a restrictive fluid regimen is more beneficial than a liberal regimen. However, the exact definitions of what is "liberal" and "restrictive" have varied between studies, as have patient groups and endpoints, meaning comparison between the studies is difficult. A review by Bundgaard-Nielson concluded that fluid excess was detrimental [140]. Varadhan and Lobo examined the evidence in these earlier studies and concluded that it is more important to reclassify patients as being in a state of "fluid balance" or "fluid imbalance": the former fared better [138].

Minimally invasive cardiac output monitors such as the oesophageal Doppler (OD) device target fluid on an individualised basis by challenging the patient with a fluid bolus (e.g., 200 ml colloid) and seeing if there is an increase in stroke volume of ≥10 %. This fluid challenge is repeated every 10–15 min until there is no further increase in stroke volume. At this point, the stroke volume is "optimised". A meta-analysis of the use of OD to target fluid therapy in major surgery has demonstrated LOSH, fewer complications, faster return of bowel function, reduced infection rates, less nausea and vomiting, a lower incidence of acute kidney injury, and the possible improvement of survival after surgery [89, 141]. There have been few studies using OD within an ERAS protocol for colorectal surgery, particularly in laparoscopic surgery. In 2009, Senagore et al. [142] showed minimal benefit of outcome when comparing goal-directed administration of balanced salt solution or hetastarch using OD within an ERAS protocol. They did conclude, however, that less crystalloid was given when using OD.

Other minimally invasive cardiac output monitors that use arterial waveform analysis or thoracic bioimpedance/bioreactance are available but no RCTs in elective colorectal surgery using these devices have been carried out. Dynamic variables using arterial waveform analysis such as stroke volume variation (SVV) or pulse pressure variation (PPV) have been shown in ventilated patients to help predict fluid responsiveness [143]. The advantage of arterial waveform analysis is that it can be used postoperatively to target stroke volume and cardiac output.

Central venous catheters are not used routinely for monitoring of central venous pressure as this is a poor predictor of fluid responsiveness. Hence, they are inserted only if there is a genuine need for central venous access for drug infusions. The use of central venous saturation to represent oxygen extraction in the early postoperative period to guide fluid therapy has been validated by some studies, and may be useful in high-risk patients [144, 145].

Postoperative intravenous fluids should be minimised to maintain normovolaemia and avoid fluid excess. The enteral route should be used in preference and the drip taken down at the earliest opportunity (preferably no later than the morning after surgery). Traditionally, there has been a reluctance to take the drip down in patients with TEA. Hypotensive normovolaemic patients with TEA should be treated with vasopressors and not an excess of fluid [146]. Balanced crystalloids have been shown to be superior to 0.9 % saline for the maintenance of electrolyte balance [147].

Summary and recommendation:

Balanced crystalloids should be preferred to 0.9 % saline. In open surgery, patients should receive intraoperative fluids (colloids and crystalloids) guided by flow measurements to optimise cardiac output. Flow measurement should also be considered if: the patient is at high risk with comorbidities; if blood loss is >7 ml/kg; or in prolonged procedures. Vasopressors should be considered for intra- and postoperative management of epidural-induced hypotension provided the patient is normovolaemic. The enteral route for fluid postoperatively should be used as early as possible, and intravenous fluids should be discontinued as soon as is practicable.

Evidence level:

Balanced crystalloids: High
Flow measurement in open surgery: High
Flow measurement in other patients: Moderate (extrapolated data). Vasopressors: High
Early enteral route: High

Recommendation grade:

Strong

Drainage of the peritoneal cavity after colonic anastomosis

Peritoneal drainage has traditionally been used to prevent accumulation of fluid in the bed of dissection, infection, and anastomotic breakdown. At least 8 RCTS of $\approx$1,390 participants have tested the efficacy of drainage in colorectal surgery; most trials evaluated closed-suction drainage for 3–7 days in elective colonic surgery. Meta-analyses did not demonstrate effects on clinical or radiological anastomotic dehiscence, wound infection, re-operation, extra-abdominal complications or mortality [148, 149]. Subgroup analyses of trials in elective colon resection replicated these findings [149].

Peri-anastomotic drainage has also been thought to allow early detection and/or control of anastomotic dehiscence. However, pooled data show that enteric content or pus is observed in only 1 in 20 drains in patients with clinical leaks [150].

Thus, peritoneal drainage is not associated with any advantage or disadvantage in the available literature. Empirical observation suggests that many drainage systems significantly impair independent mobilisation.

Summary and recommendation:

Routine drainage is discouraged because it is an unsupported intervention that probably impairs mobilisation.

Evidence level:

High

Recommendation grade:

Strong

Urinary drainage

Bladder drainage is used during and after major surgery to monitor urine output and prevent urinary retention. Only low-grade evidence is available regarding the clinical value of perioperative monitoring of urine output; in observational studies in non-cardiac surgery, intraoperative urine output was not a predictor of subsequent renal function [151] or acute kidney injury [152].

A brief duration of transurethral drainage is desirable because increasing duration is associated with increasing risk of urinary tract infection (UTI). In a recent randomised trial of early (day 1, n = 105) versus standard (approximately day 4, n = 110) removal of the transurethral catheter in patients having major abdominal and thoracic surgery, the prevalence of UTI significantly reduced with early removal (2 % versus 14 %) [153].

It has been proposed that urinary drainage is necessary for the duration of epidural analgesia. However, all patients in the quoted trial had TEA for $\geq$3 days, and the rate of urinary retention was not significantly different between the 1-day and the 4-day group (8 % versus 2 % single in–out catheterisation; 3 % versus 0 % 24-h catheterisation) [153]. This confirms findings from an uncontrolled prospective study of 100 patients treated with 48-h TEA after open colonic resection who had their transurethral catheter removed in the morning after surgery. Some 9 % had urinary retention and 4 % had a UTI [154].

A meta-analysis has shown that suprapubic bladder catheterisation in abdominal surgery is associated with lower rates of bacteriuria and lower patient discomfort than transurethral drainage [155]. However, these data are relevant for urinary drainage of 4–7 days' duration; benefit from suprapubic catheterisation in short-term transurethral drainage is uncertain.

Summary and recommendation:

Routine transurethral bladder drainage for 1–2 days is recommended. The bladder catheter can be removed regardless of the usage or duration of TEA.

Evidence level:

Low (few studies, extrapolated data)

Recommendation grade:

Routine bladder drainage: Strong
Early removal if epidural used: Weak

Prevention of postoperative ileus (including use of postoperative laxatives)

Prevention of postoperative ileus is a major cause of delayed discharge after abdominal surgery as well as a key objective of enhanced-recovery protocols. No prokinetic agent has been shown to be effective in attenuating or treating postoperative ileus, but several other types of interventions have been successful. Mid-thoracic epidural analgesia [156] as compared with intravenous opioid analgesia is highly effective at preventing postoperative ileus [83, 157]. Fluid overloading during [158] and after [159] surgery impairs gastrointestinal function and should be avoided. Avoidance of nasogastric decompression may reduce the duration of postoperative ileus [126]. Laparoscopic-assisted colonic resection also leads to faster return of bowel function, as well as resumption of an oral diet, compared with open surgery [109]. This effect of laparoscopy in comparison to open surgery has been demonstrated in a recent RCT under traditional perioperative care as well as ERAS [111]. Oral magnesium oxide was demonstrated to promote postoperative bowel function in a double-blinded RCT in abdominal hysterectomy [160] and in reports from a well-established enhanced recovery program in colonic resection [1, 161]. Another randomised trial in liver resection showed that oral magnesium enhanced the return of bowel function [162] in an ERAS setting, whereas a small RCT (49 patients) failed to show any significant effect of oral magnesium on time to first flatus or bowel movement (18.0 versus 14.0 and 42 versus 50 h; each $p > 0.15$) nor on early intake of fluids, protein drinks, solid food, nausea and vomiting, mobilisation or LOSH [163] within a well established ERAS-protocol. Bisacodyl (10 mg, p.o.) administered twice a day from the day before surgery to the third postoperative day improved postoperative intestinal function in a RCT with 189 patients undergoing colorectal surgery [164]. There was no effect of bisacodyl on tolerance to solid food or LOSH. Alvimopan (a μ-opioid receptor antagonist approved for clinical use in postoperative ileus) given via the oral route accelerates gastrointestinal recovery and reduces the LOSH in patients undergoing open colonic resection having postoperative opioid analgesia [165]. Perioperative use of chewing gum has a positive effect on postoperative duration of ileus [166].

Summary and recommendation:

Mid-thoracic epidural analgesia and laparoscopic surgery should be utilised in colonic surgery if possible. Fluid overload and nasogastric decompression should be avoided. Chewing gum can be recommended, whereas oral administration of magnesium and alvimopan (when using opioid based analgesia) can be included.

Evidence level:

Thoracic epidural, laparoscopy: High
Chewing gum: Moderate
Oral magnesium, alvimopan (when using opioids): Low (extrapolated data)

Recommendation grade:

Thoracic epidural, fluid overload, nasogastric decompression,
chewing gum, alvimopan (when using opioids): Strong
Oral magnesium: Weak

Postoperative analgesia

The optimal analgesic regimen for major surgery should give: good pain relief; allow early mobilisation, early return of gut function and feeding; and not cause complications [167]. There has been increasing recognition that different types of analgesic regimens are more suited to particular types of surgery and incision. The cornerstone of analgesia remains multimodal analgesia combining regional analgesia or local anaesthetic techniques and trying to avoid parenteral opioids and their side effects.

Postoperative analgesia in open surgery

For open midline laparotomy, TEA is the optimal established analgesic technique. It offers superior analgesia in the first 72 h after surgery [82] and earlier return of gut function provided the patient is not fluid-overloaded. A national audit by Cook et al. on behalf of the UK Royal College of Anaesthetists has quantified the risks and highlighted its safety provided good practice is adhered to [65].

Using low-dose concentrations of local anaesthetic combined with a short-acting opiate appears to offer the best combination of analgesia while minimising the risk of motor block and hypotension due to sympathetic blockade. Several meta-analyses have shown improved outcomes with TEA compared with opioid-based analgesia, including pain, complications, PONV and insulin resistance [81–85]. Hypotension induced by sympathetic block should be treated with vasopressors provided the patient is not hypovolaemic. The aim should be to remove the epidural ≈48–72 h postoperatively by the time the patient has had a bowel movement.

Postoperative analgesia in Laparoscopic surgery

Recent publications have shown that the duration of pain after laparoscopic surgery requiring major analgesics is much shorter than for open surgery, thereby allowing discharge from hospital as soon as 23 h after surgery [93]. Provided early feeding is tolerated in the laparoscopic group, analgesic requirements at 24 h postoperatively are often addressed with oral multimodal analgesia without the need of regional blocks or strong opiates. However, even in laparoscopic surgery there is the need for a small, low transverse abdominal incision to deliver the specimen. There is increasing interest in looking at alternatives to TEA or morphine using spinal analgesia or TAP blocks. A RCT by Levy et al. comparing spinal analgesia, morphine and low TEA in fluid-optimised patients provided interesting results because patients with TEA had a longer LOSH [92].

However, 3 RCTs reported contradictory effects on gastrointestinal function depending on the level of block: low-thoracic epidurals were not associated with benefits [92, 168], whereas a trial using a mid-thoracic epidural demonstrated significantly earlier return of flatus, stools and tolerance of oral diet as compared with parenteral opioid analgesia [169]. Other work has confirmed that, although analgesia is superior in the early postoperative period using TEA, LOSH is not reduced [170]. Work by Virlos et al. confirmed that spinal analgesia allows earlier mobilisation and hospital discharge compared with TEA [171].

TAP blocks have been used in laparoscopic surgery to cover the lower abdominal incision and combined with intravenous paracetamol to reduce opioid administration [172]. They are, however, short-acting and no significant RCT has compared TAP with spinal or epidural analgesia [101].

Postoperative multimodal analgesia

During the postoperative phase, a multimodal analgesic regimen has been employed aiming to avoid the use of opioids. Paracetamol is a vital part of multimodal analgesia. It is available in an intravenous preparation and can be given as 1 g four times daily.

NSAIDs

NSAIDS are also an important part of multimodal analgesia. There have been clinical case series linking voltarol (150 mg, p.o. once a day) and celecoxib (cyclo-oxygenase (COX)-2 inhibitor) to an increased incidence of anastomotic dehiscence [173–176]. However, until more thorough studies addressing this question have been carried out, there is not sufficient evidence to stop using NSAIDS as a component of multimodal analgesia in the postoperative period. Tramadol is an alternative to NSAIDs (although there are no recent studies relevant to colorectal surgery).

Other drugs that can be used to reduce postoperative opiate use

There are several ongoing studies on alternative drugs to avoid the use of opioids, but no medication can be recommended for routine use.

Summary and recommendation:

> TEA using low-dose local anaesthetic and opioids should be used in open surgery. For breakthrough pain, titration to minimise the dose of opioids may be used. In laparoscopic surgery, an alternative to TEA is a carefully administered spinal analgesia with a low-dose, long-acting opioid. In connection with TEA withdrawal, NSAIDs and Paracetamol should be used.

Evidence level:

TEA, open surgery: High
Local anaesthetic and opioid: Moderate (inconsistency).
TEA not essential in laparoscopic surgery: Moderate (inconsistency)
NSAID/Paracetamol: Moderate (inconsistency/few studies)

Recommendation grade:

Strong

Perioperative nutritional care

Most patients undergoing elective colonic resection can eat normally before surgery, and many have a seemingly normal nutritional status. In an ERAS setting, if the stress of surgery is minimised, a low body mass index (BMI) does not appear to be an independent risk factor for complications or prolonged LOSH, suggesting that, in this setting, baseline nutritional status may not be as critical as in more traditional perioperative-care situations [177]. The epidemic of obesity in Western society means that the average BMI of patients is often in the overweight or obese range, and this may hide underlying muscle wasting. A recent study has demonstrated that the presence of low muscle mass is predictive of complications and LOSH after colorectal surgery [178]. Whether such muscle wasting relates to pre-existing comorbidity or is related to cancer-associated myopenia is not known.

Regardless of the BMI, consumption of energy and protein is often low in the preoperative phase in patients about to undergo colonic surgery. Therefore, careful history-taking directed towards recent unplanned weight loss and reduced nutritional intake should be carried out. Normal food is the basis for nutrition before and after surgery for most patients treated according to ERAS. In the context of traditional perioperative care, addition of oral supplements can improve overall intake to reach nutritional goals [179]. In enhanced-recovery programmes, oral nutritional supplements (ONS) have been used on the day before surgery and for at least the first 4 postoperative days to achieve target intakes of energy and protein during the very early postoperative phase [180, 181]. One study combining preoperative oral treatment of carbohydrates, epidural analgesia, and early enteral nutrition showed that these three components of ERAS allowed nitrogen equilibrium while keeping glucose levels normal without the need for exogenous insulin by minimising insulin resistance [182]. If significant unplanned weight loss is present, oral supplements should be prescribed in the perioperative period, and consideration should be given to continuing the prescription once the patient returns home [179, 183]. For significantly malnourished patients, nutritional supplementation (oral and/or parenteral) has the greatest effect if started 7–10 days preoperatively, and is associated with a reduction in the prevalence of infectious complications and anastomotic leaks [184].

Special nutritional considerations should be taken for elderly patients as well as those with chronic diseases and alcohol problems who may also have micronutrient deficiencies or ingest vitamins and minerals below recommended doses and who may need supplementation before and after surgery [185–188].

In the postoperative phase, patients undergoing ERAS can drink immediately after recovery from anaesthesia and then eat normal hospital food and, in doing so, spontaneously consume $\approx$1,200–1,500 kcal/day [189, 190]. This is safe. RCTs of early enteral or oral feeding versus 'nil by mouth' show that early feeding reduces the risk of infection and LOSH, and is not associated with an increased risk of anastomotic dehiscence [191–193]. However, with early oral feeding, the risk of vomiting increases, especially in the absence of multimodal anti-ileus therapy.

Different combinations of diets containing components aimed to enhance immune function in surgical patients have been studied. These diets, often called 'immunonutrition' (IN) usually contain combinations of arginine, glutamine, omega-3 fatty acids, and nucleotides. Several meta-analyses have been published on the clinical effectiveness of IN (two recent with references to most others) [194, 195]. Overall, most studies show that there is clinical benefit from this treatment due to a reduction in the prevalence of complications and shortened LOSH in the context of traditional care, but results are heterogeneous. There is evidence suggesting that the treatment is most effective in malnourished patients, and there are no trials of the effectiveness of these formulas in an ERAS setting if stress is minimised.

Summary and recommendation:

Patients should be screened for nutritional status and, if deemed to be at risk of under-nutrition, given active nutritional support. For the standard ERAS patient, preoperative fasting should be minimised and postoperatively patients should be encouraged to take normal food as soon as possible after surgery. ONS can be used to supplement total intake.

Evidence level:

Postoperative early enteral feeding, safety: High
Improved recovery and reduction of morbidity: Low (study quality, extrapolated data)
Perioperative ONS (well-fed patient): Low (study quality, extrapolated data)

Perioperative ONS (malnourished patient): Low (study quality, extrapolated data, small effect)
IN: Low (study quality, extrapolated data)

Recommendation grade:

Postoperative early feeding and perioperative ONS: Strong
IN: IN could be considered in open colonic resections: Weak (different formulas, timing, dose)

Postoperative control of glucose

Insulin resistance is the cause of postoperative hyperglycaemia. Increasing insulin resistance [196] and glucose levels [87] have been shown to be associated with complications and mortality after major abdominal surgery, and also when adjusted for key confounders. This risk increases with higher insulin resistance and/or higher glucose levels. These data are primarily from glucose values during the day of surgery and postoperative day 1 with minimal food intake (i.e., not typical ERAS settings).

There are very little data on glucose control in an ERAS setting when patients are eating. However, available data with patients undergoing colorectal surgery in an ERAS protocol eating 1,500 kcal from day 1 after elective colorectal surgery show that, as expected, glucose levels are higher after food intake compared with morning fasting levels [189]. Patients with higher preoperative levels of glycated haemoglobin (HBA1c) remain $\approx$1 mmol/l higher compared with patients with normal preoperative HbA1c levels, and they also develop more complications. A small study combining epidural, preoperative carbohydrate and postoperative continuous complete enteral tube feeding after major colorectal surgery showed that glucose levels were maintained at normal levels without the need for insulin in the first 3 postoperative days [182]. Several treatments in the ERAS protocol affect insulin action/resistance [197, 198] and hence glucose levels directly or indirectly (bowel preparation prolonging preoperative fasting; preoperative carbohydrate treatment instead of overnight fasting). The prophylaxis and treatment of PONV to support nutritional intake involves: avoiding fasting; maintenance of fluid balance to support bowel movements; epidural anaesthesia to reduce the endocrine stress response from the adrenal glands; avoiding the use of opioids disturbing bowel movements; avoiding anti-inflammatory treatments to reduce stress; avoiding tubes and drains; and active mobilisation. None of these treatments carry the risk of hypoglycaemia.

Treatment of hyperglycaemia in surgical patients in the Intensive Care Unit (ICU) consistently shows improved results in that complications are avoided [199–202]. Any reduction in hyperglycaemia, regardless of the degree or level, improves outcomes. At levels >10–12 mmol/l, the risk of osmotic diuresis increases and causes additional disturbances in fluid balance [203]. However, using intravenous insulin carries the risk of hypoglycaemia [200], especially in the ward setting.

Summary and recommendation:

Hyperglycaemia is a risk factor for complications and should therefore be avoided. Several interventions in the ERAS protocol affect insulin action/resistance, thereby improving glycaemic control with no risk of causing hypoglycaemia. For ward-based patients, insulin should be used judiciously to maintain blood glucose as low as feasible with the available resources.

Evidence level:

Using stress reducing elements of ERAS to minimise hyperglycaemia: Low (study quality, extrapolations).
Insulin treatment in the ICU: Moderate (inconsistency, uncertain target level of glucose).
Glycaemic control in the ward setting: Low (inconsistency, extrapolations)

Recommendation grade:

Using stress reducing elements of ERAS to minimise hyperglycaemia: Strong
Insulin treatment in the ICU (severe hyperglycaemia): Strong
Insulin treatment in the ICU (mild hyperglycaemia): Weak (uncertain target level of glucose)
Insulin treatment in the ward setting: Weak (risk of hypoglycaemia, evidence level)

Early mobilisation

Early mobilisation has been postulated to reduce chest complications and may counteract insulin resistance from immobilisation [9]. Combining forced mobilisation with nutritional support results in improved muscle strength but only during the early postoperative phase [204]. Another RCT in 119 patients showed that postoperative muscle training had little effect of long-term postoperative outcomes [205]. A recent review confirmed these earlier results [206]. Conversely, prolonged bed rest has several negative effects, including reduced work capacity [207]. Also, a multivariate linear regression analysis of data collected during the LAFA trial [111], supported the notion that mobilisation on postoperative days 1, 2 and 3 is a factor significantly associated with a successful outcome of ERAS. Conversely, failure to mobilise on the first postoperative day may be due to inadequate control of pain, continued intravenous intake of fluids, indwelling urinary catheter, patient motivation, and preexisting co-morbidities. In a recent study in Yeovil, failure to mobilise was one of the most common reasons for ERAS deviation and was associated with prolonged LOSH [208].

Summary and recommendation:

Available RCTs do not support the direct beneficial clinical effects of postoperative mobilisation. Prolonged immobilisation, however, increases the risk of pneumonia, insulin resistance, and muscle weakness. Patients should therefore be mobilised.

Evidence level:

Low (extrapolated data, weak effect)

Recommendation grade:

Strong

Audit

Measuring standards and auditing the quality of healthcare drive continue to improve practice [209]. Auditing compliance is shown to be a key instrument to assist clinicians implementing the ERAS programme [210].

Auditing ERAS can be discussed under three domains:(i) measuring clinical outcomes of ERAS such as LOSH, readmission rates and complications (as reviewed above) (ii) determining functional recovery and patient experience and (iii) measuring compliance with (or deviation from) the ERAS protocol.

The original clinical outcome of ERAS programmes as described by Kehlet et al. resulting in a reduction of median LOSH after open colonic resection to 2 days [1] have not been reproduced widely. However, there is now robust evidence to support the benefits of ERAS over traditional postoperative care. This has been demonstrated in several meta-analyses in terms of shorter postoperative LOSH, lower complication rates, and acceptable readmission rates [211–214]. Hence, these measures of clinical outcome should be included in the clinical audit.

Measuring patients' experiences with ERAS, however, has not been investigated very thoroughly. This is mostly due to the lack of reliable and valid tools that can be used widely across many centres to report patients' experiences. Nevertheless, in the literature on this subject, ERAS does not seem to adversely influence quality of life (QoL) or psychomotor functions such as sleep quality, pain and fatigue levels after surgery [215]. In a recent unpublished Delphi consensus in the UK, measuring patient experience has been highlighted as a fundamental element of ERAS.

Measuring compliance has proven to be an instrumental factor in investigating the success of ERAS [210]. By auditing the details of the key elements of the clinical pathway, it is often easier to understand the occurrence of certain failures that lead to complications. In addition, measuring compliance helps to direct future education and the modification of other interventions (if necessary). ERAS-care outcomes were reported in relation to compliance to the ERAS-protocol in a large cohort study of nearly 1,000 consecutive patients [210]. This study concluded that the proportion of patients with postoperative morbidity and symptoms delaying discharge and readmission to hospital were significantly reduced (38–69 %) with higher levels of ERAS compliance. Nearly all of the pre- and perioperative ERAS items influenced the different outcomes in a beneficial way. However, only intravenous fluid management and intake of preoperative carbohydrate drink were identified as independent predictors of outcome.

In the LAFA study [111], overall compliance to ERAS items of 60 % was reported in laparoscopic and open colonic surgery. A follow-up study [216] showed that enforced advancement of oral intake, early mobilisation, laparoscopic surgery and female gender were independent determinants of early recovery. However, two of the variables determining outcomes—postoperative oral intake and mobilisation—could also be regarded as outcomes and dependent on the pre- and postoperative care. A third study investigating factors influencing outcomes in an ERAS setting [6] reported that fluid overload and non-functioning epidural analgesia were independent predictors of postoperative complications. It is difficult to compare the three studies except that all show that compliance with certain care elements known to improve outcomes also does so in the ERAS setting. The importance of the individual elements is likely to be influenced by variation in compliance in any given study situation.

There are several tools to audit compliance and ERAS outcomes. Within the ERAS society, a systematic process of audit has been built into the ERAS Interactive Audit System and data collection system to facilitate implementation of ERAS (www.erassociety.org) [217]. The ERAS database differs from other common audit tools in that it collects data on patient demographics, treatment and outcomes. Additionally included in the ERAS system is the recording of compliance using a series of evidence-based treatment interventions that have been shown to influence outcomes. A raft of measures which provide information on different aspects of postoperative recovery (and potential factors delaying it) is incorporated into the dataset to allow interrogation of the care process. The ERAS audit system also provides relevant feedback on clinical outcomes that are important for patients, healthcare providers and other decision-makers. Within England, there are various local systems and one national toolkit to record ERAS elements and outcomes. The Enhanced Recovery Partnership Programme (ERPP) has designed a toolkit to measure compliance in ERAS [www.natcansatmicrosite.net/enhancedrecovery/].

Summary and recommendation:

A systematic audit is essential to determine clinical outcome and measure compliance to establish successful implementation of the care protocol. The system should also report patient experience and functional recovery, but validated tools are required for this aspect.

Evidence level:

Systematic audit: Moderate (extrapolation, study quality)
Patient experience/functional recovery: Very low (lack of valid tools)

Recommendation grade:

Strong

Outcomes of ERAS

Eras versus traditional care in elective colonic surgery: clinical outcomes

Several studies have demonstrated that the ERAS programmes compared with traditional perioperative care is associated with earlier recovery and discharge after colonic resection [1, 2, 218–223]. Recently, the effect of perioperative treatment with the ERAS protocol on four outcome parameters (mortality, morbidity, LOSH, hospital readmissions) after mainly colonic surgery was reported in two systematic reviews: Spanjersberg et al., Cochrane, 2011 [224] and Varadhan et al. [214]. Different variations of the ERAS programme were compared with traditional perioperative care based on 4 and 6 RCTs, respectively ([4, 5, 222, 225] (n = 237) and [4–6, 222, 225, 226] (n = 452)).

The mortality in patients undergoing surgery within an ERAS programme was 0.4 and 1.3 % in patients within traditional perioperative care. The difference was not significant, RR, 0.53 (0.12–2.38) [224] and RR, 0.53 (0.09–2.15) [214]. However, there was a significant reduction in RR for postoperative morbidity in patients undergoing surgery within an ERAS programme of 48 %, RR, 0.52 (0.38–0.71) [224] and 47 %, RR, 0.53 (0.41–0.69) [214], respectively. Furthermore, LOSH after surgery was significantly shorter in patients within an ERAS protocol compared with patients undergoing surgery within traditional perioperative care, –2.94 days (–3.92 to –2.19) [224], –2.51 days (–3.54 to –1.47) [214]. Finally, there was no difference in hospital readmissions among patients within an ERAS programme (3.3–4.4 % versus 4.2–5.7 %) in patients within traditional care (RR, 0.87 (0.08–9.39) [224], RR, 0.80 (0.32–1.98) [214]. In a third meta-analysis (Adamina et al.) [227] investigating the same 6 randomised studies as in the meta-analysis of Varadhan et al. [214], these results were confirmed.

Summary and recommendation:

ERAS protocols should be used in elective colonic surgery. Using more evidence-based elements of perioperative care from an ERAS protocol is likely to improve outcomes further.

Evidence level:

LOSH: High
Morbidity: Low (inconsistensy, study quality, low rate of difference)
Hospital readmissions: Low (inconsistency)

Recommendation grade:

Strong

Effect of ERAS on health economics and QoL

The literature examining the impact of ERAS on health economics and QoL after colonic surgery is sparse. Two cohort studies collected data on the cost before and after the introduction of ERAS. The first [228], analyzed cost during the 3-months after intervention in 60 patients undergoing surgery for colon cancer or rectal cancer within an ERAS protocol. This was compared with a tight control group of 86 individuals treated by the same surgeon and who were recruited immediately before the introduction of the ERAS protocol. There were non-significant reductions in hospital, indirect, and total costs after the introduction of ERAS. The second study [229] looked at cost savings within a university hospital in New Zealand using a case-matched comparison of 50 patients in each group. After the introduction of enhanced recovery, 30-day costs were reduced by a mean of €4,240 per patient, even taking into account start-up costs. A review containing US cost analyses indicated a saving of ≈2,000 USD per patient [227]. Recently, the Dutch multicenter LAFA trial [111] examined in-hospital costs after colonic resection within and outside an ERAS protocol, finding (surprisingly) that there were no significant differences between groups. Despite the limited evidence for ERAS reducing the cost of care within the literature, the fact that it reduces the prevalence of complications and postoperative stay in RCTs lends support to the notion that it imparts cost benefits.

Table 1 Guidelines for perioperative care in elective colonic surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations

Item	Recommendation	Evidence level	Recommendation grade
Preoperative information, education and counseling	Patients should routinely receive dedicated preoperative counselling. Preoperative general medical optimisation is necessary before surgery	Low	Strong
Preoperative optimisation	Smoking and alcohol consumption (alcohol abusers) should be stopped four weeks before surgery	Alcohol: Low Smoking: High	Strong
Preoperative bowel preparation	Mechanical bowel preparation should not be used routinely in colonic surgery	High	Strong
Preoperative fasting and carbohydrate treatment	Clear fluids should be allowed up to 2 h and solids up to 6 h prior to induction of anaesthesia	Solids and fluids: Moderate	Fasting guidelines: Strong
	Preoperative oral carbohydrate treatment should be used routinely. In diabetic patients carbohydrate treatment can be given along with the diabetic medication	Carbohydrate loading, overall: LoCarbohydrate loading, diabetic patients: Very low	Preoperative carbohydrate drinks: Strong Preoperative carbohydrate drinks, diabetic patients: Weak
Preanaesthetic medication	Patients should not routinely receive long- or short-acting sedative medication before surgery because it delays immediate postoperative recovery	High	Strong
Prophylaxis against thromboembolism	Patients should wear well-fitting compression stockings, have intermittent pneumatic compression, and receive pharmacological prophylaxis with LMWH. Extended prophylaxis for 28 days should be given to patients with colorectal cancer	High	Strong
Antimicrobial prophylaxis and skin preparation	Routine prophylaxis using intravenous antibiotics should be given 30–60 min before initiating surgery Additional doses should be given during prolonged operations according to half life of the drug used Preparation with chlorhexidine-alcohol should be used	High	Strong
Standard anaesthetic protocol	A standard anaesthetic protocol allowing rapid awakening should be given	Rapid awakening: Low	Strong
	The anaesthetist should control fluid therapy, analgesia and haemodynamic changes to reduce the metabolic stress response	Reduce stress response: Moderate	
	Open surgery: mid-thoracic epidural blocks using local anaesthetics and low dose opioids	Open surgery: High	
	Laparoscopic surgery: spinal analgesia or morphine PCA is an alternative to epidural anaesthesia	Laparoscopic surgery: Moderate	
PONV	A multimodal approach to PONV prophylaxis should be adopted in all patients with $\geq$2 risk factors undergoing major colorectal surgery If PONV is present, treatment should be given using a multimodal approach	Low	Strong
Laparoscopy and modifications of surgical access	Laparoscopic surgery for colonic resections is recommended if the expertise is available	Oncology: High Morbidity: Low Recovery/LOSH: Moderate	Strong
Nasogastric intubation	Postoperative nasogastric tubes should not be used routinely. Nasogastric tubes inserted during surgery should be removed before reversal of anaesthesia	High	Strong
Preventing intraoperative hypothermia	Intraoperative maintenance of normothermia with a suitable warming device and warmed intravenous fluids should be used routinely to keep body temperature >36 °C	High	Strong

Table 1 continued

Item	Recommendation	Evidence level	Recommendation grade
Perioperative fluid management	Patients should receive intraoperative fluids (colloids and crystalloids) guided by flow measurements to optimise cardiac output	Balanced crystalloids: High Flow measurement in open surgery: High Flow measurement in other patients: Moderate	Strong
	Vasopressors should be considered for intra- and postoperative management of epidural-induced hypotension provided the patient is normovolaemic	Vasopressors: High	
	The enteral route for fluid postoperatively should be used as early as possible, and intravenous fluids should be discontinued as soon as is practicable	Early enteral route: High	
Drainage of peritoneal cavity after colonic anastomosis	Routine drainage is discouraged because it is an unsupported intervention that is likely to impair mobilisation.	High	Strong
Urinary drainage	Routine transurethral bladder drainage for 1–2 days is recommended	Low	Routine bladder drainage: Strong
	The bladder catheter can be removed regardless of the usage or duration of thoracic epidural analgesia		Early removal if epidural used: Weak
Prevention of postoperative ileus	Mid-thoracic epidural analgesia and laparoscopic surgery should be utilised in colonic surgery if possible	Thoracic epidural and laparoscopy: High	Thoracic epidural, fluid overload, nasogastric decompression, chewing gum, alvimopan: Strong
	Fluid overload and nasogastric decompression should be avoided	Chewing gum: Moderate	
	Chewing gum can be recommended, whereas oral magnesium and alvimopan may be included.	Oral magnesium, alvimopan: Low	Oral magnesium: Weak
Postoperative analgesia	Open surgery: TEA using low-dose local anaesthetic and opioids.	TEA, open surgery: High Local anaesthetic and opioid: Moderate	Strong
	Laparoscopic surgery: an alternative to TEA is a carefully administered spinal analgesia with a low-dose, long-acting opioid	TEA not mandatory in laparoscopic surgery: Moderate	
Perioperative nutritional care	Patients should be screened for nutritional status and if at risk of under nutrition given active nutritional support	Postoperative early enteral feeding, safety: High Improved recovery and reduction of morbidity: Low	Postoperative early feeding and perioperative ONS: Strong
	Perioperative fasting should be minimised. Postoperatively patients should be encouraged to take normal food as soon as lucid after surgery	Perioperative ONS (well-fed patient): Low Perioperative ONS (malnourished patient): Low	IN: IN could be considered in open colonic resections: Weak
	ONS may be used to supplement total intake.	IN: Low	
Postoperative glucose control	Hyperglycaemia is a risk factor for complications and should therefore be avoided	Using stress reducing elements of ERAS to minimise hyperglycaemia: Low	Using stress reducing elements of ERAS to minimise hyperglycaemia: Strong
	Several interventions in the ERAS protocol affect insulin action/resistance, thereby improving glycaemic control with no risk of causing hypoglycaemia	Insulin treatment in the ICU: Moderate	Insulin treatment in the ICU (severe hyperglycaemia): Strong Insulin treatment in ICU (mild hyperglycaemia): Weak
	For ward-based patients, insulin should be used judiciously to maintain blood glucose as low as feasible with the available resources	Glycaemic control in the ward setting: Low	Insulin treatment in the ward setting: Weak

Table 1 continued

Item	Recommendation	Evidence level	Recommendation grade
Early mobilisation	Prolonged immobilisation increases the risk of pneumonia, insulin resistance and muscle weakness. Patients should therefore be mobilised	Low	Strong

QoL was assessed before 2006 by King and colleagues [228], who reported only non-significant trends after introduction of ERAS. Fatigue was measured by the New Zealand group in a separate case-controlled prospective study [230], which elicited similar results to those reported by Jakobsen et al. [231]. Patients within an ERAS programme suffered less fatigue ≤30 days after surgery, and there were reduced consequences of fatigue even at 60 days in the New Zealand study. The lack of blinding and randomisation weakened the results of both studies, but there are clear methodological problems blinding patients to ERAS. More recently, the LAFA trial [111] randomised between ERAS and standard perioperative care but did not identify improvements in health-related QoL—one explanation for this having been discussed above. A recent review [215] did not find consistent disadvantages to ERAS care during colonic surgery if recovery was measured using QoL instruments. This is possibly because the tools used are not sufficiently sensitive to detect the improvements in clinical recovery that clinicians perceive are present. Delaney et al. addressed this problem by designing a novel postoperative scoring system [232], which may be of use in this area.

Summary and recommendation:

ERAS can be recommended because it is likely to reduce the cost of colorectal surgery and improve the quality of recovery

Evidence level:

Cost reduction: Very low (inconsistency, few studies)
Quality of recovery: Very low (inconsistency, few studies)

Recommendation grade:

Weak

Comment

The practice of surgery and anaesthesia is continuously changing. This creates the need for regular updates of the knowledge base and for continuous training of those involved in the treatment of surgical patients. The ERAS Society for Perioperative Care (www.erassociety.org) was initiated by the former ERAS Study Group and was formed in 2010 to support these processes. The Society participates in the improvement of perioperative care by developing new knowledge through research, education and also by being involved in the implementation of best practice.

Current recommendations from the ERAS Society for clinical perioperative care of patients undergoing elective colonic surgery are based on evidence evaluated according to the GRADE system. The evidence-based recommendations present the ERAS protocol interventions separately and overall, and are intended to be used by units undertaking colonic surgery to implement and upgrade to what the current literature shows to be best practice: the ERAS protocol.

Current recommendations are a development of the previous two versions published by the ERAS Study Group [8, 9]. We used a more stringent system for the evaluation of the evidence and recommendations. The currently used grading of the evidence is very demanding, and it may seem to the reader that some of the protocol items have weak levels of evidence. Simultaneously, current review of the evidence must be put into the perspective of the level of evidence in general for common medical practices and treatments. The evidence for components in the ERAS protocol is at a level that is commonly in use throughout medicine today. A summary of the guidelines is shown in Table 1.

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Conflict of interest The ERAS Society® receives an unrestricted grant from Nutricia. OL has served as an external advisor to Nutricia and has occasionally received travel and lecture honoraria from Nutricia, Fresenius-Kabi, BBraun, Baxter and Nestle. OL also previously held a patent for a preoperative carbohydrate drink formerly licensed to Nutricia. OL initiated a company that runs the ERAS society data by contract with the ERAS society. DNL has received unrestricted research funding, travel grants and speaker's honoraria from Baxter Healthcare, Fresenius Kabi and BBraun. All other authors declare no conflicts of interests.

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