Review Article

Peri-operative nutrition

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Summary
Patients are frequently malnourished or are at risk of malnutrition before surgery. Peri-operative nutritional support can improve their outcomes. This review focuses on new developments in peri-operative nutrition, including: patient preparation and pre-operative fasting; the role of nutritional supplementation; the optimal route and timing of nutrient delivery; and the nutritional management of specific groups including critically ill, obese and elderly patients.

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Introduction
Malnutrition is associated with morbidity, mortality and increased healthcare costs [1–5]. The prevalence of malnutrition varies with the definition and concomitant diseases, affecting one in four patients with chronic obstructive pulmonary disease and four in five patients with pancreatic cancer or head and neck cancer [1]. Pre-operative malnutrition is associated with increased susceptibility to infection, impaired wound healing, pressure ulceration and prolonged hospital stay [2, 6–10]. Malnutrition is exacerbated by additional weight loss during hospitalisation, which occurs in up to two-thirds of patients [11], and is due in part to the substantial catabolic response to surgery [12].

The implications of malnutrition are significant. For example, malnutrition is the third most frequent reason cited for postoperative hospital re-admission [13]. Critically ill surgical patients are at particular risk of both malnutrition and associated poor outcomes [3]. Appropriate peri-operative nutrition can reduce complications and shorten hospitalisation and intensive care. Accordingly, peri-operative nutritional therapy may be a very cost-effective intervention [5, 14–16].

The aim of this review is to describe the evidence for nutrition in the peri-operative period and to highlight areas for future research.

Before surgery
Nutritional assessment
Nutritional status is difficult to quantify accurately [2]. A history of chronic disease, infection, surgery and recent reduced dietary intake and weight loss help identify patients at risk of malnutrition. Assessment may include a calculation of body mass index (BMI), an estimate of recent loss of subcutaneous fat and muscle mass, as well as signs of specific nutritional deficiencies [17].

Importantly, malnutrition can accompany morbid obesity [5]. The macronutrient excess of obesity can co-exist with malnutrition that is associated with chronic inflammation, sarcopenia and micronutrient deficiency [18, 19]. Epidemiological studies have reported an inconsistent relationship between body fat composition, particularly as defined by the BMI, and outcomes following surgery [20]. However, data from large cohorts of postoperative patients suggest that the morbidly obese (BMI $\geq$ 40 kg.m^{-2}) have more postoperative ventilatory support, more infections, and prolonged critical care [18, 20, 21]. The distinct needs of these patients need to be identified.

Numerous laboratory indices have been proposed as markers of nutritional status. For example, low pre-operative serum albumin concentrations are associated with delayed wound healing [22, 23] and can be used to predict morbidity in patients undergoing elective operations [5, 24, 25]. However, as albumin concentration is suppressed by surgery and illness, its postoperative measurement is of limited value [5]. The peri-operative measurements of serum transferrin and pre-albumin have more potential, along with serum cholesterol and lymphocyte count, as their half-lives are shorter than albumin [26]. However, the clinical value of these markers is indicative rather than diagnostic, as they are not specific for malnutrition.

A number of tools incorporate history, examination findings and laboratory values to identify malnutrition. None are widely accepted [5]. They include 'subjective global assessment' and the 'malnutrition universal screening tool'. The 'nutritional risk survey 2002' (NRS 2002) is the best validated for surgical patients [27], but the amount of time required to calculate a score for each patient has restricted its widespread use [5]. Furthermore, there is limited evidence to suggest that interventions triggered by the NRS 2002 score have improved patient outcomes [28]. For example, a non-blinded prospective observational study of patients undergoing abdominal surgery found that one week or more of pre-operative enteral or parenteral nutrition in patients with an NRS 2002 score > 5 reduced complications and hospital stay [28]. However, causation cannot be concluded, due to the substantial risks of bias in observational studies. Because no single method comprehensively assesses a patient's nutritional status, it is intuitive that an integrated approach will identify patients at greatest risk of malnutrition in the peri-operative period, particularly those expected to be starved for 5–7 days after surgery [5]. Implementing validated assessment tools and nutrition protocols in busy 'real-world' settings beyond clinical trials is challenging [29].

Fasting

Concerns about the potential for aspiration, anastomotic breakdown and postoperative ileus resulted in the traditional peri-operative fast: no food or drink for 6–12 h before the induction of anaesthesia and then for up to several postoperative days, particularly after laparotomy [30, 31]. Intravenous fluids were infused until bowel function returned, followed by the graded introduction of diet [31]. Delays in theatre availability frequently meant that patients awaiting non-elective operations fasted for longer. Prolonged pre-operative fasting may be harmful, as fasting induces metabolic stress and impairs mitochondrial function and insulin sensitivity [2]. Recent evidence and a more sophisticated understanding of gastrointestinal motility have challenged the historical fast.

Gastric emptying is controlled by neural and hormonal pathways and is determined by a number of intraluminal and extraluminal factors. Intraluminal factors include meal composition (caloric load, volume, temperature and nutrient type), the osmolality of small intestinal contents and the length and the region of small intestine exposed to nutrient [32]. Extraluminal factors include glycaemia, posture, pain, sex and age [33, 34]. The optimal duration of fasting for a particular patient depends on numerous factors. The rate of emptying of nutrient from the stomach is linear, with emptying occurring more rapidly for liquids than solids. In contrast, water is emptied from the stomach exponentially, with an approximate half-life of 10 min [35–37].

A reduction in the standard fasting periods has little to no effect on the volume or pH of gastric contents [38]. A fast of 2 h for clear fluids is sufficient to ensure an empty stomach for the majority of otherwise well elective surgical patients, whereas no solid food should be consumed 6 h before anaesthetic induction [38, 39]. However, aspiration is uncommon – studies have not quantified the rate of aspiration or related morbidity associated with different fasting periods. Recommendations are therefore based on the indirect measures of gastric volume and pH. Gastric emptying is slowed for patients with certain chronic illnesses or receiving specific therapies (Table 1) [38–41]. Standard fasting guidelines should not be applied uniformly for these populations, particularly as they have not been studied by the studies on which the recommendations have been based [21, 38]. The risk of aspiration for such patients should be individually assessed by the anaesthetist and fasting times adjusted accordingly: some patients may need to be managed as non-fasted regardless of the fasting period.

Gastro-oesophageal regurgitation and pulmonary aspiration is thought to be more likely in critically ill patients, due to disturbed gastric and oesophageal motility [33]. Pre-operative fasting, particularly when six or more hours in duration, will starve critically ill patients who require frequent operations [42–45]. There is some evidence that critically ill patients with a protected airway (defined as a cuffed tracheal or tracheostomy tube) can be fed enterally until the time of surgery [42–44]. Our experience is that such an approach is safe, with the exception of patients who require surgery on the airway or gastrointestinal tract [42, 43].

Table 1 Factors associated with slower gastric emptying.

Disease States
Autonomic dysfunction: diabetes mellitus, amyloidosis, Parkinson's disease, multiple sclerosis, HIV, spinal injury
Hyperglycaemia
Alcoholism
Hypothyroidism
Malignancy
Critical illness
Gastrointestinal disease: gastric dysmotility, gastric outlet or bowel obstruction
Surgical: vagotomy, fundoplication, Roux-en-Y anastomosis
Drugs
Opiates
Tricyclic antidepressants
Calcium channel blockers
Dopamine agonists
Alpha-2-adrenergic agonists
Glucagon-like peptide-1 receptor agonists
Muscarinic cholinergic receptor antagonists
Catecholamines
Cyclosporine
Somatostatin analogues (e.g. octreotide)
Composition of meal ingested
High caloric load
Large lipid component
Other
Pregnancy or postpartum state
Advanced age

Carbohydrate loading

Patient outcomes may be improved by a shorter fasting period preceded by prescribed carbohydrate intake [46]. Studies have reported that postoperative insulin sensitivity is preserved by carbohydrate drinks (100 g the night before surgery and 50 g 2 h before surgery) [47] or intravenous glucose (5 $mg.kg^{-1}.min^{-1}$) [48], possibly through suppression of fat and glucose oxidation and attenuation of pyruvate dehydrogenase kinase [18].

A recent systematic review of randomised controlled trials, predominantly of patients having abdominal surgery, reported that pre-operative carbohydrate drinks reduced insulin resistance and improved a number of subjective markers of patient wellbeing, including hunger, thirst, anxiety and nausea, without increased rates of adverse events [49]. Another meta-analysis of 21 randomised trials reported that oral carbohydrate loading was associated with reduced length of stay and reduced insulin resistance in patients undergoing major abdominal surgery [50]. However, as the authors acknowledge, the individual studies were of low to moderate quality and had small sample sizes, while the definitions of outcomes and assessment methods for insulin resistance varied. For these reasons, there is the potential for bias and over-estimation of the true effect. More evidence is required before pre-operative carbohydrate loading is unequivocally established as beneficial. Pre-operative carbohydrate loading has been incorporated into bundles of care for patients undergoing elective colorectal surgery [51]. It is important to note that studies of oral pre-operative carbohydrate loading have not typically studied patients at risk of slow gastric emptying and presumably, aspiration [49].

Nutritional support

The interpretation of studies that have evaluated several days of pre-operative oral or enteral tube feeding or parenteral nutrition is challenging, as different operations, populations and definitions of malnutrition have been studied and used.

Pre-operative nutritional support appears unnecessary for nourished patients or those with mild to moderate malnutrition [28, 52, 53]. International guidelines recommend nutritional support for severely malnourished patients 7–14 days before elective major surgery, although there is limited evidence supporting any specific time period [54]. Severely malnourished patients have at least one of the following: weight loss more than 10–15% within 6 months; BMI less than 18.5 $kg.m^{-2}$; subjective global assessment grade C; or serum albumin below 30 $g.l^{-1}$ without hepatic or renal dysfunction [54].

The optimal route of pre-operative nutritional support is also contentious. In general, enteral feeding is preferred [55]. Major limitations to prescription of pre-operative parenteral nutrition include the complications of central line placement, infections, hyperglycaemia and refeeding syndrome in malnourished patients [18]. These limitations frequently mean that parenteral nutrition requires expensive hospitalisation [56, 57].

A number of studies have evaluated the role of pre-operative parenteral nutrition, with varying results. One of the foremost was the Veterans Affairs TPN Co-operative study [58]. Participants who were previously malnourished and scheduled for laparotomy or non-cardiac thoracotomy were randomly allocated to standard care or parenteral nutrition for 7–15 days before surgery and 3 days after surgery [58]. There was no difference in major complications. However, infection rates were higher after parenteral nutrition, although non-infective complications were reduced in the severely malnourished subgroup. This may have occurred because of the development of hyperglycaemia and the amount and type of lipid administered [18]. Infection control measures and blood glucose management may reduce infections associated with parenteral nutrition [59, 60]. A subsequent meta-analysis of 26 randomised trials reported reduced complication rates when parenteral nutrition was commenced pre-operatively, particularly in malnourished patients, without effect on mortality [61].

In summary, in the absence of substantial malnutrition, there is no evidence to support delaying surgery to institute nutritional support pre-operatively. Although the enteral route is generally preferred, a limited subgroup of patients with gastrointestinal dysfunction (e.g. intestinal obstruction, bowel in discontinuity or severe ileus) may benefit from pre-operative parenteral nutrition for 7 days [17, 56].

Immunonutrition

A comprehensive evaluation of peri-operative immunonutrition can be found elsewhere [62, 63]. In brief, major surgery is associated with immune dysregulation and oxidative stress, that can predispose patients to infection [64]. Enteral or parenteral supplementation with specific nutrients such as arginine, glutamine and omega-3 fatty acids may modulate inflammation and upregulate immune responses postoperatively [62]. A recent review included a meta-analysis of trials investigating immunonutrition in gastrointestinal surgery and demonstrated reduced postoperative infective complications and hospital length of stay [53]. Other meta-analyses have found reduced hospital length of stay and reduced infections in patients receiving glutamine [65] or arginine [66] supplementation. However, individual studies included in the meta-analyses had methodological flaws, often studying several compounds simultaneously. The short-term benefits of immunonutrition have mainly been demonstrated in patients undergoing gastrointestinal surgery, particularly patients diagnosed with malnutrition or cancer [62]. When administered, immunonutrition should be started 5–7 days pre-operatively (500–1000 ml per day) and continued in the post-operative period [54, 55].

During surgery

There are few randomised controlled trials assessing intra-operative enteral feeding. Studies are limited to surgery following burn injury and non-gastrointestinal trauma [18]. Following burn injury, the small intestine can be fed during surgery, which reduces cumulative calorie deficits and does not appear to increase the risk of aspiration of gastric contents [67]. Intra-operative enteral nutrition, except during surgery on the airway or gastrointestinal tract, can shorten the duration of fasting in mechanically ventilated critically ill patients, in whom the lungs are ostensibly protected by tracheal intubation. The safety of this technique and its effects on outcomes need to be researched.

After surgery

Optimising nutrient delivery

Following uncomplicated abdominal surgery, the myoelectric function of the stomach returns to relatively normal patterns within 24–48 h, the small bowel within 12–24 h and the colon within 48–72 h [5]. Several studies have now reported that resumption of oral or enteral nutrition within 24 h of surgery is well tolerated and safe, and does not increase rates of anastomotic dehiscence or postoperative ileus [68–71]. Earlier feeding is associated with reduced infectious complications [70], improved wound healing [72], resolution of ileus [68] and reduced length of stay [68, 70]. Following an uncomplicated operation, patients should eat as soon as they can tolerate food, ideally within 24 h [39]. The rate of successful feeding within 6–24 h of surgery ranges from 75% to 95%, with early initiation of feeding associated with improved feed tolerance [5]. Table 2 lists the interventions that increase the chance of successful postoperative feeding [5, 33, 41, 73]. Peri-operative bundles of care, such as the enhanced recovery protocols, may improve patients' nutrition and metabolic state [74].

Postoperative nutritional support

Enteral nutrition is generally preferred, with parenteral nutrition reserved for patients who cannot otherwise meet their caloric requirements within 7–10 days of an operation [56, 75]. Parenteral nutrition may be started earlier for patients with high output enterocutaneous fistulae, partly obstructing gastro-intestinal lesions, severe ileus, intestinal ischaemia or bowel in discontinuity [54, 56]. In general, there is no proven benefit in supplementing enteral nutrition with parenteral nutrition, although most studies have been small and retrospective [57]. Moderately and severely malnourished patients have not been specifically studied.

Table 2 Strategies used to reduce postoperative gastrointestinal dysmotility and increase success of postoperative enteral feeding.

Correction of pH imbalance
Correction of electrolyte abnormalities (especially potassium and magnesium)
Limiting excessive fluid administration
Minimisation of exogenous opiates
Optimisation of glycaemic control to avoid hyperglycaemia-induced slowing of gastric emptying
Early institution of enteral feeding
Use of prokinetic medications to treat established feed intolerance

While the optimal caloric load for the hypermetabolic patient is controversial, 20–30 $kcal.kg^{-1}.day^{-1}$ is considered safe [24]. Estimated requirements are 3–6 $mg.kg^{-1}.min^{-1}$ carbohydrate and 1.25–2.00 $g.kg^{-1}.day^{-1}$ protein. Lipids should comprise 10–25% of total calories [76]. There have been a few studies examining the concept of permissive underfeeding in patients requiring short-term nutritional support [77]. However, it is difficult to draw definite conclusions from these studies because of clinical heterogeneity and differing outcomes.

Specific patient groups

The critically ill

Critically ill surgical patients often do not receive adequate nutrition [5], although only two specific situations arise where concerns about the safety of enteral nutrition may be valid, namely for patients receiving vasopressor drugs and those with laparostomies.

Feeding practices are particularly heterogeneous for critically ill patients receiving vasopressor drugs [78], for whom there is little evidence on when to start enteral feeding. The rationale for avoiding enteral nutrition is that it might exacerbate subclinical gut ischaemia in patients receiving vasoconstrictor agents. However, in health, mesenteric artery blood, flow increases with nutrient load [79, 80], as it does in the critically ill, albeit to a lesser extent [81]. Retrospective observational data have suggested that enteral feeding during shock is safe and may be associated with reduced mortality [82]. A recent large multicentre cohort study conducted in France reported that nutrition within 48 h of intubation in shocked patients was associated with reduced mortality, irrespective of the route of feeding [83]. Similarly, enteral nutrition does not appear to delay closure of laparostomies and has been associated with a reduction in the frequency of both fistulae formation and pneumonia [84, 85].

There is conflicting evidence about the optimal amount of energy that should be administered to critically ill patients. International guidelines recommend a daily energy intake of 25 $kcal.kg^{-1}$ of body weight for critically ill patients, including 1.0–1.5 $g.kg^{-1}$ of protein per day [86]. There has been recent interest in the concept of hypocaloric feeding, based upon the rationale that anorexia associated with critical illness may be protective and that supply of nutrients during critical illness may induce a pro-inflammatory state that worsens the patient's condition [24]. A large randomised open-label study compared full enteral feeding (~1300 $kcal.day^{-1}$) with low-dose 'trophic' feeding (~400 $kcal.day^{-1}$) for the first 6 days of mechanical ventilation in a previously well-nourished population with acute lung injury. Reduced calories did not increase ventilator-free days (the primary outcome) [87]. It is important to note that this study was designed to test whether intentional underfeeding was superior to full-feeding and these data cannot be used to prove non-inferiority or equivalence of low-dose feeding. The benefits and safety of hypocaloric feeding are yet to be proven in prospective randomised trials, in which, it would be important to consider whether enterally fed critically ill patients experience worse outcomes when they fail to achieve their caloric goals [88–90]. Random allocation of 112 critically ill patients to 1.0 $kcal.ml^{-1}$ or 1.5 $kcal.ml^{-1}$ enteral nutrition in a recent feasibility study suggested that a larger study might detect lower mortality in the group that received the most calories (~1800 $kcal.day^{-1}$) [91]. Based on these observations, more data are required to determine the optimal amounts of calorie required, but there is insufficient evidence to support clinicians administering less than 50% of the energy that is recommended in current guidelines.

The obese

Despite a considerable fat store, obese patients are at risk of loss of lean body mass through gluconeogenesis and micronutrient deficiency during times of acute stress [92]. Fasting insulin concentrations are increased, which suppress lipid mobilisation from stores and result in accelerated protein breakdown to fuel gluconeogenesis [21]. These risks may be increased because of an incorrect assumption that obese patients have a greater 'nutritional reserve' than non-obese patients [92]. Obese patients may benefit from pre-operative dietary optimisation and education before major elective surgery, but this is as yet unexplored. Screening and supplementation for micronutrient deficiency may be of benefit. For example, patients undergoing laparoscopic sleeve gastrectomy can be deficient in vitamin D, iron, thiamine and vitamin B_{12} [93].

Postoperative nutrition should contain enough protein to minimise muscle loss and aid wound healing and should contain enough calories to prevent severe ketoacidosis [92]. However, what constitutes 'enough' is unknown. Preliminary data suggest that glucose targets in the critically ill should be adjusted to account for periods of pre-morbid hyperglycaemia, which may be relevant in the obese patient [94, 95]. High-protein hypocaloric feeding of critically ill obese patients has been evaluated with the aim of allowing fat stores to be utilised for energy and sparing muscle protein from excessive catabolism [96, 97]. Suggested caloric requirements for this group of patients are 22–25 $kcal.kg^{-1}$ ideal body weight per day (or 11–14 $kcal.kg^{-1}$ actual body weight per day) with 2 $g.kg^{-1}$ per day of protein, but the evidence upon which the recommendation is based is weak [96].

The elderly

Ageing is associated with a reduction in lean body mass, increase in body fat, decrease in total body water and a reduction in bone density [21]. Advanced age is independently associated with poor nutritional status in hospitalised patients [98]. Deficiencies of vitamins B_6, B_{12}, C, D, folate and calcium are prevalent in this group [21, 99]. Elderly patients who have experienced $\geq$ 10% weight loss in the previous 6 months, or who are hypoalbuminaemic, experience more adverse postoperative outcomes [98]. Peri-operative nutritional support is indicated in malnourished elderly patients, who are not in a terminal phase of illness, and the enteral route is preferred [100]. Although the evidence is limited, nutritional supplementation may reduce morbidity in elderly patients who suffer a hip fracture [101] or who undergo total hip or total knee arthroplasty [102].

Conclusion

Attention to peri-operative nutrition, particularly for patients who are moderately or severely malnourished, critically ill, obese or elderly, has the capacity to improve patient outcomes and reduce healthcare costs.

Ideally, patients at risk of malnutrition should be identified early, but the method with which to screen patients remains uncertain. Periods of prolonged fasting should be minimised and nutrition should be commenced as early as possible after surgery, preferably via the enteral route. However, nutritional therapies should be started and adjusted according to each patient's circumstances. Patients with substantial malnutrition and ongoing gastro-intestinal dysfunction have the potential to benefit most from parenteral nutrition. The optimal route, amount and timing of nutrients delivered in the peri-operative period remains the focus of ongoing studies.

Competing interests

No external funding and no competing interests declared.

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