What's new in perioperative nutritional support?

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Purpose of review

To highlight recent developments in the field of perioperative nutritional support by reviewing clinically pertinent English language articles from October 2008 to December 2010, that examined the effects of malnutrition on surgical outcomes, optimizing metabolic function and nutritional status preoperatively and postoperatively.

Recent findings

Recognition of patients with or at risk of malnutrition remains poor despite the availability of numerous clinical aids and clear evidence of the adverse effects of poor nutritional status on postoperative clinical outcomes. Unfortunately, poor design and significant heterogeneity remain amongst many studies of nutritional interventions in surgical patients. Patients undergoing elective surgery should be managed within a multimodal pathway that includes evidence-based interventions to optimize nutritional status perioperatively. The aforementioned should include screening patients to identify those at high nutritional risk, perioperative immuno-nutrition, minimizing 'metabolic stress' and insulin resistance by preoperative conditioning with carbohydrate-based drinks, glutamine supplementation, minimal access surgery and enhanced recovery protocols. Finally gut-specific nutrients and prokinetics should be utilized to improve enteral feed tolerance thereby permitting early enteral feeding.

Summary

An evidence-based multimodal pathway that includes interventions to optimize nutritional status may improve outcomes following elective surgery.

Keywords

malnourished, nutrition, outcomes, perioperative, surgery

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Introduction

Despite decades of research into therapeutic nutrition, the prevalence of malnutrition has remained alarmingly high, ranging from 24 to 88%, depending on definitions used and populations studied [1•]. Up to 65% of patients undergoing gastrointestinal surgery are malnourished [2,3] and two-thirds of patients lose weight during hospitalization [4]. The association of malnutrition with adverse outcomes was recognized as early as 1936, when Studley [5] showed that mortality after elective surgery for peptic ulcer disease was 3.5% in patients with less than 20% preoperative weight loss and 33% in those with at least 20% weight loss. Remarkably, 50 years of progress in anesthesia and surgery have led to little change in these figures: a study of 365 consecutive patients undergoing abdominal operations for malignant disease showed that malnourished patients had a significantly higher incidence of complications (72 vs. 29%) and mortality (23 vs. 4%) than well nourished ones [6].

Whilst there exist several screening tools such as the Malnutrition Universal Screening Tool (MUST), Nutritional Risk Screening (NRS) 2002 and Subjective Global Assessment (SGA) [7–10] to aid recognition of malnutrition, and guidelines on the provision of nutritional support [11], current clinical practice (nutritional assessment and provision of nutritional support) [12••] and knowledge amongst medical personnel remain poor [13].

This review focuses on developments in the field of perioperative nutritional support from October 2008 to December 2010, limited to clinically relevant English language articles addressing the effects of malnutrition on surgical outcomes, optimizing metabolic function and nutritional status preoperatively and postoperatively.

Nutritional status of surgical patients

Although the problem of malnutrition within community and hospital settings is widely recognized [1•,14,15], and guidelines recommending formal nutritional assessment at hospital admission exist [10,11], a report by the UK National Confidential Enquiry into Patient Outcome and Death (NCEPOD) has highlighted several serious failings [12••]. Having reviewed the care of 820 patients aged 80 or older who died within 30 days of surgery, the authors found 11% of UK hospitals surveyed did not have formal policies/protocols for nutritional assessment and 35% did not have a nutrition support team [12••]. The admitting teams failed to recognize malnutrition in 43% of admissions, and a nutritional assessment was not undertaken in 73% of patients admitted with an acute abdomen [12••]. European investigators have similarly reported that nutrition-related problems were rarely recognized and treated in geriatric medical patients [14]. Finally, although patients with resectable colorectal cancer were traditionally not considered a group at risk of malnutrition, a study of 132 such patients, enrolled 2–4 weeks prior to surgery, identified that half were weight-losing and 20% were malnourished [16].

Effects of malnutrition on perioperative outcomes

A number of recent studies (Table 1) have further characterized the relationship between preoperative nutritional status, risk of malnutrition and postoperative outcomes [17–23], and confirm previous observations [5,6] that disease-related malnutrition is associated with increased morbidity, mortality and length of hospital stay. Malnutrition also results in greater risks of readmission, institutionalization and higher costs of care [1•,17–22,24,25]. However, most of these studies [17–23] were retrospective observational cohort studies on small numbers of participants with severe malnutrition. The difficulties of undertaking good-quality randomized studies in these patient groups are also compounded by the lack of an accepted definition of malnutrition. The resultant heterogeneity [1•] precludes systematic review and meta-analysis [11], but an International Guideline Committee is developing a consensus approach to defining malnutrition syndromes [26].

Optimizing and delivering nutritional support

The past decade has witnessed a paradigm shift in the management of patients undergoing elective surgery, specifically with respect to avoidance of preoperative fasting, implementation of enhanced recovery protocols and perioperative optimization of nutritional status and metabolic function.

Avoidance of preoperative fasting and minimizing insulin resistance

Preoperative fasting, a traditional and dogmatic practice [27], has been shown to induce metabolic stress, impair mitochondrial function and produce insulin resistance [28,29•–31•]. Insulin resistance, characterized by decreased responsiveness of tissues to the actions of insulin [29•], is associated with prolonged hospital stay [32], morbidity [33,34••] and mortality [33,34••]. A prospective study of 273 patients undergoing elective cardiac surgery has demonstrated that for each 1 mg/kg/min decrease in intraoperative insulin sensitivity, there was increased incidence of major complications [odds ratio (OR) (95% confidence intervals, CIs) 2.23 (1.3–3.85), $P = 0.004$], death [OR 2.33 (0.94–5.78), $P = 0.067$], severe infection [OR 4.95 (1.48–16.8), $P = 0.01$] and minor infection [OR 1.97 (1.27–3.06), $P = 0.003$] [34••]. Measures to attenuate insulin resistance such as preoperative ingestion of carbohydrate-based drinks 2–3 h before surgery, as pioneered by Ljungqvist's group in Sweden [35,36] may, therefore, lead to clinical benefits. Such regimens have been shown to attenuate the development of insulin resistance by up to 50% [29•,30•] and form part of Enhanced Recovery After Surgery (ERAS, *vide infra*) protocols [31•]. Recent studies have helped elucidate some of the mechanisms by which these drinks attenuate insulin resistance. A randomized, placebo-controlled study of 40 patients undergoing laparoscopic cholecystectomy who ingested a carbohydrate-based drink that also contained glutamine and antioxidants demonstrated significantly increased intraoperative liver glycogen reserves in the intervention group [37•]. Furthermore, ingestion of the study drink was associated with a four-fold ($P < 0.001$), 44% ($P < 0.05$) and 1.5-fold ($P < 0.001$) lower expression of muscle pyruvate dehydrogenase kinase 4 (PDK4) mRNA, PDK4 protein and metallothionein 1A (Mt1A) expression, respectively, when compared with placebo. PDK4 acts to phosphorylate and inactivate pyruvate dehydrogenase complex (PDC). The latter plays a key role in muscle metabolism by controlling the entry of carbohydrate-derived pyruvate into the tricarboxylic acid cycle thereby regulating carbohydrate oxidation (COX). The postoperative insulin-resistant state is characterized by defective oxidative glucose disposal (i.e. COX) [29•]. Lower muscle PDK4 expression may enable PDC activity and COX, thereby improving insulin sensitivity [37•]. Reduced Mt1A expression in the carbohydrate-conditioned group was indicative of decreased cellular oxidative stress; however, the relationship between oxidative stress and insulin resistance remains unclear [29•]. Another randomized study examined the effects of preoperative carbohydrate loading on insulin signalling pathways in 52 patients undergoing elective surgery [38]. Carbohydrate loading enhanced tyrosine kinase activity, and phosphatidyl-inositol 3-kinase and protein kinase B expression. This cellular pathway is responsible for most of the metabolic actions of insulin and the aforementioned changes were associated with decreased postoperative insulin resistance [38], as determined by homeostasis model assessment (HOMA) modelling [39]. mRNA expression of inflammatory and insulin signalling genes in muscle and adipose tissues has also been examined [40,41]. Major surgery was associated with marked up-regulation

Table 1 Recent studies examining the effects of preoperative nutritional status on postoperative outcomes

Study	Population studied and summary of methods	Main findings	Study limitations
Schwegler *et al.* [17]	186 patients undergoing elective surgery for colorectal Ca over a 24-month period (2003–2005) Switzerland. Nutritional risk scores determined at hospital admission using 2 methods [Nutritional Risk Screening 2002 (NRS-2002) and Reilly's Nutrition Risk Score (Reilly's NRS)]. In-hospital mortality and postoperative complications studied.	Mean overall hospital LOS was 20.2 days. Overall in-hospital MR and morbidity were 3.8 and 48.4%, respectively. 39.2 and 31.7% of study population identified at nutritional risk by the NRS-2002 and Reilly's NRS, respectively. MR for patients at nutritional risk or not grouped by NRS-2002 was 7 vs. 1.8%, $P = 0.085$, whereas patients grouped by Reilly's NRS was 8 vs. 1.6%, $P = 0.033$. Patients identified by NRS-2002 as being at nutritional risk had significantly higher complication rates compared to those without risk 62 vs. 39.8%, $P = 0.004$. Respective figures for Reilly's NRS were 58 vs. 44.1%, $P = 0.086$. Multivariate analysis demonstrated that nutritional risk identified by NRS-2002 was an independent predictor of postoperative complications (OR 2.79, $P = 0.002$). Summary: Reilly's NRS was a significant predictor for mortality but not for morbidity. NRS-2002 was a significant predictor for morbidity but not for mortality.	Observational cohort study. Only in-hospital, not 30-day outcomes reported.
Skipworth *et al.* [18]	Single surgeon series of 93 patients undergoing resection of oesophagogastric Ca over a 38-month period (2001–2004) in the UK. Preoperatively, all patients maintained solid, oral nutrition. Postoperative feeding jejunostomy in all patients. Weight loss defined as a 10% decrease in weight compared to documented stable weight. Patients allocated into 4 subgroups: A – no WL & BMI >25; B – No WL and BMI <25; C – WL and BMI >25; and D – WL and BMI <25. 3-year postoperative FU.	48% of all patients displayed preoperative WL. 27% of patients were in subgroup D. 57% of all patients underwent total gastrectomy, the remainder ILO. 46% of patients had stage I and II disease. No significant differences between the subgroups groups in rates of postoperative complications, mortality and hospital LOS.	Observational cohort study. Small number of patients in each subgroup and low overall complication rates in this study may have lead to a type II statistical error.
Merli *et al.* [19]	38 consecutive patients undergoing elective liver transplantation for end-stage liver disease over 18 months (2006–2008) in Italy. SGA amongst methods for nutritional assessment.	73% of patients had one or more infective episodes. Both total number of infective episodes (85 vs. 11, $P < 0.001$) and number of infections per patient [mean (SD), 4.5 (3.1) vs. 0.6 (0.9), $P < 0.001$] significantly higher in malnourished patients than those with no malnutrition, respectively. After adjusting for confounding variables, multivariate analysis demonstrated patients with malnutrition experienced 1.33 additional infections compared to those without. After adjusting for confounders, presence of malnutrition increased the length of ICU and hospital LOS by a factor of 5. No differences in hospital MR.	Observational cohort study. Small number of participants. Study groups unmatched for severity of underlying disease. Dietary recall interviews and questionnaire to determine total energy balance. Postoperative infective complications defined as the identification of microorganisms requiring systemic antibiotics. Study outcomes and follow-up limited to period of hospital in patient stay.
Pacelli *et al.* [20]	196 patients undergoing surgery for gastric Ca over a 6-year period (2000–2006) in Italy. Patients stratified according to % preoperative WL (0 to 5%, 5.1 to 10%, and >10%), serum Alb (<3, 3–3.4, and >3.5 g/dl) and BMI (<18.5, 18.5–24.9, 25–29.9 and >30 kg/m^2).	Overall postoperative MR was 0%. Major infectious complications occurred in 10.2%, major noninfectious in 9.2% and minor infections in 10.7%. No differences in postoperative major infectious, major noninfectious and minor infections complications in patients stratified for preoperative WL, Alb or BMI.	Retrospective observational cohort study. Preoperative weight loss estimated by patients. Only 15.8% of cohort had >10% weight loss and 8.7% had BMI <18.5 so possibility of a type II statistical error. Short-term (30-day) only outcomes reported.

Table 1 (*continued*)

Study	Population studied and summary of methods	Main findings	Study limitations
Kanda *et al.* [21]	268 patients undergoing elective resection of pancreatic Ca over 19-year period in Japan. Predictive value of preoperative nutritional status [assessed using Onodera's prognostic nutrition index (PNI)] on postoperative survival and complications was studied.	27.6% of patients defined as moderate to severe malnutrition (PNI<45) had poorer outcomes than those with a PNI>45: median survival time 9 vs. 15.7 months (OR 2.06, 95% CI 1.46–2.91, $P<0.001$). Multivariate analysis identified PNI<45 as one of 5 independent prognostic factors for survival outcome: HR 1.73 (95% CI 1.21–2.47, $P=0.003$). But accuracy of a preoperative PNI<45 in predicting postoperative survival was 66.4 and 56.3% at 12 and 24 months FU, respectively. Patients with PNI<45 had higher incidence of postoperative complications (45 vs. 27.3%, $P=0.007$. Low preoperative albumin (<4g/dl) associated with adverse outcomes (survival and complications).	Retrospective observational cohort study. Long study duration thus possible confounding by changes in surgical and anesthetic techniques. Excluded patients who preoperatively were unable to tolerate oral intake.
Garth *et al.* [22]	37 and 58 patients undergoing elective surgery for upper GI and colorectal Ca, respectively, over 19 months (2006–2007) in Australia. Retrospective audit of preoperative WL, nutritional intake and biochemistry. Preoperative WL deemed significant if >2% in week prior to admission, 5% in last month, 7.5% last 3 months or 10% in last 6 months. Subset of 25 patients underwent SGA (A – well nourished, B – mild-moderately malnourished and C – severely malnourished).	Significant preoperative WL was present in 55% and 52% of upper GI and colorectal patients, respectively. Mean (SD) hospital LOS was 14 (12.2) days and was longer for patients who experienced significant preoperative WL compared to those who did not [17 (15.8) vs. 10 (6.8), $P<0.05$]. Low preoperative albumin (<3.5 g/dl) and postoperative WL also predicted increased LOS. Of the 25 patients who underwent nutritional assessment, 32% were SGA-B and 16% SGA-C. Malnourished patients (SGA-B+C) were hospitalized twice as long as SGA-A [15.8 (12.8) vs. 7.6 (3.5) days, $P<0.05$]. Overall complications rates of 35%, with a trend towards higher complications in malnourished patients (but $N=25$).	Retrospective cohort study. Small number of patients received formal nutritional assessment and defined as malnourished ($N=12$).
Ben-Ishay *et al.* [23]	96 consecutive ambulant admissions to a general surgical ward in Israel. Nutritional screening using the MUST tool.	33% of patients had high malnutrition risk (MUST score of 2 or more). High-risk group had higher prevalence of malignant conditions (43.7 vs. 18.7%, $P=0.02$). High-risk group had a higher mean (SD) hospital LOS [18.8 (11.5) vs. 7 (5.3), $P=0.02$], in-hospital mortality (9.4 vs. 0%, $P=0.017$), cumulative 6-month (18.8 vs. 1.6%, $P=0.006$) and 12-month mortalities (21.9 vs. 1.6%, $P=0.002$).	Observational study. Time period of study not stated. Included only ambulant patients. Insufficient detail of patient co-morbidities, admission diagnosis and surgery performed.

Alb, albumin; Ca, cancer; CI, confidence interval; FU, follow-up; GI, gastrointestinal; HR, hazard ratio; ILO, Ivor-Lewis oesophagectomy; LOS, length of stay; MUST, malnutrition universal screening tool; MR, mortality rate; OR, odds ratio; SD, standard deviation; SGA, subjective global assessment; WL, weight loss.

of mRNA expression of inflammatory genes in muscle [40] and adipose tissue [41]. However, as protein expression and postoperative insulin sensitivity were not measured [40,41], the associations of these variables with the development of insulin resistance remain unknown.

Enhanced recovery after surgery

Enhanced recovery after surgery programmes integrate a range of perioperative interventions aimed to maintain physiological function, minimize the stress of major surgery and facilitate recovery [31•]. Of note are avoidance of bowel preparation (grade A evidence), preoperative carbohydrate loading (grade A), utilization of minimal access surgery, avoidance of fluid overload and maintenance of normovolemia [42•] (grade A), and finally, early feeding after surgery (grade A) [31•]. However, most studies of interventions within the ERAS protocol were undertaken in patients undergoing elective colorectal resection [31•], not all the individual interventions have been subjected to randomized studies, and few studies have demonstrated actual clinical benefit. There is, however, clear evidence that implementation of ERAS protocols attenuates the development of postoperative insulin resistance [43] and significantly reduces length of hospital stay [weighted mean difference (WMD), −2.55 (95% CI −3.24 to −1.85) days] [44•].

Preoperative nutritional support

There is no role for routine nutritional support in patients undergoing major surgery [45]. Guidelines advocate preoperative nutritional support, preferably enteral, for patients at severe nutritional risk for 7–14 days prior to major surgery (grade A) [45,46]. Patients at severe nutritional risk were defined by the European guidelines [46] to have at least one of the following: weight loss more than 10–15% within 6 months; a BMI less than 18.5 kg/m^2; Subjective Global Assessment Grade C; or serum albumin below 30 g/l (with no evidence of hepatic/renal dysfunction). In patients with severe undernutrition who cannot be fed adequately orally or enterally, 7–10 days of preoperative parenteral nutrition are recommended (grade A) [47•].

A randomized study of 34 moderately and severely malnourished patients undergoing major abdominal surgery examined the effects of 5 days of intravenous glutamine dipeptide supplementation (0.3 g/kg/day) of preoperative nutrition (mainly parenteral) [48]. Whilst there were increases in preoperative white blood cell, granulocyte and lymphocyte counts, these changes were not sustained into the first postoperative week and did not alter clinical outcomes [48]. Furthermore, glutamine supplementation was not continued postoperatively [48], when glutamine is known to become a conditionally essential amino acid.

In cancer patients undergoing neoadjuvant therapy, intensive dietary counselling and, if necessary, oral or enteral nutritional support is recommended [25]. However, there is a lack of robust evidence that this improves morbidity and mortality [25]. Finally, the role of preoperative carbohydrate-based drinks containing additional metabolic conditioning agents (such as glutamine and antioxidants) [37•,49] on postoperative insulin resistance and outcome remains to be examined. However, it has been suggested that preoperative glutamine supplementation may be used as an adjunct to modulate glucose utilization and insulin sensitivity [49].

Postoperative nutritional support

Studies on the application of postoperative nutritional support via differing routes (enteral, parenteral, oral) were reviewed.

Enteral nutrition

Current data [50•,51] and consensus recommendations [31•] advocate early institution of enteral nutrition postoperatively. A systematic review and meta-analysis of the effects of early enteral feeding within 24 h of intestinal surgery (vs. no feeding within 24 h) demonstrated a significant reduction in mortality [relative risk (RR) 0.42 (95% CI 0.18–0.96)], a trend towards decreased length of stay [WMD −0.89 (95% CI −1.58 to −0.2) days] and no benefit or harm related to anastomotic dehiscence [RR 0.62 (95% CI 0.3–1.28)] in the early fed group [50•]. However, the aforementioned meta-analysis [50•], whilst updating an earlier Cochrane review [52], has been criticized [53] for including data from an immune-enhancing feed trial and for omitting studies that appeared to meet the inclusion criteria.

There are conflicting data regarding the significance of inadequate energy provision during early critical illness, probably resultant from poor study design, heterogeneity of patients and differing feed regimens. A retrospective medical ICU study [54] allocated patients to one of three groups depending upon caloric intake. Group 1 received less than 33%, group 2 33–65% and group 3 more than 65% of estimated energy requirements. Group 2 achieved spontaneous ventilation quickest, but there were no differences between the groups in nosocomial sepsis [54]. The authors concluded that moderate underfeeding (33–65% estimated energy requirements) may improve outcomes [54], conclusions that were at odds with those of two other studies [55,56•]. A retrospective observational study on patients in a medical ICU [55] demonstrated that those who received less than 60% of their recommended energy intake during the first week of critical illness had a higher risk of ICU mortality [OR 2.43, (95% CI 1.1–5.11)] than those who received more than 60% of their recommended energy intakes [55]. However, the latter study utilized crude methods to estimate energy requirements (multiplying patient's actual weight by 25–30 kcal/kg/day), did not differentiate between patients who received enteral or mixed enteral-parenteral feeding, nor was it possible to determine if inadequate gut function (enteral intolerance [57••]) underlay decreased energy provision. A prospective multicentre observational study [56•] of 207 mixed ICU patients demonstrated that greater energy provision, by means of enteral feeding, was associated with a dose-dependent reduction in infectious complications (particularly after 96 h of ICU admission) [56•]. Whilst the study design [56•] did not prove causality and the authors did not define how nutritional goals were determined for individual patients, the findings highlight that the relationship between enteral feed tolerance and clinical outcome is worthy of further investigation. Indeed, a contemporary study has examined the effects of gut-specific nutrients (GSNs, substances with specific effects on gut function, morphology, ecoflora or physiology, over and above their roles as nutrient substrates) on enteral tolerance [57••]. In a randomized, double-blind, placebo-controlled study of 50 critically ill patients with inadequate gut function (defined as oral or enteral tolerance of less than 80% of calculated nutritional requirements for a minimum consecutive period of 48 h) patients received either a 30-day cocktail of GSNs (multivitamins, probiotics, prebiotics and glutamine) or placebo. The administration of GSNs resulted in significantly earlier return to normal of gut function compared with controls [median (interquartile range) 164 (120–225) vs. 214 (184–401) h, respectively]. Earlier return of gut function did not impact on clinical endpoints such as length of stay, complications and mortality, outcomes that this study was not powered for [57••].

Other strategies to increase enteral feed tolerance include using prokinetic agents and placement of postpyloric feeding tubes. Metoclopromide, at a dose of 10 mg 4 times/day, stimulates gastric and duodenal motility in the short term but the effects rapidly diminish after 3 days [58]. Erythromycin, at a dose of 3 mg/kg, stimulates motilin receptors but administration for more than 3–4 days is associated with reduced efficiency [58]. Used in combination, the aforementioned drugs have been shown to be effective in promoting prolonged feeding [59]. Lately, there has been interest in the concept of permissive underfeeding during short-term nutritional support, as this may be associated with improved outcomes and reduced morbidity [60]. However, most of the studies reviewed [60] were designed poorly, included small numbers of heterogeneous patients and few had set out investigation of the role of underfeeding as their primary objective, making it difficult to draw firm conclusions [60].

Parenteral nutrition

Postoperative parenteral nutrition is recommended in patients who cannot meet their caloric requirements orally or enterally within 7–10 days [47•]. There is grade A evidence for the use of parenteral nutrition in undernourished patients in whom enteral nutrition is not feasible nor tolerated, and in patients with postoperative complications impairing gastrointestinal function [47•]. Supplementing postoperative parenteral nutrition with fish oils reduced nonseptic infective complications (23.1 vs. 78.6%, $P = 0.007$) in a randomized study of 27 patients undergoing elective major gastrointestinal surgery [61]. A meta-analysis that compared studies of fish-oil-enriched parenteral nutrition with standard parenteral nutrition demonstrated a positive effect on length of stay [WMD, −2.98; (95% CI −4.65 to −1.31), $P < 0.001$, $N = 627$] and postoperative infection rate [OR 0.56 (95% CI 0.32–0.98), $P = 0.04$, $N = 539$] [62•].

Glutamine supplementation

A meta-analysis of 31 randomized studies on glutamine-supplemented parenteral and enteral nutrition in critical illness and surgery identified poor trial quality, mixed patient populations, inappropriate postoperative administration of parenteral nutrition following elective gastrointestinal surgery and possible publications bias [63••]. However, parenteral glutamine in critical illness was associated with a nonsignificant reduction in mortality [RR 0.71 (95% CI 0.49–1.03), $P = 0.07$, $N = 680$] but significant reductions in infections [RR 0.78 (95% CI 0.63–0.97), $P = 0.03$, $N = 481$] and organ failure [RR 0.60 (95% CI 0.42–0.85), $P = 0.004$, $N = 439$] [63••]. In patients who were given glutamine-containing parenteral nutrition after surgery, whether they required parenteral nutrition or not, there was a significant reduction in infection [RR 0.43 (95% CI 0.27–0.69), $P < 0.001$, $N = 297$] [63••]. No beneficial effect was seen in patients who received enteral glutamine postoperatively. There was also evidence that higher doses of glutamine ($\geq$4.2 g glutamine/kg) were more effective in reducing mortality [63••]. The meta-analysis [63••] did not examine whether preoperative nutritional status affected outcomes in patients who received glutamine-supplemented feeds postoperatively. This is of importance given findings from a multicentre randomized study in which no beneficial effects were demonstrated following intravenous glutamine supplementation for 1 day preoperatively and 5 days postoperatively, on the clinical outcomes of 428 well nourished patients undergoing surgery for gastrointestinal cancer [64•]. However, this study [64•] reported a higher rate of infectious morbidity than previous studies and patients did not receive any artificial nutrition for 5 days postoperatively. Current evidence, therefore, supports the use of parenteral glutamine supplementation for critically ill patients. However, the subgroups of surgical patients who would benefit from parenteral glutamine supplementation remain unclear.

Oral nutrition

There are limited data on the adequacy of oral intake after extubation of critically ill patients. One such observational study in a mixed ICU demonstrated that average daily energy and protein intake failed to exceed 50% of recommendations in all 50 patients studied for a week after extubation [65], mainly due to nausea, vomiting and anorexia. In a randomized study of 143 patients, early oral feeding (within 48 h) following major laparotomy for gynecological malignancy was associated with significantly decreased overall (17 vs. 39%) and infective complications (3 vs. 14%), and shortened length of stay (4.7 vs. 5.8 days, $P=0.006$), when compared with a 'traditional' regimen of nil by mouth pending resumption of bowel function (presence of bowel sounds and passage of flatus), with no differences in nausea, vomiting, analgesic or antiemetic requirements [51]. Preoperative nutritional status was not described [51], and the 'traditional' postoperative regimen of nil by mouth pending return of bowel function, although not in line with current best practice [31•], does reflect common postoperative practice in many hospitals [66]. Indeed, a recent national collaborative effort in the Netherlands succeeded in implementing early oral nutrition in 65% of ERAS patients undergoing colorectal surgery by the second postoperative day [66]. Multimodal management of postoperative nausea and vomiting, which occurs in 1:5 patients, was key to the success of the programme [66].

Perioperative optimization of nutritional status and immuno-metabolic function

Perioperative immunonutrition (enteral nutrition supplemented with a combination of immuno-modulating substrates such as arginine, glutamine, ω-3 fatty acids and nucleotides), independent of nutritional risk, is recommended for patients undergoing major neck or abdominal surgery for cancer [46]. These formulae should be started 5–7 days before surgery and continued for 5–7 days postoperatively after uncomplicated surgery (grade C recommendation) [46]. Findings from a recent meta-analysis of 21 trials supported these guidelines, whereby perioperative immunonutrition reduced overall complications [OR 0.39 (95% CI 0.28–0.54), $N=1039$] and length of hospital stay [WMD −2.12 (95% CI −2.97 to −1.26), $N=2279$ days], but not mortality, following major gastrointestinal surgery [67••].

Compared to severely malnourished patients, undergoing surgery for head and neck cancer who received perioperative standard enteral nutrition, those who received arginine-supplemented enteral nutrition (Ar-EN) had improved long-term survival in a randomized double-blind study [68•]. Patients received enteral feeds for approximately 9 days preoperatively and 10 days postoperatively. There was improved median overall long-term (34.8 vs. 20.7 months, $P=0.019$) and disease-specific survival (94.4 vs. 20.8 months, $P=0.022$) in the Ar-EN group with differences remaining significant after adjusting for confounding variables [68•]. The differences in survival were speculated to result from improved immune function in the Ar-EN group [68•]. Another randomized study of patients undergoing surgery for oesophageal cancer compared a standard enteral nutrition formula with enteral nutrition enriched with eicosapentaenoic acid (EPA) [69]. Patients received the feeds for 5 days preoperatively and 21 days postoperatively. EPA-enriched enteral nutrition was associated with preservation of lean body mass and a significantly attenuated stress response postoperatively [69].

A randomized, open-labelled study of perioperative oral nutritional supplementation (ONS) vs. no supplementation, in normal/mildly undernourished geriatric patients ($N=60$) undergoing surgery for hip fracture, failed to demonstrate clinical benefits in the ONS group [70]. However, this study was underpowered to detect clinical outcomes, used crude methods to estimate total dietary energy intakes and patients in the intervention arm only ingested 52% of the prescribed supplements.

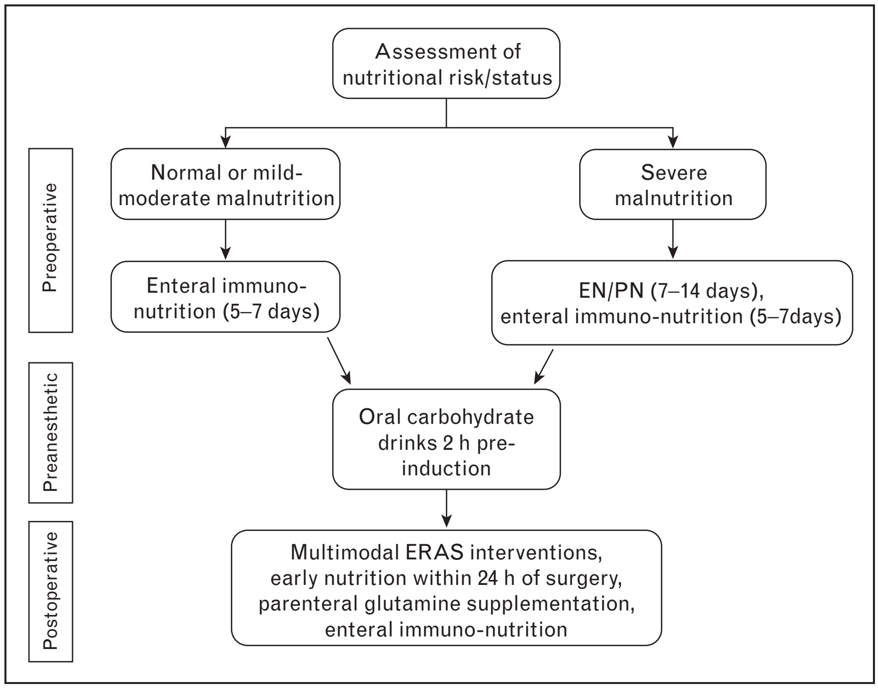
Postdischarge nutritional support

A recent systematic review of studies of postdischarge oral nutritional supplementation (using commercially available nutritional supplements given for 1–4 months postdischarge) of patients who underwent gastrointestinal surgery found little evidence of clinical benefit, principally due poor methodological study quality, on morbidity, quality of life, fatigue or hand-grip strength [71].

Future research

A review of perioperative nutritional support of patients with oesophageal cancer highlighted the importance of nutritional intervention (intensive dietetic surveillance and oral nutritional supplementation) during the neo-adjuvant period [72], but, data that this improves clinical outcomes are lacking. Preliminary work has shown that 85% of patients lost 6.8% skeletal muscle (i.e. developed sarcopenia) over the 2-month course of neo-adjuvant chemotherapy for oesophagogastric cancer [73]. The effects of such marked changes in body composition on outcomes of chemotherapy and surgery remain unknown. Existing data suggest that sarcopenia may be associated with adverse outcomes during neoadjuvant therapy [74–76] and may induce inflammation and insulin resistance [77]. Future studies should also investigate whether nutritional interventions can ameliorate development of sarcopenia during neoadjuvant therapy, further identify mechanisms underlying postoperative inflammatory and insulin-resistant responses and, finally, rigorously validate and optimize individual ERAS

Figure 1 Multimodal pathway illustrating current best practices in delivering nutritional support to patients undergoing gastrointestinal surgery during the perioperative period



EN, enteral nutrition; ERAS, enhanced recovery after surgery; PN, parenteral nutrition.

interventions and the ERAS programme applied outside the field of colorectal surgery.

Conclusion

The review has outlined recent advances in the field of perioperative nutritional support. Although poor study design and heterogeneity persist, there is much scope for more rigorous studies in better defined [26] patient subgroups. Implementation of an evidence-based multimodal perioperative pathway (Fig. 1) that includes interventions to optimize nutritional status and metabolic function, and the utilization of minimal access surgery [78], may improve postoperative outcomes.

Summary of main findings

(1) Recognition of patients with or at risk of malnutrition remains poor.
(2) Poor design and significant heterogeneity remain amongst studies of nutritional interventions.
(3) An evidence-based multimodal pathway including interventions to minimize insulin resistance and optimize nutritional status may improve outcomes following elective surgery.

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References and recommended reading

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

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 359–361).

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