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ESPEN GUIDELINES

ESPEN Guidelines on Enteral Nutrition: Surgery including Organ Transplantation ☆

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Summary Enhanced recovery of patients after surgery ("ERAS") has become an important focus of perioperative management. From a metabolic and nutritional point of view, the key aspects of perioperative care include:

- avoidance of long periods of pre-operative fasting;
- re-establishment of oral feeding as early as possible after surgery;
- integration of nutrition into the overall management of the patient;
- metabolic control, e.g. of blood glucose;
- reduction of factors which exacerbate stress-related catabolism or impair gastrointestinal function;
- early mobilisation

Enteral nutrition (EN) by means of oral nutritional supplements (ONS) and if necessary tube feeding (TF) offers the possibility of increasing or ensuring nutrient

Abbreviations: EN, enteral nutrition (oral nutritional supplements and tube feeding); ONS, oral nutritional supplements; TF, tube feeding; Normal food/normal nutrition: normal diet as offered by the catering system of a hospital including special diets

☆For further information on methodology see Schütz et al.[231] For further information on definition of terms see Lochs et al.[232]

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Undernutrition;
Complications

intake in cases where food intake is inadequate. These guidelines are intended to give evidence-based recommendations for the use of ONS and TF in surgical patients. They were developed by an interdisciplinary expert group in accordance with officially accepted standards and are based on all relevant publications since 1980. The guideline was discussed and accepted in a consensus conference.

EN is indicated even in patients without obvious undernutrition, if it is anticipated that the patient will be unable to eat for more than 7 days perioperatively. It is also indicated in patients who cannot maintain oral intake above 60% of recommended intake for more than 10 days. In these situations nutritional support should be initiated without delay. Delay of surgery for preoperative EN is recommended for patients at severe nutritional risk, defined by the presence of at least one of the following criteria: weight loss >10–15% within 6 months, BMI < 18.5 kg/m^2, Subjective Global Assessment Grade C, serum albumin < 30 g/l (with no evidence of hepatic or renal dysfunction).

Altogether, it is strongly recommended not to wait until severe undernutrition has developed, but to start EN therapy early, as soon as a nutritional risk becomes apparent.

The full version of this article is available at www.espen.org.

Summary of statements: Surgery

Subject	Recommendations	Grade[231]	Number
General	Preoperative fasting from midnight is unnecessary in most patients.	A	1
	Interruption of nutritional intake is unnecessary after surgery in most patients.	A	3
Indications			
Perioperative	Use nutritional support in patients with severe nutritional risk for 10–14 days prior to major surgery even if surgery has to be delayed.	A	4.1
	Severe nutritional risk refers to at least one: – Weight loss >10–15% within 6 months – BMI < 18.5 kg/m^2 – Subjective Global Assessment Grade C – Serum albumin < 30 g/l (with no evidence of hepatic or renal dysfunction)		4.1
	Initiate nutritional support (by the enteral route if possible) without delay:		
	• even in patients without obvious undernutrition, if it is anticipated that the patient will be unable to eat for more than 7 days perioperatively	C	4
	• in patients who cannot maintain oral intake above 60% of recommended intake for more than 10 days.	C	4
	Consider combination with parenteral nutrition in patients in whom there is an indication for nutritional support and in whom energy needs cannot be met (<60% of caloric requirement) via the enteral route.	C	4

Contraindications	Prefer the enteral route except for the following contraindications: Intestinal obstructions or ileus, severe shock, intestinal ischemia.	C	4
Application			
Preoperative	Encourage patients who do not meet their energy needs from normal food to take oral nutritional supplements during the preoperative period.	C	**4.1**
	Administer preoperative enteral nutrition (EN) preferably before admission to the hospital.	C	4.1
	Patients undergoing surgery who are considered to have no specific risk for aspiration, may drink clear fluids until 2 h before anaesthesia. Solids are allowed until 6 h before anaesthesia.	A	**1**
	Use preoperative carbohydrate loading (the night before and 2 h before surgery) in most patients undergoing major surgery.	B	2
Postoperative	Initiate normal food intake or enteral feeding early after gastrointestinal surgery.	A	4.2.1
	Oral intake, including clear liquids, can be initiated within hours after surgery to most patients undergoing colon resections.	A	3
	Oral intake should, however, be adapted to individual tolerance and to the type of surgery carried out.	C	3
	Apply tube feeding in patients in whom early oral nutrition cannot be initiated, with special regard to those		4.2.2
	● undergoing major head and neck or gastrointestinal surgery for cancer	A	4.2.2
	● with severe trauma	A	4.2.2
	● with obvious undernutrition at the time of surgery	A	4.2.2
	● in whom oral intake will be inadequate (<60%) for more than 10 days	C	4.2.2
	Initiate tube feeding for patients in need within 24 h after surgery.	A	4.2.1,4.2.4
	Start tube feeding with a low flow rate (e.g. 10–max. 20 ml/h) due to limited intestinal tolerance.	C	4.2.4
	It may take 5 to 7 days to reach the target intake and this is not considered harmful.	C	4.2.4
	Reassess nutritional status regularly during the stay in hospital and, if necessary, continue nutritional support after discharge, in patients who have received nutritional support perioperatively.	C	5
Type of tube feeding	Placement of a needle catheter jejunostomy or naso-jejunal tube is recommended for all candidates for TF undergoing major abdominal surgery.	A	4.2.4
	When anastomoses of the proximal gastrointestinal tract have been performed,	B	4.2.1

	deliver EN via a tube placed distally to the anastomosis.		
	Consider placement of a percutaneous endoscopic tube (e.g. PEG) if long term tube feeding (>4 weeks) is necessary, e.g. in severe head injury.	C	4.2.4
Type of formula	In most patients a standard whole protein formula is appropriate.	C	4.2.3
	Use EN preferably with immuno-modulating substrates (arginine, ω-3 fatty acids and nucleotides) perioperatively independent of the nutritional risk for those patients • undergoing major neck surgery for cancer (laryngectomy, pharyngectomy) • undergoing major abdominal cancer surgery (oesophagectomy, gastrectomy, and pancreatoduodenectomy) • after severe trauma.	A	4.2.3
	Whenever possible start these formulae 5–7 days before surgery	C	4.2.3
	and continue postoperatively for 5 to 7 days after uncomplicated surgery.	C	4.2.3

Grade: Grade of recommendation; Number: refers to statement number within the text.

Summary of statements: Organ transplantation

Subject	Recommendations	Grade[231]	Number
Indication			
Before transplantation	Undernutrition is a major factor influencing outcome after transplantation so optimising nutritional status is important.	C	6
	In undernutrition, use additional ONS or even TF.	C	6
	Assess nutritional status regularly while monitoring patients on the waiting list before transplantation.	C	6
	Recommendations for the living donor and recipient are not different from those for patients undergoing major abdominal surgery.	C	6
After transplantation	Initiate early normal food or EN after heart, lung, liver, pancreas, and kidney transplantation.	C	7
	Even after transplantation of the small intestine, nutritional support can be initiated early, but should be increased very carefully.	C	7
	Long-term nutritional monitoring and advice is recommended for all transplants.	C	7

Grade: Grade of recommendation; Number: refers to statement number within the text.

Preliminary remarks

To make proper plans for the nutritional support of patients undergoing surgery, it is essential to understand the basic changes in body metabolism that occur as a result of injury. In addition, recent studies have shown that not only does surgery itself influence the response to nutritional support, but many of the perioperative routines also have a major impact on how well different nutritional treatments are tolerated by the postoperative patient.

Surgery, like any injury to the body elicits a series of reactions including release of stress hormones and inflammatory mediators, i.e. cytokines. This release of mediators to the circulation has a major impact on body metabolism. They cause catabolism of glycogen, fat and protein with release of glucose, free fatty acids and amino acids into the circulation, so that substrates are diverted from their normal purposes, e.g. physical activity, to the task of healing and immune response. For optimal rehabilitation and wound healing, the body needs to be in an anabolic state. Recent studies have shown that measures to reduce the stress of surgery can minimize catabolism and support anabolism throughout surgical treatment and allow patients to recover substantially better and faster, even after major surgical operations. Such programs for enhanced recovery after surgery (ERAS)[7] involve a series of components that combine to minimize stress and to facilitate the return of function: these include preoperative preparation and medication, fluid balance, anaesthesia and postoperative analgesia, pre- and postoperative nutrition, and mobilization.

Severe undernutrition has long been known to be detrimental to outcome[1–3]: it has also been shown that even 12 h of preoperative fasting has been associated with prolonged recovery after uncomplicated surgery.[4,5] Furthermore, to improve patients' tolerance of normal food and to some extent of enteral feeding, a combination of treatments are needed to facilitate earlier return of gastrointestinal function.[6,7]

Insulin, one of the key factors regulating metabolism after surgery, was recently shown to be far more important in the postoperative period than previously recognized. A large randomized trial, in postoperative patients in intensive care, showed that when postoperative hyperglycemia was controlled by insulin infusion to maintain normoglycemia, morbidity and mortality was reduced by almost half,[8] showing that metabolic regulation is one of the key measures to reduce complications after major surgery. This has implications for nutritional management since patients with marked insulin resistance cannot tolerate feeding without developing hyperglycemia, necessitating the use of insulin to keep glucose levels within normal limits.

Some degree of insulin resistance develops after all kinds of surgery, but its severity is related to the size of the operation and any complications, e.g. sepsis. It lasts for about 2–3 weeks, even after uncomplicated moderate surgery, and its development is independent of the preoperative state of the patient. In one study[9,228] the three main variables influencing length of stay were; the type of operation, perioperative blood loss and the degree of postoperative insulin resistance. Several measures, with additive effects, may contribute to a reduction in insulin resistance, including pain relief,[9] continuous epidural analgesia using local anaesthetics,[10] and preparation of the patient with preoperative carbohydrates (12 and 2–4 h preoperatively) instead of overnight fasting.[4] Using this approach of preoperative carbohydrate loading and continuous epidural analgesia, in patients undergoing colorectal surgery, postoperative insulin resistance and nitrogen losses were reduced.[11]

Another factor that directly affects tolerance of normal food or EN is postoperative ileus, which may be exacerbated and prolonged by opiates and errors in fluid management. Experimental results demonstrate the impact of intraoperative manipulation and subsequent panenteric inflammation as the cause of dysmotility. This emphasizes the advantages of minimal invasive and gentle surgical technique.[12]

Traditionally, many patients undergoing major gastrointestinal resections receive large volumes of crystalloids intravenously during and after surgery. Excess fluid administration would result in several kilos in weight gain and even oedema. This was recently shown to be a major cause for postoperative ileus and delayed gastric emptying.[13] When fluids were restricted to the amount needed to maintain salt and water balance, gastric emptying returned sooner and patients were capable of tolerating oral intake and had bowel movements several days earlier than those in positive balance. The effect of opioids, used for pain relief, can be avoided or substantially minimized by the use of epidural analgesia instead.[6,7]

In conclusion: Enhanced recovery of patients after surgery (ERAS) has become an important focus of perioperative management. After colorectal surgery particularly, the so-called "fast track" programs have been successful in promoting rapid recovery and shortened length of hospital stay.[7] From a metabolic and nutritional point of view, therefore, the key aspects of perioperative care include:

- avoidance of long periods of pre-operative fasting,
- re-establishment of oral feeding as early as possible after surgery,
- integration of nutrition into the overall management of the patient,
- metabolic control, e.g. of blood glucose,

- reduction of factors which exacerbate stress-related catabolism or impair GI function,
- early mobilisation.

1. Is preoperative fasting necessary?

Preoperative fasting from midnight is unnecessary in most patients. Patients undergoing surgery, who are considered to have no specific risk of aspiration, may drink clear fluids until 2 h before anaesthesia. Solids are allowed until 6 h before anaesthesia (A).

Comment: There is no evidence that patients given fluids 2–3 h preoperatively are at any greater risk of aspiration/regurgitation than those fasted for the traditional 12 h (or even longer in some cases), since fluid clears the stomach rapidly in most patients[14] (Ia). Many national anaesthesia societies have changed their fasting guidelines[15–17] (III) and now recommend that patients may drink clear fluids up until 2 h before anaesthesia for elective surgery. Exceptions to this recommendation are patients "at special risk", undergoing emergency surgery, and those with known delayed gastric emptying for any reason[14] (Ia). Since the implementation of these guidelines, there has been no report of a dramatic rise in the incidence of aspiration, regurgitation, or associated morbidity or mortality.[14]

2. Is preoperative metabolic preparation of the elective patient using carbohydrate treatment useful?

Instead of overnight fasting, preoperative carbohydrate loading (the night before and 2 h before surgery) is recommended in most patients undergoing major surgery (B).

Comment: Preoperative intake of a carbohydrate drink (CHO) with 800 ml the night before and 400 ml before surgery does not increase the risk of aspiration.[14,16–18,23,24]

In colorectal patients, and those with hip replacement the intake of an hypo-osmolar 12.5% carbohydrate rich drink has been shown to reduce postoperative insulin resistance[19–21] (Ib) and preserve skeletal muscle mass[18] (Ib). Muscle strength was improved up at 1 month after surgery[22] (Ib). Oral carbohydrates have also been reported to improve preoperative well being[23] (Ib).[24]

Two studies have investigated the effect of a preoperative carbohydrate drink (CHO) on postoperative nausea and vomiting (PONV) in patients undergoing laparoscopic cholecystectomy.[25,26] One showed a reduction in PONV with CHO compared to fasting, while neither showed a clear difference between CHO and placebo[25,26] (Ib).

After major upper gastrointestinal surgery, no effect of this treatment was found on complication rate, and length of hospital stay: further studies are needed in this group of patients[18] (Ib).

3. Is postoperative interruption of oral nutritional intake generally necessary after surgery?

In general, interruption of nutritional intake is unnecessary after surgery (A). Oral intake should, however, be adapted to individual tolerance and to the type of surgery carried out (C).

Oral intake, including clear liquids, can be initiated within hours after surgery in most patients undergoing colon resections (A).

Comment: Oral nutrition (normal food and/or ONS) can be initiated, in most cases, immediately after surgery, since neither oesophago-gastric decompression nor delayed oral intake, after cholecystectomy or colorectal resection have proven beneficial[27–30] (Ib), especially in using ERAS protocol for colorectal surgery. However, the situation with regard to major upper GI surgery is less clear. Early normal food or EN, including clear liquids on the first or second postoperative day, did not cause impairment of healing of anastomoses in the colon or rectum[6,28,29,31,32] (Ib),[33] (Ia). In comparison to conventional open surgery, early oral intake is even better tolerated after laparoscopic colonic resection, due to earlier onset of peristalsis and bowel movement with this technique[34] (Ib),[35,36] (IIa). However, no differences were found between laparoscopic and conventional open colonic surgery when the full ERAS protocol was employed[37] (Ib).

The amount of initial oral intake should be adapted to the state of gastrointestinal function and to individual tolerance[33] (Ia),[28,31,32] (Ib),[35,38,39] (IIa),[40] (IIb).

4. When is perioperative nutritional support indicated?

Inadequate oral intake for more than 14 days is associated with a higher mortality (Ib). EN is therefore indicated even in patients without obvious undernutrition, if it is anticipated that

the patient will be unable to eat for more than 7 days perioperatively. It is also indicated in patients who cannot maintain oral intake above 60% of recommended intake for more than 10 days. In these situations nutritional support (by the enteral route if possible) should be initiated without delay (C).

The enteral route should always be preferred except for the following contraindications:

- ***intestinal obstructions or ileus***,
- ***severe shock***,
- ***intestinal ischemia***.

Combination with parenteral nutrition should be considered in patients in whom there is an indication for nutritional support and in whom energy needs cannot be met (<60% of caloric requirement) via the enteral route, e.g. in upper GI fistulae (C).

Comment: The influence of nutritional status on postoperative morbidity and mortality has been well documented in both retrospective[41–46] and prospective studies.[1,47–58] Inadequate oral intake for more than 14 days is associated with a higher mortality[59] (Ib).

Two multivariate analyses have shown, for hospitalised patients in general and for those undergoing surgery for cancer in particular, that undernutrition is an independent risk factor for the incidence of complications, as well as increased mortality, length of hospital stay, and costs.[60,61]

Undernutrition frequently occurs in association with underlying disease (e.g. cancer) or with chronic organ failure[2,60,62–69] (***see respective guidelines***). In a recent prospective multicenter observational study of patients with gastric cancer[70] dysphagia and gastric outlet syndrome due to stenosis have been shown independent factors for the risk of anastomotic leakage after total gastrectomy. It also influences outcome after transplantation[3,71–77] as well as increasing the morbidity and mortality of geriatric patients undergoing surgery.[78]

The general indications for nutritional support in surgery are in the prevention and treatment of undernutrition, i.e. the correction of undernutrition before surgery and the maintenance of nutritional status after surgery, when periods of prolonged fasting and/or severe catabolism are expected. Morbidity, length of hospital stay, and mortality are considered principal outcome parameters when evaluating the benefits of nutritional support.

After discharge from hospital or when palliation is the main aim of nutritional support, improvement in nutritional status and in quality of life are the main evaluation criteria.[79–91]

The current American Society for Parenteral and Enteral Nutrition guidelines (ASPEN) recommend postoperative nutritional support for patients who cannot meet their caloric requirements within 7–10 days.[92]

The effect of EN on the outcome after surgery has not been assessed in a consistent manner[93–127] (Ib) (see Table 1).

The current ESPEN working group reviewed 35 prospective randomized controlled trials, focusing on endpoints of outcome, and including patients after gastrointestinal surgery (without transplantation), trauma, and hip fracture. EN was defined as the use of ONS and TFs. Early EN was compared to normal food, administration of crystalloids and total parenteral nutrition (TPN). Twenty-four of these 35 trials reported significant advantages of EN with particular regard to the reduction of infectious complications, length of hospital stay and costs (Ib).

In eight of these 35 studies no benefits were observed[98,109,113,115,119,120,125,126] (Ib). Some authors have pointed out possible disadvantages of EN which have not been observed by others. These are increased length of stay[97] (Ib), reduced lung function after oesophageal or pancreatic resection through abdominal distension[112] (Ib) or delayed gastric emptying with increased length of stay following pancreatic surgery[128] (IIa). These problems may have been related to too rapid administration of feed in the early stages. In patients with severe trauma tolerance of enteral intake has to be carefully monitored[107] (Ib) (***see guidelines "Intensive care"***). Compared to TPN, early EN decreased postoperative infection rate in undernourished GI cancer patients, but not in those who were well nourished[121] (Ib).

In seven out of 11 randomised controlled trials[129–139] (Table 2) only surrogate measures of outcome were used, e.g. positive effects of EN on nitrogen balance and substrate tolerance. In four out of 11 studies no significant differences were shown between early EN and standard hospital feeding practice[131,132,137,138] (Ib).

Two meta analyses of studies, in which EN was compared with PN in both surgery and internal medicine, showed a significantly reduced rate of infections[140] (Ia) and a shortened length of hospital stay[141] (Ia) in the enterally fed patients.

It was claimed by the authors of the latter metaanalysis that no significant influence on mortality was shown.

Table 1 Enteral nutrition in the surgical patient: Review of the literature regarding prospective randomized controlled trials with end points of outcome.

Author	Year	*N*	Surgery	Nutritional regimen	Start	Results	Rating
Sagar et al.[93]	1979	30	Abdominal	TF vs. crystalloids+dextrose	POD 1, nasojejunal, 25 ml/h l	Less weight loss, reduced neg. N balance, shortened LOS	+
Ryan et al.[94]	1981	14	Abdominal	TF vs. crystalloids	POD 1, NCJ, 50 ml/h	Less weight loss	+
Bastow et al.[95]	1983	122	Moderately and severely undernourished women with fracture of the femoral neck	TF vs. normal food	Within 5 days, nasogastric	In particular in severe MN: shorter rehabilitation, reduced LOS, improvement of anthropometric parameters and serum protein	+
Shukla et al.[96]	1984	110	Abdominal and orolaryngeal	Preop TF vs. normal food	Preop. hypercaloric for 10 days	Less complications, reduced mortality, reduced LOS	+
Smith et al.[97]	1985	50	Abdominal	TF vs. crystalloids	POD 3, NCJ	No difference in nutritional parameters, increased LOS	–
Muggia-Sullam et al.[98]	1985	19	Abdominal	TF vs. TPN	POD 1–10, NCJ	No difference	±
Adams et al.[99]	1986	46	Trauma	TF vs. TPN	POD 1–14, jejunostomy	No difference in rate of complications and N balance	+
Bower et al.[100]	1986	20	Abdominal	TF vs. TPN	POD 1–7, NCJ	Reduced cost	+
Moore et al.[101]	1989	59	Trauma	TF vs. TPN	12 h, NCJ	Less severe infections, no difference in N balance	+
Delmi et al.[102]	1990	59	Hip fracture (age >60 yr)	ONS vs. normal food	After randomisation, for mean 32 days, 1 × daily 254 kcal	Significantly less complications and mortality in hospital and after 6 months, significantly reduced LOS	+
Schroeder et al.[103]	1991	32	Abdominal	TF vs. crystalloids+dextrose	Day of surgery, nasojejunal, 50 ml/h	Improved wound healing, no other difference	+
Kudsk et al.[104]	1992	98	Trauma	TF vs. TPN	POD 1, NCJ	Significantly less infections	+
Von Meyenfeldt et al.[105]	1992	101	Abdominal	Preop TF or ONS vs. TPN	At least 10 days in case of undernutrition, nasogastric or oral, 150% BEE after Harris Benedict	Lower rate of intraabdominal abscess in undernourished patients compared to undernourished controls	+
Iovinelli et al.[106]	1993	48	Laryngectomy	TF vs. TPN	After 24 h, PEG, energy: Harris Benedict+40%	No difference in weight, triceps skin folds, mid-arm circumference, Alb, TFN, reduced LOS	+
Dunham et al.[107]	1994	37	Severe trauma (ISS >15)	TF vs. TPN vs. PN/TF	ca. 24 h	No difference in mortality, higher mortality in intestinal dysfunction	–
Beier-Holgersen and Boesby[108]	1996	30	Abdominal	TF vs. placebo	Day of surgery, nasoduodenal	Less infections	+
Baigrie et al.[109]	1996	97	Abdominal	TF vs. TPN	POD 3, NCJ	Trend towards less infections.	± Safe
Carr et al.[110]	1996	30	Abdominal	TF vs. crystalloids	Day of surgery, NCJ	Significantly improved N-balance on day 1, no difference in intestinal permeability in the intervention group, but increase in control group, less complications	+ Safe
Keele et al.[111]	1997	100	Abdominal	Normal food+ONS (in- and outpatients)	ONS (1.5 kcal/ml) ad lib—start with oral nutrition	Supplemented group: ● inpatient period: less weight loss, maintenance of hand grip strength, less fatigue, less complications ● outpatient period: no significant difference	+
Watters et al.[112]	1997	28	Oesophageal+pancreatic resection	TF vs. crystalloids	Day of surgery, NCJ	Reduced, resp. function, less mobility	–
Reynolds et al.[113]	1997	67	Abdominal	TF vs. TPN	POD 1, NCJ	No difference in complications	±

Table 1 (*continued*)

Author	Year	*N*	Surgery	Nutritional regimen	Start	Results	Rating
Sand et al.[114]	1997	29	Gastrectomy	TF vs. TPN	POD 1, NCJ	Less expensive	+
Shirabe et al.[115]	1997	26	Liver resection	TF vs. TPN	POD 2, nasojejunal	No significant difference in outcome	±
Singh et al.[116]	1998	43	Perforation-peritonitis	TF vs. crystalloids	NCJ, 12 h postop.	Less complications	+
Sullivan et al.[117]	1998	17	Fracture of femoral neck	Nocturnal TF vs. normal food	Not consistent	No significant difference in "in-hospital Outcome", but in 6-months mortality	+
Beattie et al.[118]	2000	101	Abdominal	Normal food+ONS	In parallel to start of oral nutrition	Improved nutritional status, QOL, reduced mortality	+
MacFie et al.[119]	2000	100	Abdominal	Normal food +ONS (periop; preop; postop) vs. normal food alone	Approx. 2 weeks preop., from POD 1 for a minimum of 7 days	No difference in outcome	No routine ±
Espaulella et al.[120]	2000	171	Fracture of femoral neck	Normal food+ONS vs. normal food+placebo	Within 48 h for 60 days: ONS:150 kcal/d, 20 g protein, Ca, Vit D, along with other minerals and vitamins Placebo; 155 kcal/d; mainly carbohydrates	No advantages in regard to rehabilitation and mortality, significantly less complications over 6 months	No routine ±
Pacelli et al.[126]	2001	241	Undernutrition—abdominal	TF vs. PN	POD 1, NCJ or nasojejunal, 30 ml/h	No difference in rate of complications and mortality	No benefits ±
Bozzetti et al.[127]	2001	317	Undernutrition—abdominal	TF vs. PN	POD 1, NCJ or nasojejunal, isocaloric	EN: significantly less complications and reduced LOS	+
Braga et al.[121]	2001	257	Abdominal—upper GI cancer	TF vs. PN	6 h postop., NCJ or nasojejunal, nutritional goal 25 kcal/kg/d, EN and TPN were isocaloric and continued until adequate oral intake of 800 kcal/d	EN: significantly less (four-fold) expensive tendency to less infections and shorter length of hospital stay	+
Malhotra et al.[122]	2004	200	Peritonitis following gut perforation	TF vs. PN (dextrose only)	POD 2, nasogastric, TF: 50 ml/h, 600 kcal/d plus 300 kcal i.v.versus PN: 600 kcal/d i.v.	TF: safe, significantly less weight loss, tendency to less complications and shorter LOS in ICU and in hospital, tendency to higher rate of vomiting, diarrhoea, abdominal distension	+ safe
Smedley et al.[123]	2004	179	Abdominal—lower gastrointestinal	Periop ONS vs. no ONS vs. preop only vs. postop only	Minimum 7 days preop, up to 4 weeks after discharge, 1.5 kcal/ml ad libitum resulting in mean additional intakes of 300–540 kcal/d	Periop. ONS.: postop. significantly less weight loss, fewer minor complications, cost-effective	+
Mack et al.[124]	2004	36	Pancreatoduodenectomy	TF via double-gastrojejunostomy tube vs. standard care	POD 1 or 2, start with 20 ml/h, increase with 20 ml/h each day as tolerated, goal rate: 25 kcal/kg/d	TF: significantly less gastro-paresis, significantly shorter LOS and hospital charges	+
Sullivan et al.[125]	2004	57	Geriatric patients with hip fracture	TF/ONS vs. standard care	Test group: up to 1.375 kcal via nasoenteral TF overnight	TF: greater total daily nutrient intake during the first week, high rate of intolerance to -TF, no difference in the rate of postoperative life–threatening complications or mortality within 6 months	±

Abbreviations: (T)EN = enteral nutrition; TF = tube feeding; ONS = oral nutritional supplements; (T)PN = total parenteral nutrition; NCJ = needle catheter jejunostomy; LOS = length of stay; QOL = quality of life; NK cell = natural killer cells; N = nitrogen; POD = postoperative day.

In one trial of overnight nasogastric feeding[95] (Ib), in which the patients were first stratified by nutritional status before randomisation, there was a significant reduction in rehabilitation time and postoperative stay in the undernourished groups. In another study of TF, there was no influence on hospital outcome, although 6-month mortality was reduced[117] (Ib). In the study by Delmi et al.[102] (Ib) ONS once daily significantly improved outcome at 6 months with a lower rate of complications and mortality.

There are no controlled data with regard to combined EN and PN after elective surgery. For critically ill patients, a recently published systematic review[142] (Ib) including five controlled trials revealed no advantages of combined EN and PN on mortality or infections, or on length of hospital stay. However, the quality of the data is not good enough to draw further conclusions for patients after elective surgery.

4.1. When is preoperative EN indicated?

Patients with severe nutritional risk benefit from nutritional support for 10–14 days prior to major surgery even if surgery has to be delayed (A). Whenever feasible, the enteral route should be preferred (A).

In cancer patients undergoing upper major abdominal surgery preoperative EN preferably with immune modulating substrates (arginine, ω-3 fatty acids and nucleotides) is recommended for 5–7 days independently of their nutritional risk (A).

Many patients do not meet their energy needs from normal food and therefore they should be encouraged to take ONS during the preoperative period (C).

Preoperative EN should preferably be administered before admission to the hospital (C).

Comment: For surgical patients the benefits of nutritional support were shown in cases of severe undernutrition[96,105,143] (Ib),[144] (Ia), particularly with regard to the rate of complications[96,105] (Ib). These patients were fed preoperatively for at least 10 days.

"Severe" nutritional risk is defined by the ESPEN working group as the presence of at least one of the following criteria:

- weight loss >10–15% within 6 months,
- BMI < 18.5 kg/m^2,
- Subjective Global Assessment (SGA) Grade C[229],
- serum albumin < 30 g/l (with no evidence of hepatic or renal dysfunction).

These parameters reflect undernutrition as well as disease associated catabolism.

Preoperative ONS, using a standard whole protein formula, was studied in general surgical patients in two PRCTs[145,123] (Ib). Although one study showed no significant impact on outcome, Smedley et al.[123] found a significant reduction in minor complications. Furthermore, preoperative ONS continued postoperatively, minimized postoperative weight loss.

Preoperative intake of ONS (3 × 250 ml) enriched with immune modulating substrates (arginine, ω-3 fatty acids and nucleotides) for 5–7 days reduced postoperative morbidity and length of stay after major abdominal cancer surgery[146–149] (Ib). Undernourished patients, in particular, appear to benefit[150] (Ib).

The prospective controlled trial by Gianotti et al.[151] (Ib) randomised 305 gastrointestinal cancer patients without severe undernutrition to receive either preoperative or perioperative immune modulating formulae. A reduction in infectious complications and length of hospital stay were observed in both groups. These authors also showed the cost-effectiveness of preoperative immune modulating formulae in this group of patients[152] (IIb). However, this study did not include a group with standard formula. Therefore, It can be argued, that the observed effects would have been also obtained with standard formulae.

4.2. Postoperative EN

4.2.1. Is early normal food intake or EN (<24 h) following gastrointestinal surgery beneficial?

Early initiation of normal food intake or enteral feeding is recommended after gastrointestinal surgery (A). When anastomoses of the proximal gastrointestinal tract have been performed, EN can be delivered via a tube whose tip is placed distal to the anastomosis (B).

Comment: In several prospective studies, beneficial effects of early normal food or EN were shown with regard to the rate of infectious complications and the length of hospital stay[33,153] (Ia),[154,155] (Ib),[156] (IIa). Early TF was not a risk factor for gastric intolerance and pneumonia[157] (Ib).

Limited data are available regarding immediate oral nutrition in patients with anastomoses in the proximal gastrointestinal tract, e.g. following gastrectomy, pancreatoduodenectomy or oesophageal resection[230]. Many studies have shown the benefits and feasibility of feeding via a tube either inserted distal to the anastomosis, e.g. jejunostomy, or inserted via the nose with its tip passed distally at the time of operation, e.g. nasojejunal tube[126,127,158–160] (IIb).

Table 2 Enteral nutrition in the surgical patient: Review of the literature regarding prospective randomized controlled trials with surrogate end points.

Author	Year	*N*	Surgery	Nutritional regimene	Results	Rating
Lim et al.[129]	1981	19	Oesophagus	TF (gastrostomy) vs. TPN for 4 wks	TPN: quicker pos. N-balance a. weight loss	+
McArdle et al.[130]	1986	20 (no strict randomisation)	Cystectomy	TF (jejunal) vs. TPN or normal food	Improvement of intestinal function	+
Fletcher and Little[131]	1986	28	Aortic replacement	TF vs. PN vs. cristalloids	No difference in N-balance	±
Nissila et al.[132]	1989	22	Abdominal	TF vs. TPN	No difference in NK-cell-function	±
Magnusson et al.[133]	1989	20	Colorectal	TF with glucose only vs. glucose i.v.	Improvement of glucose tolerance	+
Hwang et al.[134]	1991	24	Bile duct	TF (nasoduodenal) vs. crystalloids	Improved N-balance	+
Suchner et al.[135]	1995	34	Neurosurgery	TF vs. TPN	Improvement of visc. protein synthesis, of nutr. index, tolerance of substrates and of intestinal function	+
Hochwald et al.[136]	1997	29	Abdominal	TF vs. crystalloids	Decrease of fat oxidation and catabolism, improvement of N-balance	+
Beier-Holgersen and Brandstrup[137]	1999	60	Abdominal	TF vs. placebo	No impact on cell-mediated immunity	±
Brooks et al.[138]	1999	19	Abdominal	TF vs. crystalloids	No impact on intestinal permeability	±
Hu and Zheng[139]	2003	135	Abdominal-impaired liver function	TF vs. TPN vs. control	EN: earlier reaching positive N-balance, lower loss of body weight, postop. no change in intestinal permeability (significant in TPN)	+

Abbreviations: (T)EN = enteral nutrition; TF = tube feeding; ONS = oral nutritional supplements; (T)PN = total parenteral nutrition; NCJ = needle catheter jejunostomy; LOS = length of stay; QOL = quality of life; NK cell = natural killer cells; N = nitrogen , POD = postoperative day.

A recent study in patients undergoing total laryngectomy with primary pharyngeal closure showed that initiation of oral feeding on the first postoperative day was safe[161] (Ib).

4.2.2. Which patients benefit from early postoperative TF?

Early TF (within 24 h) is indicated in patients in whom early oral nutrition cannot be initiated (see Table 1), in case of patients:

- ***undergoing major head and neck or gastrointestinal surgery for cancer(A),***
- ***with severe trauma (A),***
- ***with obvious undernutrition at the time of surgery (A),***
- ***in whom oral intake will be inadequate (<60%) for more than 10 days (C).***

Comment: Patients undergoing major surgery for head and neck, and abdominal cancer (larynx, pharynx or oesophageal resection, gastrectomy, partial pancreatoduodenectomy) often exhibit nutritional depletion before surgery[1,50,53–55,62,65,67,68] (***see guidelines "Oncology"***) and run a higher risk of developing septic complications.[1,50,53–55,61,68] Postoperatively, oral intake is often delayed due to swelling, obstruction or impaired gastric emptying, or in order to prevent straining the anastomosis, making it difficult to meet nutritional requirements. Nutritional support reduces morbidity with an increasing protective effect of TPN, EN, and immune-modulating formulae[61] (IIb).

Trauma patients with normal nutritional status have a high risk of developing septic complications and multiple organ failure. Early EN has been claimed to reduce septic complications[44] (Ia),[101,104] (Ib) and, has been suggested to reduce the rate of multiple organ failure when initiated within 24 h[162] (Ib).

4.2.3. Which formulae should be used?

In most patients a standard whole protein formula is appropriate (C).

With special regard to patients with obvious severe nutritional risk, those undergoing major cancer surgery of the neck (laryngectomy, pharyngectomy) and of the abdomen (oesophagectomy, gastrectomy, and pancreatoduodenectomy) as well as after severe trauma benefit from the use of immune modulating formulae (enriched with arginine, omega-3 fatty acids and nucleotides) (A). Whenever possible administration of these supplemented formulae should be started before surgery (A) and continued postoperatively for 5–7 days after uncomplicated surgery (C).

Comment: Data are available from several randomised controlled trials on the use of immune modulating ONS and TF formulae, including arginine, ω-3-fatty acids and ribonucleotides, with or without glutamine[146,147,163–175] (Ib). In some of these trials there is no clear distinction made between critically ill and elective surgical patients undergoing major surgery (***see guidelines "intensive care"***). Four meta analyses of trials, in general surgical and trauma patients, suggest that immune modulating nutritional formulae have contributed to a decreased rate of postoperative complications and consequently to a decreased length of stay in the hospital[175–178] (Ia).

Three randomised controlled trials showed that postoperative immune modulating formulae are effective in both undernourished[150] and well nourished gastrointestinal cancer patients[149,151] (Ib). In patients undergoing gastrectomy for gastric cancer, early EN with immune modulating formula was associated with significantly less wound-healing problems, suture failure, and infectious as well as global complications[179] (Ib).

A National US-Database evaluation also supported the cost-effectiveness of nutritional formulae modulating immune-function. In order to reduce resource consumption and total cost, a breakeven infection rate was also calculated for well nourished as well as undernourished surgical patients[180] (IIb).

The US experts summit[181] issued consensus recommendations concerning undernourished patients. Their indications for nutritional support were:

Patients undergoing elective gastrointestinal surgery

- Moderately or severely undernourished patients (serum albumin <35 g/l[†]) undergoing major elective upper gastrointestinal tract procedures.
- Severely malnourished patients (albumin <28 g/l (see footnote [†])) undergoing lower gastrointestinal surgery.

Although benefits of enteral formulae enriched with glutamine alone have been found in several randomised controlled trials in critically ill patients, particularly those suffering from severe trauma or burns[182–185] (Ib), no strong data for

[†]The ESPEN-working group agrees that hypoalbuminia is a clear surgical risk factor, however, it reflects disease associated inflammation and disease severity rather than undernutrition. It is also influenced by the dilutional effect of intravenous crystalloids.

patients after major neck or abdominal cancer surgery are available.

For formulae containing synbiotics with fibre and Lactobacillus, a significantly lower incidence of infections was shown after major abdominal surgery, particularly that involving gastric and pancreatic resections. No difference was observed between the effects of living or heat-killed lactobacilli[186] (Ib).

A recent study in brain injured patients[187] showed significant advantages of a formula containing glutamine and probiotics with regard to infection rate and length of stay in the intensive care unit (Ib).

4.2.4. How should patients be tube fed after surgery?

Placement of a needle catheter jejunostomy or naso-jejunal tube is recommended for all candidates for TF undergoing major abdominal surgery (A).

TF should be initiated within 24 h after surgery (A).

TF should start with a low flow rate (e.g. 10—max. 20 ml/h) due to limited intestinal tolerance (C). It may take 5–7 days to reach the target intake and this is not considered harmful (C).

If long-term TF (>4 weeks) is necessary, e.g. in severe head injury, placement of a percutaneous tube (e.g. percutaneous endoscopic gastrostomy—PEG) should be considered (C).

Comment: In several PRCTs the feasibility of needle catheter jejunostomy for EN after major abdominal surgery has been well documented.[147,158,160]

Open or even laparoscopic placement of the needle catheter jejunostomy according to standardized techniques is associated with low risk[160,188–196] (IIb,III),[197] (IIa). Insertion of a double-gastrojejunostomy tube during pancreaticoduodenectomy has also been shown to be safe[124] (Ib).

In anecdotal reports a too rapid administration of feed may lead to the development of small bowel ischemia.[198–205] Tolerance of TF has to be monitored closely in patients with impaired gastrointestinal function[107] (Ib). It may therefore take 5–7 days before nutritional requirements can be achieved by the enteral route.[100,108,159]

Percutaneous endoscopic gastrostomy should be considered where there is an indication for long-term enteral feeding when abdominal surgery is not indicated, e.g. after severe head injury or neurosurgery. For patients with upper GI stenosis due to esophageal cancer and scheduled surgery after neoadjuvant radio-chemotherapy, a preoperative PEG should be only placed according to the discretion of the surgeon. The guidelines for PEG placement[206] recommend the intervention for enteral feeding of more than 2–3 weeks duration. However, recent results from the FOOD Trial in dysphagic stroke patients[207] do not support early PEG feeding.

5. Which patients will benefit from EN after discharge from the hospital?

Regular reassessment of nutritional status during the stay in hospital and, if necessary, continuation of nutritional support after discharge, is advised for patients who have received nutritional support perioperatively (C).

Comment: In six randomised controlled trials postoperative and post hospital administration of ONS have been investigated[102,111,118,120,123] (Ib). The available data do not show with certainty that routine administration improves outcome but they do show benefit in terms of nutritional status, rate of minor complications and well-being in patients who cannot meet their nutritional requirements at home from normal food. This applies mainly to major gastrointestinal surgery, e.g. colorectal resections,[208] gastrectomy[209] and to geriatric patients with fractures.[45,52] Among geriatric patients, compliance with nutritional intake was low, independently of nutritional status. However, total energy intake was still significantly higher in the treatment compared to the control group[52] (IIa).

Organ transplantation

6. When is EN necessary before solid organ transplantation?

Undernutrition is a major factor influencing outcome after transplantation, so optimising nutritional status is important (C).

In undernutrition, additional ONS or even TF is advised (C).

Regular assessment of nutritional status is necessary while monitoring patients on the waiting list before transplantation (C).

Recommendations for the living donor and recipient are no different from those for patients undergoing major abdominal surgery (C).

Comment: Undernutrition is likely to lead to a faster progression of the underlying disease, especially in cardiac and respiratory insufficiency, and leads to impaired functional status (***see respective guidelines***). Particular issues regarding the influence of EN on the course/progression of liver disease are discussed in the hepatology section. Nutritional parameters have been shown to correlate with outcome after transplantation[74,210,211] (IIa+b). During the, often long, preoperative waiting period, there is time to try to replete patients nutritionally. Four intervention studies (two randomised) of preoperative nutrition in patients waiting for organ transplantation have been performed[212,213] (Ib),[214,215] (IIa). Improvement in parameters of nutritional status was shown in all four studies. There was no difference in mortality for the patients with nutritional supplementation on the waiting list and patients after transplantation[213] (Ib). This was however only investigated in one study. In case of nutritional intervention no association was found between mortality and nutritional status[211] (IIb). In one randomised study the improved parameters of nutritional status pretransplant did not affect outcome and mortality[213] (Ib).

Early results concerning the benefits of immune modulating formulae during the waiting period and 5 days after liver transplantation show favourable long-term impact on total body protein and a possible reduction of infectious complications[215] (IIa).

At present, there are no data available with regard to metabolic preconditioning of the (living) donor and recipient. Experimental results[216] showing the impact of nutritional status on liver preservation injury also favour the concept of metabolic preparation by preoperative carbohydrate drink.

7. When is EN indicated after organ transplantation?

After heart, lung, liver, pancreas, and kidney transplantation, early normal food or EN should be initiated (C).

Even after transplantation of the small intestine, nutritional support can be initiated early, but should be increased very carefully (C).

No recommendation can be given with regard to the use of immune modulating formulae.

Long-term nutritional monitoring and advice is recommended for all transplants (C).

Comment: It is generally agreed that early normal food or EN should be administered in transplant patients.[217,218] In cases of undernutrition it should be combined with PN.

Absorption and blood levels of tacrolimus are not affected by EN[219] (IIb).

EN is at least equal to PN in patients after liver transplantation[220] (Ib) and has been shown to reduce the incidence of viral infections[221] (Ib). Compared to standard formulae, combined with selective decontamination of the small intestine, the use of a high fibre formula with probiotic bacteria (*lactobacillus plantarum*) has been shown to reduce significantly the rate of infections[222] (Ib). Early EN enriched with a mixture of probiotic bacteria and fibre significantly reduced bacterial infection rate compared with a supplement containing only fibre[223] (Ib).

Insertion of a needle catheter jejunostomy is feasible in liver transplant patients[224] (IIb).

EN is possible despite increased intestinal secretion in small bowel transplantation and can be performed at low rates in the first week.[225–227]

Experience with the use of immune modulating formulae is still only small. The first controlled data on the use of an immune modulating formulae after liver transplantation suggest that unfavourable effects on immunosuppression are unlikely[215] (IIa).

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