ESPEN Practical Guideline: Clinical Nutrition in Surgery

Arved Weimann[a*], Marco Braga[b], Franco Carli[c], Takashi Higashiguchi[d], Martin Hübner[e], Stanislaw Klek[f], Alessandro Laviano[g], Olle Ljungqvist[h], Dileep N. Lobo[i], Robert G. Martindale[k], Dan Waitzberg[l], Stephan C. Bischoff[m], Pierre Singer[n]

Based on

ESPEN guideline: Clinical nutrition in surgery

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[a] Department of General, Visceral and Oncological Surgery, St. George Hospital, Leipzig, Germany

[b] University of Milano-Bicocca, San Gerardo Hospital, Monza, Italy

[c] Department of Anesthesia of McGill University, School of Nutrition, Montreal General Hospital, Montreal, Canada

[d] Yonaha General Hospital, Kuwana-city, Mie, Japan

[e] Service de chirurgie viscérale, Centre Hospitalier Universitaire de Lausanne, Lausanne, Switzerland

[f] General Surgical Oncology Clinic, National Cancer Institute, Krakow, Poland

[g] Department of Translational and Precision Medicine, Sapienza University, Rome, Italy

[h] Department of Surgery, Faculty of Medicine and Health, Orebro University, Orebro, Sweden

[i] Gastrointestinal Surgery, Nottingham Digestive Diseases Centre, National Institute for Health Research Nottingham Biomedical Research Centre, Nottingham University Hospitals and University of Nottingham, Queen's Medical Centre, Nottingham, United Kingdom

[k] Oregon Health Sciences University, Portland, Oregon, USA

[l] University of Sao Paulo Medical School, Ganep – Human Nutrition, Sao Paulo, Brasil

[m] Institut für Ernährungsmedizin, Universität Hohenheim, Stuttgart, Germany

[n] Institute for Nutrition Research, Rabin Medical Center, Beilison Hospital, Petah Tikva, Israel

Key words

Surgery; perioperative nutrition; nutritional therapy; enteral nutrition; parenteral nutrition; bariatric surgery; organ transplantation; ERAS; prehabilitation.

Abbreviations

BMI, body mass index; EN, enteral nutrition; ERAS, Enhanced Recovery after Surgery; LOS, hospital length of stay; NCJ, needle catheter jejunostomy; ONS, oral nutritional supplements; PEG, percutaneous endoscopic gastrostomy; PN, parenteral nutrition; RCT, randomized controlled trial; SOP, standard operating procedure

*Corresponding author
Professor Dr. Arved Weimann,
Klinik für Allgemein-, Viszeral- und Onkologische Chirurgie
Klinikum St. Georg gGmbH,
Delitzscher Straße 141,
04129 Leipzig / Germany
Phone +49 341 909 2200,
Fax: +49 341 909 2234
E-Mail: Arved.Weimann@sanktgeorg.de

Abstract

Early oral feeding is the preferred mode of nutrition for surgical patients. Avoidance of any nutritional therapy bears the risk of underfeeding during the postoperative course after major surgery. Considering that malnutrition and underfeeding are risk factors for postoperative complications, early enteral feeding is especially relevant for any surgical patient at nutritional risk, especially for those undergoing upper gastrointestinal surgery. The focus of this guideline is to cover both nutritional aspects of the Enhanced Recovery After Surgery (ERAS) concept and the special nutritional needs of patients undergoing major surgery, e.g. for cancer, and of those developing severe complications despite best perioperative care. From a metabolic and nutritional point of view, the key aspects of perioperative care include the integration of nutrition into the overall management of the patient, avoidance of long periods of preoperative fasting, re-establishment of oral feeding as early as possible after surgery, the start of nutritional therapy immediately if a nutritional risk becomes apparent, metabolic control e.g. of blood glucose, reduction of factors which exacerbate stress-related catabolism or impaired gastrointestinal function, minimized time on paralytic agents for ventilator management in the postoperative period, and early mobilization to facilitate protein synthesis and muscle function.

Preliminary remarks

1. PRINCIPLES OF METABOLIC AND NUTRITIONAL CARE

As a key component of Enhanced Recovery after Surgery programs (ERAS), nutritional management is an inter-professional challenge. These ERAS programs also include a metabolic strategy to reduce perioperative stress and improve outcomes (1). "Prehabilitation" aims at conditioning metabolic risk for ERAS meaning a trimodal approach including a nutrition, physical exercise, and stress-reducing psychological component (2). A significant reduction in the number of complications was shown in elderly high-risk patients with American Society of Anesthesiologists (ASA) classifications Grade III and IV, (3). Meta-analyses showed that prehabilitation may contribute to decreased postoperative complication rates and shortened hospital length of stay (LOS) in patients undergoing major abdominal surgery (4-6).

Evidence of nutritional therapy

Obscured by obesity reduced muscle mass (sarcopenia) and malnutrition may be underestimated and ignored in surgical patients. There is clear evidence that malnutrition is associated with worse outcomes, and major surgical stress and trauma will induce catabolism. The extent of catabolism is related to the magnitude of surgical stress but also the outcome.

In a recent meta-analysis of 29 studies including 7,179 patients, sarcopenia was associated with an increased risk of postoperative major and total complications in patients undergoing surgery for gastrointestinal cancer (7).

Perioperative nutritional supplementation has been shown in a recent meta-analysis of 56 trials including 6,370 patients to decrease postoperative infectious and non-infectious complications, and also LOS in patients undergoing gastrointestinal cancer surgery (8).

In complex medical conditions like the perioperative patient undergoing major surgery, the geriatric patient, or in the critically ill the outcome will be related to multiple associated factors. Regarding a nutritional intervention, an existing effect may be too weak to show significant impact in a prospective randomized controlled trial (RCT) with a feasible number of patients to be included, even in a multicenter setting. However, the combination of the nutritional intervention with some other therapeutic items as a treatment bundle like in the ERAS program may show significant benefit (9).

2. METHODOLOGY

The present practical guideline consists of 37 recommendations and is based on the ESPEN guideline: Clinical nutrition in surgery(10). The original guideline was shortened by restricting the commentaries to the gathered evidence and literature on which the recommendations are based on. The recommendations were not changed, only the language was adapted to American English, but the presentation of the content was transformed into a graphical presentation consisting of decision-making flow charts wherever possible. The original guideline was developed according to the standard operating procedure (SOP) for ESPEN guidelines (11). This SOP is oriented on the methodology of the Scottish Intercollegiate Guidelines Network (SIGN). Literature was searched and graded into 1-4 according to evidence, and recommendations were created and graded into four classes (A/B/0/GPP). All recommendations were not only based on evidence but also underwent a consensus process, which resulted in a percentage of agreement (%). Whenever possible, representatives from different professions (physicians, dieticians, nurses, others) as well as patient representatives were involved.

The guideline process was funded exclusively by the ESPEN society. The guideline shortage and dissemination were funded in part by the UEG society, and also by the ESPEN society. For further details on methodology, see the full version of the ESPEN guideline (10) and the ESPEN SOP (11).

3. BASIC QUESTIONS

3.1 Is preoperative fasting necessary?

Recommendation 1

Preoperative fasting from midnight is unnecessary in most patients. Patients undergoing surgery, who are considered to have no specific risk of aspiration, shall drink clear fluids until two hours before anesthesia. Solids shall be allowed until six hours before anesthesia.

Grade of recommendation A – strong consensus (97 % agreement)

Commentary

There is no evidence that patients given clear fluids up to two hours before elective operations are at any greater risk of aspiration or regurgitation than those fasted for the traditional twelve hours or longer since clear fluids empty the stomach within 60 – 90 minutes (12-14). Many national anesthesia societies have changed their fasting guidelines (15-17) and now recommend that patients may drink clear fluids up to two hours before anesthesia 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 (12) or gastroesophageal reflux. 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. Avoidance of fasting is also a key component of ERAS. Allowing intake of clear fluids including coffee and tea minimizes the discomfort of thirst and headaches from withdrawal symptoms.

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

Recommendation 2

In order to reduce perioperative discomfort including anxiety oral preoperative carbohydrate treatment (instead of overnight fasting, the night before and two hours before surgery) should be administered (B). To impact postoperative insulin resistance and LOS, preoperative carbohydrates can be considered in patients undergoing major surgery (0).

Grade of recommendation B/0 – strong consensus (100% agreement)

Commentary

Preoperative intake of a carbohydrate drink with 800 ml the night before and 400 ml before surgery does not increase the risk of aspiration (12, 17, 18). Fruit-based lemonade may be considered a safe alternative with no difference in gastric emptying time (19). Oral carbohydrates have been reported to improve postoperative well being (20-23). A meta-analysis of 21 RCT on preoperative oral carbohydrate treatment in elective surgery including 1,685 patients showed a significant reduction of LOS only in the patients undergoing major surgery. There was no difference in complication rates (24). Another meta-analysis including 27 RCT with 1,976 patients, confirmed the reduction of LOS. There was no clear influence on the complication rate after elective surgery. Lack of adequate blinding in many placebo-controlled studies was considered a potential bias (25). Another meta-analysis, including 43 trials with 3,110 participants showed only a small reduction in length of postoperative stay compared with fasting, and no benefit in comparison with water and placebo. No difference in the postoperative complication rate was observed (26). For a detailed methodological discussion see the long guideline version (10). The most recent multicentric RCT included 662 patients. While significantly less patients had the requirement of one dose insulin/day and blood glucose levels >140mg/dl, no difference in clinical complications could be found (27). In order to avoid any harm carbohydrate drink should not be used in patients with severe diabetes with special regard to those with anticipated gastroparesis.

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

<u>Recommendation 3</u>

In most instances, oral nutritional intake shall be continued after surgery without interruption.

Grade of recommendation A – strong consensus (90 % agreement)

Commentary

Oral nutrition (balanced hospital diet and/or ONS) can be initiated, in most cases, immediately after surgery. Early oral nutrition is also a key component of ERAS, which demonstrated a significantly lower rate of complications and LOS in meta-analyses of the

randomized studies (28, 29). Neither esophagogastric decompression nor delayed oral intake, even after cholecystectomy or colorectal resection have proven beneficial (30-32).

Recommendation 4

It is recommended to adapt oral intake according to individual tolerance and to the type of surgery carried out with special caution to elderly patients.

Grade of recommendation GPP – strong consensus (100 % agreement)

Commentary

In comparison with conventional open surgery, early oral intake is tolerated even better after laparoscopic colonic resection, due to earlier return of peristalsis and bowel function with this technique (33-35). However, in combination with ERAS no differences were found between laparoscopic and conventional open colonic surgery when the full ERAS protocol was employed (36). In the multicenter RCT postoperative LOS was significantly shorter in the ERAS group undergoing laparoscopic surgery (37). A recent meta-analysis confirmed the reduction of major morbidity and LOS by the combination of laparoscopic surgery and ERAS (38). The amount of initial oral intake should be adapted to the state of gastrointestinal function and individual tolerance.

Recommendation 5

Oral intake, including clear liquids, shall be initiated within hours after surgery in most patients.

Grade of recommendation A – strong consensus (100 % agreement)

Commentary

Early normal food or EN, including clear liquids on the first or second postoperative day, does not cause impairment of healing of anastomoses in the colon or rectum (32, 39-42) and leads to significantly shortened LOS (43). This has been emphasized by a Cochrane Systematic Review (44). Recent meta-analyses (45-47) showed significant benefits concerning postoperative recovery and infection rate. Early postoperative nutrition is associated with significant reductions in total complications compared with traditional postoperative feeding practices and does have no negative effect on outcomes such as mortality, anastomotic dehiscence, resumption of bowel function, or LOS (47). This has

been also shown for patients after total gastrectomy (48) and minimally invasive esophagectomy (49). A meta-analysis of 15 studies (eight RCT) with 2112 adult patients undergoing upper gastrointestinal surgery showed significantly shorter postoperative LOS in early orally fed patients without a difference in complications with special regard to anastomotic leaks (50).

4. INDICATION FOR NUTRITIONAL THERAPY (Figure 1)

4.1 When is nutritional assessment and support therapy indicated in the surgical patient?

Recommendation 6

It is recommended to assess the nutritional status before and after major surgery.

Grade of recommendation GPP – strong consensus (100 % agreement)

Commentary

The influence of nutritional status on postoperative morbidity and mortality has been documented well in both retrospective and prospective studies (10). Inadequate oral intake for more than 14 days is associated with higher mortality (51). Two multivariate analyses have shown, for hospitalized patients in general and those undergoing surgery for cancer in particular, that undernutrition is an independent risk factor for the incidence of complications, as well as increased mortality, LOS, and costs (52, 53).

Recommendation 7

Perioperative nutritional support therapy is indicated in patients with malnutrition and those at nutritional risk. Perioperative nutritional therapy should also be initiated if it is anticipated that the patient will be unable to eat for more than five days perioperatively. It is also indicated in patients expected to have low oral intake and who cannot maintain above 50% of the recommended intake for more than seven days. In these situations, it is recommended to initiate nutritional support therapy (preferably by the enteral route – oral nutritional supplements – tube feeding) without delay.

Grade of recommendation GPP – strong consensus (92 % agreement)

Commentary

The general indications for nutritional support therapy in patients undergoing surgery are 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, LOS, and mortality are considered principal outcome parameters when evaluating the benefits of nutritional support (54-63). After discharge from the hospital or when palliation is the main aim of

nutritional support therapy, improvement in nutritional status and quality of life are the main evaluation criteria.

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

- Intestinal obstructions or ileus,
- Severe shock
- Intestinal ischemia
- High output fistula
- Severe intestinal hemorrhage

The advantages of early EN within 24 h versus later commencement have been clearly shown in two meta-analyses (one Cochrane systematic review) (44, 45). The American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines from 2016 (64) recommend postoperative EN when feasible within 24 hours.

Recommendation 8

If the energy and nutrient requirements cannot be met by oral and enteral intake alone (<50% of caloric requirement) for more than seven days, a combination of enteral and parenteral nutrition (PN) is recommended (GPP). PN shall be administered as soon as possible if nutrition therapy is indicated and there is a contraindication for enteral nutrition (EN), such as in intestinal obstruction. (A)

Grade of recommendation GPP/A – strong consensus (100 % agreement)

Commentary

Enteral vs. parenteral. The meta-analysis of Mazaki et al. based on 29 RCT with 2,552 patients confirmed the beneficial effects of EN for a lower rate of infectious complications, anastomotic leaks, and shorter LOS in patients after gastrointestinal surgery (46). The meta-analysis of Zhao et al. based on 18 RCT with 2540 patients showedd a shorter time to flatus, shorter LOS, and a greater increase in albumin levels (65). However, no significant influence on mortality was observed.

Enteral tolerance and timing of PN. For the surgical patient, PN may be beneficial in the following circumstances (ESPEN Guideline (66)): in undernourished patients in whom EN is not feasible or not tolerated, and in patients with postoperative complications impairing gastrointestinal function who are unable to receive and absorb adequate

amounts of oral/enteral feeding for at least seven days (66). There might be an advantage of PN when there is a limited tolerance of EN due to intestinal dysfunction especially in the early postoperative phase, which is associated with lower energy intake (67). A Cochrane systematic review and meta-analysis suggests that chewing gum may improve the postoperative recovery of gastrointestinal function (68). However, when an ERAS program was used, the benefits could not be confirmed in a randomized multicenter trial (69). The tolerance of enteral intake especially in patients with severe trauma needs to be considered (70). Adequate energy intake is better secured by PN in patients with a limited gastrointestinal tolerance (71). There is still a paucity of controlled data concerning combined EN and PN ("dual nutrition") after elective surgery. An increase in caloric intake is the main objective in combined EN/PN.

Recommendation 9

For the administration of PN, an all-in-one (three-chamber bag or pharmacy prepared) should be preferred instead of a multibottle system.

Grade of recommendation B – strong consensus (100 % agreement)

Commentary

In two RCTs the cost benefits of using a three-chamber bag were better than a multibottle system (72, 73). A retrospective analysis of a US data bank showed a significantly lower rate of blood stream infections using a three-chamber-bag (74).

Recommendation 10

SOPs for nutritional support are recommended to secure effective nutritional support therapy.

Grade of recommendation GPP – strong consensus (100 % agreement)

Commentary

Feeding protocols and SOPs have proven benefits concerning the safety and feasibility of achieving the caloric target (75, 76). Adequate supply with micronutrients is considered essential for long-term total PN.

4.2 Is there an indication for supplementing glutamine?

Recommendation 11

Parenteral glutamine supplementation may be considered in patients who cannot be fed adequately enterally and, therefore, require exclusive PN.

Grade of recommendation 0 –consensus (76 % agreement)

Commentary

Most surgical patients requiring PN have prolonged or even complicated courses that often require intensive care treatment. Numerous RCTs have been performed for glutamine supplemented PN in a standard dosage of 0.35g/kg body weight in surgical patients (10). In a large multicenter RCT including 428 well-nourished patients undergoing major gastrointestinal surgery no significant benefit was found for the postoperative complication rate and the LOS for those patients, who had been supplemented with 0.4 g dipeptide/kg/d parenterally the day before and five days after surgery (77). Two meta-analyses that included 14 RCTs with 587 surgical patients, or 40 RCTs with more than 2000 patients, respectively, have emphasized significant advantages of glutamine supplementation concerning infections and LOS (78, 79). Another RCT not comprised in the previous meta-analyses included 150 surgical intensive care patients who received isonitrogenous isocaloric PN (1.5 g/kg/d aminoacids). In the intervention, group glutamine was administered at 0.5 g/kg/d. No significant differences were seen with the primary endpoints of hospital mortality and infection rate (80). While the working group still considered beneficial effects of glutamine supplementation, there is no strong evidence from the literature to recommend the use of parenteral glutamine. Exclusive PN over five to seven days is not indicated in most surgical patients particularly after elective colorectal surgery with an uncomplicated course (28, 29, 81). The extent to which parenteral glutamine administration in combination with oral nutrition / EN may have a positive effect, cannot be clarified at present due to lack of available data.

Currently, no clear recommendation can be given regarding the supplementation of oral glutamine (0).

Commentary

Data regarding oral glutamine supplementation as a single substance are limited. In pancreatic surgery oral preconditioning with glutamine, antioxidants, and green tea extract versus placebo elevated plasma vitamin C concentrations significantly and improved total endogenous antioxidant capacity without reducing oxidative stress and inflammatory response (26).

4.3 Is there an indication for supplementing arginine (IV or EN) alone?

Currently, no clear recommendation can be given regarding the intravenous or enteral supplementation of arginine as a single substance (0). Evidence is insufficient to suggest the use of arginine alone.

Commentary

Data regarding arginine supplementation as a single substance are limited. For patients undergoing surgery for head and neck cancer, a meta-analysis included six studies with 397 patients receiving peri/postoperative enteral supplementation with arginine in different dosages (6.25-18.7g/l) and also in combination with other substances. There was a reduction in fistulas (OR=0.36, 95% CI: 0.14 to 0.95, p=0.039), and LOS (mean difference: -6.8 d, 95% CI: -12.6 to -0.9 d, p=0.023). Interestingly, no reduction in wound infections (OR=1.04, 95% CI 0.49 to 2.17, p=0.925) or other infections was observed (82). A 10 year-long observation in 32 patients with head and neck cancer who had been perioperatively administered an arginine-enriched diet showed a significantly longer overall, better disease-specific survival, and less loco-regional tumor recurrence in the intervention group (83). It must be emphasized that this study was underpowered to detect differences in survival which was not the primary endpoint of this trial.

4.4 Is there an indication for supplementing i.v. omega-3-fatty acids?

Recommendation 12

Postoperative PN including omega-3-fatty acids should be considered only in patients who cannot be adequately fed enterally and, therefore, require PN.

Grade of recommendation B - majority agreement (65 % agreement)

Commentary

For parenteral supplementation of omega-3-fatty acids, a meta-analysis of 13 RCTs on 892 surgical patients revealed significant advantages concerning the postoperative infection rate and LOS (84). This has been confirmed by more recent meta-analysis including 23 studies with 1,502 patients (85, 86). The methodological analysis of the meta-analysis and the single studies brings up concerns concerning the lack of homogenous criteria for the definition of infectious complications and the considerable heterogeneity of LOS (87). Tian et al. performed a meta-analysis for the comparison of a new lipid emulsion containing soybean oil, medium-chain triglycerides, olive oil, and fish oil versus other olive oil and medium-and long-chain triglyceride-based emulsions (88). No clear evidence was found. It has also to be argued that in most of the studies the majority of patients, with special regard to colorectal surgery, were not appropriate candidates for PN alone. Due to these methodological problems of the individual studies, the working group voted for a limited B recommendation. The possible benefits of a short-term perioperative omega-3-fatty acid infusion for a total duration of 72 hours before elective surgery, needs to be clarified further (89).

4.5 Is there an indication for specific oral/enteral formula enriched with immunonutrients?

Recommendation 13

Peri- or at least postoperative administration of specific formula enriched with (arginine, omega-3-fatty acids, ribonucleotides) should be given in malnourished patients undergoing major cancer surgery (B). There is currently no clear evidence for the sole use of these formulas enriched with immunonutrients vs. standard oral nutritional supplements (ONS) in the preoperative period (0).

Grade of recommendation B/0 – consensus (89 % agreement)

Commentary

15 meta-analyses of RCT, in general, surgical patients, and one in head/neck cancer surgery suggest that perioperative administration of immune-modulating nutritional formula has contributed to a decreased rate of postoperative complications and a decreased LOS (90-114). This was confirmed by a more recent meta-analysis including 83

RCTs with 7116 patients (115). Concerning the immunomodulating substrates, most of the RCTs were performed with arginine, omega-3-fatty acids, and ribonucleotides.

It has been discussed controversially of there is an advantage of pre-, peri- and postoperative intake of immune-modulating substrates such as arginine, omega-3 fatty acids, and nucleotides. The reduction of postoperative morbidity and LOS after major abdominal cancer surgery (116-119) has been shown, particularly in malnourished patients (120, 121). In the meta-analysis of Hegazi et al. a clear differentiation was made between studies comparing preoperative immunonutrition vs. ONS and those vs. no supplements (122). Only in studies with a control group of an oral non-supplemented standard diet, a significant difference was found for infectious complications (OR 0.49, 95% CI 0.30 to 0.83, $p<0.01$) and for LOS (mean difference -2.22 d, 95% CI -2.99 to -1.45 d, $p<0.01$). In another meta-analysis, the sole use of immunonutrition before surgery again led to a significant decrease of infectious complications when compared with normal diet but also with isonitrogenous standard nutritional supplement (OR 0.52; 95% CI 0.38-0.71, $p<0.0001$). For the LOS a significant reduction was found for immunonutrition vs. hospital diet, and a tendency vs. standard nutritional supplement (123). These data provide arguments for a preferentially preoperative use. The cost-effectiveness of such a formula, e.g. because of reduced complication rates, has been shown (121, 124-126).

5. NUTRITIONAL THERAPY in THE PREOPERATIVE PERIOD (Figure 2)

5.1 Which patients benefit from nutritional therapy in the preoperative period?

Recommendation 14

Patients with severe nutritional risk shall receive nutritional therapy prior to major surgery (A) even if operations including those for cancer have to be delayed (BM). A period of seven to 14 days may be appropriate (0).

Grade of recommendation A/0 – strong consensus (95 % agreement)

Commentary

Recently, an international Global Leadership Initiative, for the definition of Malnutrition driven by the clinical nutrition societies, has proposed a definition of malnutrition

including phenotypical (non-volitional weight loss, low body mass index (BMI), reduced muscle mass) and etiological criteria (reduced food intake or assimilation, inflammation or disease burden) (127).

In the surgical patient sarcopenic obesity may not be underestimated, "severe" nutritional risk has been defined according to the ESPEN working group (2006) as the presence of at least one of the following criteria:

- Weight loss >10-15% within six months
- BMI <18.5 kg/m^2
- SGA Grade C or NRS >5 (subjective global assessment, nutritional risk screening)
- Serum albumin <30g/l (with no evidence of hepatic or renal dysfunction)

These parameters reflect undernutrition as well as disease-associated catabolism. The working group agrees that hypoalbuminemia is a clear surgical risk factor (128, 129), however, it reflects disease-associated catabolism and disease severity rather than undernutrition. The impact of hypoalbuminemia has been emphasized by recent data (130-132). For patients at high-risk preoperative conditioning has been a traditional approach to optimize the patient's status before major elective surgery. The benefits of nutritional therapy were shown in cases of severe undernutrition (133-135); and confirmed in two meta-analyses (134, 136) both, particularly concerning the rate of postoperative complications (133, 135-137). These patients were fed preoperatively for at least seven to ten days. In 800 patients with gastric cancer undergoing gastrectomy and with severe nutritional risk according to the ESPEN definition, the incidence of surgical-site-infections was significantly lower in the group receiving adequate energy support for at least ten days than in the group with inadequate or even no support for less than ten days (17.0% vs. 45.4%, p=0.00069). In multivariate analysis, nutritional therapy was an independent factor associated with fewer surgical site infections (odds ratio 0.14, 95% CI 0.05 to 0.37, p=0.0002) (138).

<u>Recommendation 15</u>

Whenever feasible, the oral/enteral route shall be preferred (A).

Grade of recommendation A – strong consensus (100 % agreement)

Commentary

With special regard to cancer patients undergoing multimodal therapy support of a dietitian should be integrated very early (139). If PN is necessary to meet energy needs e.g. in stenosis of the upper gastrointestinal tract, it should be combined with oral nutrition (e.g. ONS) whenever possible. To avoid refeeding syndrome in severely malnourished patients PN should be increased stepwise including laboratory and cardiac monitoring with adequate precautions to replace potassium, magnesium, phosphate, and thiamine (140). There is insufficient data available on the comparison of EN with PN preoperatively. Jie et al. presented a consecutive series of 1085 patients undergoing nutritional risk screening (NRS-2002) before abdominal surgery (141) and found that 512 were at nutritional risk. At the discretion of the surgeon, patients received EN or PN for seven days before surgery. While no difference in infection rate and LOS was found for patients with Nutrition Risk Score of 3 and 4 for patients with and without preoperative nutritional support, of 120 patients with nutritional risk screening (NRS) score of at least 5 those with preoperative nutrition had significantly fewer complications (25.6% vs. 50.6%, p=0.008) and a shorter hospital stay (13.7$\pm$7.9 d vs. 17.9$\pm$11.3 d, p=0.018).

Duration of preoperative nutritional therapy according to nutritional risk

5.2 When is preoperative ONS /EN indicated?

Recommendation 16

When patients do not meet their energy needs from normal food it is recommended to encourage these patients to take ONS during the preoperative period unrelated to their nutritional status.

Grade of recommendation GPP – consensus (86 % agreement)

Commentary

It is the consensus of the working group that ONS should comprise a standard fully balanced non-disease-specific formula which may be used as a sole source for nutrition and is composed according to the European Union regulatory directives for Food for Special Medical Purposes (FSMP) (142, 143). Because many patients do not meet their energy needs from normal food it is the consensus of the working group to encourage them to take standard ONS during the preoperative period unrelated to their nutritional status.

Unrelated to the nutritional status preoperative ONS were studied in general surgical patients in three RCTs (144-146). Although two studies showed no significant impact on the outcome, Smedley et al. found a significant reduction in minor complications. Furthermore, preoperative ONS continued postoperatively, minimized postoperative weight loss (147). It has to be argued that most of the patients who underwent surgery for colorectal cancer were not at nutritional risk. This might explain why the meta-analysis of these studies did not show significant benefits (148). It is noteworthy that Burden et al. observed some benefits for surgical site infections according to the Buzby definition in selected weight losing patients (146). The cost-effectiveness of standard ONS in hospitalized patients was shown in a systematic review of the literature and meta-analysis (142).

Recommendation 17

Preoperatively, ONS shall be given to all malnourished cancer and high-risk patients undergoing major abdominal surgery. A special group of high-risk patients are the elderly people with sarcopenia.

Grade of recommendation A – strong consensus (97 % agreement)

See recommendations 14 and 16.

Recommendation 18

Immune modulating ONS including (arginine, omega-3 fatty acids, and nucleotides) can be preferred (0) and administered for five to seven days preoperatively (GPP).

Grade of recommendation 0/GPP – majority agreement, 64 % agreement

Commentary

See also recommendation 13

Because patient compliance to take ONS seems to be a matter of motivation patients should be informed well about the potential benefits (149).

Recommendation 19

Preoperative EN / ONS should preferably be administered prior to hospital admission to avoid unnecessary hospitalization and to lower the risk of nosocomial infections.

Grade of recommendation GPP – strong consensus (91 % agreement)

Commentary

The benefits of nutritional therapy prior to hospital admission are obvious regarding the risk of nosocomial infection and also economy.

For specific immune modulating diets – see recommendation 13 and 18

5.3 When is preoperative PN indicated?

See also 5.2 „ When is preoperative ONS /EN indicated?"

Recommendation 20

Preoperative PN shall be administered only in patients with malnutrition or severe nutritional risk where energy requirement cannot be adequately met by EN (A). A period of 7-14 days is recommended (0).

Grade of recommendation A/0 – strong consensus (100 % agreement)

Commentary

The benefits of preoperative PN for seven to 14 days are only evident in patients with severe malnutrition (weight loss 10-15 %) before major gastrointestinal surgery (135, 137). When PN is given for ten days preoperatively and continued for nine days postoperatively the rate of complications is 30 % lower and there is a reduction in mortality (137). According to the recovery of physiological function and total body protein, a considerable increase can be achieved within seven days of PN. However further significant improvement will be obtained within the second week (150). No controlled studies are comparing seven days with ten to 14 days of PN. While the ASPEN guidelines 2009 recommend seven days of PN (64), it is the opinion of the working group, that in patients with severe nutritional risk the potential increase in benefit will justify the preoperative extension of LOS with ten to 14 days. A recent Cochrane analysis of

preoperative PN in patients undergoing gastrointestinal surgery confirmed a significant reduction of complications from 45% to 28% (148).

6. POSTOPERATIVE NUTRITION (Figure 3a and b)

6.1 Which patients benefit from early postoperative EN?

Recommendation 21

Early EN (within 24 h) shall be initiated in patients in whom early oral nutrition cannot be started, and in whom oral intake will be inadequate (<50%) for more than seven days

- **patients undergoing major head and neck or gastrointestinal surgery for cancer (A)**
- **patients with severe trauma including brain injury (A)**
- **patients with obvious malnutrition at the time of surgery (A) (GPP)**

Grade of recommendation A/GPP - strong consensus (97 % agreement)

Commentary

Recent data from RCTs and one meta-analysis confirm that immediate oral nutrition can be administered safely in patients with anastomoses after partial and total gastrectomy (50, 151, 152). A recent RCT in patients undergoing minimally invasive esophagectomy showed that direct oral feeding is feasible without any harm (49). An RCT in patients undergoing total laryngectomy with primary pharyngeal closure also showed that initiation of oral feeding on the first postoperative day was safe (153). Nevertheless, patients undergoing major surgery for head and neck, and abdominal cancer (larynx, pharynx or esophageal resection, gastrectomy, partial pancreatectomy) often exhibit nutritional depletion before surgery (154-162) and have a higher risk of developing septic complications (52, 154-158, 161, 163). Postoperatively, oral intake is often delayed due to swelling, obstruction, or impaired gastric emptying, making it difficult to meet nutritional requirements. Any postoperative complications may delay oral and enteral feeding, and diminish predefined caloric uptake (164). Nutritional support reduces morbidity with an increasingly protective effect of PN, EN, and immune-modulating formula (52). Trauma patients with a normal nutritional status have a high risk of developing septic complications and multiple organ failure. Early EN has been claimed to reduce septic complications (60, 165), and has been suggested to reduce the rate of multiple organ failure when initiated within 24 hours (166). For head-injured patients, early feeding may be associated with fewer infections and a trend towards better outcomes in terms of survival and disability (167).

6.2 Which formula should be used?

Recommendation 22

In most patients, a standard whole protein formula is appropriate. For technical reasons with tube clotting and the risk of infection, the use of home-made diets for EN is not recommended in general.

Grade of recommendation GPP - strong consensus (94 % agreement)

Commentary

Most patients can be appropriately fed by a standard diet. Even in case of small bowel access e.g. by a needle catheter jejunostomy (NCJ) no oligopeptide diet is required. Home-made diets for EN may be considered in the home care setting (preparation is solely for one patient, and risk for contamination is lower than in an institution where several preparations are made at the same time). For immune-modulating formula see comment 4.5.

6.3 How should patients be tube fed after surgery?

Recommendation 23

With special regard to malnourished patients, placement of a nasojejunal tube or NCJ should be considered for all candidates for EN undergoing major upper gastrointestinal and pancreatic surgery.

Grade of recommendation B – strong consensus (95 % agreement)

Commentary

Many studies have shown the benefits and feasibility of feeding via a tube either inserted distal to the anastomosis, e.g. NCJ, or inserted via the nose with its tip passed distally at the time of operation e.g. nasojejunal tube (168-173). Open or even laparoscopic placement (174) of the NCJ according to standardized techniques in a specialized center is associated with low risk and a complication rate of about 1.5-6 % in most series (120, 168, 170, 175-185). Some authors consider the routine use of NCJ and overtreatment and propose consideration of NCJ only in high-risk patients (186-188). For patients undergoing esophageal resection, an observational study demonstrated the benefits of

safe long term EN by NCJ with special regard to anastomotic complications (172, 183). The complication rate was low: 1.5% (183). In an RCT including 68 patients undergoing pancreaticoduodenectomy no significant difference in the complication rate was found (15% vs.13%) (189). The postoperative LOS was significantly shorter in the NCJ group (189). A meta-analysis of five RCTs including 344 patients did not elucidate a clear difference between enteral NCJ feeding and parenteral access (190). In patients undergoing esophagectomy, an RCT showed no significant differences between naso-duodenal tube and feeding jejunostomy for early EN and catheter-associated complications (191). Because nasojejunal and nasoduodenal tubes are associated with a significant rate of early accidental dislodgement (187, 190), the working group agrees with Markides et al. that for patients at nutritional risk, "feeding jejunostomy may be superior to nasojejunal or duodenal tubes". In these patients, it may be reasonable to leave NCJ and to continue nutritional support therapy after discharge.

Recommendation 24

EN shall be initiated within 24 hours after surgery.

Grade of recommendation A – strong consensus (91 % agreement)

Commentary

see commentary recommendation 25

Recommendation 25

It is recommended to start EN with a low flow rate (e.g. 10 – max. 20 ml/h) and to increase the feeding rate carefully and individually due to limited intestinal tolerance. The time to reach the target intake can be very different and may take five to seven days.

Grade of recommendation GPP – consensus (85 % agreement)

Commentary

Tolerance of EN has to be monitored closely in all patients with impaired gastrointestinal function (192). It may therefore take five to seven days before nutritional requirements can be achieved by the enteral route (171, 173, 193, 194). In anecdotal reports, strangulation or too rapid administration of feed may lead to the development of small bowel ischemia with a high risk of mortality (187, 195-201).

Recommendation 26

If long-term EN (>4 weeks) is necessary, e.g. in severe head injury, placement of a percutaneous tube (e.g. percutaneous endoscopic gastrostomy - PEG) is recommended.

Grade of recommendation GPP – strong consensus (94 % agreement)

Commentary

Percutaneous endoscopic gastrostomy should be considered in case of the indication for long-term EN when abdominal surgery is not indicated e.g. severe head injury, neurosurgery. For patients with upper gastrointestinal stenosis due to esophageal cancer and scheduled surgery after neoadjuvant radio-chemotherapy preoperative PEG should be only placed according to the discretion of the surgeon. The guidelines for PEG placement (202) recommend the intervention for EN of two to three weeks.

6.4 Which patients will benefit from EN after discharge from the hospital?

Recommendation 27

Regular reassessment of nutritional status during the stay in hospital and, if necessary, a continuation of nutritional support therapy including qualified dietary counseling after discharge, is advised for patients who have received nutritional support therapy perioperatively and still do not cover appropriately their energy requirements via the oral route.

Grade of recommendation GPP – strong consensus (97 % agreement)

Commentary

Despite perioperative nutritional therapy, patients developing postoperative complications lose weight and are at risk for further deterioration of nutritional status. These patients require continuing nutritional follow-up after discharge. Furthermore, in some patients after major gastrointestinal or pancreatic surgery the oral calorie intake will be inadequate for a longer period with a risk for postoperative malnutrition. A meta-analysis of 18 studies in patients with esophagectomy indicated a weight loss of 5-12% at six months postoperatively. More than half of patients lost >10% of body weight at twelve

months (203). Dietary counseling is strongly recommended and appreciated by most patients. If implemented during surgery, NCJ is advantageous because it need not be removed at the time of discharge from the hospital. If necessary supplementary EN can be continued via NCJ e.g. with 500 or 1000 kcal/d overnight. Appropriate training will enable most of the patients to administer jejunostomy tube feeds themselves. The data from six RCTs do not show with certainty that routine postoperative or post-hospital administration of ONS improves outcome but there is benefit in terms of nutritional status, rate of minor complications, well-being, and quality of life in patients who cannot meet their nutritional requirements at home from normal food (64, 70, 147, 204, 205). This applies mainly to patients after major gastrointestinal surgery (206), colorectal resections (207), and geriatric patients with fractures (208-210). 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 with the control group (209, 211).

7. ORGAN TRANSPLANTATION (Figure 4)

7.1 When is EN necessary before solid organ transplantation?

Recommendation 28

Malnutrition is a major factor influencing outcome after transplantation, so monitoring of the nutritional status is recommended. In malnutrition, additional ONS or even EN is advised.

Grade of recommendation GPP – strong consensus (100 % agreement)

Commentary

Undernutrition is likely to lead to a faster progression of the underlying disease, especially in the presence of cardiac and respiratory insufficiency, and leads to impaired functional status (see respective guidelines). Negative energy balance is highly prevalent among patients on the waiting list for liver transplantation and is associated with the severity of the liver disease. Nutritional parameters have been shown to correlate with outcome after transplantation (212-217). During the often long preoperative waiting period, there is time to try to replete patients nutritionally. Food composition may be inadequate and intake of energy and protein overall too low (218). Four interventional studies (two randomized) on preoperative nutrition in patients waiting for organ transplantation have been performed (219-222). Improvement in parameters of nutritional status was shown in all four studies. There was no difference in mortality between patients on the waiting list and patients after transplantation. In the case of nutritional intervention, no association was found between mortality and nutritional status (215). In one RCT, the improved parameters of nutritional status before transplantation did not affect outcome and mortality (220).

Recommendation 29

Regular assessment of nutritional status and qualified dietary counselling shall be required while monitoring patients on the waiting list before transplantation.

Grade of recommendation GPP – strong consensus (100 % agreement)

Commentary

Besides malnutrition, and despite the obesity paradox, obesity remains a significant metabolic risk factor for the outcome of patients undergoing organ transplantation (223).

Therefore, nutritional monitoring and treatment should also include obesity and metabolic syndrome to obtain weight loss and risk minimization. Early results concerning the benefits of immune-modulating formula during the waiting period and five days after liver transplantation show a favorable long-term impact on total body protein and a possible reduction of infectious complications (222). In a Japanese pilot study, 23 living donors for liver transplantation were randomized for the intake of a supplement enriched with antioxidants for five days before surgery. While an increase in antioxidant capacity was observed in the intervention group no significant differences were found for any immunological or clinical parameter (224).

Recommendation 30

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

Grade of recommendation GPP – strong consensus (97 % agreement)

Commentary

At present, there is a paucity of data available concerning the metabolic preconditioning of the (living) donor and recipient. Experimental results (225) showing the impact of nutritional status on liver preservation injury also favor the concept of metabolic preparation by preoperative carbohydrate drink. Particular issues regarding the influence of EN on the course/progression of liver disease are discussed in the hepatology guideline (226).

7.2 When is nutritional therapy indicated after solid organ transplantation?

Recommendation 31

After heart, lung, liver, pancreas, and kidney transplantation, early intake of normal food or EN is recommended within 24h.

Grade of recommendation GPP – strong consensus (100 % agreement)

Commentary

It is generally agreed that early normal food or EN should be administered in patients undergoing transplantation (226-228). In cases of undernutrition, it should be combined

with PN if the enteral delivery of nutrients is inadequate. Insertion of an NCJ is feasible in patients undergoing liver transplantation (229). For the first 48h caloric intake <18 kcal/kg/day may be beneficial for the early graft function after liver transplantation (230). Absorption and blood levels of tacrolimus are not affected by EN (231). EN is at least equal to PN in patients after liver transplantation (232) and has been shown to reduce the incidence of viral and bacterial infections (228, 233). Compared with standard EN formula plus the use of selective digestive decontamination, the use of a high soluble fiber formula with probiotic bacteria (*Lactobacillus plantarum*) has been shown to reduce significantly the rate of infections (234). Early EN enriched with a mixture of probiotic bacteria and soluble fiber significantly reduced bacterial infection rate compared with a supplement containing only fiber (235).

Recommendation 32

Even after transplantation of the small intestine, EN can be initiated early but should be increased very carefully within the first week.

Grade of recommendation GPP – strong consensus (93 % agreement)

Commentary

EN is possible despite increased intestinal secretion in small bowel transplantation and can be performed at low delivery rates in the first week (236-238). Micronutrients and minerals should be monitored and supplemented because deficiencies were observed in 21 pediatric and young adult patients undergoing intestinal transplantation with special regard to those who received jejunal tube feeding (239).

Recommendation 33

If necessary EN and PN should be combined. Long-term nutritional monitoring and qualified dietary counseling are recommended for all transplants.

Grade of recommendation GPP – strong consensus (100 % agreement)

Commentary

EN and PN may be equally important in patients after liver transplantation (232). Benefits have been reported with administration of Medium Chain Triglycerides / Long Chain Triglycerides lipid emulsions compared to Long Chain Triglycerides emulsions, with more

favorable regeneration of the function of the reticuloendothelial system after liver transplantation (240). There was no difference in the metabolism of both lipid preparations (241). When compared with routine treatment including an oral diet or additional PN with 20% Medium Chain Triglycerides / Long Chain Triglycerides emulsion the use of an omega-3 fish oil lipid emulsion for seven days after liver transplantation showed significant benefits concerning ischemia-reperfusion graft injury, infectious morbidity, and post-transplant hospital stay (242, 243). The advantages regarding the recovery of the graft may be expected from the results of a meta-analysis of 21 RCTs (85). For parenteral and enteral use of omega-3-fatty acids, the meta-analysis from Lei et al. (244) included four heterogeneous studies (245), and two studies published in Chinese. No significant decrease was found in the rate of infectious complications.

Long-term nutritional monitoring and dietary counseling are reasonable because many patients undergoing transplantation show inadequate body composition. Increased fat and reduced lean body mass were observed in 145 patients undergoing renal transplantation and patients with a normal BMI had better renal graft function than those with obesity (246). To improve kidney function, rejection rates, patient and graft survival fish oil use after renal transplantation was analyzed in a Cochrane Systematic Review including 15 RCT with733 patients (247). Besides a modest improvement in High-Density Lipoproteins (HDL) cholesterol and diastolic blood pressure no benefit in clinical outcome was found (246).

8. BARIATRIC SURGERY (Figure 5)

8.1 When is perioperative nutritional therapy indicated in the bariatric patient?

Recommendation 34

Early oral intake can be recommended after bariatric surgery.

Grade of recommendation 0 – strong consensus (100 % agreement)

Commentary

Nutritional care in patients undergoing bariatric surgery extends well beyond the perioperative period. ERAS principles have been applied also in bariatric surgery (248). Standardized pathways have been shown to facilitate implementation and to improve process quality, while clinical benefits were minimal at best (248, 249). The preoperative assessment should include screening for malnutrition and deficiency in vitamins and trace elements. Potential benefits of preoperative carbohydrate loading and postoperative peripheral PN vs. standard management were studied in a cohort of 203 laparoscopic Roux-en-Y bypass patients. While the nutritional interventions appeared to be safe even in patients with type 2 diabetes, careful analysis of various nutritional parameters and clinical outcomes did not show any statistically significant difference between the groups (250). Consensus exists about early oral nutrition after bariatric surgery (251-254). There is no difference in management when compared with any other (upper) gastrointestinal surgical procedures. Clinical practice guidelines were elaborated by an American expert panel first in 2008 and regularly updated since (last update: (253)).

Recommendation 35

PN is not required in uncomplicated bariatric surgery.

Grade of recommendation 0 – strong consensus (100 % agreement)

Commentary

While hypocaloric nutrition is part of the treatment strategy in patients with an uncomplicated course, there is no need for supplemental PN. The Allied Health Nutritional Guidelines for the Surgical Weight Loss Patient do not recommend PN regularly (247). In

these patients, the gastrointestinal tract is usually working and catheter-associated complications have to be considered (255).

Recommendation 36

In case of a major complication with relaparotomy, the use of a nasojejunal tube / NCJ may be considered.

Grade of recommendation 0 – consensus (87 % agreement)

Commentary

Even in the case of major complications after bariatric procedures, EN has proven advantages concerning mortality and higher cost-effectiveness (256-258). For EN nasojejunal tubes, NCJ or gastrostomy in the gastric remnant may be considered carefully (256-259). NCJ and PEG have a considerably higher risk of leakage in the obese patient. A nasojejunal tube may be placed in the operating room.

Recommendation 37

Further recommendations are not different from those for patients undergoing major abdominal surgery (0).

Grade of recommendation 0 – strong consensus (94 % agreement)

Commentary

Early postoperative food intake is advocated, and supplementation with protein powders is suggested to meet daily requirements of 60 g protein/day. Of note, standard oral supplements contain high glucose concentrations and are problematic in bariatric patients as they can cause dumping syndrome. Postoperative nutritional follow-up by a dedicated team is a must in these patients for dietary counseling, to monitor weight loss, and to prevent deficiencies (vitamins, micronutrients) with special emphasis on bone health (vitamin D3, Ca). In this context, physical exercise should be encouraged strongly, although evidence is lacking.

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Figure legends:

Figure 1: Flow scheme of perioperative nutrition therapy

Figure 2: Flow scheme of preoperative nutrition

Figure 3a: Flow scheme of postoperative nutrition and indication for nutrition therapy

Figure 3b: Flow scheme of postoperative nutrition therapy

Figure 5: Flow scheme of perioperative nutrition in organ transplantation and bariatric surgery

Figure

Figure 1: Flow scheme of perioperative nutrition therapy

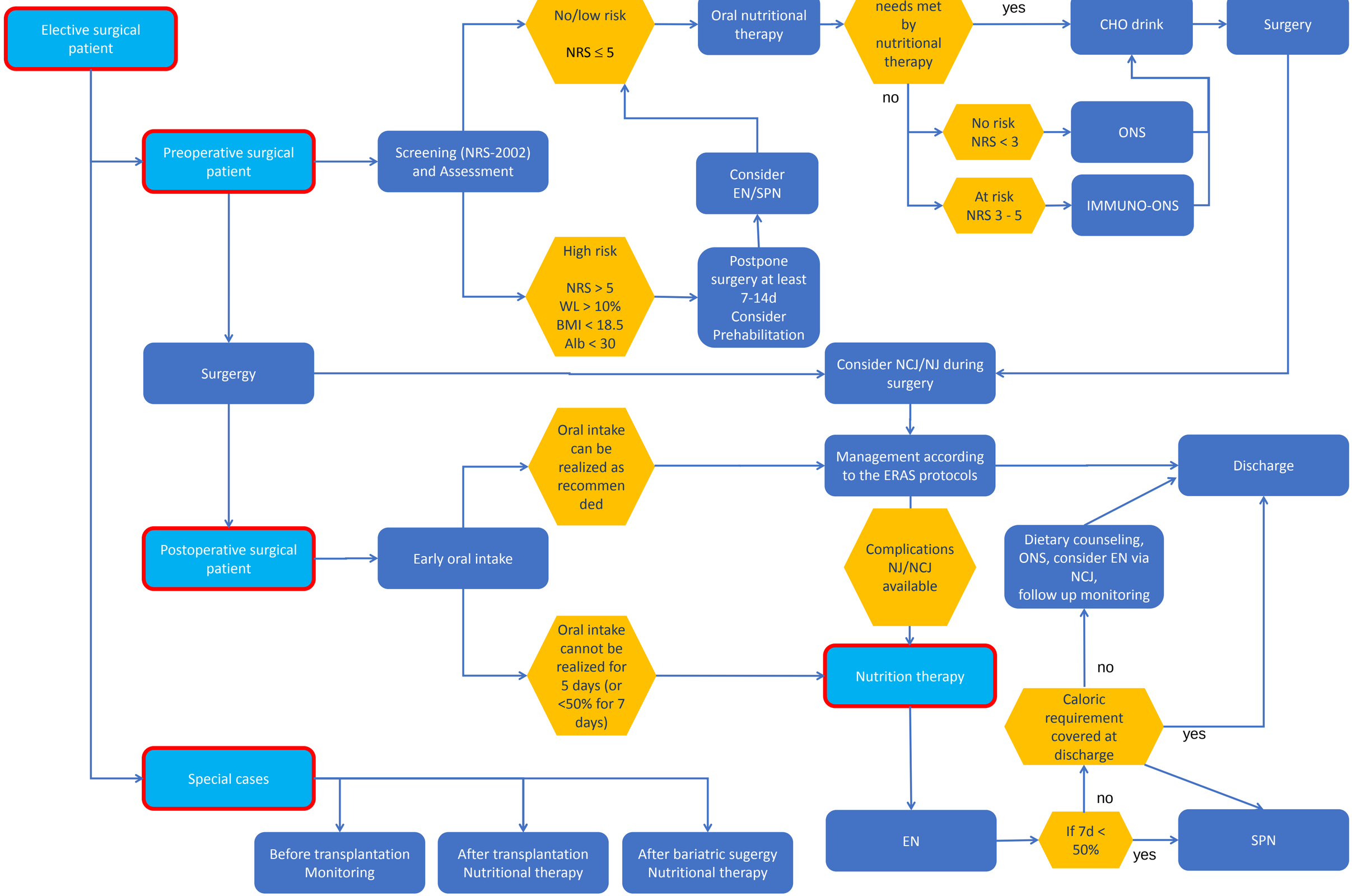


Figure 2: Flow scheme of preoperative nutrition

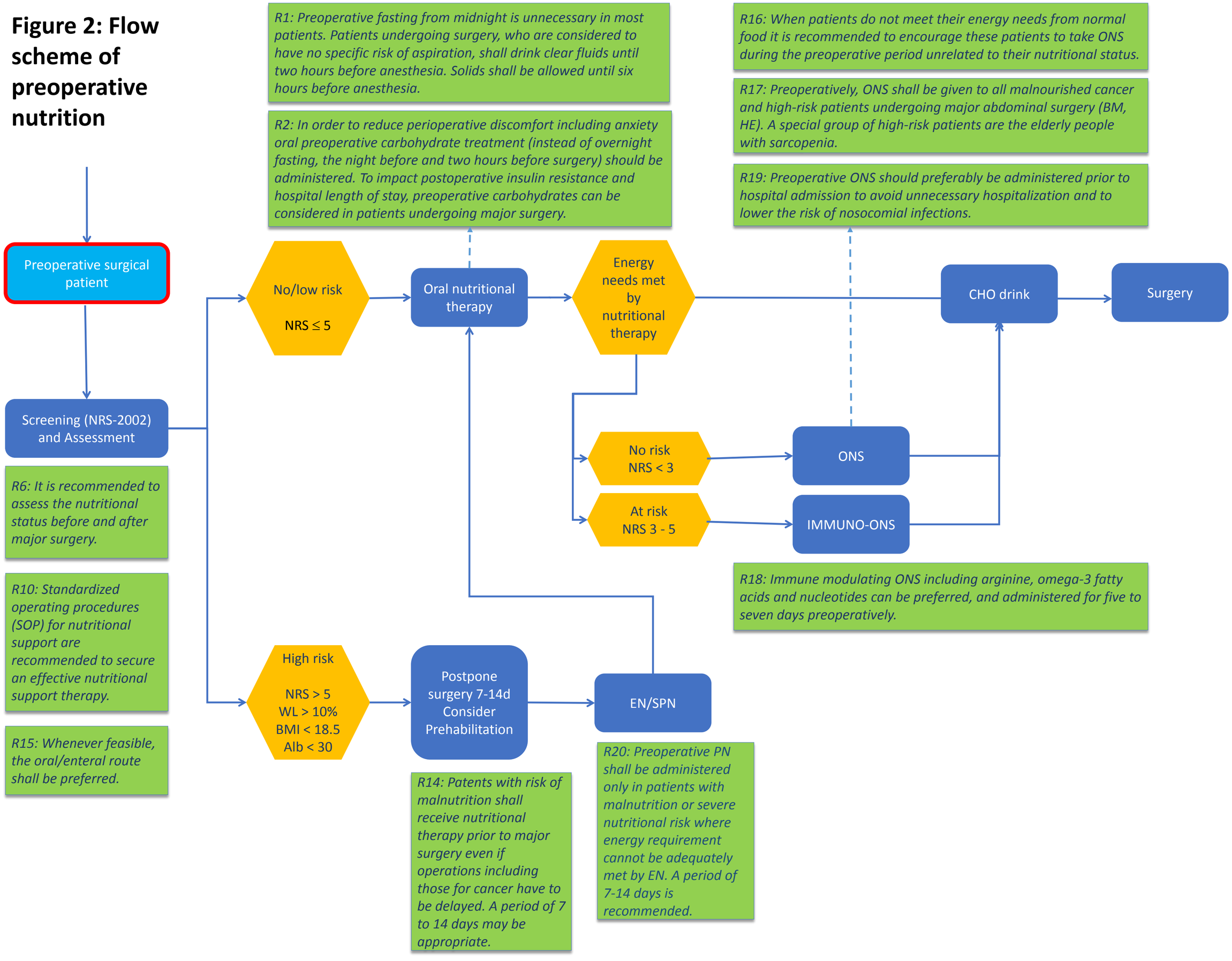


Figure 3a: Flow scheme of postoperative nutrition and indication for nutrition therapy

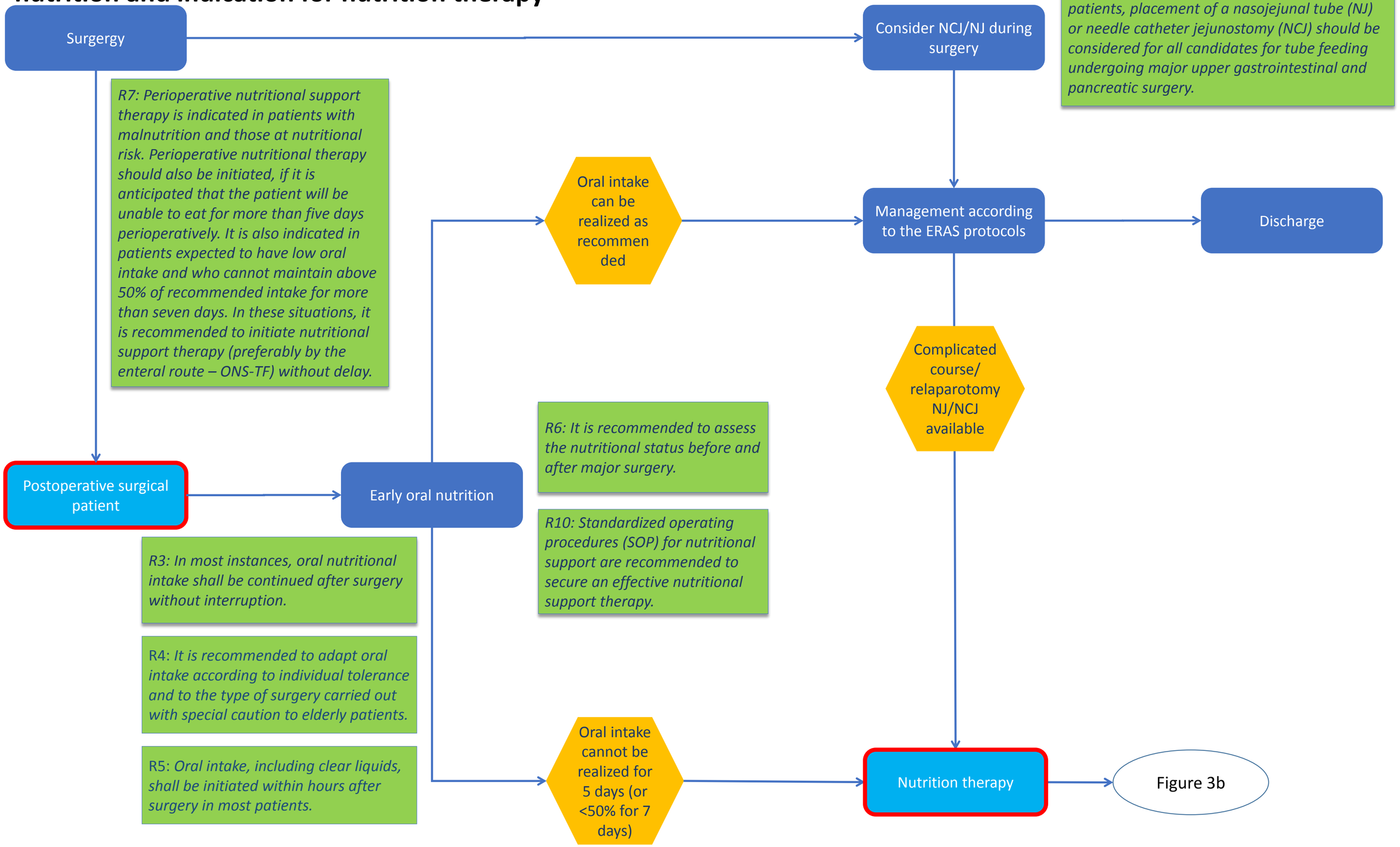
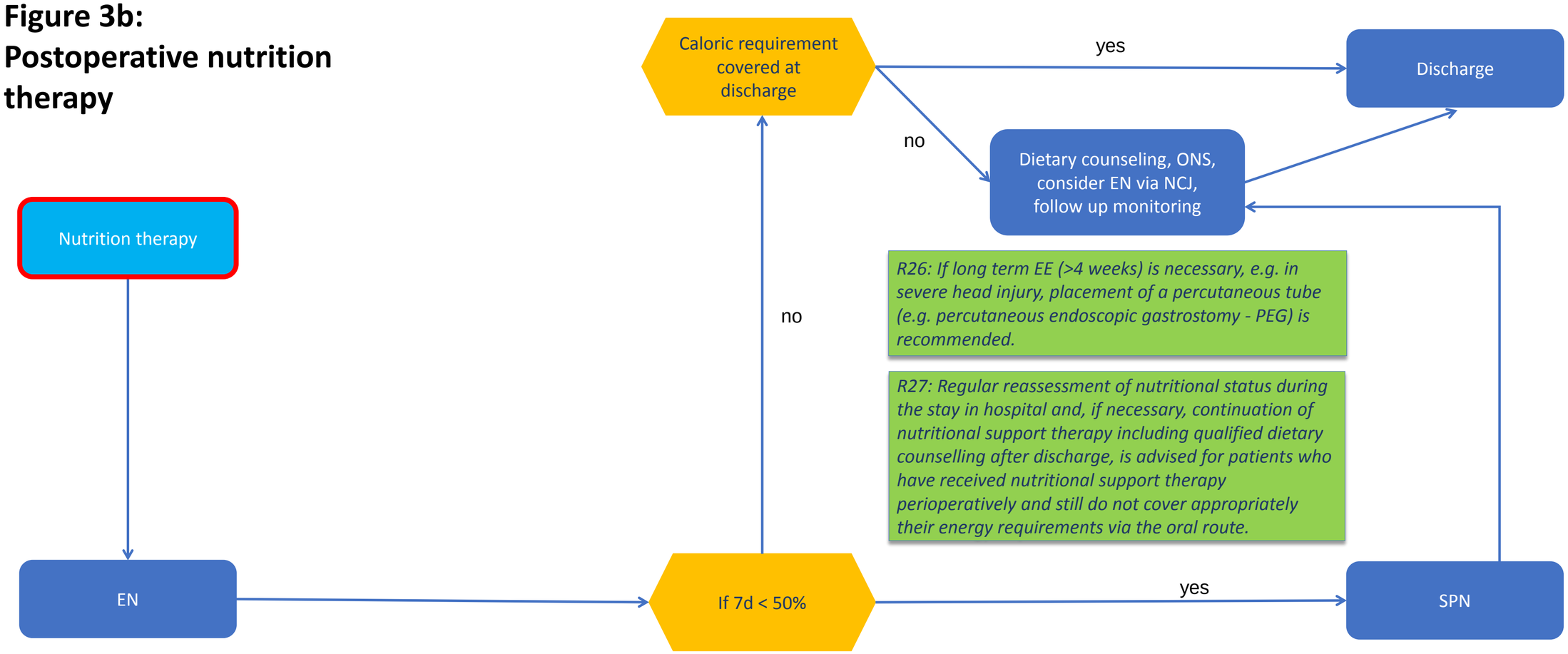


Figure 3b: Postoperative nutrition therapy



R26: If long term EE (>4 weeks) is necessary, e.g. in severe head injury, placement of a percutaneous tube (e.g. percutaneous endoscopic gastrostomy - PEG) is recommended.

R27: Regular reassessment of nutritional status during the stay in hospital and, if necessary, continuation of nutritional support therapy including qualified dietary counselling after discharge, is advised for patients who have received nutritional support therapy perioperatively and still do not cover appropriately their energy requirements via the oral route.

R24: Tube feeding shall be initiated within 24 hours after surgery.

R21: Early tube feeding (within 24 h) shall be initiated in patients in whom early oral nutrition cannot be started, and in whom oral intake will be inadequate (<50%) for more than 7 days

- *patients undergoing major head and neck or GI surgery for cancer*
- *patients with severe trauma including brain injury*
- *patients with obvious malnutrition at the time of surgery*

R22: In most patients, a standard whole protein formula is appropriate. For technical reasons with tube clotting and the risk of infection the use of home-made diets for tube feeding is not recommended in general.

R25: It is recommended to start tube feeding with a low flow rate (e.g. 10 – max. 20 ml/h) and to increase the feeding rate carefully and individually due to limited intestinal tolerance. The time to reach the target intake can be very different, and may take five to seven days.

R13: Peri- or at least postoperative administration of specific formula (enriched with arginine, omega-3-fatty acids, ribonucleotides) should be given in malnourished patients undergoing major cancer surgery.

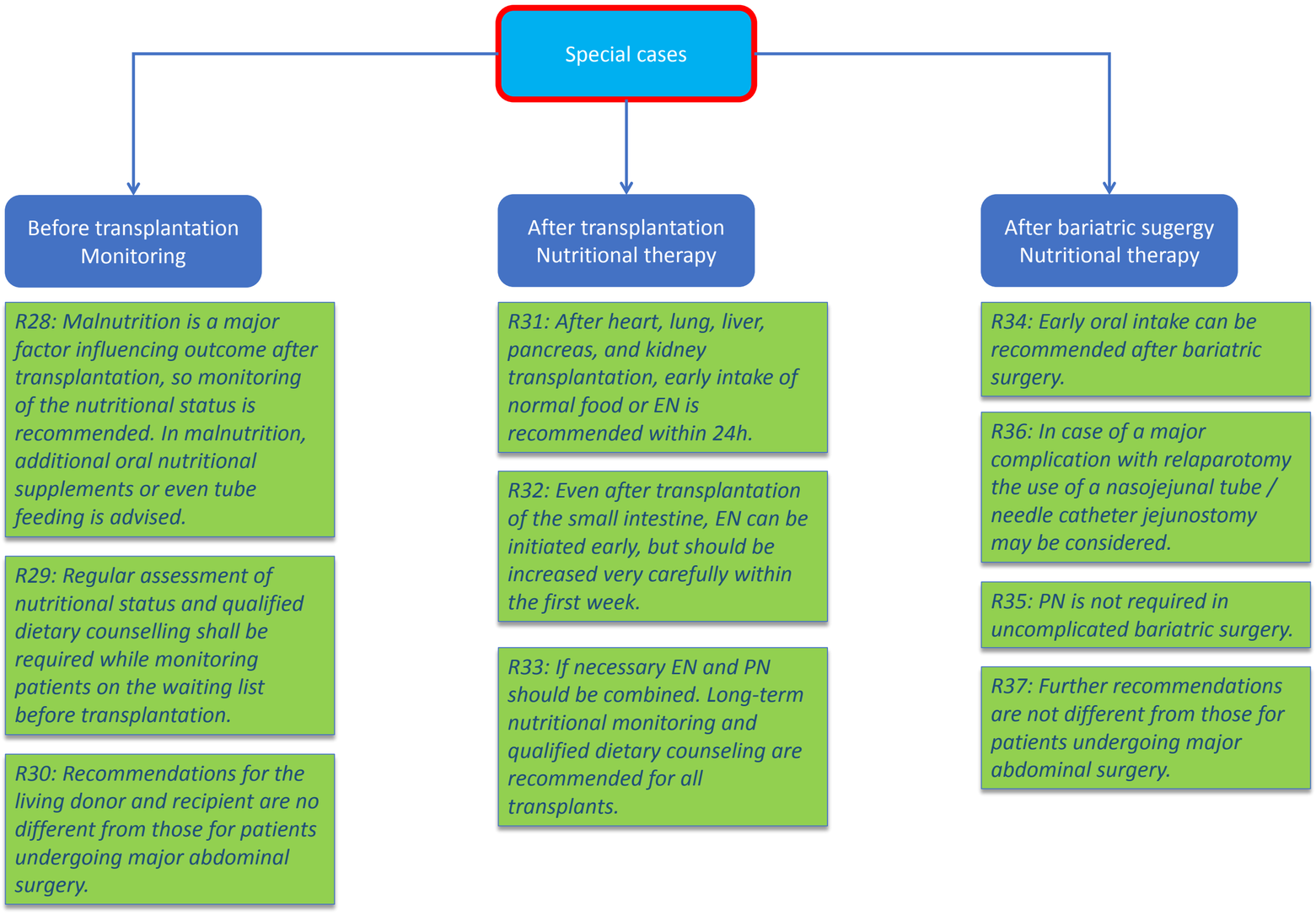
R8: If the energy and nutrient requirements cannot be met by oral and enteral intake alone (<50% of caloric requirement) for more than seven days, a combination of EN and PN is recommended. PN shall be administered as soon as possible if nutrition therapy is indicated and there is a contraindication for EN, such as in intestinal obstruction.

R9: For administration of PN an all-in–one (three-chamber bag or pharmacy prepared) should be preferred instead of multibottle system.

R11: Parenteral glutamine supplementation may be considered in patients who cannot be fed adequately enterally and, therefore, require exclusive PN.

R12: Postoperative PN including omega-3-fatty acids should be considered only in patients who cannot be adequately fed enterally and, therefore, require PN.

Figure 4: Special cases: organ transplantation and bariatric surgergy



ESPEN Practical Guideline: Clinical Nutrition in Surgery

Arved Weimann[a*], Marco Braga[b], Franco Carli[c], Takashi Higashiguchi[d], Martin Hübner[e], Stanislaw Klek[f], Alessandro Laviano[g], Olle Ljungqvist[h], Dileep N. Lobo[i], Robert G. Martindale[k], Dan Waitzberg[l], Stephan C. Bischoff[m], Pierre Singer[n]

Based on

ESPEN guideline: Clinical nutrition in surgery

Arved Weimann, Marco Braga, Franco Carli, Takashi Higashiguchi, Martin Hübner, Stanislaw Klek, Alessandro Laviano, Olle Ljungqvist, Dileep N. Lobo, Robert Martindale, Dan L. Waitzberg, Stephan C. Bischoff, Pierre Singer

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[a] Department of General, Visceral and Oncological Surgery, St. George Hospital, Leipzig, Germany

[b] University of Milano-Bicocca, San Gerardo Hospital, Monza, Italy

[c] Department of Anesthesia of McGill University, School of Nutrition, Montreal General Hospital, Montreal, Canada

[d] Yonaha General Hospital, Kuwana-city, Mie, Japan

[e] Service de chirurgie viscérale, Centre Hospitalier Universitaire de Lausanne, Lausanne, Switzerland

[f] General Surgical Oncology Clinic, National Cancer Institute, Krakow, Poland

[g] Department of Translational and Precision Medicine, Sapienza University, Rome, Italy

[h] Department of Surgery, Faculty of Medicine and Health, Orebro University, Orebro, Sweden

[i] Gastrointestinal Surgery, Nottingham Digestive Diseases Centre, National Institute for Health Research Nottingham Biomedical Research Centre, Nottingham University Hospitals and University of Nottingham, Queen's Medical Centre, Nottingham, United Kingdom

[k] Oregon Health Sciences University, Portland, Oregon, USA

[l] University of Sao Paulo Medical School, Ganep – Human Nutrition, Sao Paulo, Brasil

[m] Institut für Ernährungsmedizin, Universität Hohenheim, Stuttgart, Germany

[n] Institute for Nutrition Research, Rabin Medical Center, Beilison Hospital, Petah Tikva, Israel

Key words

Surgery; perioperative nutrition; nutritional therapy; enteral nutrition; parenteral nutrition; bariatric surgery; organ transplantation; ERAS; prehabilitation.

Abbreviations

BMI, body mass index; EN, enteral nutrition; ERAS, Enhanced Recovery after Surgery; LOS, hospital length of stay; NCJ, needle catheter jejunostomy; ONS, oral nutritional supplements; PEG, percutaneous endoscopic gastrostomy; PN, parenteral nutrition; RCT, randomized controlled trial; SOP, standard operating procedure

*Corresponding author
Professor Dr. Arved Weimann,
Klinik für Allgemein-, Viszeral- und Onkologische Chirurgie
Klinikum St. Georg gGmbH,
Delitzscher Straße 141,
04129 Leipzig / Germany
Phone +49 341 909 2200,
Fax: +49 341 909 2234
E-Mail: Arved.Weimann@sanktgeorg.de

Abstract

Early oral feeding is the preferred mode of nutrition for surgical patients. Avoidance of any nutritional therapy bears the risk of underfeeding during the postoperative course after major surgery. Considering that malnutrition and underfeeding are risk factors for postoperative complications, early enteral feeding is especially relevant for any surgical patient at nutritional risk, especially for those undergoing upper gastrointestinal surgery. The focus of this guideline is to cover both nutritional aspects of the Enhanced Recovery After Surgery (ERAS) concept and the special nutritional needs of patients undergoing major surgery, e.g. for cancer, and of those developing severe complications despite best perioperative care. From a metabolic and nutritional point of view, the key aspects of perioperative care include the integration of nutrition into the overall management of the patient, avoidance of long periods of preoperative fasting, re-establishment of oral feeding as early as possible after surgery, the start of nutritional therapy immediately if a nutritional risk becomes apparent, metabolic control e.g. of blood glucose, reduction of factors which exacerbate stress-related catabolism or impaired gastrointestinal function, minimized time on paralytic agents for ventilator management in the postoperative period, and early mobilization to facilitate protein synthesis and muscle function.

Preliminary remarks

1. PRINCIPLES OF METABOLIC AND NUTRITIONAL CARE

As a key component of Enhanced Recovery after Surgery programs (ERAS), nutritional management is an inter-professional challenge. These ERAS programs also include a metabolic strategy to reduce perioperative stress and improve outcomes (1). "Prehabilitation" aims at conditioning metabolic risk for ERAS meaning a trimodal approach including a nutrition, physical exercise, and stress-reducing psychological component (2). A significant reduction in the number of complications was shown in elderly high-risk patients with American Society of Anesthesiologists (ASA) classifications Grade III and IV, (3). Meta-analyses showed that prehabilitation may contribute to decreased postoperative complication rates and shortened hospital length of stay (LOS) in patients undergoing major abdominal surgery (4-6).

Evidence of nutritional therapy

Obscured by obesity reduced muscle mass (sarcopenia) and malnutrition may be underestimated and ignored in surgical patients. There is clear evidence that malnutrition is associated with worse outcomes, and major surgical stress and trauma will induce catabolism. The extent of catabolism is related to the magnitude of surgical stress but also the outcome.

In a recent meta-analysis of 29 studies including 7,179 patients, sarcopenia was associated with an increased risk of postoperative major and total complications in patients undergoing surgery for gastrointestinal cancer (7).

Perioperative nutritional supplementation has been shown in a recent meta-analysis of 56 trials including 6,370 patients to decrease postoperative infectious and non-infectious complications, and also LOS in patients undergoing gastrointestinal cancer surgery (8).

In complex medical conditions like the perioperative patient undergoing major surgery, the geriatric patient, or in the critically ill the outcome will be related to multiple associated factors. Regarding a nutritional intervention, an existing effect may be too weak to show significant impact in a prospective randomized controlled trial (RCT) with a feasible number of patients to be included, even in a multicenter setting. However, the combination of the nutritional intervention with some other therapeutic items as a treatment bundle like in the ERAS program may show significant benefit (9).

2. METHODOLOGY

The present practical guideline consists of 37 recommendations and is based on the ESPEN guideline: Clinical nutrition in surgery(10). The original guideline was shortened by restricting the commentaries to the gathered evidence and literature on which the recommendations are based on. The recommendations were not changed, only the language was adapted to American English, but the presentation of the content was transformed into a graphical presentation consisting of decision-making flow charts wherever possible. The original guideline was developed according to the standard operating procedure (SOP) for ESPEN guidelines (11). This SOP is oriented on the methodology of the Scottish Intercollegiate Guidelines Network (SIGN). Literature was searched and graded into 1-4 according to evidence, and recommendations were created and graded into four classes (A/B/0/GPP). All recommendations were not only based on evidence but also underwent a consensus process, which resulted in a percentage of agreement (%). Whenever possible, representatives from different professions (physicians, dieticians, nurses, others) as well as patient representatives were involved.

The guideline process was funded exclusively by the ESPEN society. The guideline shortage and dissemination were funded in part by the UEG society, and also by the ESPEN society. For further details on methodology, see the full version of the ESPEN guideline (10) and the ESPEN SOP (11).

3. BASIC QUESTIONS

3.1 Is preoperative fasting necessary?

Recommendation 1

Preoperative fasting from midnight is unnecessary in most patients. Patients undergoing surgery, who are considered to have no specific risk of aspiration, shall drink clear fluids until two hours before anesthesia. Solids shall be allowed until six hours before anesthesia.

Grade of recommendation A – strong consensus (97 % agreement)

Commentary

There is no evidence that patients given clear fluids up to two hours before elective operations are at any greater risk of aspiration or regurgitation than those fasted for the traditional twelve hours or longer since clear fluids empty the stomach within 60 – 90 minutes (12-14). Many national anesthesia societies have changed their fasting guidelines (15-17) and now recommend that patients may drink clear fluids up to two hours before anesthesia 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 (12) or gastroesophageal reflux. 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. Avoidance of fasting is also a key component of ERAS. Allowing intake of clear fluids including coffee and tea minimizes the discomfort of thirst and headaches from withdrawal symptoms.

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

Recommendation 2

In order to reduce perioperative discomfort including anxiety oral preoperative carbohydrate treatment (instead of overnight fasting, the night before and two hours before surgery) should be administered (B). To impact postoperative insulin resistance and LOS, preoperative carbohydrates can be considered in patients undergoing major surgery (0).

Grade of recommendation B/0 – strong consensus (100% agreement)

Commentary

Preoperative intake of a carbohydrate drink with 800 ml the night before and 400 ml before surgery does not increase the risk of aspiration (12, 17, 18). Fruit-based lemonade may be considered a safe alternative with no difference in gastric emptying time (19). Oral carbohydrates have been reported to improve postoperative well being (20-23). A meta-analysis of 21 RCT on preoperative oral carbohydrate treatment in elective surgery including 1,685 patients showed a significant reduction of LOS only in the patients undergoing major surgery. There was no difference in complication rates (24). Another meta-analysis including 27 RCT with 1,976 patients, confirmed the reduction of LOS. There was no clear influence on the complication rate after elective surgery. Lack of adequate blinding in many placebo-controlled studies was considered a potential bias (25). Another meta-analysis, including 43 trials with 3,110 participants showed only a small reduction in length of postoperative stay compared with fasting, and no benefit in comparison with water and placebo. No difference in the postoperative complication rate was observed (26). For a detailed methodological discussion see the long guideline version (10). The most recent multicentric RCT included 662 patients. While significantly less patients had the requirement of one dose insulin/day and blood glucose levels >140mg/dl, no difference in clinical complications could be found (27). In order to avoid any harm carbohydrate drink should not be used in patients with severe diabetes with special regard to those with anticipated gastroparesis.

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

<u>Recommendation 3</u>

In most instances, oral nutritional intake shall be continued after surgery without interruption.

Grade of recommendation A – strong consensus (90 % agreement)

Commentary

Oral nutrition (balanced hospital diet and/or ONS) can be initiated, in most cases, immediately after surgery. Early oral nutrition is also a key component of ERAS, which demonstrated a significantly lower rate of complications and LOS in meta-analyses of the

randomized studies (28, 29). Neither esophagogastric decompression nor delayed oral intake, even after cholecystectomy or colorectal resection have proven beneficial (30-32).

Recommendation 4

It is recommended to adapt oral intake according to individual tolerance and to the type of surgery carried out with special caution to elderly patients.

Grade of recommendation GPP – strong consensus (100 % agreement)

Commentary

In comparison with conventional open surgery, early oral intake is tolerated even better after laparoscopic colonic resection, due to earlier return of peristalsis and bowel function with this technique (33-35). However, in combination with ERAS no differences were found between laparoscopic and conventional open colonic surgery when the full ERAS protocol was employed (36). In the multicenter RCT postoperative LOS was significantly shorter in the ERAS group undergoing laparoscopic surgery (37). A recent meta-analysis confirmed the reduction of major morbidity and LOS by the combination of laparoscopic surgery and ERAS (38). The amount of initial oral intake should be adapted to the state of gastrointestinal function and individual tolerance.

Recommendation 5

Oral intake, including clear liquids, shall be initiated within hours after surgery in most patients.

Grade of recommendation A – strong consensus (100 % agreement)

Commentary

Early normal food or EN, including clear liquids on the first or second postoperative day, does not cause impairment of healing of anastomoses in the colon or rectum (32, 39-42) and leads to significantly shortened LOS (43). This has been emphasized by a Cochrane Systematic Review (44). Recent meta-analyses (45-47) showed significant benefits concerning postoperative recovery and infection rate. Early postoperative nutrition is associated with significant reductions in total complications compared with traditional postoperative feeding practices and does have no negative effect on outcomes such as mortality, anastomotic dehiscence, resumption of bowel function, or LOS (47). This has

been also shown for patients after total gastrectomy (48) and minimally invasive esophagectomy (49). A meta-analysis of 15 studies (eight RCT) with 2112 adult patients undergoing upper gastrointestinal surgery showed significantly shorter postoperative LOS in early orally fed patients without a difference in complications with special regard to anastomotic leaks (50).