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ESPEN guideline: Clinical nutrition in surgery

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SUMMARY

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 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:

- 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
- start of nutritional therapy early, as soon as a nutritional risk becomes apparent
- metabolic control e.g. of blood glucose
- reduction of factors which exacerbate stress-related catabolism or impair gastrointestinal function
- minimized time on paralytic agents for ventilator management in the postoperative period
- early mobilisation to facilitate protein synthesis and muscle function

The guideline presents 37 recommendations for clinical practice.

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Important abbreviations and terms

BM	biomedical endpoints
EN	enteral nutrition (enteral tube feeding)
ERAS	enhanced recovery after surgery
ESPEN	European Society for Clinical Nutrition and Metabolism
HE	health care economy endpoint
IE	integration of classical and patient-reported endpoints
ONS	oral nutritional supplements
PN	parenteral nutrition
QL	quality of life
TF	tube feeding
Normal food/normal nutrition	normal diet as offered by the catering system of a hospital including special diets
Perioperative nutrition	period starting prior to surgery from hospital admission until discharge after surgery

1. Preliminary remarks – Principles of metabolic and nutritional care

In order to make proper plans for the nutritional support of patients undergoing surgery, it is essential to understand the basic changes in metabolism that occur as a result of injury, and that a compromised nutritional status is a risk factor for postoperative complications. Starvation during metabolic stress from any type of injury differs from fasting under physiological conditions [1]. Surgery itself leads to inflammation corresponding with the extent of the surgical trauma, and leads to a metabolic stress response. To achieve appropriate healing and functional recovery ("*restitutio ad integrum*") a metabolic response is necessary, but this requires nutritional therapy especially when the patient is malnourished and the stress/inflammatory response is prolonged. The negative effect of long term caloric and protein deficits on outcome for critically ill surgical patients has been shown again recently [2]. The success of surgery does not depend exclusively on technical surgical skills, but also on metabolic interventional therapy, taking into account the ability of the patient to carry a metabolic load and to provide appropriate nutritional support. In patients with cancer, management during the perioperative period may be crucial for long-term outcome [3,4].

Surgery, like any injury, elicits a series of reactions including release of stress hormones and inflammatory mediators, i.e. cytokines. The cytokine response to infection and injury, the so-called "Systemic Inflammatory Response Syndrome", has a major impact on metabolism. The syndrome causes 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 purpose of maintaining peripheral protein (especially muscle) mass, to the tasks of healing and immune response [5,6]. The consequence of protein catabolism is the loss of muscle tissue which is a short and long-term burden for functional recovery which is considered the most important target [7]. In order to spare protein stores, lipolysis, lipid oxidation, and decreased glucose oxidation are important survival mechanisms [8]. Nutritional therapy may provide the energy for optimal healing and recovery, but in the immediate postoperative phase may only minimally counteract muscle catabolism, or not at all. To restore peripheral protein mass the body needs to deal with the surgical trauma and possible infection adequately. Nutritional support/intake and physical exercise are prerequisites to rebuild peripheral protein mass/body cell mass.

Patients undergoing surgery may suffer from chronic low-grade inflammation as in cancer, diabetes, renal and hepatic failure [9]. Other non-nutritional metabolic factors interfering with an adequate immune response have to be taken into account and, whenever possible, corrected or ameliorated before surgery. These are diminished cardio-respiratory organ function, anaemia, acute and chronic intoxications (e.g. alcohol, recreational drugs), medical treatment with anti-inflammatory and cytotoxic drugs.

The surgeon has to balance the extent of surgery according to nutritional state, inflammatory activity and anticipated host response. Severe pre-existing inflammation and sepsis influence healing negatively (wounds, anastomoses, immune function, etc.) but also decrease the benefit of nutritional therapy. Severely malnourished patients may exhibit an adynamic form of sepsis with hypothermia, leukopenia, somnolence, impaired wound healing and pus production, altogether leading to slow deterioration and mortality. In this situation nutritional therapy will not maintain or build up muscle mass but may restore an adequate stress response, promoting the chances of recovery. Awareness for the impaired inflammatory stress response means limiting the extent of the surgical trauma and may lead to uneventful recovery.

Severely compromised patients should receive perioperative nutritional therapy of longer duration or when acute intervention is required, surgery should be limited or minimally invasive interventional techniques should be preferred to relieve infection/ischaemia.

In order to optimize the mildly malnourished patient short-term (7–10 days) nutritional conditioning has to be considered. In severely malnourished patients longer periods of nutritional conditioning are necessary and this should be combined with resistance exercise. In the truly infected patient immediately dealing with the focus of sepsis ("source control") should have priority and no major surgery should be performed (risky anastomoses, extensive dissections etc.). Definitive surgery should be performed at a later stage when sepsis has been treated adequately.

In elective surgery it has been 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 programmes for Fast Track surgery [10] later developed into Enhanced Recovery after Surgery (ERAS). A series of components that combine to minimize stress and to facilitate the return of function have been described: these include preoperative preparation and medication, fluid balance, anaesthesia and postoperative analgesia, pre- and postoperative nutrition, and mobilization [5,11–13]. The ERAS programmes have now become a standard in perioperative management that has been adopted in many countries across several surgical specialties. They were developed in colonic operations [11,14–17] and are now being applied to all major operations. ERAS programmes have been also successful in promoting rapid "functional" recovery after gastrectomy [18], pancreatic resections [19,20], pelvic surgery [21,22], hysterectomy [23], gynaecologic oncology [24]. In times of limitations in health care economy ERAS is also a reasonable contribution for the purpose of saving resources [25]. ERAS protocols have been also shown to be safe and beneficial in the elderly [26]. High adherence to ERAS protocols may be associated with improved 5-year cancer specific survival after major colorectal surgery [4].

As a key component of ERAS, nutritional management is an inter-professional challenge. The ERAS programmes also include a metabolic strategy to reduce perioperative stress and improve outcomes [12]. While early oral feeding is the preferred mode of nutrition, avoidance of any nutritional therapy bears the risk of underfeeding during the postoperative course after major surgery. Keeping in mind that the nutritional status is a risk factor for postoperative complications, this is especially relevant for patients at nutritional risk and those undergoing upper gastrointestinal (GI) surgery. For this reason, ERAS guidelines recommend liberal subscription of oral supplements pre- and postoperatively. Equally ERAS protocols support early oral intake for the return of gut function.

From a metabolic and nutritional point of view, the key aspects of perioperative care include:

- 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
- start of nutritional therapy early, as soon as a nutritional risk becomes apparent
- metabolic control e.g. of blood glucose
- reduction of factors which exacerbate stress-related catabolism or impair gastrointestinal function
- minimize time on paralytic agents for ventilator management in the postoperative period
- early mobilisation to facilitate protein synthesis and muscle function.

1.1. Nutrition therapy

Nutrition therapy. Synonym: nutritional support is defined according to the European Society for Clinical Nutrition and Metabolism (ESPEN) [27,28]:

Nutrition therapy is the provision of nutrition or nutrients either orally (regular diet, therapeutic diet, e.g. fortified food, oral nutritional supplements) or via enteral nutrition (EN) or parenteral nutrition (PN) to prevent or treat malnutrition. “Medical nutrition therapy is a term that encompasses oral nutritional supplements, enteral tube feeding (enteral nutrition) and parenteral nutrition” [27]. Enteral and parenteral nutrition have traditionally been called artificial nutritional support. Nutrition therapies are individualized and targeted nutrition care measures using diet or medical nutrition therapy. Dietary advice or nutritional counselling can be part of a nutrition therapy.

In the surgical patient, the indications for nutritional therapy are prevention and treatment of catabolism and malnutrition. This affects mainly the perioperative maintenance of nutritional state in order to prevent postoperative complications [29]. Therapy should start as a nutritional risk becomes apparent. Criteria for the success of the “therapeutic” indication are the so-called “outcome” parameters of mortality, morbidity, and length of hospital stay, while taking into consideration economic implications. The improvement of nutritional status and functional recovery including quality of life are most important nutritional goals in the late postoperative period.

Nutrition therapy may be indicated even in patients without obvious disease-related malnutrition, if it is anticipated that the patient will be unable to eat or cannot maintain appropriate oral intake for a longer period perioperatively. In these situations, nutrition therapy may be initiated without delay. Altogether, it is strongly recommended not to wait until severe disease-related malnutrition has developed, but to start nutrition therapy early, as soon as a nutritional risk becomes apparent.

Nutritional care protocols for the surgical patient must include

- a detailed nutritional and medical history that includes body composition assessment
- a nutrition intervention plan
- an amendment of the intervention plan, where appropriate
- clear and accurate documentation assessment of nutritional and clinical outcome
- resistance exercise whenever possible

Therefore, as a basic requirement a systematic nutritional risk screening (NRS) has to be considered in all patients on hospital admission [30]. The items of the NRS comprise BMI <20.5 kg/m^2, weight loss >5% within 3 months, diminished food intake, and severity of the disease. In older adults comprehensive geriatric assessment is necessary and should definitely include NRS [31].

In order to improve oral intake documentation of food intake is necessary and nutritional counselling should be provided as needed. Oral nutritional supplements (ONS) and EN (tube feeding) as well as PN offer the possibility to increase or to ensure nutrient intake in case of insufficient oral food intake.

1.2. Preoperative nutritional care

1.2.1. Nutritional “metabolic” risk and disease-related malnutrition

Assessment before surgery means risk assessment according to pathophysiology [32]. Severe undernutrition has long been known to be detrimental to outcome [33–36]. Malnutrition is generally considered to be associated with starving and lack of food. Its presence in the Western world with an increasing percentage of obese people is frequently neither realized nor well understood. Disease Related Malnutrition (DRM) is more subtle than suggested by the World Health Organization (WHO) definition of undernutrition with a body mass index (BMI) < 18.5 kg/m^2 (WHO) [28,37]. Disease related weight loss in patients who are overweight is not necessarily associated with a low BMI. However, this weight loss results in changes in body composition with a loss of fat free mass inducing a “metabolic risk” which has to be kept in mind for patients undergoing major surgery with special regard to cancer. Additionally, chronic low-grade inflammation may be a component of malnutrition [9].

ESPEN has recently defined diagnostic criteria for malnutrition according to two options [28]

- option 1: BMI <18.5 kg/m^2
- option 2: combined: weight loss >10% or >5% over 3 months and reduced BMI or a low fat free mass index (FFMI).

Reduced BMI is <20 or <22 kg/m^2 in patients younger and older than 70 years, respectively. Low FFMI is <15 and <17 kg/m^2 in females and males, respectively.

Because DRM is frequently not recognized and therefore untreated, metabolic factors will usually not be considered for the critical analysis of surgical morbidity and outcome. In traditional surgical care many retrospective and prospective studies (References in ESPEN guidelines 2006, [38]) have shown clearly the prognostic influence of nutritional status on complications and mortality. A systematic review of ten studies revealed a validated nutritional tool a predictor for length of hospital stay in gastrointestinal cancer patients requiring surgery [39]. DRM is also relevant for outcome after organ transplantation (see references [38]). Data from the European “NutritionDay” in about 15,000 patients clearly showed that “metabolic risk” is a factor for hospital mortality, with special focus on the elderly [40].

According to the prospective data from a multicentre trial, most patients at risk will be found in hospital in the departments of surgery, oncology, geriatrics, and intensive care medicine. The univariate analysis revealed significant impact for the hospital complication rate: severity of the disease, age >70 years, surgery and cancer [41]. Bearing in mind the demographic development in the Western world, surgeons will have to deal with an increased risk of developing complications in the elderly undergoing major surgery for cancer.

The metabolic risk associated with DRM can be detected easily by the “Nutritional Risk Score” [30]. This tool has been validated prospectively in recent studies for surgical patients as well [41,42].

Recently, one study reported that a lower food intake before hospital admission alone was an even better risk predictor than NRS [43]. A systematic review of 15 studies on elderly general surgery patients (>65 years) from 1998 to 2008 revealed that weight loss and serum albumin concentration were predictive parameters for postoperative outcome [44]. This has been confirmed in a recent cohort study of patients undergoing major upper gastrointestinal surgery [7].

For clinical practice these data emphasize:

- screening for malnutrition (e.g. Nutritional Risk Screening – NRS) on admission or first contact
- observation and documentation of oral intake
- regular follow-up of weight and BMI
- nutritional counselling

Preoperative serum albumin is a prognostic factor for complications after surgery [7,45–50] and also associated with impaired nutritional status. Therefore, albumin may also be considered to define surgical patients at severe nutritional risk 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 (SGA) Grade C or NRS >5
- preoperative serum albumin <30 g/l (with no evidence of hepatic or renal dysfunction).

For patients at high risk preoperative conditioning has been a traditional approach to optimize the patient's status before major elective surgery. After earlier surgery with infectious complications, at least 6 weeks and sometimes longer may be required to restore a metabolic and nutritional state allowing a successful reoperation [51,52]. In case of severe metabolic risk 10–14 days of nutritional therapy may be beneficial, but without measurable change in body composition or serum albumin concentration. While this concept focuses on EN or PN support only, “prehabilitation” has been recently introduced, and is an inter-professional multimodal approach [5]. The premise of the multimodal prehabilitation approach with a nutrition and physical exercise component rests on their synergy. Regarding the clinical impact of prehabilitation two recent meta-analyses concluded that preoperative exercise therapy contributed to decreased postoperative complication rates and shortened length of stay in patients undergoing cardiac and abdominal surgery [53,54]. The training of inspiratory muscles was also associated with decreased postoperative pulmonary complications.

While physical activity is the main part of this multimodal prehabilitation programme, other functional reserve factors need to be included, such as adequate nutrition, medical and pharmacological optimization and relaxation techniques. There is strong evidence supporting prehabilitation to mitigate the side effects of therapy in patients with cancer [55]. Meaningful changes in functional capacity take 4–5 weeks of prehabilitation and were recently shown for patients undergoing liver resection [56]. Patients with low functional and physiological reserve such as the elderly, frail, sarcopenic and cancer patients could benefit more from prehabilitation than other patient populations. This possibility needs to be studied. Further studies with special regard to elderly cancer patients are needed to determine the impact of prehabilitation as part of the preoperative optimization on postoperative outcome (complications, length of hospital stay, readmission rate).

“Metabolic conditioning” of the patient focuses on prevention and treatment of insulin resistance, which is also a measure to reduce complications after major surgery. Preoperative carbohydrates may reduce insulin resistance, prevent hypoglycaemia and may reduce stress. Focussing on the magnitude of stress-induced inflammation and the ability of the patient to generate an adequate host response has led to the concept of “immunonutrition”. So-called “ecoimmunonutrition” using pre- and probiotics aims at the microbiome in the gut and the enhancement of mucosal immunity [57].

1.3. Surgery

To balance the extent of surgery with the ability of the body to deal with the metabolic load may be a considerable challenge for the surgeon. This refers to relevant comorbidity with special regard to the cardiopulmonary capacity and the presence of inflammation or even more infection and sepsis. If the extent and risk of surgery are not tailored to the capacity of the patient to generate an adequate host response, there is a high risk for anastomotic leakage, infectious/septic complications, and mortality.

After abdominal surgery postoperative ileus may inhibit early oral food intake. Experimental results demonstrate the impact of intraoperative manipulation and subsequent panenteric inflammation as the cause of dysmotility [58,59]. This emphasizes the advantages of minimal invasive and gentle surgical technique [60] in order to minimize the trauma and favours laparoscopic surgery [61].

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 [62]. This was shown to be a major cause for postoperative ileus and delayed gastric emptying [63] and development of complications [64]. When fluids were titrated to the amount needed to maintain intravascular volume, blood pressure and (modest) urine production balance, gastric emptying returned sooner and patients were capable of tolerating oral intake and had bowel movements several days earlier than those with a strongly positive balance, amounting to 8–10 L during operation and the three days after operation [63,64].

The surgeon should anticipate the ability of the patient for appropriate postoperative oral feeding. If considerable problems may be foreseen, the operation offers a unique chance to create safe access for long-term nutrition. Therefore, it may be reasonable to place a nasojejunal tube or needle catheter jejunostomy (NCJ) for EN at the end of major gastrointestinal surgery.

1.4. Postoperative management of metabolism and gut function

Insulin resistance is a response mechanism to starvation predominantly caused by the inhibition of glucose oxidation. It is a protein sparing evolutional “survival” mechanism [8]. Some degree of insulin resistance develops after all kinds of surgery, but its severity is related to the magnitude of the operation and development of complications e.g. sepsis.

Several measures, with additive effects, may contribute to a reduction in insulin resistance, including pain relief [65], continuous epidural analgesia using local anaesthetics [66], and preparation of the patient with preoperative carbohydrates two to three hours before surgery. This has implications for nutritional management since patients with marked insulin resistance cannot tolerate feeding without developing hyperglycaemia, necessitating the use of insulin to limit hyperglycaemia.

Using this approach of preoperative carbohydrate loading and continuous epidural analgesia, and immediate postoperative complete enteral feeding in patients undergoing colorectal surgery, postoperative insulin resistance was reduced greatly. Glucose concentrations were maintained within the normal range during feeding without any exogenous insulin, and nitrogen losses were also reduced [67]. Another factor that affects tolerance of normal food or EN directly is postoperative ileus, which may be exacerbated and prolonged by opiates and errors in fluid management [58]. The effect of opioids, used for pain relief, can be avoided or substantially minimized in open surgery by the use of epidural analgesia instead [10–12]. Nasogastric or nasojejunal decompression does not facilitate the recovery of bowel function or reduce the risk of postoperative complications even after gastrectomy [68].

Functional recovery is clearly related to the tolerance of oral food intake, restored gastrointestinal motility, and mobilization. During the postoperative course, this should be observed carefully and documented by the surgical team. Vomiting and/or abdominal meteorism, accompanied by an elevation of inflammatory parameters like C-reactive protein (CRP) may be first signals of a complicated course e.g. anastomotic leakage or intraabdominal abscess. This has to be excluded by appropriate diagnostic measures. In order to assess metabolic recovery the CRP/Albumin ratio is a promising new prognostic parameter which has to be validated in the future [69]. Another important parameter is whether the patient has reached the "turning point" successfully. In uneventful recovery after 2–3 days the fluid balance changes from positive to negative. The inflammatory effect of the surgical trauma leads to increased capillary escape of fluid, electrolytes and plasma proteins into the interstitium, which reverts when inflammation subsides leading to re-entry of interstitial fluid into the vascular space. This leads to overhydration and increased urinary output if patients have good renal and cardiac function. Interestingly the increase in interstitial volume and the vascular volume represent the distribution volume of albumin electrolytes and other plasma elements, explaining the rapid decrease in albumin concentration after surgery and increase 3 days after uneventful major surgery. A persistently low, even decreasing or increasing serum albumin concentration is, therefore, a good parameter of whether recovery is successful or not [70]. The magnitude of the postoperative systemic inflammatory response shown in the CRP may be even significantly associated with long-term outcome after surgery independent of postoperative complications or disease stage [71].

1.5. Evidence of nutritional therapy

There is evidence that malnutrition is associated with worse outcome, and it is evident that major surgical stress and trauma will induce catabolism. The extent of catabolism is clearly related to the magnitude of surgical stress but also to the outcome. In complex medical conditions like the perioperative patient undergoing major surgery, the geriatric patient or in the critically ill the outcome will be clearly related to multiple associated factors. Regarding a nutritional intervention an existing effect may be too weak to show significant impact in a prospective controlled randomized study 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 programme may show significant benefit [72].

The evidence for nutritional therapy interventions in surgical patients has been critically assessed in several meta-analyses and Cochrane Database Systematic Reviews [73,74]. There is considerable heterogeneity and inconsistency. In many aspects the evidence is still of low quality and is unconvincing. There are many shortcomings in these studies and subsequent meta-analyses. Most did not select patients at nutritional risk for inclusion. Of course, there is need for more well-designed randomized controlled trials (RCTs), sufficiently powered in homogenous groups of patients with clearly defined endpoints. It is the typical dilemma that Gerritsen et al. demonstrated with a systematic review of 15 studies with 3474 patients that there is no evidence to support either enteral or parenteral feeding after pancreatoduodenectomy [73]. The study suggested that an oral diet should be the first choice of feeding in these patients. However the quality of the studies was too low to perform a meta-analysis. Soeters et al. have recently criticized that strong reliance on meta-analyses and guidelines will shift the focus away from studying clinical and nutritional physiology [1]. The authors of the present guideline share this emphasis on physiologic knowledge to personalize nutrition in clinical practice. Clinical observation with a "metabolic" view will remain mandatory.

2. Methodology

2.1. Aim of the guideline

The guideline is a basic framework of evidence and expert opinion aggregated in a structured consensus process. The idea is to cover nutritional aspects of the ERAS concept, that is aimed at most patients undergoing surgery and covers their nutritional needs, and also the special nutritional needs of patients at risk that is based on the traditional principles of metabolic and nutritional care.

Therefore, this guideline focuses on the issue of nutritional support therapy in patients at risk being unable to cover appropriately by oral intake their energy requirements for a longer period of time. The working group attempted to summarize the evidence from a metabolic point of view and to give recommendations for

- surgical patients at nutritional risk
- those undergoing major surgery, e.g. for cancer
- those developing severe complications despite best perioperative care

2.2. Methodology of guideline development

This is the update of the ESPEN Guideline for Enteral Nutrition: Surgery and Transplantation from 2006 [38] the ESPEN Guideline for Parenteral Nutrition: Surgery from 2009 [105] and the Guideline of the German Society for Nutritional Medicine (DGEM) Clinical Nutrition in Surgery from 2013 [75]. Both ESPEN guidelines were merged. The guideline update was developed by an expert group of surgeons of different specialties including an anaesthesist and an internist. All members of the working group had declared their individual conflicts of interest according to the rules of the International Committee of Medical Journal Editors (ICMJE).

The guideline was developed in accordance with official standards of the Guideline International Network (GIN) and based on all relevant publications since 1980 – in the update since 2006 (the German DGEM Guideline had included the period 2006–2012). The process followed in detail the ESPEN Standard Operative Procedure for the development of guidelines [76].

During the working process the internet portal www.guideline-services.com provided access to the draft and the literature at any time exclusively for members of the working group. Revisions of the first drafts incorporating the points discussed were prepared by the working groups and were made available to the other ESPEN Guideline working groups on the internet platform for commenting and voting (Delphi technique). The updated recommendations and the first voting were intensively discussed in a consensus conference on April 18, 2016 and accepted after revision by voting consent of at least 95% the same day.

2.3. Search strategy

The Embase, PubMed and Cochrane Library databases were searched for studies and systematic reviews published between 2010 and 2015 using a broad filter with the key words "enteral nutrition AND surgery" and "parenteral nutrition AND surgery" (Table 1). Further key words were "immunonutrition" and "bariatric surgery AND nutrition" (see Table 1). Only articles published in English and German, and studies in humans were considered. All fields were covered. Additionally, RCTs, meta-analyses, and systematic reviews were hand-searched for studies that were missed in the initial database search. The search for literature was updated several times during the working process for the last time on October 31, 2016. According to the abstracts all studies considered to be appropriate were listed with the pdf file in the internet portal and, therefore, available for all members of the working group at any time. Practice guidelines were assessed using the DELBI instrument (Deutsches Leitlinien Bewertungs Instrument).

The quality and strength of the supporting evidence was graded according to the criteria of the Scottish Intercollegiate Guidelines Network (SIGN) (Scottish) and the Agency for Health Care Policy and Research (AHCPR). This grading system relies primarily on studies of high quality, i.e. prospective RCTs. Evidence levels were then translated into recommendations, taking into account study design and quality as well as consistency and clinical relevance (Tables 2–4). The highest grade (A) is assigned to recommendations which are based on at least one RCT whereas the lowest recommendation (0) is based on expert opinion, including the view of the working groups. These two grading systems were chosen because they were used in the German guideline development and were proposed in the German Manual for Clinical Practice Guidelines [AWMF 2001]. For the update RCTs were assessed in part by using the AWMF template (see Table 4).

Those areas where guidelines are being classified as being based on class IV data reflect an attempt to make the best recommendations possible within the context of the available data and expert clinical experience. Some of the recommendations of these guidelines were developed on the basis of expert opinion because of the ethical dilemma of conducting prospective RCTs involving patients at risk of starvation.

In the case of inconsistent data the following approach was chosen. The recommendations were not only based on the evidence levels of the studies but also on the judgement of the working group concerning the consistency, clinical relevance and validity of the evidence [77]. For perioperative enteral and parenteral immunonutrition several systematic reviews and meta-analyses had been published in the past years. These meta-analyses were analysed by an external methodologist from the Ärztliches Zentrum für Qualität in der Medizin (ÄZQ). The guideline recommendations were based on this ÄZQ report [78].

Using a new approach to differentiate outcome parameters [72], the recommendations were weighed according to the type of evidence-based endpoints: biomedical, multidimensional, health economy, and quality of life.

The draft was reviewed by two senior surgeons and Professors Emeriti Federico Bozzetti (Milan, Italy) and Peter Soeters (Maastricht, The Netherlands), who were not involved in the guideline development themselves and had also declared their conflicts of interest.

Table 1
Criteria for systematic search for literature – databases and keywords.

Publication date	From 01.01.2010 to 17.05.2015
Language	English, German
Databases	Medline, EMBASE, Pubmed, Cochrane
Filter	"human"
Publication type	Original publications, practice guidelines, recommendations, meta-analyses, systematic reviews, randomized controlled trials, observational studies
Default keywords	Enteral nutrition AND surgery, parenteral nutrition AND surgery, Nutrition AND elective surgery, Nutritional risk Enteral nutrition AND surgery Parenteral nutrition AND surgery Perioperative nutrition Perioperative nutritional support Preoperative nutrition Postoperative nutrition
Optional keywords	Bariatric surgery AND nutrition Transplantation AND nutrition Oral nutritional supplements AND surgery Sip feeding AND surgery Immunonutrition AND surgery Pharmaconutrition AND surgery Glutamine AND surgery Arginine AND surgery Fish oil AND surgery Omega-3-fatty acids AND surgery Probiotics AND surgery Prebiotics AND surgery Tube feeding AND surgery Fine-needle-catheter jejunostomy Feeding jejunostomy Jejunostomy

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 anaesthesia. Solids shall be allowed until six hours before anaesthesia (BM, IE, QL).

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

Table 2
Levels of evidence.

1++	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1+	Well-conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
1-	Meta-analyses, systematic reviews, or RCTs with a high risk of bias
2++	High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
2+	Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
2-	Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
3	Non-analytic studies, e.g. case reports, case series
4	Expert opinion

Table 3
Grades of recommendations (SIGN).

A	1++ or 1+	At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results
B	2++ or 2+	A body of evidence including studies rated as 2++, directly applicable to the target population; or a body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results: or extrapolated evidence from studies rated as 1++ or 1+.
0	3 or 4	Evidence level 3 or 4; or extrapolated evidence from studies rated as 2++ or 2+
GPP		Good practice points. Recommended best practice based on the clinical experience of the guideline development group

Table 4
Forms of recommendation.

Judgement	Recommendation
Undesirable consequences clearly outweigh desirable consequences	Strong recommendation against
Indesirable consequences probably outweigh desirable consequences	Conditional recommendation against
Balance between desirable and undesirable consequences is closely balanced or uncertain	Recommendation for research and possibly conditional recommendation for use restricted to trials
Desirable consequences probably outweigh undesirable consequences	Conditional recommendation for
Desirable consequences clearly outweigh undesirable consequences	Strong recommendation for

Terminology and definitions follow the ESPEN guidelines [28].

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 12 h or longer, since clear fluids empties the stomach within 60–90 min [79] (1++), [80,81] (both 1+). Many national anaesthesia societies have changed their fasting guidelines [82–84] and now recommend that patients may drink clear fluids up to two hours 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 [79] or gastro-oesophageal reflux [81 (1++). 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) (QL). To impact postoperative insulin resistance and hospital length of stay, preoperative carbohydrates can be considered in patients undergoing major surgery (0) (BM, HE).

Consensus Conference: Grade of recommendation A/B – strong consensus (100% agreement)- downgraded by the working group during the finalization process according to the very recent meta-analysis [102] (with 100% agreement within the working group members)

Commentary:

Preoperative intake of a carbohydrate drink (so-called "CHO-loading") with 800 ml the night before and 400 ml before surgery does not increase the risk of aspiration [79,84,85]. Fruit-based lemonade may be considered a safe alternative with no difference in gastric emptying time [86] (2++).

Oral carbohydrates have been reported to improve postoperative well being [87–90]. Two studies have investigated the effect of a preoperative carbohydrate drink (CHO) on postoperative nausea and vomiting (PONV) in patients undergoing laparoscopic cholecystectomy [91,92] (both 1+). One showed a reduction in PONV with CHO compared to fasting, while neither showed a clear difference between CHO and placebo [91,92] (both 1+).

In colorectal patients, the intake of a hypo-osmolar 12.5% carbohydrate rich drink has been shown to reduce postoperative insulin resistance [67,93] (both 1+). In another PRCT no improvement of the grip strength was found within the first seven days postoperatively [89] (1+). With regard to the control group cardiac ejection fraction and psychosomatic status proved to be significantly better. In the patients of the control group with conventional fasting insulin resistance significantly increased what was not observed in der CHO-group. Complication rate and hospital length of stay between CHO– and control group did not differ [89] (1+). In several studies so called insulin resistance has been determined using methods based in basal fasting glucose and insulin. These methods, HOMA (Homeostasis Model Assessment) and QUICKI (Quantitative Insulin Sensitivity Check Index) do not capture insulin resistance and hence these methods measure something different from the true method of determination the hyperinsulinemic euglycemic clamping [94]. In the latter study "insulin resistance" was measured by QUICKI. In another PRCT with 36 patients undergoing elective colorectal (fasting *vs.* water *vs.* maltodextrin drink) surgery showed a significantly shorter length of hospital stay (study drink *vs.* water, $p = 0.019$) and a tendency for earlier recovery of gut function [95] (1+). A PRCT with 142 patients undergoing open colorectal or liver surgery did not reveal any significant advantage for the CHO drink with regard to early postoperative plasma glucose sensitivity, insulin resistance (HOMA), and inflammation (C reactive protein). However, plasma cortisol level was significantly lower on pod 1, which might be related to stress reduction. Within a postoperative 28 days observation period no difference was found for grip strength and mean arm circumference [96] (1+). It may be criticised that epidural analgesia was not performed in all patients and that open and laparoscopic cases were mixed in both treatment groups thereby widening the variation in length of stay.

Three studies in cardiac surgery patients, which examined the influence of preoperative oral CHO on postoperative insulin sensitivity as primary outcome, could not show a significant influence

[97–99] (both 1+), while gastric emptying was not affected in either of the studies and PONV increased in one study [97–99] (both 1+).

A meta-analysis of 21 PRCT on preoperative oral carbohydrate treatment in elective surgery including 1685 patients showed a significant reduction of length of hospital stay only in the patients undergoing major surgery. There was no difference in complication rates. However, the studies were of low or moderate quality [100] (1++). A recent meta-analysis including 27 PRCT with 1976 patients confirmed the reduction of length of hospital stay. There was no clear influence on complication rate after elective surgery. Lack of adequate blinding in many placebo-controlled studies was discussed as potential bias [101] (1++). Another meta-analysis including 43 trials with 3110 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 [102] (1++). It has to be argued that obviously a large number of clinical studies were analysed including patients with minor surgery and very short hospital length of stay.

There are preoperative drinks available which are additionally enriched with glutamine, antioxidants, and green tea extract. In patients undergoing laparoscopic cholecystectomy supplementation of glutamine to CHO showed additional advantages with regard to postoperative insulin resistance (HOMA-IR), antioxidant defence (serum glutathione concentrations), and inflammatory response (serum-interleukin 6) [103] (1−). In pancreatic surgery preconditioning with glutamine, antioxidants, and green tea extract versus placebo significantly elevated plasma vitamin C concentrations and improved total endogenous antioxidant capacity without reducing oxidative stress and inflammatory response [104] (1−). The use of homemade products e.g. sweetened tea has not been investigated in controlled studies.

In order to avoid any harm CHO drink should not be given in patients with severe diabetes with special regard to those with anticipated gastroparesis. CHO drinks are unlikely to be of benefit in patients with Type I diabetes as they are insulin deficient rather than insulin resistant, and the drinks may result in hyperglycaemia.

The ESPEN guideline for parenteral nutrition: surgery recommends in patients who cannot be fed enterally, an intravenous administration of 200 g glucose preoperatively [105]. Positive effects on postoperative stress adaption were reported after parenteral infusion of 1.5–2 g/kg glucose and 1 g/kg amino acids preoperatively (16–20 h) [106] (2+).

From pathophysiological considerations, the metabolic impact of carbohydrate loading is endorsed by the working group with special regard to those patients undergoing major abdominal surgery. So far, no definite conclusions may be drawn with regard to the impact on clinical outcome. Further large scale RCTs will be required.

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

Recommendation 3:

In general, oral nutritional intake shall be continued after surgery without interruption (BM, IE).

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

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)

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:

Oral nutrition (balanced hospital diet and/or ONS) can be initiated, in most cases, immediately after surgery, since neither oesophago-gastric decompression nor delayed oral intake, even after cholecystectomy or colorectal resection have proven beneficial [107–109] (both 1+). 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 [109–112] all (1+), [113] (1++), and leads to significantly shortened hospital length of stay [114] (1+). This has been emphasized by a Cochrane Systematic Review [115] (1++). Recent meta-analyses [116–118] (both 1++) showed significant benefits with regard to 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 a beneficial effect on outcomes such as mortality, anastomotic dehiscence, resumption of bowel function, or hospital length of stay [118] (1++). Early oral nutrition is also a key component of ERAS, which demonstrated a significantly lower rate of complications and hospital length of stay in meta-analyses of the randomized studies [15,16] (both 1++). Early oral feeding is also feasible and safe in patients after colorectal surgery and shortens hospital length of stay outside an ERAS programme [119] (2+).

With regard to traditional feeding, a free diet after surgery resulted in significantly earlier tolerance of an oral diet on pod 2 without higher rate of reinserting a nasogastric tube. No difference was found for the duration of postoperative ileus, and quality of life in the early postoperative period [120] (1+). Even after gastrectomy omission of nasojejunal tubes led to significantly shorter length of hospital stay [121] (1+).

A meta-analysis of 15 studies (eight RCTs) with 2112 adult patients undergoing upper gastrointestinal surgery showed significantly shorter postoperative hospital stay in early orally fed patients without difference in complications with special regard to anastomotic leaks [122] (both 1++).

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 [123] (1−), [124,125] (both 2++). However, in combination with ERAS no differences were found between laparoscopic and conventional open colonic surgery when the full ERAS protocol was employed [126] (1−). In the multicentre RCT postoperative hospital length of stay was significantly shorter in the ERAS group undergoing laparoscopic surgery [127] (1+). A recent meta-analysis confirmed reduction of major morbidity and hospital stay by combination of laparoscopic surgery and ERAS [61] (1++).

The amount of initial oral intake should be adapted to the state of gastrointestinal function and to individual tolerance [110–112,128–130] (all 1+), [118] (1++). Impaired tolerance to early oral intake in the ERAS group with more nausea, vomiting, stomach retention, intestinal obstruction and a higher readmission rate respectively was shown in a comparison of Fast Track surgery and conventional care in elderly Chinese patients with gastric cancer (75–89 years) [131] (1−).

It must be emphasized, that good evidence is available only for patients undergoing colorectal surgery. With special regard to the elderly the benefits are less clear in patients undergoing upper gastrointestinal and pancreatic surgery [131,132] both (1−).

So far, no controlled data are available for patients with oesophageal resection. The study protocol for an ongoing multicentre study in the Netherlands has been recently published [23].

4. Indication for nutritional therapy

4.1. When is nutritional assessment and 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)

Recommendation 7:

Perioperative nutritional 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 recommended intake for more than seven days. In these situations, it is recommended to initiate nutritional therapy (preferably by the enteral route — ONS-TF) without delay.

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

Commentary:

The influence of nutritional status on postoperative morbidity and mortality has been documented well in both retrospective [133–137] (both 2−) and prospective studies [34,46,138–149] (all 2+). Inadequate oral intake for more than 14 days is associated with a higher mortality [150] (1−).

The energy and protein requirements can be estimated with 25–30 kcal/kg and 1.5 g/kg ideal body weight [105].

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 [50,151] (both 2++).

Undernutrition occurs frequently in association with underlying disease (e.g. cancer) or with chronic organ failure [34–36,151–158] (both 2−) (see respective guidelines). In a prospective multicentre observational study of patients with gastric cancer [159] (2+) dysphagia and gastric outlet obstruction have been shown independent factors for the risk of anastomotic leakage after total gastrectomy. Nutritional status also influences outcome after transplantation [36,160–168] (all 2+) as well as increasing the morbidity and mortality in geriatric patients undergoing surgery [40] (2+).

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, length of hospital stay, and mortality are considered principal outcome parameters when evaluating the benefits of nutritional support [169–178] (all 2−).

After discharge from hospital or when palliation is the main aim of nutritional therapy, improvement in nutritional status and in 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 ischaemia
- High output fistula
- Severe intestinal haemorrhage

The effect of EN on the outcome after surgery has not been assessed in a consistent manner.

The working group reviewed thirty-five controlled trials [179–213] (all 1), focussing on endpoints of outcome, and including patients after gastrointestinal surgery (without transplantation), trauma, and hip fracture. EN was defined as the use of oral nutritional supplements (ONS) and tube feedings (TF). Early EN was compared with normal food, administration of crystalloids and PN. 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.

In eight of these 35 studies no benefits were observed [180,188,192,196,197,202,211,212] (all 1). Some authors have pointed out possible disadvantages of EN which have not been observed by others. These are increased length of stay [206] (1−), reduced lung function after oesophageal or pancreatic resection through abdominal distension [209] (1−) or delayed gastric emptying with increased length of stay following pancreatic surgery [213] (2+). 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 [214] (1−). Compared with PN, early EN decreased postoperative infection rate in undernourished GI cancer patients, but not in those who were well nourished [185] (1−).

In seven out of eleven RCTs [215–225] only surrogate measures of outcome were used, e.g. positive effects of EN on nitrogen balance and substrate tolerance. In four out of eleven studies no significant differences were shown between early EN and standard hospital feeding practice [215–217,224] (all 1−).

The advantages of early EN within 24 h versus later commencement have been clearly shown in two meta-analyses (one Cochrane systematic review) [115,116] (both 1++).

The American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines from 2016 [226] recommend postoperative EN when feasible within 24 h.

In three older trials enteral feeding in patients with fracture of the hip and the femur neck was studied. In one trial of overnight nasogastric feeding [181] (1−), 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 six-month mortality was reduced [207] (1−). In the third study ONS given once daily significantly improved outcome at six months with a lower rate of complications and mortality [187] (1−).

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 is recommended (GPP). Parenteral nutrition shall be administered as soon as possible if nutrition therapy is indicated and there is a *contraindication for enteral nutrition, such as in intestinal obstruction (A) (BM).*

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

Commentary:

For the surgical patient PN is beneficial in the following circumstances (ESPEN Guidelines [105]): 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 7 days [105].

The recent ASPEN Guidelines [226] recommend postoperative PN for patients who cannot meet their energy needs orally/enterally within 5–7 days. PN should only be initiated if the duration of therapy is anticipated to be >7 days.

4.1.1. Enteral vs. parenteral

The effect of PN in comparison with oral/enteral standard nutrition with regard to the prognosis of surgical patients has been controversial. Twenty randomised studies of patients undergoing abdominal surgery, including patients after liver transplantation and trauma, were reviewed by the working group [179,180,185,189,191,195–197,202,204,208,210,211,227–233] (all 1). In these studies (total) PN was compared with EN, or with crystalloid solutions or with a normal hospital diet.

EN was compared with PN in 15 studies, of which 6 studies showed significant benefits of EN, mainly, a lower incidence of infectious complications, shorter length of stay, and lower costs (1+). No significant difference, was found in 8 of the 15 studies, which led most authors to favour EN because of its lower costs [183,192,195,208] (all 1+).

Heyland et al. incorporated 27 studies in a meta-analysis of PN in surgical patients [234] (2+). An influence of PN on the mortality of surgical patients was not shown. A lower complication rate, especially in those with malnutrition, was observed in patients receiving PN.

A meta-analysis by Braunschweig et al. comparing EN with PN incorporated the results of 27 studies with 1828 patients, (both surgical and non-surgical) [235] (2++). It showed a significantly lower risk of infection with oral/enteral nutrition. In malnourished patients, however, PN resulted in a significantly lower mortality with a tendency towards lower rates of infection. Lower infection rates and a shortened length of hospital stay was found in the enterally fed patients by Peter et al. [236] (1++).

Focussing on patients after gastrointestinal surgery the meta-analysis of Mazaki et al. including 29 randomized studies with 2552 patients confirmed the beneficial effects of enteral nutrition for a lower rate of infectious complications, anastomotic leaks, and shorter hospital length of stay [117] (1++); Zhao et al. including 18 randomized studies with 2540 patients for a shorter time to flatus, shorter hospital length of stay, and a greater increase in albumin levels [237] (1++). It must be emphasized that no significant influence on mortality was shown. A very recent multicentre randomized study investigated EN and PN in 2388 critically ill patients. No difference in mortality, infectious complication rate, and hospital length of stay was observed between the two groups [238] (1+).

4.1.2. Enteral tolerance and timing of PN

Several authors have pointed out the possible advantages of PN when there is a limited tolerance of EN due to intestinal dysfunction especially in the early postoperative phase, which is associated with a lower energy intake [209] (1–). There is some evidence from a Cochrane systematic review and meta-analysis that chewing gum may improve the postoperative recovery of gastrointestinal function [239] (1++). However, when an ERAS programme was used, the benefits could not be confirmed in a recent randomised multicenter trial [240] (1+). Attention must be paid to the tolerance of enteral intake especially in patients with severe trauma [214] (1–). An adequate energy intake is better provided by PN when there is an obvious limitation of gastrointestinal tolerance [241] (2+).

There is still a paucity of controlled data with regard to combined enteral and parenteral ("dual") nutrition after elective surgery. An increase in caloric intake is the main objective in combined EN/PN. A prospective RCT in patients undergoing oesophagectomy showed significantly improved insulin sensitivity and reduced blood glucose concentrations in case of dual feeding [242] (1+). A retrospective cohort analysis in 69 patients undergoing pancreaticoduodenectomy showed safety and especially in combination with NCJ delivery of caloric requirements [243] (2–).

More data have been available for critically ill patients and were analysed by Heyland et al. [244] and Dhaliwal et al. [245] (both 1–) Two of these studies from the 1980s came from the same study group, and were carried out on patients with extensive burns and severe trauma respectively. In the meta-analysis of these studies no advantage was found for combined nutrition with respect to mortality, infection, LOS and length of artificial ventilation [245] (1–).

Two recent large-scale multicentre studies investigated whether PN should be supplemented "early" (within 4 days) or "late" (after 7 days) in the event of impaired enteral tolerance [246,247] (both 1++). The results provide arguments to start PN in malnourished patients and those with special risks on day 4 at the latest [248]. In major elective surgery placement of a central venous catheter is still a routine procedure in many institutions. It is the opinion of this expert group that in the presence of a suitable indication this access should be used for PN, especially in malnourished patients, and if necessary also as a part of hypocaloric regime.

An RCT has shown that provision of PN of 25 kcal/kg and 1.5 g/kg protein presented no increased risk of hyperglycaemia and infectious complications, but resulted in a significant improvement in nitrogen balance [249] (1+). In elderly patients undergoing surgery for gastrointestinal cancer combined EN/PN showed clinical benefits when compared with EN or PN alone [250] (1-). An increase in energy intake can be achieved in the short-term by administration of lipids using peripheral venous access. When insertion of a central venous catheter is required for the purpose of nutrition therapy, this indication must be considered critically in relation to the expected time period of PN.

Combined nutrition is not necessary if the expected time period of PN is <4 days. If the expected PN period is expected to last between 4 and 7 days, nutrition can be hypocaloric with 2 g carbohydrate and 1 g amino acids/kg body weight administered via a peripheral catheter, and if it is likely to last more than 7–10 days, it is recommended that a central venous catheter should be inserted.

For long-term parenteral nutrition appropriate devices are a port, Broviac or Hickman catheter.

4.1.3. Hyperglycaemia

In order to avoid hyperglycaemia, intensive insulin therapy has been recommended for critically ill patients. Due to an incalculable risk of hypoglycaemia, it is the opinion of the working group that intensive insulin therapy is not appropriate in postsurgical patients on the general ward with less staffing. Therefore, the amount of glucose-based calories in PN should be reduced in case of blood sugar levels exceeding 180mg/dl. For patients with very unstable and high glucose levels ICU care is to be preferred.

Recommendation 9:

For administration of parenteral nutrition an all-in–one (three-chamber bag or pharmacy prepared) should be preferred instead of multibottle system (BM, HE).

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

In two RCTs the cost benefits of using a three-chamber bag were better than a multibottle system [251,252] (both 1+). A retrospective analysis of a US data bank showed a significantly lower rate of blood steam infections using a three-chamber-bag [253] (2+).

Recommendation 10:

Standardised operating procedures (SOP) for nutritional support are recommended to secure an effective nutritional support therapy.

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

Feeding protocols and SOP have proven benefits with regard to safety and feasibility of achieving the caloric target [254,255] (both 2+).

Adequate supply with micronutrients is considered essential for long-term TPN.

4.2. Is there an indication for supplementing i.v. glutamine

Recommendation 11:

Parenteral glutamine supplementation may be considered in patients who cannot be fed adequately enterally and, therefore, require exclusive PN (0) (BM, HE).

Consensus Conference: Grade of recommendation B – consensus (76% agreement) – downgraded by the working group during the finalization process according to the recent PRCT [257] (with 100% agreement within the working group members).

Commentary:

There is no convincing evidence to recommend the use of parenteral glutamine. The parenteral supplementation of glutamine dipeptide in a standard dosage of about 0.5 g/kg/d in 7 RCTs with non-enterally fed surgical patients was reviewed by the working group 2009 with regard to the end-points of morbidity and outcome [256,258–263] (all 1+). In six of these studies, the patients were to undergo elective surgery and in one after emergency visceral surgery. All studies showed significant benefits of glutamine supplementation five with respect to postoperative LOS and two with respect to complications. This was in line with the results of an earlier meta-analysis examining elective surgical patients [264] (1++). A systematic analysis of European and Asian non-enterally nourished surgical patients resulted in 10 studies with the endpoint of infectious complications and 8 studies of postoperative LOS. Significant benefits of glutamine supplementation were also seen [265] (1+). Significant improvement in postoperative immune function was shown in two studies with immunological endpoints [266–269] (all 1+).

In a large multicentre RCT on 428 well-nourished patients undergoing major gastrointestinal surgery no significant benefit was found for the postoperative complication rate and the hospital length of stay for those patients who had been supplemented with 0.4 g dipeptide/kg/day parenterally the day before and five days after surgery [270] (1+). Taking these controversial results into account no recommendation for the surgical patient was given in the ESPEN guidelines 2009 [105].

A multicentre RCT of high dose administration of glutamine in the critically ill patients with organ dysfunction was associated with a significant increase in mortality [271] (1+). This also raised concerns for the use in surgical patients receiving even the standard dosage of 0.5 g/kg/day.

In a recent RCT on 60 patients undergoing colonic resection, glutamine infusion (0.5 g/kg/day) 24 h before and 1 h after the commencement of surgery proved to be significantly beneficial for intra- and postoperative glucose–insulin homeostasis, and recovery of bowel function with shortened time to first stool passage after colonic resection [272] (1–).

Another recent multicentre double-blind RCT included 150 surgical ICU patients (gastrointestinal, vascular, cardiac) without renal or hepatic failure, or shock. All received isonitrogenous isocaloric PN (1.5 g/kg/day). In the intervention group glutamine was administered in the standard dosage of 0.5 g/kg/day. No significant differences were seen with the primary endpoints of hospital mortality and infection rate (mortality glutamine *vs*. standard 14.7% *vs*. 17.3%, bloodstream infection rate 9.6 *vs*. 8.4 per 1000 hospital days [257] (1+)).

Two meta-analyses (including 14 RCTs with 587 surgical patients, 40 RCTs with more than 2000 patients totally) have emphasized significant advantages of glutamine supplementation with regard to infectious morbidity and hospital length of stay [273,274] (both 1++). In addition, an improvement of immune parameters has been emphasized in a recent meta-analysis by Kang et al. on 13 RCTs including 1034 surgical patients with gastrointestinal tumour. In three of the studies glutamine was administered via the enteral route [275] (1+). Another meta-analysis included 19 RCTs with 1243 patients. Here a significant reduction of hospital stay was found without a difference in the complication rate [276] (1++).

A methodological review of the meta-analysis and the quality of the single studies for the German guideline update brought up concerns about the lack of clear criteria for the definition of infectious complications and the heterogeneity of hospital length of stay [78]. The low and medium quality of the studies – most of them underpowered – was also discussed by Sandini et al. [276], and it was emphasized that an exclusive effect on the hospital length of stay without difference in morbidity can hardly be interpreted (1++). Furthermore, it must be argued that in most of the studies the majority of patients with special regard to colorectal surgery were not appropriate candidates for parenteral feeding alone.

Based on the current understanding, exclusive PN over 5–7 days is definitely not indicated in most surgical patients particularly after elective colorectal surgery with an uncomplicated course [11,15,16] (all 1++). Therefore, according to the available data glutamine is safe in a standard dosage while a strong recommendation for the use in parenterally fed surgical patients may not be justified.

The extent to which parenteral glutamine administration in combination with oral/enteral nutrition may have a positive effect, cannot be clarified at present due to lack of available data.

4.2.1. Is there an indication for supplementing oral glutamine?

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 [102] (1–).

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 (6.25–18.7 g/l) and also in combination with other substances. There was a reduction in fistulas (OR = 0.36, 95% CI: 0.14–0.95, p = 0.039), and length of hospital stay (Mean difference: −6.8 days, 95% CI: −12.6 to −0.9 days, p = 0.023). Interestingly, no reduction in wound infections (OR = 1.04, 95% CI: 0.49–2.17, p = 0.925) or other infections was observed [277] (1+). 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 tumour recurrence in the intervention group [278] (2+). It must be emphasised that this study was actually 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 parenteral nutrition including omega-3-fatty acids should be considered only in patients who cannot be adequately fed enterally and, therefore, require parenteral nutrition (BM, HE).

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 with regard to the postoperative infection rate and hospital length of stay [279] (1++). This has been confirmed by more recent meta-analysis including 23 studies with 1502 patients [280,281] (both 1++). The methodological analysis of the meta-analysis and the single studies brings up concerns with regard to the lack of homogenous criteria for the definition of infectious complications and the considerable heterogeneity of hospital length of stay [78]. Tian et al. performed a meta-analysis for the comparison of a new lipid emulsion containing soy bean oil, medium-chain triglycerides, olive oil and fish oil versus other olive oil and medium- and long-chain triglyceride based emulsions [282] (1++). 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 parenteral feeding 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 h before elective surgery, needs to be clarified further [283] (1+).

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 immunonutrients (arginine, omega-3-fatty acids, ribonucleotides) should be given in malnourished patients undergoing major cancer surgery (B) (BM, HE).

There is currently no clear evidence for the use of these formulae enriched with immunonutrients vs. standard oral nutritional supplements exclusively in the preoperative period (0).

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

Commentary:

Data are available from numerous RCTs on the use of immune modulating ONS and TF formulae, including arginine, omega-3-fatty acids and ribonucleotides, with or without glutamine [195,284–294] (all 1+).

15 meta analyses of trials, in general surgical patients, and one in head and neck cancer surgery suggest that perioperative administration of immune modulating nutritional formulae have contributed to a decreased rate of postoperative complications and consequently to a decreased length of stay in the hospital [195,286–309] (all 1++). With regard to the immunomodulating substrates, most of the RCTs were performed with arginine, omega-3-fatty acids, and ribonucleotides. No additional benefits were found in an RCT in high-risk cardiac surgery patients by supplementation of glycine [310] (1+).

In some of these trials there is no clear distinction made between critically ill and patients undergoing major elective surgery (see guidelines on intensive care).

For undernourished oncological patients undergoing surgery the ASPEN guidelines from 2009 give a strong recommendation [311]. For elective digestive cancer surgery the French guidelines from 2012 recommend preoperative "pharmacotherapy" for 5–7 days, whether or not the patient is malnourished [29]. The ESPEN guideline on nutrition in cancer patients from 2016 gives a strong recommendation for patients undergoing resection for upper gastrointestinal cancer in the context of conventional perioperative care [312].

However, the methodological analysis of these meta-analyses and the included RCTs raise reservations to give a strong recommendation for the general use of immunomodulating formulae. This is due to the considerable heterogeneity of the single studies including different periods of application, and the lack of homogenous criteria for the definition of complications and hospital discharge [78]. Furthermore, the most recent review of the literature by the working group shows that the evidence for the appropriate risk groups and the timing of the intervention is not clear.

4.5.1. Pre-, peri- or postoperative timing

Pre- or perioperative intake of ONS (3 × 250 ml) enriched with immune modulating substrates (arginine, omega-3 fatty acids and nucleotides) for five to seven days reduces postoperative morbidity and length of stay after major abdominal cancer surgery [313–316] (all 1+). Undernourished patients, in particular, appear to benefit [317] (1+).

Three RCTs showed that perioperative immunomodulating formulae were effective in both undernourished [317] (1+) and well-nourished gastrointestinal cancer patients [313,315] (both 1+). Klek et al. [318] found significant advantages regarding a reduction of postoperative complications only in malnourished patients (1+).

The RCT by Gianotti et al. [319] randomised 305 gastrointestinal cancer patients without severe undernutrition to receive either preoperative or perioperative immunomodulating formulae (1−). A reduction in infectious complications and length of hospital stay were observed in both groups. However, this study did not include a group with standard formula. Therefore, it can be argued, that the observed effects could have been also obtained with standard formulae.

Comparing preoperative immunonutrition with a standard oral nutritional supplement Hübner et al. [320] performed a double-blinded RCT in surgical patients at risk according to NRS >3 (1+). Another PRCT included well-nourished patients with the nutritional intervention for three days [321] (1+). In both studies no benefits were observed in the intervention group.

In the meta-analysis of Hegazi et al. [322] a clear differentiation was made between studies comparing preoperative immunonutrition *vs.* ONS (8 PRCT with 561 patients) and those *vs.* no supplements (9 PRCT with 895 patients) (1++). Only in studies with a control group of an oral non-supplemented standard diet a significant difference was found: decrease of infectious complications (OR 0.49, 95% CI 0.30 to 0.83, $p < 0.01$) and length of hospital stay (mean difference −2.22 days, 95% CI −2.99 to −1.45 days, $p < 0.01$).

Therefore, the superiority of immune-enriched supplements has not been proven in the preoperative period. This has been supported by a small RCT in 35 patients undergoing surgery for pancreatic cancer with 40% being at nutritional risk. No significant differences were found either in the complication rate or in functional capability and body weight [323] (1−).

In the meta-analysis from Marimuthu et al. [302] (1++), significant benefits with regard to infectious complications were found for the pre-, peri- and postoperative use of the immunomodulating diet. The non-infectious complications and the hospital length of stay were reduced significantly in case of peri- or postoperative initiation of the diet. The meta-analysis from Osland et al. and Song et al. confirmed the benefits for the perioperative and sole postoperative use [307,308] (both 1++).

4.5.2. Special indications

There is also a dearth of well-designed RCTs focussing on homogenous groups of patients undergoing major surgery for cancer. In patients undergoing gastrectomy for gastric cancer, early EN with an immunomodulating formula was associated with significantly less wound-healing problems, suture failure, and infectious as well as global complications [324] (1+).

Another RCT (n = 244) on preoperative enteral immunonutrition (arginine, omega-3-fatty acids and ribonucleotides) versus a regular diet for five days in well-nourished patients undergoing elective gastrectomy for gastric cancer failed to demonstrate any clinical advantages [325] (1+).

Sultan et al. investigated 195 patients undergoing surgery for oesophagogastric cancer in three groups: omega-3-fatty acid supplemented EN or standard EN for 7 days before and after surgery, or postoperative supplementation alone [326] (1+). No difference was found between the groups when morbidity, mortality and hospital stay were considered. HLA-DR expression in monocytes or activated T-lymphocytes were also not different. In another trial the perioperative use of an immunomodulating formula for 3 days before and after oesophagectomy led to a significant increase in the total lymphocyte count on days 3 and 5 and a shift toward B cell proliferation on days 5 and 7 [327] (1+).

A meta-analysis focussing on patients undergoing surgery for gastric cancer included 9 studies with 785 patients. Some increase in IgA, IgG, IgM, CD3, CD4/CD8 ratio, and NK cells was found, and a decrease of IL-6 and TNFalpha was observed. However, the clinical outcome parameters were not improved significantly. Again, heterogeneity, timing and sample size were discussed critically [328] (1++).

A meta-analysis of six RCTs including 628 patients undergoing surgery for oesophagogastric cancer with enteral immunonutrition did not demonstrate consistency in clinical outcome parameters [329] (1+). While this meta-analysis did not support a routine recommendation of immunonutrition in this group of patients, it must be criticized as it did not include and evaluate more homogeneous studies. In addition to methodological weaknesses, the studies differed in composition of immunomodulating diet, the type of administration (peri-/pre-/postoperatively), and three of the studies were underpowered for clinical outcome parameters.

In a Cochrane meta-analysis of six high quality studies in patients undergoing gastrointestinal surgery Burden et al. demonstrated significant benefits with regard to postoperative complications [330] (1++). Due to some bias these authors saw limited generalizability [330]. Wong et al. found in their meta-analysis of 19 RCTs with 2016 patients undergoing oesophagectomy, gastrectomy, and pancreatectomy (2.2:1.2:1.0) significant benefits for the postoperative use of immunonutrition regarding a decrease of wound infections and the hospital length of stay [309] (1++). The integration of immunonutrition in an ERAS protocol was recommended, which has been shown in a randomized controlled study in 264 patients undergoing colorectal surgery [331] (1+). A diet enriched with immunonutrients was compared with a standard oral nutritional supplement and administered 7 days before surgery and continued for 5 days postoperatively. In the immunonutrition group a significant decrease in the rate of infectious complications was found (23.8% *vs.* 10.7%; $p = 0.0007$).

4.5.3. Cost effectiveness

A National US Database evaluation as well as data from Braga et al. and Chevrou-Séverac et al. [332–334] (both 2+) showed the cost-effectiveness of these formulae regarding decreased treatment of complications. In order to reduce resource consumption and total cost, a breakeven infection rate was calculated for well nourished (0.91%) as well as undernourished patients (>3.31%) [332] (2+).

4.5.4. Long-term outcome

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 locoregional tumour recurrence in the intervention group [278] (2+). A post-hoc analysis of a PRCT in 99 patients with gastric carcinoma showed no improvement in long-term survival by use of postoperative EN with the combination of glutamine, arginine and omega-3-fatty acids [335] (2+). Both studies were not powered adequately to detect differences in survival, which was not the primary endpoint.

Although benefits of enteral formulae enriched with glutamine alone have been found in several RCTs in critically ill patients, particularly those suffering from severe trauma or burns [336–339] (all 1+), no strong data for patients after major abdominal cancer or head and neck surgery are available currently.

4.5.5. Synbiotics

The concept of “ecoimmunonutrition” refers to formulae containing synbiotics with fibre and *Lactobacillus*. A significant reduction of the rate of postoperative pneumonia (2.4 *vs.* 11.3%, $p = 0.029$), of surgical site infections (7.1 *vs.* 20.0%, $p = 0.020$) and of anastomotic leakage (1.2 *vs.* 8.8%, $p = 0.031$) was shown in patients after colorectal surgery [340] (1+), and for the incidence of infections after pancreatic and hepatobiliary resections, as well as liver transplantation [341–346] (all 1+). A marked but not significant difference was observed between the effects of living or heat-killed lactobacilli [347] (1+).

In addition to the rate of infectious complications Kanazawa et al. found significant advantages with regard to cumulative length of antibiotic therapy and hospital length of stay in patients undergoing hepato-biliary resection for biliary tract cancer [343] (1+).

A meta-analysis of 13 RCTs with 962 patients revealed that probiotic and symbiotic use in elective surgical patients resulted in a reduction of postoperative sepsis ($p = 0.03$ and $p = 0.02$) [348] (1++). For trauma patients a meta-analysis of 5 studies with 281 patients showed significant benefits with regard to a reduction of nosocomial infections ($p = 0.02$), the rate of ventilator associated pneumonia (3 studies, $p = 0.01$) and the length of intensive care stay (2 studies, $p = 0.001$). No difference in mortality was observed [349] (1++). The authors highlighted considerable heterogeneity in the included studies.

A study in brain injured patients [350] (1+) showed significant advantages of a formula containing glutamine and probiotics with regard to infection rate and length of stay in the intensive care unit. The most appropriate species of probiotic has not been elucidated yet. Therefore more high quality clinical studies with adequate power are required.

It remains uncertain whether future studies should focus on the dietary combination of metabolic and immunologic conditioning with mixed substances or pure "pharmaconutrition" using a single substance approach. Regarding RCTs in malnourished patients, it may be hard to define an appropriate control group for ethical reasons.

4.6. 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 7–14 days may be appropriate (0).

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

Recommendation 15:

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

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

Commentary:

For surgical patients the benefits of nutritional therapy were shown in cases of severe undernutrition [208,233,351] (all 1+); and confirmed in two meta-analyses [234,352] both (2+), particularly with regard to the rate of postoperative complications [208,233,351,352].

These patients were fed preoperatively for at least 7–10 days.

For surgical patients "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 6 months
- BMI <18.5 kg/m^2
- SGA Grade C or NRS >5
- Serum albumin <30 g/l (with no evidence of hepatic or renal dysfunction)

These parameters reflect undernutrition as well as disease-associated catabolism.

The working group agrees that hypoalbuminaemia is a clear surgical risk factor [45,46] (both 2+), however, it reflects disease-associated catabolism and disease severity rather than undernutrition. The impact of hypoalbuminaemia has been emphasized by recent data [all 48, 49, 51] (2+).

Kuppinger et al. [43] showed that for patients undergoing abdominal surgery lower food intake before hospital admission was an independent risk factor for postoperative complications (2+).

Related to the percentage of preoperative weight loss and the serum albumin concentration, Pacelli et al. [353] did not observe any significant difference in the postoperative complication rate in 145 patients undergoing total or subtotal gastrectomy (2+). However, the percentage of patients in the risk group with postoperative complications was higher. While underpowered, this study showed that the number of patients with a critical weight loss or serum albumin level is less than 20% (14 and 27/145 resp.).

4.6.1. Duration of preoperative nutritional therapy according to nutritional risk

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 10 days than in the group with inadequate or even no support for <10 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 0.05–0.37, $p = 0.0002$) [149] (2+).

There are insufficient data available on the comparison of EN with PN preoperatively.

Preoperative PN and EN have been compared in only one RCT. Clear advantage of preoperative PN could not be shown [208] (1+). The results of the meta-analysis by Braunschweig et al. including non-randomized studies as well, however, do favour PN for malnourished patients [235] (2++). A significantly lower mortality with a tendency towards lower rates of infection was found in malnourished patients receiving PN. Heyland et al. incorporated 27 studies in a meta-analysis of PN in surgical patients [233] (2++), while clinical trials comparing EN with PN were excluded. An influence of PN on the mortality of surgical patients was not shown except a trend in one study [351] (1+). A lower complication rate, especially in those with malnutrition, was observed in the parenterally nourished patients (see 4.1). Jie et al. presented a consecutive series of 1085 patients undergoing nutritional risk screening (NRS-2002) before abdominal surgery [354] (2+) 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 hospital length of stay was found for patients with NRS of 3 and 4 for patients with and without preoperative nutritional support, of 120 patients with NRS score of at least 5 those with preoperative nutrition had significantly less complications (25.6% *vs.* 50.6%, $p = 0.008$) and a shorter hospital stay (13.7 ± 7.9 days *vs.* 17.9 ± 11.3 days, $p = 0.018$).

It is the opinion of the working group, that oral or enteral supplementation should be preferred whenever possible. With special regard to cancer patients undergoing multimodal therapy support of a dietitian should be integrated very early [355] (2+). 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. oral nutritional supplements) whenever possible. In order 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 [356] (3).

4.6.2. When are preoperative oral nutritional supplements and enteral nutrition indicated?

Recommendation 16:

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

Grade of recommendation GPP – consensus (86% agreement)

Recommendation 17:

Preoperatively, oral nutritional supplements shall be given to all malnourished cancer and high-risk patients undergoing major abdominal surgery (BM, HE). A special group of high-risk patients are the elderly people with sarcopenia.

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

Recommendation 18:

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

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

Recommendation 19:

Preoperative enteral nutrition/oral nutritional supplements should preferably be administered prior to hospital admission to avoid unnecessary hospitalization and to lower the risk of nosocomial infections (BM, HE, QL).

Grade of recommendation GPP – strong consensus (91% 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) [357,358].

Unrelated to the nutritional status preoperative ONS were studied in general surgical patients in three RCTs [192,205,359] (all 1+). Although two studies showed no significant impact on outcome, Smedley et al. found a significant reduction in minor complications. Furthermore, preoperative ONS continued postoperatively, minimized postoperative weight loss [207] (1+).

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 [330] (1++).

It is noteworthy that Burden et al. [359] observed some benefits for surgical site infections according to the Buzby definition in selected weight losing patients (1+). 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. Because patient compliance to take ONS seems to be a matter of motivation patients should be informed well about the potential benefits [360] (2+). Cost effectiveness of standard oral nutritional supplements in hospitalized patients was shown in a systematic review of the literature and meta-analysis [357] (1+).

For specific immune modulating diets – see comment 4.5. There is currently no clear evidence for the sole use of specific formula enriched with immunonutrients *vs*. standard oral nutritional supplements in the preoperative period.

4.7. When is preoperative parenteral nutrition 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) (BM). 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 7–14 days are only evident in patients with severe malnutrition (weight loss >15%) prior to major gastrointestinal surgery [233,351] (both 1+). When PN is given for 10 days preoperatively and continued for 9 days postoperatively the rate of complications is 30% lower and there is a tendency for a reduction in mortality [351] (1+).

According to the recovery of physiological function and total body protein a considerable increase can be achieved within 7 days of PN. However further significant improvement will be obtained within the second week [361] (2+). There are no controlled studies comparing 7 days with 10–14 days of PN. While the ASPEN guidelines 2009 recommend 7 days of PN [362], 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 hospital length of stay with 10–14 days.

A recent Cochrane analysis of preoperative PN in patients undergoing gastrointestinal surgery confirmed a significant reduction of complications from 45% to 28% [330] (1++). While the authors discussed a high risk bias in the three trials which were more than 20 years old, surprisingly two important studies with positive results [233,351] (1+) had not been included.

5. Postoperative nutrition

5.1. Which patients benefit from early postoperative tube feeding?

Recommendation 21:

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. Special risk groups are:

- *patients undergoing major head and neck or gastrointestinal surgery for cancer (A) (BM)*
- *patients with severe trauma including brain injury (A) (BM)*
- *patients with obvious malnutrition at the time of surgery (A) (BM) (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 [14,122,363] (all 1+). Another RCT showed that a nasojejunal tube is unnecessary after gastrectomy and that this is beneficial with regard to the hospital length of stay [121] (1+). No controlled data are available for patients with oesophageal resection. A study protocol for an ongoing multicentre study in the Netherlands has been recently published [23].

A RCT in patients undergoing total laryngectomy with primary pharyngeal closure showed that initiation of oral feeding on the first postoperative day was safe [364] (1+).

Patients undergoing major surgery for head and neck, and abdominal cancer (larynx, pharynx or oesophageal resection, gastrectomy, partial pancreatectomy) often exhibit nutritional depletion before surgery [34,139,140,147,148,152,156,157,365] and have a higher risk of developing septic complications [34,50,139,140,147,148,157,366] (all 2). Postoperatively, oral intake is often delayed due to swelling, obstruction or impaired gastric emptying, making it difficult to meet nutritional requirements. Nutritional therapy reduces morbidity with an increasing protective effect of PN, EN, and immune-modulating formulae [50] (2+).

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 [175,191] (both 1+), and has been suggested to reduce the rate of multiple organ failure when initiated within 24 h [367] (1+). For head-injured patients early feeding may be associated with fewer infections and a trend towards better outcomes in terms of survival and disability [368] (1++). However, many of the studies have methodological weaknesses.

5.2. Which formulae should be used?

Recommendation 22:

In most patients, a standard whole protein formula is appropriate.

For technical reasons with tube clotgging and the risk of infection the use of kitchen-made (blenderized) diets for tube feeding 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 NCJ no oligopeptide diet is required.

Kitchen made (blenderized) diets are nutritionally inconsistent, have a short shelf-life, and bear a risk for infection by contamination with variable microorganisms.

There is also a high risk for tube clogging.

Home-made diets for tube feeding 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). Tube blockage due to high viscosity may be reduced if the concentration is 1 cal/ml and if standard enteral formulae are added as milk base.

For immune modulating formulae see comment 4.5.

5.3. How should patients be tube fed after surgery?

Recommendation 23:

With special regard to malnourished patients, placement of a nasojejunal tube (NJ) or needle catheter jejunostomy (NCJ) should be considered for all candidates for tube feeding undergoing major upper gastrointestinal and pancreatic surgery (BM).

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

Recommendation 24:

If tube feeding is indicated, it shall be initiated within 24 h after surgery (BM).

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

Recommendation 25:

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.

Grade of recommendation GPP — consensus (85% agreement)

Recommendation 26:

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) is recommended.

Grade of recommendation GPP — strong consensus (94% 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 [287,369–374] (all 2+).

Open or even laparoscopic placement [375] of the NCJ according to standardized techniques in a specialized centre is associated with low risk and a complication rate of about 1.5–6% in most series [371,376–386] (all 2−), [317,369] (both 2+).

Some authors consider routine use of NCJ an overtreatment and propose consideration of NCJ only in high-risk patients [387–389] (all 2−). For patients undergoing pancreaticoduodenectomy a prognostic score was recently developed and validated to predict major postoperative complications including pancreas texture, pancreatic duct diameter, operative blood loss, and ASA score [390] (2+).

For patients undergoing oesophageal resection an observational study demonstrated benefits of safe long term EN by NCJ with special regard to anastomotic complications [373] (2−), [384] (3). The complication rate was low: 1.5% [384] (3). In a RCT including 68 patients undergoing pancreaticoduodenectomy no significant difference in the complication rate was found (15% *vs.* 13%) [391] (1+). The rate of intestinal obstruction and delayed gastric emptying was significantly lower in the nasojejunal tube group. Catheter-related complications were more common in the NCJ group (35.3 *vs.* 20.6%). It had to be expected that the time for removal of the feeding tube was significantly decreased in the nasojejunal tube group. The postoperative hospital length of stay was significantly shorter in the NCJ group [391] (1+).

A meta-analysis of five RCTs including 344 patients did not elucidate a clear difference between enteral NCJ feeding and parenteral access [392] (1++). In patients undergoing oesophagectomy a RCT showed no significant differences between nasoduodenal tube and feeding jejunostomy for early enteral feeding and catheter associated complications [393] (1+).

Because nasojejunal and nasoduodenal tubes are associated with a significant rate of early accidental dislodgement [388,392] (both 1++), 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.

Tolerance of TF has to be monitored closely in all patients with impaired gastrointestinal function [213] (1+). It may therefore take 5–7 days before nutritional requirements can be achieved by the enteral route [183,210,374] (all 1+), [372] (2+). In anecdotal reports, strangulation or too rapid administration of feed may lead to the development of small bowel ischaemia with a high risk of mortality [388,394–400] (3).

Percutaneous endoscopic gastrostomy should be considered in case of the indication for long-term enteral feeding when abdominal surgery is not indicated e.g. severe head injury, neurosurgery. For patients with upper GI stenosis due to oesophageal 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 [401] recommend the intervention for enteral feeding lasting for 2–3 weeks which is considered too short in surgical patients.

5.4. 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, continuation of nutrition therapy including qualified dietary counselling after discharge, is advised for patients who have received nutrition 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 preoperative nutritional therapy patients developing postoperative complications lose weight and are at risk for further deterioration of nutritional status. This was shown in a retrospective analysis of 146 patients of a prospective study by Grass et al. [402] (2−). These patients require continuing nutritional follow-up after discharge.

Furthermore, in a considerable number of patients after major gastrointestinal or pancreatic surgery the oral calorie intake will be inadequate for a longer period with a risk for postoperative malnutrition. In patients after intensive care an observational study showed a spontaneous caloric intake of 700 kcal/d after extubation. This is insufficient in an anabolic phase of rehabilitation, when a caloric intake of 1.2–1.5× resting energy expenditure REE is recommended. It also emphasizes the importance of observing the food intake in these patients [403] (2+).

After subtotal ($n = 110$) or total gastrectomy ($n = 58$) a retrospective analysis showed a decrease in BMI after one month, six months, 12 months and 24 months of 7.6, 11.7, 11.5 and 11.1% respectively [404]. After radical oesophagectomy weight loss of more than 15% within 6 months was observed in about 30% [405] (2+). A meta-analysis of 18 studies indicated a weight loss of 5–12% at six months postoperatively. More than half of patients lost >10% of body weight at 12 months [406] (1−). According to general recommendations less than 10% of 96 patients after oesophagectomy with gastric tube reconstruction had sufficient intake of all micronutrients in a prospective cohort study [407] (2+). Possible reasons may be a decrease in appetite, impaired enteral tolerance with dumping symptoms, meteorism and diarrhoea. The number of nutrition-related complaints was not an independent risk factor for the presence of suboptimal intake of nutrients [407] (2+). Therefore, these patients are at metabolic risk, and follow-up of nutritional status (minimum BMI) including documentation of the amount of oral food intake is necessary.

Follow up of the nutritional status can be easily performed by observation of the BMI. However, the BMI is not sensitive for differences in body composition without change of BMI. Bioelectrical Impedance Analysis (BIA) is a feasible non-invasive tool which is also convenient for outpatients [28]. The intra-individual course can be well documented in a three-compartment-model including extracellular (ECM) and body cell mass (BCM) as well as fat mass. From body impedance, the ratio of ECM/BCM and the phase angle may be easily calculated providing reliable information about the cell content in the body. Ideally, the first measurement will be performed before surgery [158].

Dietary counselling is strongly recommended and appreciated by most patients. If implanted during surgery, NCJ is advantageous because it must 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/day overnight. Appropriate training will enable most of the patients to administer jejunostomy tube feeds themselves. In a randomized study home enteral feeding by jejunostomy was shown to be safe and feasible. Better weight, muscle and fat store preservation was observed [408] (1−). Although further weight loss cannot be avoided completely, attenuation of weight loss can be expected as well as for oral nutritional supplementation [198] (2−).

In six RCTs postoperative and post hospital administration of ONS have been investigated [184,190,194,207,214,362] (all 1+). 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, well-being and quality of life in patients who cannot meet their nutritional requirements at home from normal food. This applies mainly to patients after major gastrointestinal surgery [409] (2+), colorectal resections [410] (2+) and to geriatric patients with fractures [136,145,187] (all 2+). 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 [145,211] (both 2+).

Further data from controlled studies are warranted to look for potential long-term benefits.

6. Organ transplantation

6.1. When is enteral nutrition 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 oral nutritional supplements or even tube feeding is advised.

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

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)

Recommendation 30:

Recommendations for the living donor and recipient are not different from those for patients undergoing major abdominal surgery.

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

Particular issues regarding the influence of EN on the course/progression of liver disease are discussed in the hepatology guidelines.

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 liver disease. Nutritional parameters have been shown to correlate with outcome after transplantation [160,161,164,166,411,412] (all 2). 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 [413] (2−). Four interventional studies (two randomized) on preoperative nutrition in patients waiting for organ transplantation have been performed [414,415] (both 1+), [416,417] (both 2+). 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 case of nutritional intervention no association was found between mortality and nutritional status [166] (2+). In one randomized study the improved parameters of nutritional status before transplantation did not affect outcome and mortality [415] (1+).

Besides malnutrition, and despite the obesity paradox, obesity remains a significant metabolic risk factor for the outcome of patients undergoing organ transplantation [418] (2+). Therefore, nutritional monitoring and treatment should also include obesity and metabolic syndrome in order to obtain weight loss and risk minimization.

Early results concerning the benefits of immune modulating formulae during the waiting period and five days after liver transplantation show favourable long-term impact on total body protein and a possible reduction of infectious complications [417] (2+). 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 prior to surgery. While an increase in antioxidant capacity was observed in the intervention group no significant differences were found for any immunological or clinical parameter [419] (1−).

At present, there is a paucity of data available with regard to metabolic preconditioning of the (living) donor and recipient. Experimental results [420] showing the impact of nutritional status on liver preservation injury also favour the concept of metabolic preparation by preoperative carbohydrate drink.

6.2. 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 enteral nutrition is recommended within 24 h.

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

Recommendation 32:

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

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

Recommendation 33:

If necessary enteral and parenteral nutrition should be combined. Long-term nutritional monitoring and qualified dietary counselling are recommended for all transplants.

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 [Guideline [421], [422,423] (both 1−). In cases of undernutrition it should be combined with PN if enteral delivery of nutrients is inadequate. (See also Recommendation 7 and 8). Insertion of a NCJ is feasible in patients undergoing liver transplantation [424] (2−).

For the first 48 h caloric intake <18 kcal/kg/day may be beneficial for the early graft function after liver transplantation [425] (2−).

Absorption and blood levels of tacrolimus are not affected by EN [426] (2+).

EN is at least equal to PN in patients after liver transplantation [231] (1+) and has been shown to reduce the incidence of viral and bacterial infections [423] (1+), [427] (1−).

Compared with standard EN formulae plus the use of selective digestive decontamination, the use of a high soluble fibre formula with probiotic bacteria (*Lactobacillus plantarum*) has been shown to reduce significantly the rate of infections [347] (1+). Early EN enriched with a mixture of probiotic bacteria and soluble fibre significantly reduced bacterial infection rate compared with a supplement containing only fibre [341] (1+).

EN is possible despite increased intestinal secretion in small bowel transplantation and can be performed at low delivery rates in the first week [428–431] (all 2−). Micronutrients and minerals should be monitored and supplemented because deficiencies were observed in 21 paediatric and young adult patients undergoing intestinal transplantation with special regard to those who received jejunal tube feeding [432] (2−).

EN and PN are equally important in patients after liver transplantation [231] (1+).

Benefits have been reported with administration of MCT/LCT lipid emulsions compared to LCT emulsions, with more favourable regeneration of the function of the reticuloendothelial system after liver transplantation [433] (2+). There was no difference in the metabolism of both lipid preparations [434] (1+).

When compared with routine treatment including an oral diet or additional PN with 20% MCT/LCT emulsion the use of a omega-3 fish oil lipid emulsion for 7 days after liver transplantation showed significant benefits with regard to ischaemia-reperfusion graft injury, infectious morbidity and postransplant hospital stay [435,436] (both 2+). Advantages regarding the recovery of the graft may be expected from the results of a meta-analysis of 21 RCTs [281] (1++).

Experience with the use of enteral immune modulating formulae is still only small. The first controlled data on the use of an immune modulating formula including arginine, omega-3-fatty acids and ribonucleotides suggest that unfavourable effects on immunosuppression are unlikely [417] (2+), [438] (1+). However, no benefits were observed in a RCT [438] (1+). Another study had been stopped early without reporting results [439].

For parenteral and enteral use of omega-3-fatty acids the meta-analysis from Lei et al. [437] (1−) included four heterogenous studies, two published in Chinese. For the use of glutamine dipeptide two studies published in Chinese were included. While for patients who received omega-3-fatty acids no significant decrease was found in the rate of infectious complications this benefit was observed for the parenteral glutamine administration (RR: 0.30; 95% C I: 0.12-0.75, $p = 0.01$). The rate of rejection reaction was without significant difference for the pooled data and the subgroups.

Long-term nutritional monitoring and dietary counselling is 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 [440] (2−). In order to improve kidney function, rejection rates, patient and graft survival fish oil use after renal transplantation was analysed in a Cochrane Systematic Review including 15 RCT with 733 patients [441] (1++). Besides a modest improvement in HDL cholesterol and diastolic blood pressure no benefit in clinical outcome was found [440] (1++).

7. Bariatric surgery

7.1. 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:

Consensus exists about early oral nutrition after bariatric surgery [442–445]. There is no difference in management when compared with any other (upper) gastrointestinal surgical procedures.

Nutritional care in patients undergoing bariatric surgery extends well beyond the perioperative period. Clinical practice guidelines were elaborated by an American expert panel first in 2008 and regularly updated since (last update: [445]). The most important issues are addressed in a recent review [446]. The preoperative assessment should include screening for malnutrition and deficiency in vitamins and trace elements. Superobese patients might benefit from preoperative weight loss (reduced complication rate). Early postoperative food intake is advocated, and supplementation with protein powders is suggested in order 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 counselling, to monitor weight loss, and to prevent deficiencies of micronutrients with special emphasis on bone health (vitamin D3, Ca). In this context, physical exercise should be encouraged strongly, although evidence is lacking.

ERAS principles have been applied also in bariatric surgery [447]. Standardized pathways have been shown to facilitate implementation and to improve process quality, while clinical benefits were minimal at best [447,448] (both 2+).

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 [449] (1+).

Recommendation 35:

Parenteral nutrition 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 on a regular basis [442]. In these patients the GI tract is usually working and catheter associated complications have to be considered [450].

Recommendation 36:

In case of a major complication with relaparotomy the use of a nasojejunal tube/needle catheter jejunostomy may be considered (0).

Grade of recommendation 0 − consensus (87% agreement)

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:

Even in case of major complications after bariatric procedures EN has proven advantages with regard to mortality and higher cost-effectiveness [451–453] (all 2+). A high protein formula can be recommended. For enteral feeding nasojejunal tubes, NCJ or gastrostomy in the gastric remnant may be considered carefully [446,451–453] (all 2+). NCJ and PEG have a considerably higher risk for leakage in the obese patient. A nasojejunal tube may be placed in the operating room.

8. Conclusion

These guidelines are based on currently best-available evidence and it must be emphasised that in certain areas the evidence is not strong. Inevitably, new evidence in the future will lead to strengthening or modification of the guidelines.

Conflict of interest

The expert members of the working group were accredited by the ESPEN Guidelines Group, the ESPEN Education and Clinical Practice Committee, and the ESPEN Executive Committee. All expert members have declared their individual conflicts of interest according to the rules of the International Committee of Medical Journal Editors (ICMJE). If potential conflicts were indicated, they were reviewed by the ESPEN guideline officers and, in cases of doubts, by the ESPEN Executive. None of the expert panel had to be excluded from the working group or from co-authorship because of serious conflicts. The conflict of interest forms are stored at the ESPEN guideline office and can be reviewed by ESPEN members with legitimate interest upon request to the ESPEN Executive.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.clnu.2017.02.013.

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