Approach to Oral and Enteral Nutrition in Adults

Topic 8

Module 8.1

Indications, Contraindications, Complications and Monitoring of EN

Michela Zanetti MD, PhD
Department of Medical Sciences
University of Trieste, Italy

Learning Objectives

- To understand the main indications and contraindications for EN;
- To identify patients who might benefit from EN;
- To understand the most important complications of EN;
- To know how to prevent or counteract complications;
- To know how to monitor patients on enteral nutritional support.

Contents

1. What exactly is EN?
2. Indications for EN
   2.1 Definition of malnutrition and nutritional risk
   2.2 Specific indications for EN according to the ESPEN guidelines
3. Contraindications to EN
4. Complications of EN
   4.1 Aspiration
   4.2 Diarrhoea
   4.3 Nausea and vomiting
   4.4 Constipation
   4.5 Tube related complications
   4.6 Metabolic complications
5. Monitoring of EN
6. Summary
7. References

Key Messages

- EN is a safe and effective approach to nutritional therapy;
- The main indication for EN is prevention and treatment of malnutrition to improve outcome;
- The main contraindications are severe disturbances of the gastrointestinal tract and metabolic instability;
- Most complications of EN are the result of application errors;
- Certain underlying diseases are associated with increased risk of specific complications;
- Acceptance of EN can be enhanced by adequate monitoring / early recognition of complications and modification of the type of EN and its application;

- Careful monitoring of EN is especially important in intensive care, in elderly patients and in patients with neurological impairment.

1. What Exactly is EN?

Enteral nutrition generally refers to any method of artificial feeding that uses the gastrointestinal (GI) tract to deliver part or all of calorie requirements. It includes the use of oral nutritional supplements or delivery of part or all of the daily requirements by use of nasogastric/enteral or percutaneous (gastric or jejunal) tube (tube feeding) (1). Thus, enteral nutrition comprises all forms of nutritional support that imply the use of "dietary foods for special medical purposes" as defined in the European legal regulation of the commission directive 1999/21/EC of 25th March 1999 and which are further strengthened in the Regulation (UE) 609/2013 that has applied since July 2016 (2). Enteral nutrition is a safe, effective and generally well tolerated approach to nutritional therapy in patients with a normal or relatively normally functioning gastrointestinal tract.
The main goal of EN is prevention or treatment of malnutrition in order to improve outcome. This is obvious from a pathophysiological point of view, but there is also strong evidence from a number of excellent studies which show that malnutrition is an independent risk factor for increased morbidity and mortality rates, length of hospital stay, worsening of functional status and higher treatment costs (3, 4). As expected, treatment of malnutrition results in improved clinical outcomes, including longer survival and fewer hospital readmission rates (5-7). Therefore, once patients who need nutrition support have been correctly identified, the appropriate nutrition treatment should be chosen and delivered timely.

2. Indications for EN

Irrespective of the underlying disease or clinical setting EN should be considered, and usually administered to maintain or improve nutritional status in patients at nutritional risk, those who are malnourished, and in those who cannot meet their nutrient requirements by oral dietary intake and are expected to experience inadequate oral food intake for more than 7 days, have a functioning gastrointestinal tract and agree to the treatment.

2.1 Definition of Malnutrition and Nutritional Risk

Malnutrition is a nutritional disorder which includes starvation-related underweight, cachexia /disease-related malnutrition, sarcopenia and frailty (8).
The term nutritional risk is used to describe a state of malnutrition with impaired outcome. According to the Global Leader Initiative on Malnutrition (GLIM) criteria, the diagnosis of malnutrition can be formulated in a simple stepwise process, first by applying the screening to identify "at risk" patients by any validated screening tool, second, by assessing for diagnosis, and finally by grading the severity of malnutrition (9) (**Fig. 1**). No specific tool is recommended, as long as it is validated for the setting where it is applied. Common criteria included in different validated screening tools include low BMI, unintentional weight loss and reduced food intake. The SGA (Subjective Global Assessment) was established by Detsky and coworkers (10) and relies on the patient´s history regarding weight loss, dietary intake, gastrointestinal symptoms, functional capacity, and physical signs of

malnutrition (loss of subcutaneous fat or muscle mass, oedema, ascites). The MNA is used to assess nutritional status in older adults and includes factors such as weight change, dietary problems, motility issues, and neuropsychological status (11). The NRS 2002 (Nutritional Risk Screening 2002) was established by Kondrup and coworkers (12) and considers weight loss, food intake, BMI, disease severity and age. MUST (Malnutrition Universal Screening Tool) is a somewhat similar screening tool to identify adults, who are malnourished or at risk of malnutrition in the hospital, in the community and in other care settings (13). All of these scores are useful to identify patients at nutritional risk who might benefit from enteral nutrition. Once the risk of malnutrition is established, malnutrition can be diagnosed when at least one phenotypic criterion (non-volitional weight loss, low body mass index, reduced muscle mass) and one aetiological criterion (reduced food intake or assimilation and inflammation or disease burden) are present. Severity grading (moderate and severe malnutrition) is based upon the phenotypic criteria while the aetiological criteria are used to guide intervention.

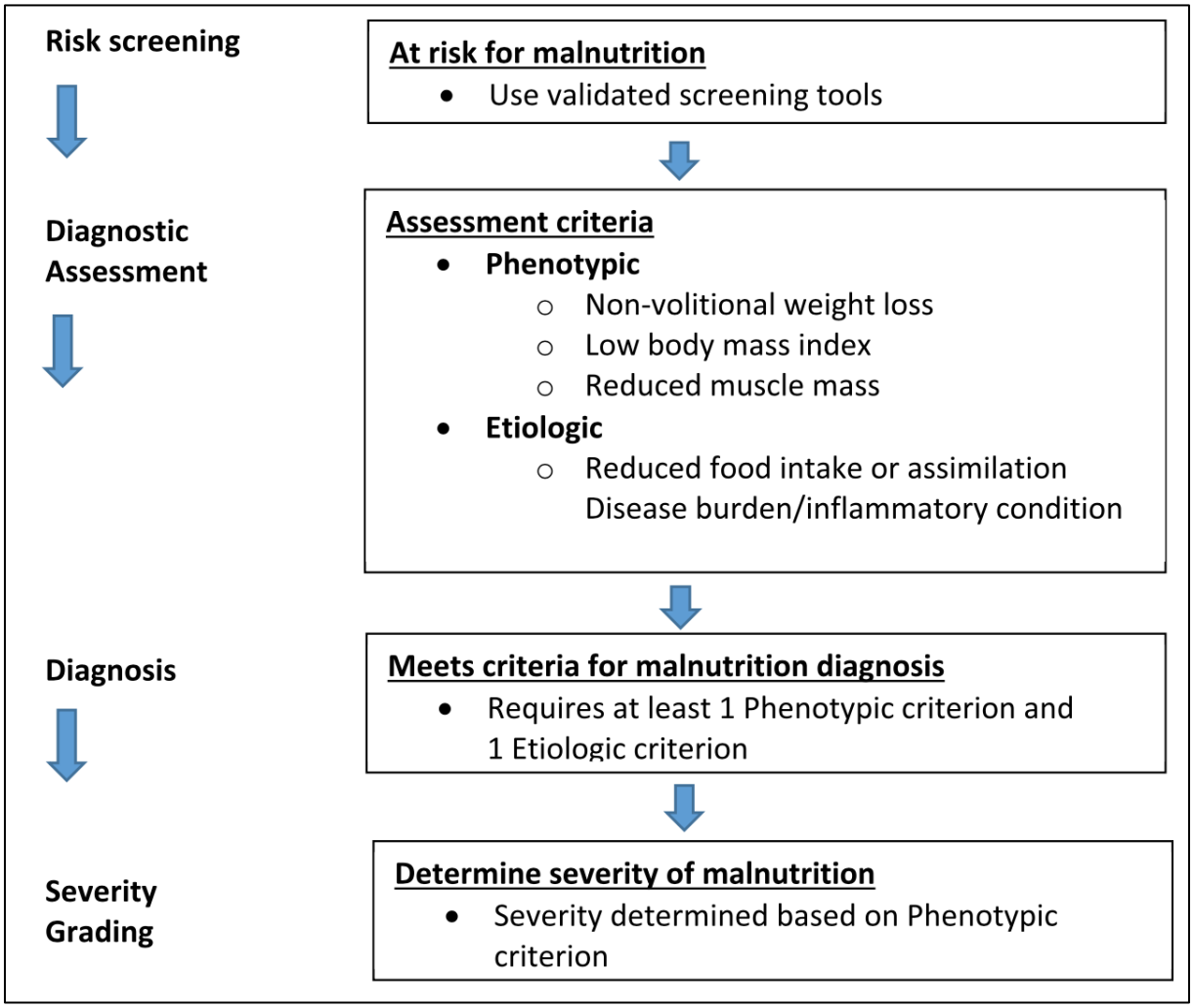

Fig. 1 GLIM diagnostic flowchart for screening, assessment, diagnosis and grading of malnutrition

2.2. Specific Indications for EN According to the ESPEN Guidelines

EN is in general the first choice in at risk/malnourished patients who are unable to meet their calorie and protein targets by oral feeding and are affected by one or more of a variety of conditions that interfere with oral intake. These include situations associated with

reduced level of consciousness or cognition, neurological disorders, head and neck and upper GI cancers and inherited metabolic diseases (14). In these situations, EN has proven to be effective in preventing weight loss and maintaining nutritional status.
The original ESPEN guidelines on EN (15) reviewed and analyzed hundreds of interventional studies to create evidence-based recommendations for the use of EN in different diseases and clinical settings, which have been implemented over the years. They include EN during inflammatory bowel disease, major burns, acute and chronic pancreatitis, liver disease, dementia, neurology, and surgery, in the intensive care unit, internal medicine, geriatrics, oncology and home enteral nutrition practice (16-27). More detailed recommendations on further clinical situations and the modes of application, including routes for enteral feeding and choice of formulae are given in the full text of the ESPEN guidelines (published on-line via: https://www.espen.org/guidelines-home/espen-guidelines)
In general, an early start to EN is recommended, including the postoperative period (23) major burns (20) and acute pancreatitis (18). Special considerations apply to severe dementia (21) and to the terminal phases of life (28). EN is recommended by the ESPEN guidelines in patients with mild or moderate dementia to overcome a crisis situation with markedly insufficient oral intake if this is caused by a potentially reversible condition. EN is not recommended in severe dementia or in the terminal phases of life. Nutritional interventions should however be used in patients with advanced incurable diseases if their expected benefit outweighs the potential harm.
The situation becomes even more complex when the patient is not able to give consent or when it is uncertain whether tube feeding will be beneficial and the prognosis of the underlying condition is uncertain. The ethical and legal aspects of such situations have been extensively discussed by Druml and colleagues (28).

3. Contraindications to EN

Contraindications to EN encompass the clinical situations associated with severe functional disturbances of the bowel, gastrointestinal obstruction or severe metabolic and circulatory instability (14) (**Table 1**).

Table 1
Contraindications to EN

Category	Example
Severe functional disturbances of the bowel	• Malassimilation or loss of nutrients (short bowel syndrome, intestinal ischaemia, small bowel mucosal disease, high output intestinal fistula) • Severe nausea/vomiting
Gastrointestinal obstruction (ileus)	• Peritonitis • Stenosis or strictures • Inflammatory disease • Peritoneal carcinomatosis
Metabolic instability	▪ Diabetic ketoacidosis ▪ Diabetic coma ▪ Hepatic coma
Circulatory instability	▪ Severe acute cardiac insufficiency ▪ Shock of any origin

Nausea and malassimilation are not strict contraindications, and EN might be possible when the underlying condition is adequately treated or specific formulae are applied. General

contraindications for endoscopic tube placement are discussed in the LLL-module 8.3 "Techniques of EN". The ESPEN guidelines advise against gastrostomy (PEG) placement in patients with cirrhosis or in those on chronic ambulatory peritoneal dialysis due to the increased risk of peritonitis and other complications. In patients with advanced cirrhosis, however, the placement of finebore nasogastric tubes is not associated with an increased risk of bleeding from oesophageal varices, and thus, nasogastric tube feeding is possible (29).

4. Complications of EN

Enteral nutrition is a safe, effective and generally well-tolerated approach to nutritional therapy in patients with a normally functioning gastrointestinal tract. There is a relative paucity of evidence regarding the frequency of adverse effects due to enteral nutrition, but it is suggested that most complications are the results of application errors. The limited evidence that exists indicates that the most common complications are aspiration, diarrhoea, and metabolic and mechanical complications (tube-related) (**Fig. 2**).

Complications of enteral nutrition

Problem	Frequency
Compliance	10 - 40%
Tube malposition/displacement	up to 50%
Nausea/vomiting	10 - 15%
Diarrhoea	25 - 50%
Infections	rare
Severe matabolic complications	?
Aspiration	?

Fig. 2 Complications of enteral nutrition. Problems with patient compliance (or adherence) are not strictly complications, but they are an important reason for failure of the technique.

4.1 Diarrhoea

Diarrhoea is a fairly common gastrointestinal complication of EN. There is a wide range for the prevalence of diarrhoea in the literature, which is most likely explained by the different definitions used. In ICU the occurrence of diarrhoea has been reported in 15-18% of patients receiving enteral nutrition, compared to 6% in those not receiving EN (30, 31).
The exact mechanism is unknown, but it is probably related to alterations of intestinal transit or of the intestinal microbiota. Other reasons include bolus administration or high feed delivery rate, bacterial contamination or inappropriate temperature of the formula diet (**Fig. 3**). There is limited evidence that low serum albumin (<25 g/L) can cause diarrhoea because of malabsorption as a consequence of intestinal wall oedema.

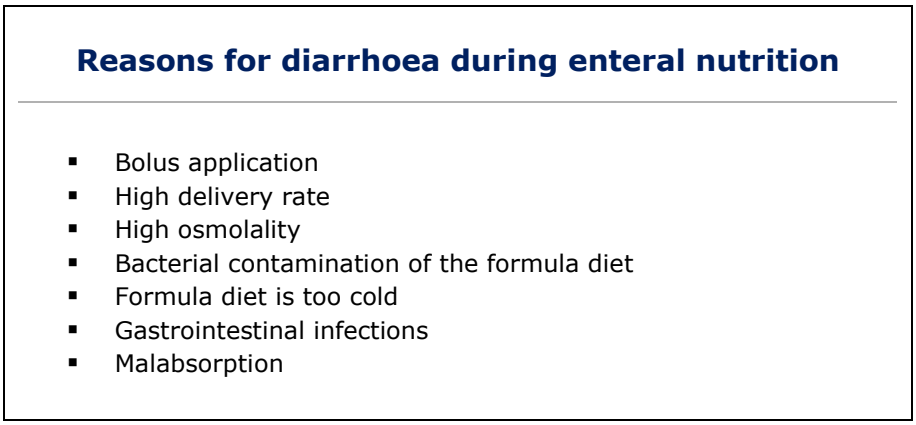

Fig. 3 Reasons for diarrhoea during enteral nutrition

The ideal temperature of the formula is 20 to 25 °C.

EN-related diarrhoea is often associated with concomitant administration of medications that affect the intestinal microbiota (especially antibiotics, but also proton pump inhibitors, etc.) or medications in suspension. The latter often contain sorbitol, a non-absorbable sugar that causes diarrhoea when administered at high doses as a vehicle. Before intolerance of EN is considered, one must also exclude gastrointestinal infections and disturbances of nutrient absorption (e.g. due to milk protein allergy, exocrine pancreatic insufficiency or lactose intolerance).

Before the inclusion of fibre into standard feeds, addition of fibre was the most widely accepted intervention for diarrhoea if no other culprit was found (32). In the event of diarrhoea it is recommended that the fibre content in the feed is reviewed and to add it if not included in the formula (14).

To date, there is contradictory evidence regarding the efficacy of probiotics in preventing diarrhoea in patients receiving enteral nutrition and therefore they should not be routinely used (33).

EN should not be interrupted for diarrhoea but should be continued while the aetiology is being investigated. A practical work-up for diarrhoea is proposed in **Fig. 4**.

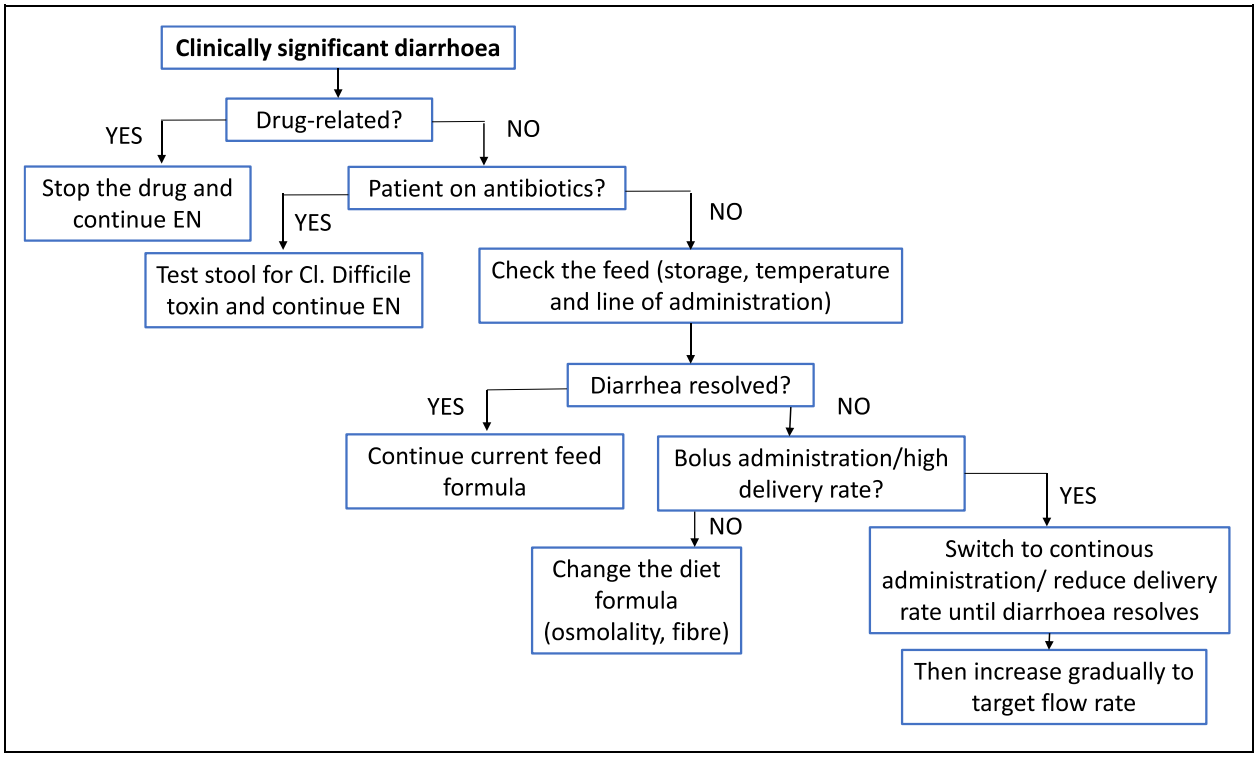

Fig. 4 Practical work-up for diarrhoea during EN

4.2 Aspiration

Abnormal entry of fluids into the lower airways may result in severe pulmonary sequelae which depend upon the volume and the composition of inhaled fluids and host defences. Aspiration of gastric and small-bowel contents into the respiratory tract is the most critical complication of EN and may finally result in pneumonia and sepsis. Aspiration of very small volumes of fluids (microaspiration), occurs during sleep in up to 50% of the normal population in whom it is not associated with untoward clinical outcomes (34). Clinically significant pulmonary aspiration is more common in critically ill patients and when patients are fed via nasogastric tubes rather than via PEG and is caused by a combination of factors including the supine position favouring gravitational back-flow, impaired lower oesophageal sphincter relaxation, infrequent oesophageal contractions, and the presence of the tube across the oesophagogastric junction. Major problems associated with EN in ICU patients are shown in **Fig. 5**. Further risk factors include: neurological impairment, decreased level of consciousness, diminished gag reflexes, postoperative or drug induced delayed gastric emptying, high GI reflux.

Major causes of enteral tube feeding in ICU and non-ICU patients (n=754) Wang K, J Parent Ent Nutr 2016	
Problem	**Incidence (%)**
Enteral tube feeding intolerance	32
Causes	
Large gastric residual volume	63
Nausea/vomiting	36
Abdominal pain of distention	29
Diarrhoea	5
Combination of symptoms and/or signs	29
Large GRV and nausea/vomiting	12
Large GRV and nausea/vomiting	9
Nausea/vomiting and abdominal pain/distention	9

Fig. 5 Clinical problems associated with EN in ICU and non ICU patients (21)
GRV = gastric residual volume

Various strategies to reduce aspiration can be adopted. They include backrest elevation, post-pyloric feeding and administration of prokinetics (35). The rationale for these measures lies in the assumption that reflux of gastric content favours aspiration and pneumonia. Since this hypothesis has not been confirmed by clinical studies, and aspiration seems more associated with oropharyngeal secretions than with aspiration of gastric material, routine checking of gastric residual volumes is not recommended in asymptomatic patients receiving EN as it doesn't impact clinical outcomes but it may hamper nutrient delivery (36). In these patients, if gastric residual volume is assessed, a volume ≤500 ml should not impact on the delivery of EN. In the presence of clinical changes, such as abdominal pain, distension, nausea or vomiting measurement of gastric residual volumes is recommended (followed by possible interruption of infusion for several hours). Nonetheless, backrest elevation to 30° to 45° is easy to perform and has been strongly advocated during EN. When this elevation cannot be achieved, the backrest should be lifted up as much as possible. The safety and efficacy of EN during the less usual prone positioning, as employed in the treatment of ARDS with mechanical ventilation, has been addressed in many studies (37-39). The available evidence shows that there are no additional risks of EN in terms of increased gastric residual volume, vomiting or regurgitation episodes per day of tube feeding when the patient is prone.
Post-pyloric feeding should not be routinely performed, but it should be considered on a case-by case basis in patients at high risk of aspiration. Similar considerations apply to the administration of prokinetic agents (eg, metoclopramide, erythromycin).

In order to **prevent aspiration** in high risk patients the following issues should be considered:

- Prefer a semi-recumbent position (30-45°)
- Prefer nasojejunal instead of nasogastric tube feeding
- In the presence of clinical changes measure gastric residual volume, adjust the delivery rate (prolong delivery period)

4.3 Nausea and Vomiting

Nausea occurs in 15-20% of patients receiving enteral nutrition, but many of them suffer from diseases which are themselves associated with a high risk of nausea and vomiting (e.g. cancer of the upper GI tract). Furthermore antineoplastic therapy (i.e. radio- or chemotherapy) is a strong trigger for nausea and vomiting and consequently requires antiemetic therapy before EN is initiated. Causes of impaired gastric emptying during EN are shown in **Fig. 6**.

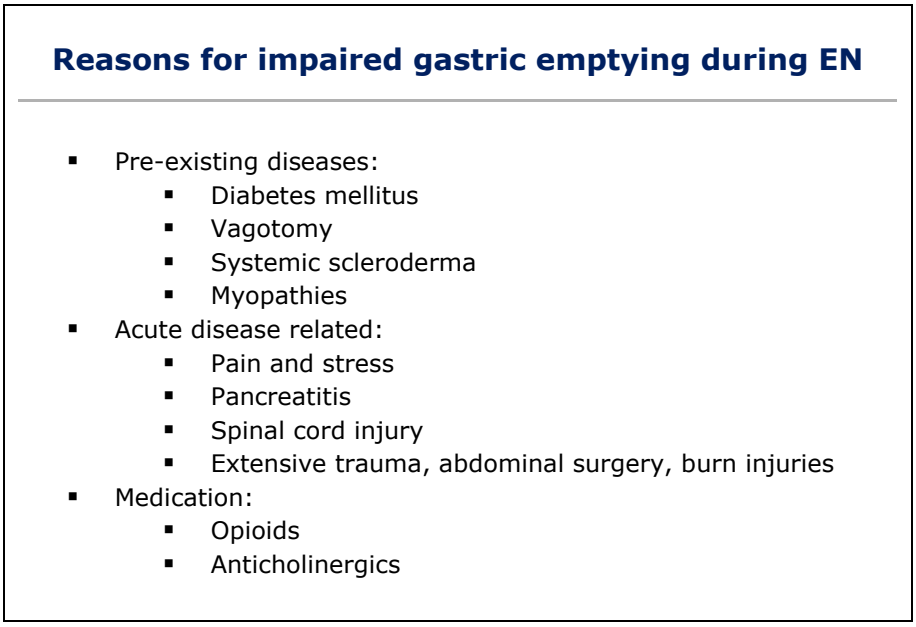

Fig. 6 Reasons for impaired gastric emptying during EN

In some cancer patients nausea might be so dominant that EN becomes impossible and total parenteral nutrition must be considered.
Delayed gastric emptying is the most common cause of nausea related to tube feeding and this may be aggravated by pain, ascites, immobilisation, sedatives, antibiotics, etc.
In ventilated patients a high positive end expiratory pressure (PEEP) might induce vomiting (with the risk of aspiration). In some patients abdominal distension and nausea might occur only transiently after initiating EN.

The **work-up of nausea/vomiting** occurring during EN should include the following issues:

- In case of cancer / antineoplastic therapy: initiate adequate antiemetic / analgesic therapy
- Exclude bowel obstruction (auscultation, x-ray abdomen)
- Review patients' prescriptions regarding nausea-inducing drugs
- If delayed gastric emptying is considered: reduce delivery rate, try prokinetic drugs

4.4 Constipation

Constipation is less common than diarrhoea during EN, and more prevalent in patients requiring long-term EN. Decreased fluid intake, high energy and energy dense formulae, and lack of dietary fibre are possible reasons for constipation associated with EN.

Furthermore, immobilisation and decreased bowel motility (as a result of sedatives or opioids) may contribute to constipation. The primary goal of constipation management is prevention.
Special caution should be taken in patients on EN with impaired peristalsis (eg those on vasopressors) because they are more prone to develop fibre bezoars. This complication, although rare, can be associated with severe sequelae and should be recognized and treated promptly.

The **work-up of constipation** occurring during EN should include the following issues:

- Review patient's EN prescription
- Increase fluid intake, reduce density of formula or switch to fibre-containing formulae if for some reason these have not been the first line choice
- Exclude bowel obstruction (auscultation, x-ray abdomen)
- If these steps fail consider stool softener (e.g. lactulose) or bowel stimulants

4.5 Tube Related Complications

The use of nasal tubes should be limited to short-term enteral feeding (4-6 weeks), in order to prevent necrosis or ulceration of the nasopharyngeal, oesophageal, gastric or duodenal mucosa. These complications however became very rare after introduction of the modern fine-bore tubes. These are made from polyurethane or silicon. They are filiform (7 to 8 Ch/Fr, maximum 12 Ch/Fr), soft and flexible. However, even with these modern and convenient fine-bore tubes, tolerance of nasogastric tubes is usually limited especially in the conscious patient and in geriatric patients with acute confusional states; in addition they may cause reflux oesophagitis and tend to dislocate.
Primary tube malposition as result of blind insertion has been described in 0.5-16% of cases, thus causing pulmonary/pleural formula infusion, pneumothorax or even pulmonary abscess (40). It is therefore mandatory to ensure adequate post-placement monitoring for immediate correction. Air instillation and auscultation are inaccurate methods for validating the position, especially in patients with neurological impairment, decreased level of consciousness or diminished gag reflexes. Misplacement is often not recognized either by the patient (who might not even cough) or by the staff unless a chest X-ray is obtained. Therefore radiological review of tube position is recommended in many countries. Validation of tube placement by demonstration of acid pH from aspiration of the luminal contents is considered sufficiently convincing in some healthcare systems, and is particularly helpful in patients in whom repeated tube replacement is required.
In patients with nasopharyngeal or facial injuries transnasal tube placement is contraindicated. In patients who are candidates for logopedic rehabilitation (eg by speech and language therapists) for potentially reversible dysphagia the presence of a nasal tube should be carefully evaluated since it significantly interferes with swallowing retraining.
When long term EN (> 4-6 weeks) is anticipated, insertion of gastrostomy tube should be considered (41, 14).
Complications of gastrostomy tube placement may be minor or major and may develop immediately after tube placement or later. Most complications are minor and range from skin maceration due to leakage of gastric contents around the stoma to peristomal pain with a frequency of 13-40%. This wide range reflects differences in the definitions used and in the populations under study. Complications are however more likely to occur in geriatric patients with comorbid conditions such as infectious illnesses, or in the presence

of a history of aspiration. Early major complications include pneumoperitoneum, oesophagus or stomach perforation or injury to other intraabdominal organs. There are small differences in the complication rates depending on whether the insertion was endoscopic (PEG) or radiologically guided (RIG).

Local wound infections are the most common complications of percutaneous gastrostomies and may occur at any time. Most of them are minor and resolve with antibiotic treatment. Factors predisposing to infection are 1) technique-related, such as lack of antibiotic prophylaxis; 2) patient-related, eg malnutrition, malignancy, diabetes, obesity, immunosuppressive therapy, 3) nursing care-related, such as inappropriate wound dressing or excessive traction. While regular skin and stomal care are crucial for the prevention of infection, the infection rate can be reduced by pre-interventional use of antibiotics (30 minutes before gastrostomy tube insertion typically using a 3rd generation cephalosporin or a broad spectrum penicillin). This is recommended especially in patients with impaired immune function or malignant disease. Other complications that may develop at any time include bleeding, peristomal leakage and inadvertent tube removal (rare with internal collars, more common where there is a fluid-filled retention balloon) or obstruction. This can be avoided by adequate flushing with water (40 ml or more) before and after feeding and after delivering medications or whenever an interruption of feeding is necessary (14). The issue of drug administration through enteral tubes is a common practice, however it deserves special considerations. First, before administration efficacy of drug through the enteral tube should be confirmed; second crushing medicines should be avoided and formulations with low osmolality and sorbitol content should be preferred (14). If possible, all medications should be completely dissolved in water prior to flushing or applied as liquid formulations. When fine-bore tubes are used flushing should be performed every 4 to 6 hours even during feeding. Application of warm water, sodium bicarbonate or pancreatic enzymes is not always successful in dislodging the blockage, and, therefore, tube replacement might be necessary. Since low pH promotes protein coagulation, aspiration of gastric residual volume should be avoided or minimized. Also flushing with saline solutions should be avoided, as salts can crystallize within the tube and promote clogging.

Haemorrhagic episodes are not uncommon following gastrostomy tube placement. Acute bleeding is usually a consequence of vessel injury at the skin level or from the gastric mucosa. Delayed bleeding after tube placement can be caused by oesophagitis, gastritis, gastric or duodenal ulcer. Acute bleeding can be prevented by a careful evaluation of concomitant anticoagulant therapy. While aspirin and non-steroidal anti-inflammatory drugs can be continued in high-risk patients, clopidogrel and warfarin, together with the newer oral anticoagulants, should normally be suspended at the time of the procedure using heparin as bridging therapy when necessary (42).

Late complications occur after the gastrostomy tract has matured. They include deterioration of the gastrostomy site, buried bumper syndrome, and colocutaneous fistula formation.

The most common complications of percutaneous endoscopy gastrostomy (PEG) are listed in **Table 2**. The list is almost identical for radiologically inserted tubes, but the rates of most of the complications are thought generally a little higher than for PEG tubes.

Table 2
Complications of percutaneous endoscopy gastrostomy (PEG) (43)

MAJOR COMPLICATIONS	
Aspiration	0.3-1%
Haemorrhage	0-2.5%
Peritonitis	0.5-1,3%
Necrotizing fasciitis	Rare
Death	0-2.1%
Tumour implantation	Rare
MINOR COMPLICATIONS	
Tube occlusion	25-35%
Peristomal infection	5.4-30%
Inadvertent removal	1.6-4.4%
Stomal leakage	1-2%
Fistulous tracks	0.3-6.7%
Buried bumper	0.3-2.4%
Gastric ulcer	0.3-1,2%
Ileus	1-2%

4.6 Metabolic Complications

Compared to parenteral nutrition EN is a more physiological approach to nutrition support which is reflected by a lower frequency and severity of metabolic complications. However, some complications may occur and they include - but are not limited to – altered hydration status, hyperglycaemia and the refeeding syndrome. If treatment is focused only on calorie administration and fluid balance is ignored, disturbances of the hydration status may occur. Feeding products generally consist of 70-80% water. They may be unable to meet normal daily water requirements alone. Additional water can be provided orally, by periodic flushing of feeding tubes (also helping to avoid clogging) or by the parenteral route, but volume balance should initially be monitored strictly to avoid dehydration and hyperhydration. A severe form of dehydration is called the "***tube-feeding syndrome***", where a hyperosmolar formula diet causes diarrhoea and intestinal fluid losses, acidosis, and impairment of renal function. Overhydration and dehydration are usually accompanied by hyponatraemia and hypernatraemia, respectively, and are treated by fluid restriction or by additional fluid supplements. Overhydration occurs frequently, particularly when patients are receiving concomitant intravenous fluids. Concomitant comorbidity impacting on the hydration state, including renal and liver failure must be taken into account. Also micronutrient disturbances can be avoided when adequate monitoring of EN is performed. A further metabolic complication is the "***refeeding syndrome***" (RFS), which is a potentially life-threatening condition determined by sudden shifts in fluid and electrolytes when severely malnourished patients are given oral, enteral or parenteral feeds. It was first clearly described in Far East prisoners after the second world war who manifested cardiac and neurological symptoms soon after starting to eat (44) (**Fig. 7**).

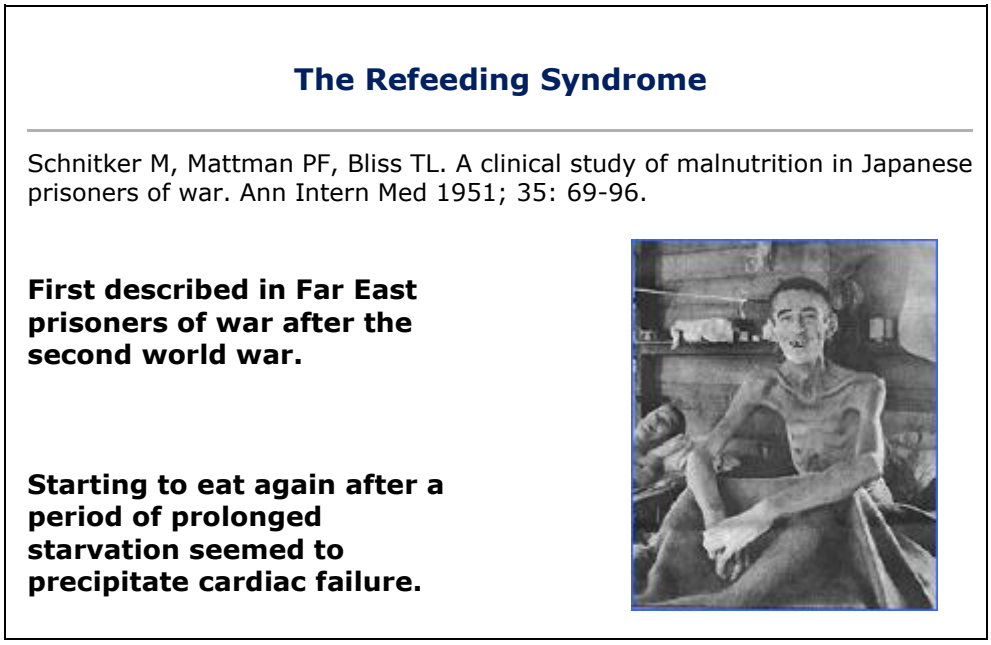

Fig. 7 The refeeding syndrome

The main biochemical feature of the refeeding syndrome is hypophosphataemia with its clinical consequences (cardiovascular and respiratory failure, seizures, rhabdomyolysis and delirium) often associated with hypokalaemia and hypomagnesaemia. Thiamine deficiency and fluid retention which also characterize the syndrome ultimately can result in cardiac arrhythmias, congestive cardiac failure and Wernicke's encephalopathy. Milder forms of the refeeding syndrome are probably not so uncommon and may be identified by biochemical alterations of micronutrient status in the absence of clinical symptoms. Laboratory and clinical findings of refeeding syndrome are shown in **Fig. 8**.

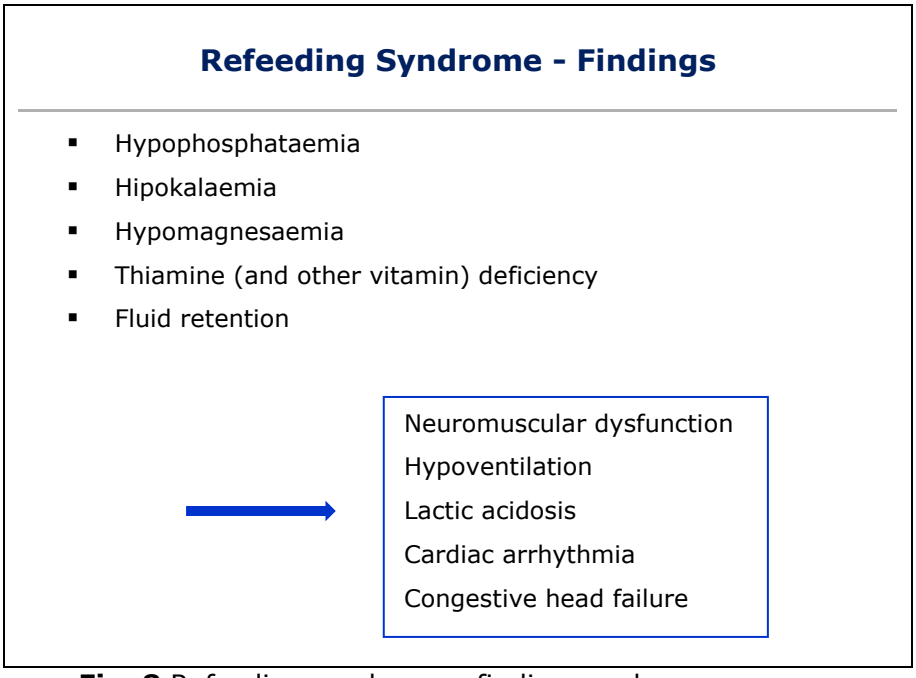

Fig. 8 Refeeding syndrome - findings and consequences

Although anorexia nervosa represents the typical syndrome complicated by RFS, other common predisposing conditions are listed in **Table 3**.

Table 3
Criteria for identifying people at high risk of developing refeeding problems (45)

Patient has one or more of the following: • BMI less than 16 kg/m^2 • unintentional weight loss greater than 15% within the last 3–6 months • little or no nutritional intake for more than 10 days • low levels of potassium, phosphate or magnesium prior to feeding
Or patient has two or more of the following: • BMI less than 18.5 kg/m^2 • unintentional weight loss greater than 10% within the last 3–6 months • little or no nutritional intake for more than 5 days • a history of alcohol abuse or of drugs including insulin, chemotherapy, antacids or diuretics

In order to prevent the RFS in patients at risk it is important to introduce and advance feeding gradually over several days while closely monitoring vital functions, plasma electrolytes (phosphate, magnesium, calcium, potassium) and renal function, heart rate and ventilatory function. To avoid fluid overload, fluid balance should be carefully controlled. Initial fluid and sodium restriction to prevent congestive heart failure can be considered. Before the onset of nutritional support electrolyte and fluid deficiencies should be corrected (46, 47). Nutrition support should be started with reduced amounts of energy (25-50% of planned energy intake, about 500-1000 kcal/day or 10-15 kcal/kg/day), particularly during the first week of refeeding, and should be increased by approximately 20% daily until the determined goal is reached. Fluids and electrolytes should be infused separately. The average weekly weight gain, particularly in extremely undernourished patients should not exceed 0.5 kg/wk. With regard to vitamin replacement, thiamine supplementation (parenteral or enteral) should be given before starting the refeeding and always if there are any features of Wernicke's encephalopathy, since once neurological symptoms develop they are rarely fully reversible (48, 49). The replacement prescription should also include a balanced multivitamin/trace element supplementation. Potassium, phosphate and magnesium should be supplemented based on their plasma levels.

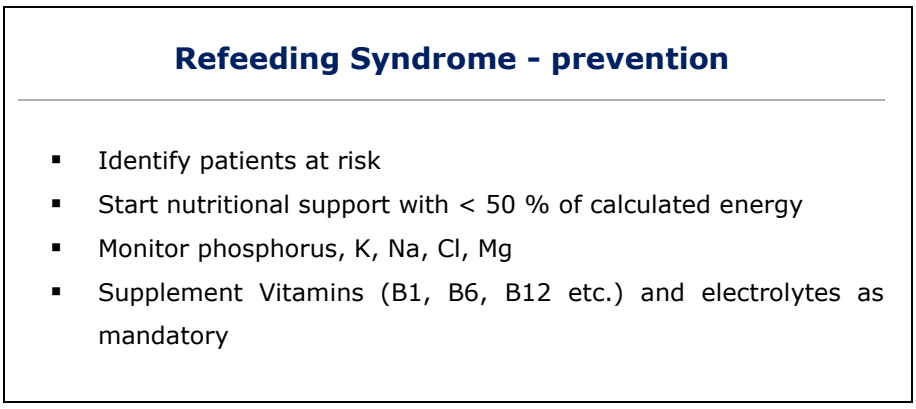

Fig. 9 Refeeding syndrome: prevention

5. Monitoring of EN

It is important to monitor EN for two reasons: 1. to monitor the patient's progress if enteral feeding is to be successful and adequate for the patient's needs; and 2. to recognize possible (metabolic) complications early.
Important general actions that should be taken when deciding to start EN and throughout the monitoring process of a patient include:

- To recognize situations in which EN is not likely to be of benefit
- To select the enteral access best suited to the patient and the planned therapy
- To implement measures to promote safety and reduce adverse outcomes
- To evaluate response to nutrition therapy
- To adjust the therapeutic prescription based on results of monitoring
- To assess continued need for EN
- To switch promptly to oral nutrition as feasible
- To collaborate across disciplines and professionals.

From a clinical standpoint, in many situations monitoring of nutrition cannot be separated from monitoring of other medical interventions (e.g. fluid balance in necrotizing pancreatitis with renal failure). Therefore, a thorough assessment of patient's nutritional, clinical and anthropometric parameters should be performed regularly. The indications, route, risks, benefits and goals of nutrition support should also be reviewed periodically. The following recommendations can only be used for rough orientation and should be adjusted to the patient's individual needs (**Table 4**).

Table 4
Protocol for nutritional, EN-related, clinical, laboratory and functional monitoring during EN

PARAMETER	**FREQUENCY**
Nutritional	
Nutrient and fluid administration	*Daily*
Fluid balance	*Daily*
Weight/BMI/bioimpedance analysis	*Weekly/every 2nd week*
Tube- and EN-related	
Nausea/vomiting	*Daily*
Diarrhoea	*Daily*
Constipation	*Daily/twice weekly*
Tube conditions and fixation	*Daily*
Stoma site	*Daily*
Clinical	
General conditions	*Daily*
Drug therapy	*Daily*
Laboratory	
Na, K glucose	*Initially daily*
P, Ca, urea, creatinine, ALT, Blood Count	*Initially twice/week*
Albumin	*Weekly/every 2nd week*
Prealbumin	*Weekly/every 2nd week*
Functional	
Handgrip strength	*Weekly*

Monitoring of EN should consider the following issues (14):

- *Feed administration*: check nutrient intake and delivery rates at intervals to ensure even flow. Measure gastric residual volumes only if problems are encountered.

- *Fluid balance*: fluid balance charts must be strictly maintained throughout enteral feeding. Check hydration status clinically; in patients with diarrhoea, fever or other non-physiological fluid losses, assess urinary output daily.
- *GI function*: nausea and vomiting, constipation and abdominal distension must be checked to ensure tolerance of feeds.
- *Tube and stoma*: Ensure daily that tube is in the correct position, it is correctly fixated and well tolerated; check stoma site to exclude infection and leakage daily as well as correct tube insertion, position and patency.
- *Nutritional status*: weigh patient daily until feeding is well established, then weigh patient weekly. If available perform analysis of body composition by bioelectrical impedance analysis every second week. A good functional outcome measure of tube feeding is hand-grip strength which can easily be performed every week.
- *Laboratory tests*: electrolytes and glucose should initially be monitored daily, with serum urea, calcium, magnesium and phosphate levels twice weekly until feeding is well established. Keep in mind that many cancer and acutely ill patients have insulin resistance and might develop diabetes mellitus under EN. Serum albumin should be measured initially and then at weekly intervals. Because of its short half-life (2 days) prealbumin better than albumin is useful to track changes of nutritional status in acute patients.

6. Summary

In this module indications and contraindications for enteral nutrition with special respect to selected diagnoses and clinical situations are highlighted. In addition, diagnosis and treatment of gastrointestinal, tube-related and metabolic complications of EN are discussed. Most complications of EN are the result of application errors and can be avoided by an adequate approach and appropriate monitoring. The recommendations are based on the published ESPEN guidelines on enteral nutrition and on available recent literature.

7. References

1. Lochs H, Allison SP, Meier R, Pirlich M, Kondrup J, Schneider St, van den Berghe G, Pichard C. Introductory to the ESPEN Guidelines on enteral nutrition: terminology, definitions and general topics. Clin Nutr 2006; 25: 180-186.
2. Regulation (EU) No 609/2013 of the European Parliament and of the Council of 12 June 2013 on food intended for infants and young children, food for special medical purposes, and total diet replacement for weight control and repealing Council Directive 92/52/EEC, Commission Directives 96/8/EC, 1999/21/EC, 2006/125/EC and 2006/141/EC, Directive 2009/39/EC of the European Parliament and of the Council and Commission Regulations (EC) No 41/2009 and (EC) No 953/2009.
3. Norman K, Pichard C, Lochs H, Pirlich M. Prognostic impact of disease-related malnutrition. Clin Nutr 2008; 27: 5-15.
4. Hersberger L, Bargetzi L, Bargetzi A, Tribolet P, Fehr R, Baechli V, et al. Nutritional risk screening (NRS 2002) is a strong and modifiable predictor risk score for short-term and long-term clinical outcomes: secondary analysis of a prospective randomised trial. Clin Nutr 2019;. doi: http://dx.doi.org/10.1016/j.clnu.2019.11.041.
5. Schuetz P, Sulo S, Walzer S, Vollmer L, Stanga Z, Gomes F, Rueda R, Mueller B, Partridge J; EFFORT trial collaborators. Economic evaluation of individualized nutritional support in medical inpatients: Secondary analysis of the EFFORT trial. Clin Nutr 2020 Feb 25. pii: S0261-5614(20)30086-8. doi: 10.1016/j.clnu.2020.02.023.
6. Schuetz P, Fehr R, Baechli V, Geiser M, Deiss M, Gomes F, Kutz A, Tribolet P, Bregenzer T, Braun N, Hoess C, Pavlicek V, Schmid S, Bilz S, Sigrist S, Brändle M, Benz C, Henzen

C, Mattmann S, Thomann R, Brand C, Rutishauser J, Aujesky D, Rodondi N, Donzé J, Stanga Z, Mueller B. Individualised nutritional support in medical inpatients at nutritional risk: a randomised clinical trial. Lancet 2019; 393: 2312-2321.
7. Gomes F, Baumgartner A, Bounoure L, Bally M, Deutz NE, Greenwald JL, Stanga Z, Mueller B, Schuetz P. Association of Nutritional Support With Clinical Outcomes Among Medical Inpatients Who Are Malnourished or at Nutritional Risk: An Updated Systematic Review and Meta-analysis. JAMA Netw Open 2019 Nov 1;2(11):e1915138. doi: 10.1001/jamanetworkopen.2019.15138.
8. Cederholm T, Bosaeus I, Barazzoni R, Bauer J, Van Gossum A, Klek S, Muscaritoli M, Nyulasi I, Ockenga J, Schneider SM, de van der Schueren MAE, l, Singer P. Diagnostic criteria for malnutrition-An ESPEN Consensus Statement. Clin Nutr 2015; 34: 335-340.
9. Cederholm T, Jensen GL, Correia MITD, Gonzalez MC, Fukushima R, Higashiguchi T, Baptista G, Barazzoni R, Blaauw R, Coats A, l, Crivelli A, Evans DC, Gramlich L, Fuchs-Tarlovsky V, Keller H, Llido L, Malone A, Mogensen KM, Morley JE, Muscaritoli M, Nyulasi I, Pirlich M, Pisprasert V, de van der Schueren MAE, Siltharm S, Singer P, Tappenden K, Velasco N, Waitzberg D, Yamwong P, Yu J, Van Gossum A, Compher C, GLIM Core Leadership Committee, GLIM Working Group. GLIM criteria for the diagnosis of malnutrition e A consensus report from the global clinical nutrition community. Clin Nutr 2019; 38: 1-9.
10. Detsky AS, McLaughlin JR Baker JP, Johnston N, Whittaker S, Mendelson RA, Jeejeebhoy KN. What is subjective global assessment of nutritional status? J Parenter Enteral Nutr 1987; 11: 8-13.
11. Rubenstein LZ, Harker JO, Salva A, Guigoz Y, Vellas B. Screening for under- nutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). J Gerontol A Biol Sci Med Sci 2001;56:M366e72.
12. Kondrup J, Allison SP, Elia M et al. ESPEN guidelines for nutrition screening 2002. Clin Nutr 2003; 22: 415-421.
13. Stratton RJ, Hackston A, Longmore D, Dixon R, Price S, Stroud M, et al. Malnutrition in hospital outpatients and inpatients: prevalence, concurrent validity and ease of use of the 'malnutrition universal screening tool' ('MUST') for adults. Br J Nutr 2004;92: 799-808.
14. Bischoff SC, Austin P, Boeykens K, Chourdakis M, Cuerda C, Jonkers-Schuitema C, Lichota M, Nyulasi I, Schneider SM, Stanga Z, Pironi L. ESPEN guideline on home enteral nutrition. Clin Nutr 2020; 39: 5-22.
15. H. Lochs, L. Valentini, T. Schütz, S.P. Allison, P. Howard, C. Pichard, S.D. Anker, J. Arends, M.E. Assis-Camilo, M.M. Berger, YN Berner, E. Berry, G. Bodoky, A. Bondolfi, F. Bozzetti, M. Braga, E. Buehler, E. Cabré, N.J.M. Cano, T. Cederholm, M.A. Cicoira, P. Coti-Bertrand, E. Dardai, C.H.C. DeJong, N.E.P. Deutz, W. Druml, K. Fearon, E. Fiaccadori, L. Furniss, R. Grimble, F. Hammarqvist, L. Harsanyi, X. Hébuterne, B. Herbst, M. Hiesmayr, M. John, P. Jolliet, C. Jonkers-Schuitema, G. Kazandjiev, U. Körner, M. Koller, J. Kondrup, K.G. Kreymann, U.G. Kyle, A. Laviano, M. León-Sanz, O. Ljungqvist, D. Macallan, J. MacFie, M.M. Meguid, R. Meier, J.C. Melchior, B. Messing, N. Milinic, A. Milne, S. Muehlebach, M. Muscaritoli, G. Nitenberg, K. Norman, J. Ockenga, A. Ödlund-Olin, F. Oehmichen, J. Palmblad, A. Pap, P.U. Pedersen, M. Page-Rodebjer, M. Pertkievicz, M. Pirlich, M. Plauth, P. Ponikowski, C. Raguso, O. Riggio, H.P. Sauerwein, S.M. Schneider, A.M.W.J. Schols, A. Schwenk, G. Selga, L. Sobotka, P. Soeters, Z. Stanga, P. Tesinsky, G. Toigo, M.A.E. Van Bokhorst-de van der Schueren, G. Van den Berghe, W. Van Gemert, A. Van Gossum, D. Volkert, M. Von Meyenfeldt, A. Weimann, J. Wernerman, C. Wheatley ESPEN Guidelines on Adult Enteral Nutrition. Clin Nutr 2006; 25: 177-360.
16. Forbes A, Escher J, Hébuterne X, Kłęk S, Krznaric Z, Schneider S, Shamir R, Stardelova K, Wierdsma N, Wiskin AE, Bischoff SC. ESPEN guideline: Clinical nutrition in inflammatory bowel disease. Clin Nutr 2017; 36: 321-347.
17. Rousseau AF, Losser M-R, Ichai C, Berger MM. ESPEN endorsed recommendations: Nutritional therapy in major burns. Clin Nutr 2013; 32: 497-502.

18. Arvanitakis M, Ockenga J, Bezmarevic M, Gianotti L, Krznarić Ž, Lobo DN, Löser C, Madl C, Meier R, Phillips M, Rasmussen HH, Van Hooft JE, Bischoff SC. ESPEN guideline on clinical nutrition in acute and chronic pancreatitis. Clin Nutr 2020; 39: 612-631.
19. Plauth M, Bernal W, Dasarathy S, Merli M, Plank LD, Schütz T, Bischoff SC. ESPEN guideline on clinical nutrition in liver disease. Clin Nutr 2019;38:485-521.
20. Rousseau AF, Losser MR, Ichai C, Berger MM. ESPEN endorsed recommendations: nutritional therapy in major burns. Clin Nutr 2013;32:497-502.
21. Volkert D, Chourdakis M, Faxen-Irving G, Frühwald T, Landi F, Suominen MH, Vandewoude M, Wirth R, Schneider SM. ESPEN guidelines on nutrition in dementia. Clin Nutr 2015; 34:1052-1073.
22. Burgos R, Bretón I, Cereda E, Desport JC, Dziewas R, Genton L, Gomes F, Jésus P, Leischker A, Muscaritoli M, Poulia KA, Preiser JC, Van der Marck M, Wirth R, Singer P, Bischoff SC. ESPEN guideline clinical nutrition in neurology. Clin Nutr 2018; 37:354-396.
23. Weimann A, Braga M, Carli F, Higashiguchi T, Hübner M, Klek S, Laviano A, Ljungqvist O, Lobo DN, Martindale R, Waitzberg DL, Bischoff SC, Singer P. ESPEN guideline: Clinical nutrition in surgery. Clin Nutr 2017; 36: 623-650.
24. Singer P, Blaser AR, Berger MM, Alhazzani W, Calder PC, Casaer MP, Hiesmayr M7, Mayer K, Montejo JC, Pichard C, Preiser JC, van Zanten ARH, Oczkowski S, Szczeklik W, Bischoff SC. ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr 2019;38: 48-79.
25. Gomes F, Schuetz P, Bounoure L, Austin P, Ballesteros-Pomar M, Cederholm T, Fletcher J, Laviano A, Norman K, Poulia KA, Ravasco P, Schneider SM, Stanga Z, Weekes CE, Bischoff SC. ESPEN guidelines on nutritional support for polymorbid internal medicine patients. Clin Nutr 2018; 37:336-353.
26. Volkert D, Beck AM, Cederholm T, Cruz-Jentoft A, Goisser S, Hooper L, Kiesswetter E, Maggio M, Raynaud-Simon A, Sieber CC, Sobotka L, van Asselt D, Wirth R, Bischoff SC. ESPEN guideline on clinical nutrition and hydration in geriatrics. Clin Nutr 2019; 38:10-47.
27. Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, Bozzetti F, Fearon K, Hütterer E, Isenring E, Kaasa S, Krznaric Z, Laird B, Larsson M, Laviano A, Mühlebach S, Muscaritoli M, Oldervoll L, Ravasco P, Solheim T, Strasser F, de van der Schueren M, Preiser JC. ESPEN guidelines on nutrition in cancer patients. Clin Nutr 2017; 36:11-48.
28. Druml C, Ballmer PE, Druml W, Oehmichen F, Shenkin A, Singer P, Soeters P, Weimann A, Bischoff SC. ESPEN guideline on ethical aspects of artificial nutrition and hydration. Clin Nutr 2016; 35: 545-556.
29. Hébuterne X, Vanbiervliet G. Feeding the patients with upper gastrointestinal bleeding. Curr Opin Clin Nutr Metab Care 2011; 14: 197-201.
30. Montejo JC. Enteral nutrition-related gastrointestinal complications in critically ill patients: a multicenter study. The Nutritional and Metabolic Working Group of the Spanish Society of Intensive Care Medicine and Coronary Units. Crit Care Med 1999; 27:1447-1453.
31. Luft VC, Beghetto MG, de Mello ED, Polanczyk CA. Role of enteral nutrition in the incidence of diarrhea among hospitalized adult patients. Nutrition 2008; 24:528-535.
32. Rushdi TA, Pichard C, Khater YH. Control of diarrhea by fiber-enriched diet in ICU patients on enteral nutrition: a prospective randomized controlled trial. Clin Nutr 2004; 23:1344-1352.
33. Jack L, Coyer F, Courtney M, Venkatesh B. Probiotics and diarrhoea management in enterally tube fed critically ill patients: what is the evidence? Intensive Crit Care Nurs 2010; 26:314–326.
34. Gleeson K, Eggli DF, Maxwell SL. Quantitative aspiration during sleep in normal subjects. Chest 1997; 111:1266-1272.
35. Drakulovic MB, Torres A, Bauer TT, Nicolas JM, Nogué S, Ferrer M. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial. Lancet 1999; 354:1851-1858.

36. Reignier J, Mercier E, Le Gouge A, Boulain T, Desachy A, Bellec F, Clavel M, Frat JP, Plantefeve G, Quenot JP, Lascarrou JB; Clinical Research in Intensive Care and Sepsis (CRICS) Group. Effect of not monitoring residual gastric volume on risk of ventilator-associated pneumonia in adults receiving mechanical ventilation and early enteral feeding: a randomized controlled trial. JAMA 2013; 309: 249-256.
37. Guèrin C, Beuret P, Constantin JM, Bellani G, Garcia-Olivares P, Roca O, Meertens JH, Maia PA, Becher T, Peterson J, Larsson A, Gurjar M, Hajjej Z, Kovari F, Assiri AH, Mainas E, Hasan MS, Morocho-Tutillo DR, Baboi L, Chrétien JM, François G, Ayzac L, Chen L, Brochard L, Mercat A; investigators of the APRONET Study Group, the REVA Network, the Réseau recherche de la Société Française d'Anesthésie-Réanimation (SFAR-recherche) and the ESICM Trials Group. A prospective international observational prevalence study on prone positioning of ARDS patients: the APRONET (ARDS Prone Position Network) study. Intensive Care Med 2018; 44:22.
38. Linn DD, Beckett RD, Foellinger K. Administration of enteral nutrition to adult patients in the prone position. Intensive Crit Care Nurs 2015; 31:38-43.
39. Saez de la Fuente I, Saez de la Fuente J, Quintana Estelles MD, Garcia Gigorro R, Terceros Almanza LJ, Sanchez Izquierdo JA, Montejo Gonzalez JC. Enteral Nutrition in Patients Receiving Mechanical Ventilation in a Prone Position. J Parenter Enteral Nutr 2016; 40: 250-255.
40. McClave SA, Chang WK. Complications of enteral access. Gastrointest Endosc 2003; 58: 739-751.
41. Löser C, ASchl G, Hebuterne X et al. ESPEN guidelines on artifical enteral nutrition – Percutaneous endoscopic gastrostomy (PEG). Clin Nutr 2005; 24: 848-861.
42. Anderson MA, Ben-Menachem T, Gan SI, Appalaneni V, Banerjee S, Cash BD, Fisher L, Harrison ME, Fanelli RD, Fukami N, Ikenberry SO, Jain R, Khan K, Krinsky ML, Lichtenstein DR, Maple JT, Shen B, Strohmeyer L, Baron T, Dominitz JA. Management of antithrombotic agents for endoscopic procedures. Gastrointest Endosc 2009; 70: 1060-1070.
43. Itkin M, DeLegge MH, Fang JC, McClave SA, Kundu S, Janne d'Othee B, Martinez-Salazar GM, Sacks D, Swan TL, Towbin RB, Walker TG, Wojak JC, Zuckerman DA, Cardella JF, Interventional Radiology and American Gastroenterological Association, American Gastroenterological Association Institute, Canadian Interventional Radiological Association, Cardiovascular and Interventional Radiological Society of Europe. Multidisciplinary practical guidelines for gastrointestinal access for enteral nutrition and decompression from the Society of Interventional Radiology and American Gastroenterological Association (AGA) Institute, with endorsement by Canadian Interventional Radiological Association (CIRA) and Cardiovascular and Interventional Radiological Society of Europe (CIRSE). J Vasc Interv Radiol 2011;22:1089-1106.
44. Schnitker M, Mattman PF, Bliss TL. A clinical study of malnutrition in Japanese prisoners of war. Ann Intern Med 1951; 35: 69-96.
45. NICE. Nutrition support for adults: oral nutrition support, enteral tube feeding and parenteral nutrition. London: NICE, 2006.
46. Marinella MA. The refeeding syndrome and hypophosphataemia. Nutr Rev 2003; 61: 320-323.
47. Maier-Dobersberger T, Lochs H. Enteral supplementation of phosphate does not prevent hypophosphataemia during refeeding of cachectic patients. JPEN 1994; 18: 182-184.
48. Gentile MG, Pastorelli P, Ciceri R, Manna GM, Collimedaglia S. Specialized refeeding treatment for anorexia nervosa patients suffering from extreme undernutrition. Clin Nutr 2010; 29: 627-632.
49. NICE. Eating disorders - core interventions in the treatment and management of anorexia nervosa, bulimia nervosa and related eating disorders. London: NICE, 2009.

Weblink:
ESPEN-guidelines
https://www.espen.org/guidelines-home/espen-guidelines