Module 18.4

How to Choose the Best Route of Feeding

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Learning Objectives

- Review the routes of feeding (oral, enteral, parenteral, supplemental parenteral nutrition);
- Understand the respective strengths and weaknesses of each route of feeding;
- Learn how to optimize enteral and parenteral nutrition.

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Key Messages

- Increased and specific nutritional requirements occurring during critical illness need to be covered by appropriate administration of energy, nitrogen and micronutrients, especially in case of pre-existing malnutrition, or chronic insufficient oral intakes or expected delay before recovery of eating;
- Early enteral nutrition must be systematically considered in patients unlikely to recover their ability to eat within 48 hours after admission into the ICU; if enteral nutrition is not feasible, parenteral nutrition should be considered case by case;
- Both insufficient and excessive amounts of energy are detrimental, especially after very low food intake or fasting for > 5 days;
- In-house written protocols are highly recommended to optimise nutrition support;
- Monitoring of nutrition support is as important as the initial prescription.

1. Implementation of Nutrition Support

Increased and specific nutritional requirements occurring during critical illness need to be covered by appropriate administration of energy, nitrogen and micronutrients, especially in the case of pre-existing malnutrition (1, 2). Optimal provision of macro- and micronutrients is mandatory throughout the Intensive Care Unit (ICU) stay to promote the best possible outcome of severely ill patients. The difficulties in feeding adequately a large proportion of patients, mainly the most severely ill, during their stay in the ICU is widely recognized (3-5). The use of enteral nutrition, whenever the oral intakes are insufficient, is rarely debated. Unfortunately, the tolerance to enteral nutrition is low in the most severely ill patients and in those with impaired digestive function (6). In addition, a number of procedures such as repeated surgery, invasive investigations such as endoscopies or computerized imaging interrupt or significantly reduce the administration of enteral nutrition. This condition results in a rapidly growing negative energy balance, which has been associated with poor outcome. In order to prevent this situation, the use of parenteral nutrition, either as a stand-alone treatment or as a supplement to the insufficient enteral nutrition seems logical. Unfortunately, recent guidelines are conflicting about the best time to start with this strategy, as well as the definition of the energy targets to aim for from the beginning of the ICU stay until discharge.

Nutritional support is indicated when at least one of the four following criteria is present:

Cardiopulmonary resuscitation is completed

- Pre-existing severe malnutrition
- Oral intake matches < 50% of the energy and nitrogen needs
- Expected delay before recovery of eating ≥ 3 days

The prescription of nutrition support is a critical step in initiating optimal treatment. It must be followed up by routine monitoring to readjust the prescription according to the clinical evolution (7).

1.1 Route of Feeding

The 2019 ESPEN guidelines (2) recommend the administration of nutritional support in critically ill patients to limit the negative energy and protein balance commonly observed in these conditions and associated with increased morbidity and mortality. Oral intakes are generally limited (8). Enteral nutrition is generally preferred to parenteral nutrition (9). Of note, a recent large trial involving 3022 patients and comparing early EN to early PN in different general ICUs has shown similar clinical outcomes, including infections, from both techniques (10). A meta-analysis has further supported the conclusion that the two techniques are equivalent, but stressed the importance of early prescription of enteral nutrition or parenteral nutrition (6). One may conclude that if both techniques are equivalent, then rather use the most physiological one (i.e. use the gut if it works).

The absence of gut feeding (also known as gut starvation) may represent an important trigger for systemic infections due to gastro-intestinal microorganisms. Numerous disturbances are found at different levels of the gastrointestinal tract during the ICU stay and are summarised in **Table 1**.

Table 1

Consequences of starvation on the gastrointestinal tract

	-			
Gut barrier (epithelial cell junction)	Increased permeability to macromolecules and			
	micro-organisms (bacteria, fungi)			
Enterocytes	Increased adherence of bacteria			
Intestinal flora	Overgrowth of pathogens			
Sub-mucosal immune system	Atrophy of Peyer's patches. Decreased production			
	of immunoglobulin A			

The absence of nutrients in the gastrointestinal tract has 4 main consequences:

- lack of fuel source for enterocytes
- lack of mechanical stimulation
- delayed capacity to resume oral feeding
- abnormal hormonal pattern

The absence of nutrients in the gut has been proposed as a trigger for the translocation of endotoxins, bacteria and fungi from the gastrointestinal tract lumen into the bloodstream despite the liver "filter", inducing a metabolic response, and a generalised whole-body response to a second "hit" that may induce a systemic inflammatory response to stress and multi-organ failure. Early enteral nutrition, even as small amounts (e.g. 250 ml/day) of nutrients into the gastrointestinal tract may prevent this translocation process.

Enteral nutrition does not always allow the nutritional targets prescribed by clinicians to be reached because of gastrointestinal tract intolerance, unavailability of the gastrointestinal tract, practical obstacles (e.g. multiple operations). Enteral nutrition is indicated mainly for patients with an expected stay in the ICU of at least 3 days.

Parenteral nutrition can be used alone in the case of failure of enteral nutrition, or as supplemental parenteral nutrition together with (insufficient) enteral nutrition. The timing of supplemental parenteral nutrition is still a subject of debate (11).

1.2 Timing of Nutritional Support

The latest ESPEN guidelines (2) recommend early (<48 hours) enteral nutrition. If the patient is not likely to benefit from early enteral nutrition, delayed enteral or parenteral nutrition should be prescribed if the patient is not expected to cover his energy and protein requirements by oral feeding for >5 days (see discussion in the "choice of route" unit of this module). Studies on early (12, 13, 14) or late (15) supplemental parenteral nutrition in critically ill patients have generated conflicting results. Of note, only two studies (12, 14) used indirect calorimetry to define the nutritional target, which is thought to have a significant influence on the outcome by avoiding under- or overfeeding. As these results are not yet conclusive, parenteral nutrition should be used only in case of failure or non-feasibility of enteral nutrition. The optimal timing to start supplemental parenteral nutrition remains uncertain.

2. Enteral Nutrition

2.1 Indications and Contraindications

Enteral nutrition is indicated in most ICU patients, as the gastrointestinal tract function is usually normal or only modestly impaired. Some precautions must be taken before initiating enteral nutrition (9). The systematic use of a checklist and of standard settings (**Table 2**) can be useful in starting and optimising enteral nutrition, and decreases the risks of enteral nutrition-related complications.

Checklist before starting enteral nutrition			
Significant gastrointestinal	Is the gastric residual volume >500 ml?		
dysfunction?			
Suspicion of ileus?	Administer enteral nutrition (20 ml/h) and check gastri		
	residual volume 4–6 h later. Perform X ray.		
Initial settings?	Pump-driven, continuous (24 hours/day)		
Position of the feeding tube?	Naso- or orogastric. In the middle of the stomach		
Catheter type?	Silicon – polyurethane		
Patient position?	Head of bed elevation at >30° if possible		
Which formula?	Polymeric, isoenergetic (1 kcal/ml), fibre-enriched in		
	most cases		

Table 2

Checklist before starting enteral nutrition

They are few absolute contraindications to enteral nutrition:

- Vomiting, aspiration and increased gastric residues (above 500 mL)
- Complete bowel obstruction
- Haemodynamic instability with increasing doses of catecholamines
- Active upper gastrointestinal tract bleeding
- Fear of inducing intestinal complications such as bowel ischaemia
- No possible access to the gastrointestinal tract
- Unsafe surgical anastomosis

• Abdominal compartment syndrome

Enteral nutrition should be delayed in the case of severe abdominal distension, abdominal compartment syndrome, significant bowel ischaemia and/or haemodynamic instability, and in active ulcer bleeding with a high risk of rebleeding. Special attention should be given when there are increasing or persisting high lactate levels as these reflect an increased risk of bowel ischaemia.

There is no contraindication in the case of uncomplicated hypoxaemia, hypercapnia, acidosis, hypothermia, after small surgical procedures, the use of muscle relaxants, or in patients suffering from acute pancreatitis, after abdominal trauma, even with an open abdomen or after aortic aneurysmal surgery (9).

2.2 Enteral Access

Gastric access has many advantages:

- easy and early access
- access performed by nurses

Gastric access should always be proposed whenever the gastrointestinal tract is functioning and available.

The disadvantages of gastric tubes include the risk of inhalation of gastric content, increased by use of the supine position, gastro-oesophageal reflux and impaired gastrointestinal peristalsis. Aspiration of gastric content into the airways is a serious complication which can be life-threatening, if massive, but this occurs rarely. In many cases, aspiration is "silent" and is associated with ventilation-associated pneumonia. Nasopharyngeal trauma related to the nasogastric access may induce profuse bleeding: this complication can be prevented by gentle introduction through the nose of a small bore nasogastric tube. Accidental tube displacement should be continuously suspected since initial correct fixation may be lost and the new positioning after refixation may not have been reconfirmed by X ray, or by other techniques such as pH measurement.

2.2.1 Gastric Access

Gastric feeding techniques include:

- nasogastric tubes available for short-term nutrition (< 3 weeks), and achievable using a manual bedside placement that can be confirmed radiologically (not mandatory).
- gastrostomy available for expected long-term nutrition through the GIT tract, and achievable using endoscopic, radiologic or surgical placement.

2.2.1.1 Naso-gastric Tubing

Tubes are made of polyvinyl (PVC), silicone or polyurethane (more flexible, less traumatic, more expensive than PVC). Their diameter varies from 6 to 14 French, and their length from 95 to 120 cm, to adapt to the anatomy of the patient. The tip of the tube can be weighted, although confirmation of the advantage of such a feature is still awaited.

The right placement of the tube must always be checked before starting enteral nutrition, by pH measurement or X-ray. Coughing, vomiting or nasotracheal suctioning of the feed (recognizable by its colour), as well as removal of endotracheal tubes can induce dislodgement of the nasogastric or nasoduodenal tube. Therefore, the position of the tube should be checked regularly by nurses. In case of undetermined position, and inconclusive pH measurement, X ray should be ordered.

Other tests for placement that are no longer recommended include auscultation during insufflation of air through the tube because proven to be unreliable. pH analysis of aspirated juice is reliable if the sample has a pH of less than 4.5. Important note: normal gastric pH is 2-3, duodenal pH is 6-7. Biliary reflux and stress ulcer prophylaxis may represent confounding factors.

2.2.1.2 Gastrostomy

Percutaneous Endoscopic Gastrostomy (PEG) has many advantages over surgical gastrostomy (2) there is no need for surgery, it can be performed at the bedside in ICU, minimal sedation is required, and it is a short procedure with reasonable costs. PEG is indicated if enteral nutrition is expected to last for > 3 weeks. Significant variations in practice are observed about this time-line in Europe. Counterintuitively, the aspiration risk is not decreased by PEG. If the patient is agitated, pulling out a nasogastric tube many times per day or in a vegetative state, PEG is recommended. The procedure is simple, and the complication rate is lower than for surgical gastrostomy. PEG is cost-effective. Immediate nutrition is recommended after PEG placement.

Some patients require a surgical or radiological procedure because of their oesophageal or abdominal condition (e.g. multiple abdominal operations, status post gastric bypass, etc.). Surgical gastrostomy during laparotomy/scopy is an alternative to PEG. Complications of operative gastrostomy tube placement are similar to those seen with PEG (i.e. rare bleeding (< 1%), dislodgement in the anterior part of the stomach). Tube site leakage is more frequent. Wound infection occurs in 2-8%.

2.2.2 Postpyloric Feeding

Postpyloric feeding is indicated in patients on enteral nutrition for prolonged periods (> 3 weeks), or those with severe gastro-duodenal dysfunction (16). The advantages of postpyloric feeding (i.e. ease of administration of drugs and nutrients) must be balanced against the disadvantages of this technique which include: higher costs, hazard of gut perforation in case of accidental dislodgement as compared to gastric feeding and the administration of prokinetics. Some teams will prefer postpyloric feeding tubes, whereas others will prefer gastric feeding and pro-motility agents. No study has yet demonstrated a relevant advantage for either of these two options.

Recently, techniques have been developed to improve the rate of success of introducing a nasoenteral tube. If the purpose is to introduce the tube into the duodenum, a "10-10-10" technique has been proposed. This technique proposes the administration of metoclopramide (10 mg), to wait 10 min and then to introduce an 10 French duodenal tube, achieving around 70% success.

Other techniques have reached similar results, and bedside introduction of gastric or duodenal tubes has been widely proposed. More invasive techniques using endoscopy or fluoroscopy are also successful. Techniques using electromagnetic localisation or special antiperistaltic tubes have also had some success. Any duodenal tube introduction must be confirmed by an X-ray.

2.3. Prevention and Handling of Current Problems of Enteral Feeding

Enteral nutrition is associated with several adverse events, frequently related to an inadequate delivery of enteral feeds. Some of the frequently asked questions and solutions are shown below (**Table 3**). Although the guidelines listed in this chapter are not evidence-based and are open to debate, they reflect current practice in several ICUs and, with minor alterations, could realistically be adopted by most ICUs.

Problem	Suggested solution			
High gastric residual volume	Could be neglected up to 500 ml			
	Administer feeds continuously over 24 hours/d			
Duranation of inholotion	Try to decrease opiates and noradrenaline use			
Prevention of inhalation	,			
pneumonia	Flush the catheter after administration of drugs t			
	prevent occlusion.			
	Keep the patient's head elevated (30 degrees)			
Prevention of sinusitis/nasal	_			
erosions	Use small tubes, preferentially of silicon or			
	polyurethane			
Diarrhoea	Exclude infectious diarrhoea, including Clostridium			
	difficile			
	Decrease administration rate by half and prescribe			
	loperamide			
	Replace by a fibre-enriched solution and add			
	probiotics.			
Constipation	Replace by a fibre-enriched solution			
	Treat when exceeding 5 days			
Oral drug administration and				
tube obstruction	Use liquid formulas in preference			
	Crunch and mix tablets			
	Rinse the tube with water after administration			
Nasogastric tube present and				
oesophageal erosions observed	calibre feeding catheter can be left in place			
at endoscopy				
Is stress ulcer prophylaxis useful				
during enteral nutrition?	nutrition partially prevents the occurrence of			
	mucosal erosions and gastrointestinal bleeding, the			
	efficacy of enteral nutrition alone for stress ulcer			
	prophylaxis is not proven. At present,			
	pharmacological stress ulcer prophylaxis should be			
	administered independently from enteral nutrition			

Table 3Troubleshooting common problems related to enteral nutrition

2.3.1 Administration Technique

Continuous enteral nutrition decreases the gastrointestinal tract secretions and is best achieved using volumetric pumps. Practical recommendations include starting enteral nutrition slowly (10-20 ml/h) and progressing cautiously with monitoring of gastrointestinal tract symptoms (7). An elevation of the head of the bed (30 degrees) is recommended. In the case of significant gastric residues (> 500 ml), try prokinetic agents. In the case of further failure, the introduction of a nasoduodenal tube can be considered, according to local practice.

In the case of high viscosity of the formula, or of obstruction risk, routine extra flushing with a saline solution should be a standard technique to prevent the tube obstruction.

Some units still use drip feeding or bolus feeding. These techniques require intensive nursing observation and gastric residue analysis every 4 to 8 hours to reduce the risk of vomiting and intestinal distension. They should be avoided.

2.3.2 Complications

The most frequently encountered complications include: clogging, diarrhoea, constipation, aspiration pneumonia, vomiting, oesophagitis, and abdominal pain. In ventilated patients, the gastric motility is decreased, and is further decreased when morphine or norepinephrine are administered. These complications justify the implementation of an in-house written protocol for nutrition support, which includes monitoring guidelines (7).

2.3.2.1 Gastro-duodenal Dysfunction

A common concern during enteral nutrition is delayed gastric emptying. This condition is defined by an increased gastric residue of > 500 mL/4-6 hours, or more than double the administration of feed for the previous hour, or more than 600 mL for the past 24 hours. Studies have shown however that this documentation of gastric residue is not reliable enough to evaluate gastric emptying adequately. A recent study has even demonstrated that not measuring the gastric residue at all generates the same clinical outcome as measuring it regularly (17). Other tests of gastric emptying, such as sophisticated isotope techniques or the paracetamol absorption test have been proposed to evaluate gastric motility at the bedside. If gastric paresis is observed, it should prompt evaluation of gastric emptying function.

Although there is no clear consensus on the best management of gastro-duodenal dysfunction, one should remember that enteral nutrition is beneficial for the gut mucosa, even at low rates (e.g. 10 ml/hr). In most cases, enteral nutrition should not be discontinued, and pro-kinetic drugs should be used when the patient cannot tolerate "a low delivery rate" of enteral nutrition. Importantly, once the gastric residual volume is below the cut-off value, the administration rate should be restored to a higher value to avoid nutritional deficits. An example algorithm is shown in **Fig. 1**.

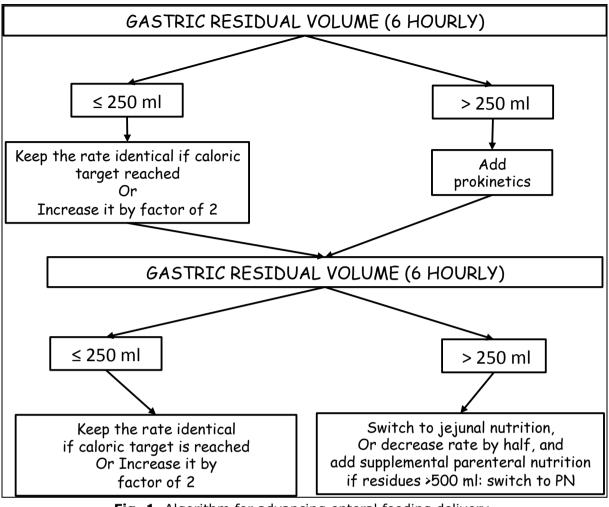


Fig. 1. Algorithm for advancing enteral feeding delivery.
Of note, the accuracy of measured gastric residues is poorly reliable due to the gastric anatomy.
Residues > 500 ml definitively reflect gastric stasis.

Many studies have tested the use of metoclopramide 10-20 mg, or erythromycin, prior to postpyloric tube placement in medical, surgical and mixed populations of patients. The rate of success was significantly better in 3 out of the 6 studies (rates of success of 61% up to 96%) (17).

A high gastric residue is not always a sign of poor gastric peristalsis. Cohen et al (18) demonstrated that half of the patients with gastric residues larger than 200 mL had normal gastric emptying as assessed by the paracetamol test. This easily achieved bedside test can be proposed to help in the decision as to whether to continue gastric enteral nutrition, to propose a naso-jejunal tube.

If the patient is due to receive enteral nutrition for > 3 weeks and will require longer enteral support, percutaneous endoscopic gastrostomy (PEG) should be considered. If the patient is undergoing abdominal surgery, the relative indications for jejunostomy should be considered.

Additional help can be obtained using prokinetic agents that increase gastric peristalsis and gastric emptying. In the case of difficult insertion of a nasoduodenal tube, erythromycin in a single dose may be proposed and facilitate the tube insertion. Prokinetic agents have shown positive effects on gastrointestinal transit and feeding in most of the studies, but without showing positive effects on clinical outcome. When

comparing erythromycin and metoclopramide, the latter has been found the safer, increasing gastrointestinal transit and the tolerance to feeding. Use of erythromycin raises the question of inducing bacterial resistance. However, metoclopramide and erythromycin exert synergistic effects and can be used together in difficult cases.

2.3.2.2 Diarrhoea

Diarrhoea is a common complication of enteral nutrition and is the most frequent cause of interruption of enteral nutrition (19). Diarrhoea is generally defined as the emission of >3 liquid stools / day. A recent prospective survey has shown that the diarrhoea incidence in a general ICU is 14%, with an incidence of *Clostridium difficile* infection of 0.7%. Enteral nutrition is not *per se* a risk factor for diarrhoea. But the combination of EN with antibiotics/antifungals doubles the incidence of diarrhoea. In most cases, continuation of enteral nutrition can be achieved using a systematic and standardized approach. However, when the volume of diarrhoea exceeds 350 mL / day, parenteral nutrition should be considered.

The causes of diarrhoea during enteral nutrition can be divided into 2 broad categories: infectious and non-infectious. Standard treatments for infectious diarrhoea associated with *Clostridium difficile* include oral/enteral metronidazole and vancomycin. In most cases, enteral nutrition can be continued, while antibiotic therapy should obviously be for as short a duration as possible. Occasionally, parenteral nutrition should replace enteral nutrition because the management of diarrhoea is a massive burden both on human and financial resources (20).

2.3.2.3 Constipation

Although frequent in patients fed enterally, constipation is not a typical feeding-related complication, but is probably linked to prolonged periods in the supine position, drugs reducing gastrointestinal peristalsis, or therapeutic negative water balance. However, if untreated, constipation can contribute to ileus, increase abdominal pressure and ultimately impair respiratory function and weaning from the ventilator. Fibre-enriched solutions are usually recommended in cases of constipation, and become progressively a standard of care in the ICU (2). Enemas should be prescribed if constipation exceeds 5 days (21).

3. Parenteral Nutrition

Parenteral nutrition is recommended if enteral nutrition is contraindicated or in the case of failure of enteral nutrition to cover energy requirements after 3-4 days of attempts (2).

3.1 Peripheral, Exclusive and Supplemental Parenteral Nutrition

Access can be central or peripheral. Central access is preferred in ICU patients, who generally require central venous catheter for other purposes (central venous pressure monitoring, fluid and vasopressor administration, etc.). Subclavian access is preferred because it is associated with the lowest rates of complications. Internal jugular or less frequently, (because of the increased infection risk) femoral, catheters could be used. Parenteral nutrition should be administered via a separate lumen of a multilumen central

catheter, to prevent incompatibilities or physicochemical interactions. Aseptic technique and continued aseptic care of central lines for any purpose are mandatory. Peripherally inserted central catheters (PICCs) are now more often used.

3.2 Indications and Contraindications

If parenteral nutrition is required for a short period of time (e.g. 3-4 days), peripheral venous access could be used as an alternative. In order to prevent damage to the peripheral vein, the osmolarity of the administered parenteral nutrition solutions should remain below 900 mOsm/L. This requires administering larger volumes of parenteral nutrition solutions to reach the nutrition target, a condition not always tolerated by fluid sensitive patients. Peripheral parenteral nutrition is sometime used as the route for supplemental parenteral nutrition when the patient requires combined enteral and parenteral nutrition.

To avoid undernutrition or aggravation of pre-existing malnutrition, a therapeutic flowchart is proposed. It recommends administering parenteral nutrition within 3 days in malnourished patients not able to match at least 50% of their resting energy expenditure on day 3 after admission (2). In non-malnourished patients, enteral nutrition is started and if not reaching the calorie target (80% of the prescription), supplementary parenteral nutrition should be considered to avoid building up a caloric debt.

3.3 Complications

Complications of parenteral nutrition:

- Insertion of the catheter may result in pneumothorax, arterial or nerve puncture
- Local or systemic infection may be located at the catheter site, the subcutaneous tunnel, the catheter extremity, or the blood. Catheter-related sepsis (CRS) is a frequent cause of sepsis in critically ill patients and requires blood and hub cultures, with replacement of the catheter in the case of fever and high suspicion of CRS.
- Metabolic complications are either immediate or delayed. Hyper- or hypoglycaemia are the most frequent acute metabolic disturbances encountered. Tight glucose control has become a recommended therapy in critically ill patients. The most feared acute metabolic complication is the **refeeding syndrome** (cf discussion, module 18.1). Electrolyte disturbances are diagnosed easily by frequent laboratory tests. Hepatic function test disturbances can be found in up to 55% of patients receiving parenteral nutrition. A reduction in lipid emulsion load is often a sufficient step to improve the liver blood tests. Fish oil supplemented parenteral nutrition is also helpful (see Module 18.2) to prevent abnormal liver function tests. Triglycerides and cholesterol should be monitored, especially in the case of a simultaneous high dose of propofol.
- Thromboses are mostly encountered with PVC catheters. Venous thrombosis or catheter occlusion are also associated with catheter misplacement and inappropriate use of hyperosmolar parenteral nutrition solutions. The diagnosis is suspected when no blood reflux can be obtained from the catheter, and is confirmed by Doppler examination. Catheter fibrinolysis, catheter removal and/or systemic anticoagulant therapy are usually indicated. The use of polyurethane or silicon catheters significantly reduces the risk of these thromboses.

The appropriate management of parenteral nutrition aims at early detection and treatment of all complications in order to reduce associated morbidity. The most frequent

complications (catheter-related or metabolic/hepatobiliary) and their specific management are listed in **Table 4**.

Table 4

Parenteral nutrition complications and specific management

Catheter-relate	-	Metabolic and			
Catheter misplac torsion	eumothorax/haemothorax H heter misplacement or H rsion sy ombosis or occlusion El ection Si C		Metabolic and hepato-biliary Hyper-/hypoglycaemia Hypertriglyceridaemia /macrophage activation syndrome Electrolytic disturbances Steatosis Cholestasis Acalculous cholecystitis		
Туре	Risk factors	Diagnosis	Prevention	Treatment	
Pneumothorax Haemothorax	Subclavian puncture	Chest X-ray	Ultrasound guidance	Insert thoracic drain	
Catheter misplacement or torsion	Internal jugular puncture	Chest X-ray		Remove the catheter	
Venous thrombosis Catheter occlusion	PVC catheters Catheter misplacement Hyperosmolar solutions	Inflammation and/or swelling (local/homo- lateral arm) No reflux Pulsed Doppler	Use polyurethane or silicon catheters Transparent dressings Use 0.22 micron filters	Remove the catheter Systemic anticoagulant therapy or catheter fibrinolysis	
Hyperglycaemia	Rate of glucose infusion > 4 mg/kg.min ⁻¹	Provide calories as a glucose + lipid mixture Check glycaemia every 4 hours	Reduce glucose supply (2–4 mg/kg.min ⁻¹) Intensive insulin therapy		
Hypoglycaemia	Abrupt withdrawal of dextrose administration Excessive insulin therapy	Check glycaemia every 4 hours	Re-infuse glucose solution	Provide continuous glucose infusion	
Hypertriglycerid aemia	Excessive lipid supply (>4-6 g/kg.day ⁻¹)			Macrophage activation syndrome	
Cholestasis	Absence of oral alimentation Sepsis	Check liver tests 2–3 times/week	Interrupt PN Re-start oral nutrition as soon as possible	Use olive oil or fish oil based lipid emulsions	

Steatosis	High caloric	Avoid excessive	Interrupt PN	Treatment of
	supply	caloric supply		hepatic failure
		Check liver		
		tests 2–3		
		times/week		
Acalculous	Fasting	Check liver		Encourage
cholecystitis	Intraluminal	tests 2-3		enteral feeding
	microbial	times/week		
	overgrowth			

4. General Comments

4.1 Is Enteral Nutrition Better than Parenteral Nutrition?

For 3 decades, enteral nutrition was unanimously considered better than parenteral nutrition. A recent study of a large and unselected population of ICU patients has shown that choosing either parenteral nutrition or enteral nutrition for early nutrition has no impact on the clinical outcome (10). The potential weakness of this work is due to the determination of the energy target based on predictive equations. A straightforward conclusion is that enteral nutrition or parenteral nutrition are equivalent and can therefore be prescribed without further analysis. A number of experts still believe that enteral nutrition should be tested in most patients, except in the case of absolute contraindications, and that parenteral nutrition should be prescribed in the case of partial or complete failure to meet the patient's nutritional needs. The reasons behind this pragmatic approach are: 1/ enteral nutrition is more physiological than parenteral nutrition; 2/ EN administration promotes the functioning of the gut and therefore paves the way for later oral feeding; 3/ parenteral nutrition is more likely to result in overfeeding, especially during the early days in the ICU and if the energy target is not defined by indirect calorimetry.

However, it must be acknowledged that enteral nutrition is insufficient to cover the nutritional needs in up to 50% of ICU patients (22). In addition, the risk of pneumonia during the ICU stay is greater when using enteral nutrition than parenteral nutrition (17, 23). These observations explain most of the divergent opinions with regard to the exclusive use of enteral nutrition versus parenteral nutrition. A pragmatic approach is described below.

4.2 EN Should Be Tested First in Most Patients

Testing the tolerance to enteral nutrition during 2-3 days after ICU admission makes sense. During this period, the intense catabolism provides energy to the body. In other words, the body feeds itself, and high level of exogenous administration of energy is likely to result in overfeeding. A wise strategy can therefore be outlined as follows:

Enteral nutrition is prescribed as soon as the patients is stable from an haemodynamic point of view. The volume of feed is progressively increased over 2-3 days. If the tolerance is good, then the prescription of the total daily feed is further increased. This progression matches the increasing need for exogenous energy as the endogenous energy from stress-related catabolism diminishes. If progression is not possible due to gastrointestinal intolerance, then parenteral nutrition should be prescribed to supplement the insufficient enteral nutrition. This concept has been proven to be of value by the so-called SPN study (24). In this work, supplemental parenteral nutrition was administered

only in the case of failure of enteral nutrition, and only to avoid an energy deficit quantified by indirect calorimetry. Such a strategy was shown to reduce by about 30% the number of nosocomial infections up to 30 days after ICU admission. In the case of absolute contraindications to enteral nutrition, parenteral nutrition should be considered as the most relevant method, but it is recommended to start parenteral nutrition carefully in order to avoid overfeeding (2).

5. Summary

Critically ill patients have increased energy and specific nutrient needs. The administration of an appropriate amount of nutrients by the oral or enteral route is preferred over parenteral nutrition. Gut protective effects of early enteral nutrition have been consistently shown in mechanically ventilated patients. However, significant barriers can impede the administration of enteral nutrition, including gastroduodenal dysfunction reflected by high gastric residual volumes, aspiration, diarrhoea and constipation. Possible solutions are suggested. In the case of contraindications to or failure of enteral nutrition after a few days of attempts, exclusive or supplemental parenteral nutrition are indicated and should be discussed case by case. The timing of supplemental parenteral nutrition (early or late) remains uncertain, and parenteral nutrition should be carefully monitored.

6. References

- 1. Berger MM, Pantet O, Schneider A, Ben-Hamouda N. Micronutrient Deficiencies in Medical and Surgical Inpatients. J Clin Med. 2019;8:7.
- 2. Singer P, Reintam-Blaser A, Berger M, Alhazzani W, Calder PC, Casaer M, et al. ESPEN guidelines on clinical nutrition in the intensive care unit. Clinical Nutrition. 2019;38:48-79.
- 3. Berger MM, Pichard C. Feeding should be individualized in the critically ill patients. Current Opinion in Critical Care. 2019;25:307–13.
- 4. Oshima T, Berger MM, De Waele E, Guttormsen AB, Heidegger CP, Hiesmayr M, et al. Indirect calorimetry in nutritional therapy. A position paper by the ICALIC study group. Clinical Nutrition 2017;36(3):651-62.
- 5. Zusman O, Kagan I, Bendavid I, Theilla M, Cohen J, Singer P. Predictive equations versus measured energy expenditure by indirect calorimetry: A retrospective validation. Clinical Nutrition. 2019;38(3):1206-10.
- Tian F, Heighes PT, Allingstrup MJ, Doig GS. Early Enteral Nutrition Provided Within 24 Hours of ICU Admission: A Meta-Analysis of Randomized Controlled Trials Crit Care Med 2018, 46: 1049–1056 46(46):1049–56.
- 7. Berger M, Reintam-Blaser A, Calder PC, Casaer M, Hiesmayr MJ, Mayer K, et al. Monitoring nutrition in the ICU. Clinical Nutrition. 2019;38:584-93.
- 8. Schindler K, Themessi-Huber M, Hiesmayr M, Lainscak M, Laviano A, Ljungqvist O, et al. To eat or not to eat? Indicators for reduced food intake in 91,245 patients hospitalized on nutritionDays 2006-2014 in 56 countries worldwide: a descriptive analysis. American Journal of Clinical Nutrition. 2016;104(5):1393-402.
- 9. Reintam-Blaser A, Starkopf J, Alhazzani W, Berger MM, Casaer MP, Deane AM, et al. Early enteral nutrition (EEN) in critically ill Patients : ESICM clinical practice guidelines. Intens Care Med 2017;43:380-98.

- Harvey SE, Parrott F, Harrison DA, Bear D, Segaran E, Beale R, et al. Trial of the Route of Early Nutritional Support in Critically Ill Adults. N Engl J Med. 2014;71(18):1673-84.
- 11. Berger MM, Pichard C. Parenteral Nutrition in the ICU: lessons learned over the last few years Nutrition. 2018;59:188-94.
- 12. Heidegger CP, Darmon P, Pichard C. Enteral versus parenteral nutrition for the critically ill patient: a combined support should be preferred ! Current Opinion Critical Care. 2008;14(4):408-14.
- 13. Doig GS, Simpson F, Sweetman EA, Finfer SR, Cooper DJ, Heighes PT, et al. Early parenteral nutrition in critically ill patients with short-term relative contraindications to early enteral nutrition: a randomized controlled trial. Jama. 2013;309(20):2130-8.
- 14. Petros S, Horbach M, Seidel F, Weidhase L. Hypocaloric vs Normocaloric Nutrition in Critically III Patients: A Prospective Randomized Pilot Trial. JPEN J Parenter Enteral Nutr. 2016;40(2):242-9.
- 15. Casaer MP, Mesotten D, Hermans G, Wouters PJ, Schetz M, G. M, et al. Early versus late parenteral nutrition in critically ill adults. N Engl J Med. 2011;365:506-17.
- 16. Deane AM, Dhaliwal R, Day AG, Ridley EJ, Davies AR, Heyland DK. Comparisons between intragastric and small intestinal delivery of enteral nutrition in the critically ill: a systematic review and meta-analysis. Crit Care. 2013(17):R12.
- Reignier J, Darmon M, Romain Sonneville R, Anne-Laure Borel A, Maite Garrouste-Orgeas M, Ruckly S, et al. Impact of early nutrition and feeding route non outcomes of mechanically ventilated patients with shock: a post hoc marginal structural model study. Intensive Care Med. 2015;41(5):875-86.
- 18. Cohen J, Aharon A, Singer P. The paracetamol absorption test: a useful addition to the enteral nutrition algorithm? Clinical Nutrition. 2000;19(4):233-6.
- 19. Thibault R, Graf S, Clerc A, Delieuvin N, Heidegger CP, Pichard C. Diarrhoea in the intensive care unit: respective contribution of feeding and antibiotics. Critical Care. 2013;17(4):R153.
- 20. Heidegger CP, Graf S, Pernegger T, Genton L, Oshima T, Pichard C. The burden of diarrhea in the ICU: A survey and observational study of the caregivers' opinions and workload. International Journal of Nursing Studies. 2016;59:163-8.
- 21. Reintam A, Parm P, Kitus R, Kern H, Starkopf J. Gastrointestinal symptoms in intensive care patients. Acta Anaesthesiol Scand. 2009;53:318-24.
- Alberda C, Gramlich L, Jones N, Jeejeebhoy K, Day AG, Dhaliwal R, et al. The relationship between nutritional intake and clinical outcomes in critically ill patients: results of an international multicenter observational study. Intensive Care Med. 2009;35(10):1728-37.
- 23. Nseir S, Le Gouge A, Lascarrou JB, Lacherade JC, Jaillette E, Mira JP, et al. Impact of nutrition route on microaspiration in critically ill patients with shock: a planned ancillary study of the NUTRIREA-2 trial. Critical Care. 2019; 23(1):111.
- 24. Heidegger CP, Berger MM, Graf S, Zingg W, Darmon P, Costanza MC, et al. Optimization of energy provision with supplemental parenteral nutrition (SPN) improves the clinical outcome of critically ill patients : a randomized controlled trial. Lancet. 2013;381:385-93.