Nutrition, Metabolism and Kidney Support

A Critical Care Approach

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Chapter 14
Complications Associated with Enteral Feeding

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Introduction

Critically ill patients often experience severe metabolic stress, increased inflammatory response, and impaired immune system regulation, leading to greater morbidity, infectious complications, and mortality [1]. Enteral feeding is a form of artificial nutrition that provides macronutrients and micronutrients through the digestive system [2] and is recommended to attenuate these harmful consequences. Moreover, it may improve outcomes of critically ill patients [3]. Enteral nutrition is preferred for patients with a functional gastrointestinal tract who cannot meet their nutritional needs through oral intake [4]. However, precautions are necessary before initiating enteral nutrition in critically ill patients; hence hemodynamic instability, severe

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hypoxemia, and acidosis are contraindication to enteral feeding [3]. Additionally, vomiting, aspiration, and gastric aspirate greater than 500 ml/6 h should be closely monitored and are indications to withhold enteral nutrition [3]. Understanding the potential complications of enteral nutrition and carefully planning enteral nutrition therapy are essential to achieve its intended aims.

Complications Related to Enteral Feeding Tubes

Selecting and inserting the proper tube to provide enteral nutrition can prevent risks associated with faulty feeding techniques. Enteral tube feeding can be inserted through the nose, such as the nasogastric, and naso-jejunal feeding tubes. The tubes are made of thin, flexible polyvinyl (PVC), silicone, or polyurethane and can be inserted at the bedside. This type of tube is usually suitable for a period of less than 4 weeks. Post-pyloric feeding should be considered for patients continuing enteral nutrition for more than 3 weeks or with dysfunctions of the gastroduodenal route [5]. However, while the feeding tube passes through the nose or mouth, it may cause significant discomfort, nausea, and injury. For patients requiring administered enteral nutrition for extended periods or when specific conditions such as anatomical or neurological defects cause difficulty swallowing, a feeding tube is directly inserted into the stomach or small bowel (gastrostomy or jejunostomy). This is achievable using endoscopic, radiologic, or surgical technique [6, 7]. Safety evaluation before using enteral nutrition includes assessing the patient's nutritional status, severity of illness, goals of nutrition support, and proper aims of suitable nutrient quantities to optimize outcomes in critically ill patients (Table 14.1). Feeding initiation after hemodynamic stabilization should be done slowly and gradually [1]. Additionally, a patient with the suspected refeeding syndrome should have laboratory exams monitored, and enteral nutrition should be given gradually [8]. This most significant risks associated with enteral nutrition are inaccurate or mispositioned insertion of feeding tubes to the trachea/lungs and aspiration. After inserting the feeding tube, radiographic confirmation of tube placement is crucial [9–11]. Studies recommend avoiding enteral nutrition until there is confirmation of the correct position of the feeding tube at the beginning of each shift, along with other safety checks [12]. Although many nurses use non-invasive clinical assessments to confirm the positioning of the feeding tube, such as indicator paper to test pH, auscultation, or using capnometry and capnography, these monitoring techniques are not always suitable or efficient for patients in intensive care [13]. Blockage inside feeding tubes is frequently caused by clotting due to the acidic environment and protein in the feeding formula. Interruptions in the continuity of the nutrition formula, gastric residual tests, or passing medication through the tube can also cause feeding tube occlusion [14, 15]. Some methods to unclog feeding tubes include flushing the tube with warm water or carbonated drinks like Coca-Cola or cranberry juice [16]. Uninterrupted feeding should be preferred over intermittent feeding, provided via a continuous movement pump to prevent obstruction of the

Table 14.1 Summarizing potential complications related to enteral nutrition tubes and recommended solutions

Complication	Description	How to deal
Occlusion of the feeding tube	Obstruction of the enteral feeding tube	Use a catheter tip syringe to flush the tube with coca cola or warm water, and try to aspirate the blockage, and if no release, change the tube
Displacement of the feeding tube	Displacement from its planned position	Evaluate the position of the tube with radiography or pH test; if necessary, change the tube, and protect the new tube with suitable measures
Aspiration	Aspirate of stomach content or feeding formula penetrating the lungs	Ensure the proper location of the feeding tube, use an elevated head 30°–45° position during feeding sessions, and inspect for signs and indications of aspiration.
Gastrointestinal symptoms	Cramping, bloating of the stomach, nausea, vomiting, diarrhea, constipation	Gradual modulation of the feeding formula rate, make the feeding formula more suitable, use prokinetic drugs
Unstable metabolic state	Hypo or hyperglycemia Electrolyte complication refeeding syndrome	Monitor blood glucose, electrolyte levels in blood, and fluid balance, regulate the rate and feeding formula
Skin soreness or damage	At the site of the tube insertion redness, sores	Assure appropriate care of the insertion site, use suitable dressings

feeding tubes. Researchers suggest that continuous feeding also has added benefits, such as decreasing the incidence of aspiration [16]. Patients receiving enteral formula with brain injuries, mechanical ventilation, low levels of consciousness, high gastric residual volumes, or accidental tube displacement are at high risk of aspiration and ventilator-associated pneumonia [17–19].

Aspiration

Oropharyngeal or gastric contents secretions and migration of bacteria along the tube from the stomach to the upper airway may contaminate and increase the risk of silent aspiration [15]. A major concern is that the patient develops nosocomial pneumonia as an outcome of aspiration. The events of aspiration often do not come with coughing or other signs of respiratory distress [20]. To reduce the risk of aspiration, assessment of gastric residual volume is recommended [18]. Patients receiving enteral feeding should not lie flat. To reduce the risk of micro aspiration, it is recommended to place the patient in a semi-recumbent position and to elevate the head of the patient bed at a minimum of 300–450 elevation [16, 21, 22]. Regular mouth care with chlorhexidine mouthwash at least twice daily was shown in two studies to reduce nosocomial pneumonia [1, 23, 24]. There is a priority for antiseptic solutions over antimicrobials to reduce the possibility of antimicrobial resistance

[12]. Placing a post pyloric tube is a suggested possibility. The ESPEN and SCCM recommendations suggest that placing a post pyloric tube is advantageous in patients with a high risk of aspiration or intolerance to gastric enteral nutrition or with motility problems [1–3]. The implementation of a post pyloric tube requires expertise [2].

Feeding Efficiency

Due to their critical condition, ICU patients have higher energy requirements resulting from increased metabolic demands [1]. However, despite this, only 50% of patients achieve their energy goal through enteral feeding. Furthermore, enteral feeding is interrupted in approximately 85% of patients for various reasons (see Table 14.2) [25].

Gastrointestinal Intolerance

Enteral nutrition should be initiated within 24–48 h of admission and progressed gradually to adjust for the patient's energy requirements while assessing tolerance to enteral feeding and adjusting the rate and volume appropriately. GI intolerance is characterized by abnormal bowel sounds, vomiting, bowel dilation, diarrhea, and high GRVs [17]. GRV is a common complication of enteral nutrition and is measured by evaluating the volume of food or formula left in the stomach before the next feeding in patients who are receiving enteral nutrition. A GRV larger than 250 mL can occur in up to 50% of patients who are receiving EN and are on mechanical ventilation or vasopressor therapy [1]. Decreased or absent bowel

Table 14.2 Summarizing potential causes of interruption/discontinuation of feeding nutrition and recommended solutions

Potential causes of interruption of enteral feeding	Possible solutions
The patient transferred to surgery or radiological examination or requiring nursing care	Notice the interruption time, secure and connect the feeding formula as soon as possible after the procedure
Patient restlessness	Evaluate the underlying factors and handle them accordingly
Gastrointestinal intolerance, nausea, vomiting, diarrhea	Inspect the placement of the feeding tube. Use another formula. Change the rate of the formula. Evaluate bacterial overgrowth.
High GRV	Define new rate, consider prokinetic medications
Occlusion of feeding tube	Flush the tube with warm water and if no release, consider changing the tube

sounds are associated with worsened patient prognosis, mortality, and longer ICU stays [26]. There is an association between high GRV volume (larger than 250 mL) and occurrence of aspiration, regurgitation, and pneumonia in ICU patients receiving enteral nutrition. Enteral feeding should not be stopped automatically unless other signs of intolerance are present such as vomiting [27–29]. Adjusting the feeding rate, changing the formula used for enteral nutrition, and using prokinetic agents such as erythromycin and metoclopramide have demonstrated improvements in gastric emptying and tolerance. However, studies show few changes in clinical outcomes [29–31]. Large GRV can be due to impaired gastric motility [3, 32]. In this case, a nasoduodenal or -jejunal tube may be inserted. However, post-pyloric tube placement requires expertise and is less physiologic than gastric EN. The use of evidence-based guidelines and protocols for ICU enteral feeding can improve clinical outcomes and increase the supply of enteral nutrition for critically ill patients [3, 16].

Diarrhea

Diarrhea is often defined as the passage of more than three liquid stools per day, according to the World Health Organization [33]. It is a common complication of enteral nutrition in ICU patients and should be recognized and controlled as quickly as possible. Diarrhea can cause hypovolemia, electrolyte and water imbalances, malabsorption of nutrients, and decreased efficiency of enteral nutrition, which can compromise a patient’s nutritional needs. Furthermore, diarrhea can increase the workload and cost of ICU care [3, 34]. Studies show that diarrhea is associated with higher illness severity grades, longer ICU stays, and higher mortality rates [35–37]. The causes of diarrhea can be roughly divided into two categories: infectious and non-infectious. Infection (such as with C. difficile), specific medications (such as metronidazole and vancomycin), and enteral nutrition can all cause diarrhea [36, 38]. However, in most cases, diarrhea results from multiple factors without any consistent causal factor [39]. A diarrhea protocol can help prevent diarrhea in the ICU population [40]. Specific formulas used for enteral nutrition may include substrates that, for some patients, can cause diarrhea, such as formulas with a high amount of fiber or lactose. In most cases of diarrhea in patients receiving enteral nutrition, it is safe to continue with EN. However, if diarrhea exceeds 350 ml/day, parenteral nutrition should be considered [10]. It is important to note that manual filling of the feeding bag with feeding solution can lead to the growth of microorganisms when new feed is added [41, 42]. Suitable hang times are required to prevent microbial growth, and closed systems have been advocated for this purpose [43]. Further research is needed in this area.

New Horizons

Does Machine Learning Support Enteral Nutrition Decisions and Prevent Complications?

In recent years, medicine witnessed the rise of artificial intelligence (AI) and machine learning (ML) [44]. ML is a domain of AI and engages in the way computers ("machines") learn from data. These technologies do not act upon preprogrammed rules but instead, they learn and improve from exposure to examples with the aim to aid clinical decision-making and to improve quality and efficiency of care [45]. ML is becoming more important in medicine as the patient's condition and medical technology increase in complexity [46]. Studies across multiple medical domains have already demonstrated potential benefits of employing ML in the detection and classification of diseases [47, 48]. While the traditional analysis requires the statistical assumptions of the independent and linear relationship between outcome and exploratory variables, the advantage of the ML approach includes the unbiased analysis of many covariates, integration of nonlinear associations, and interaction terms [49, 50]. In many studies, it was claimed that these non-linear capabilities of ML techniques may explain the superior performance compared to traditional statistics [51]. In the ICU, ML might aid clinicians on diagnostic, prognostic, and therapeutic levels to improve patient outcomes. The number of publications on ICU-ML models has increased rapidly in recent years, most aimed at predicting complications, predicting mortality, and improving prognostic models [52, 53]. Recently, advanced ML-based modeling has shown promising results for predicting the onset of sepsis in ICU patients [54] and patient survival for those admitted to the ICU [55]. ML techniques have been used in the domain of enteral nutrition for predicting enteral feeding intolerance (EFI), GI symptoms, and refeeding hypophosphatemia. Hu et al. developed and validated a predictive model for EFI in ICU patients with sepsis [56]. In this dual-center, retrospective, case-control study, a total of 195 intensive care unit patients with sepsis, who stayed at an ICU for at least 7 days and received EN, were enrolled. EFI was defined as vomiting, distention, high GRV (more than 500 mL/24 h), diarrhea, and high intra-abdominal pressure (>12 mm Hg). The deep learning model achieved the best performance with AUCROC of 0.79 (95% CI: 0.68–0.89). Lower respiratory tract infection was the most important contributing factor, followed by peptide EN and shock. A recent study by Lu et al. developed a clinical prediction model to predict the risk of EFI in patients receiving EN in the intensive care unit [57]. In a prospective cohort study, basic information, medical status, nutritional support, and gastrointestinal (GI) symptoms of 203 enrolled patients were recorded. A logistic regression model achieved AUCROC of 0.70 (95%CI: 0.63–0.77) in bootstrap resampling validation. Important predictors included age, GI disease, early feeding, mechanical ventilation before EN started, and abnormal serum sodium. Our group used a supervised ML approach to predict EFI in the first week of ICU stay, using patients' clinical data from the first 72 h [58]. In this retrospective, single-center study, critically ill patients who stayed at the ICU for at least 7 days and received EN were included. EFI was defined according to the occurrence of GI symptoms, “large” gastric volumes, and “inadequate” delivery of enteral nutrition. Admission conditions, medications, and lab results along 72 h from admission were analyzed by classification algorithms. The best performing algorithm was Extra Trees Classifier with AUCROC of 0.88 (95% CI: 0.78–0.98). The results show that intolerance to enteral feeding during the first week of ICU stay is associated with high BMI, urea/creatinine ratio, respiratory and metabolic acidosis, and gender (male). ML has been also used to predict GI symptoms. In a retrospective study, Chen et al. developed a predictive model for diarrhea in the ICU and found that the predictive power of the model was 0.81 (95%CI: 0.752–0.868) in the derivation cohort and 0.736 (95%CI: 0.634–0.837) in the validation cohort, respectively. Predicting factors included enteral nutrition days, high urea nitrogen levels, probiotics, respiratory system disease, and daily doses of nutrient solution [59]. Diarrhea has also been found to be a valid predicting feature for bacteremia [60] using a machine learning algorithm to predict bloodstream infections in the ICU. Another area of ML application is the identification of patients at risk of developing refeeding hypophosphatemia. A retrospective study was conducted including 806 patients with 2 or more days of nothing-mouth prescription, and with phosphate level measurement within 5 days of refeeding [61]. The Extra Trees Classifier showed the highest performance in predicting positive RH prediction (AUCROC:0.95, 95%CI 0.924–0.975) followed by logistic regression (AUCROC:0.76, 95%CI 0.71–0.81). Creating a risk assessment tool via ML to identify patients at risk of developing refeeding hypophosphatemia can lead to careful nutrition management planning and monitoring in the ICU, aiming to reduce the incidence of refeeding syndrome morbidity and mortality. The variables with the highest influence on the model’s decision were provided by low phosphate levels (cutoff: 3.05 mg/dL), followed by recent weight loss, high creatinine (cutoff: 2.4 mg/dL), DM with insulin use, and low hemoglobin.

In conclusion, machine learning is another step toward personalized medicine. It is gaining popularity in the field of intensive care and could be a valuable alternative for a better and more personalized approach to medical nutrition therapy of the critically ill.

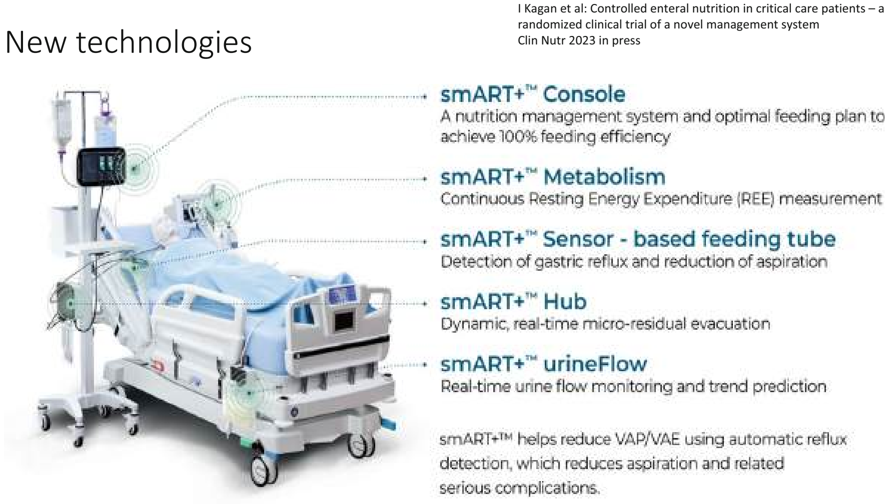
New Technologies to Prevent Enteral Nutrition Complications

Advanced Tube Feedings

Many tubes are equipped with new technologies to prevent nasogastric tube misplacement. One such device uses dual indicators, CO_2, and pH to prevent misplacement [62]. The IRIS technology uses a camera designed to provide anatomic visualization during insertion and after placement. This technology could spare the use of X-ray and prevented misplacement into the airway in about one-third of the cases [63]. The CORTRAK technology uses a magnet to localize the position of the tip of the tube and help the practitioner to progress in the stomach or in the jejunum [64]. All these technologies aim to prevent NGT misplacement.

smART Platform

A new technology [65] includes the smART+ naso-orogastric feeding tube equipped with multichannel bioimpedance sensors that can detect both minor and massive reflux events. It prevents aspiration by stopping feeding and inflating an esophageal balloon when a reflux event occurs, rerouting potential aspiration to an outer bag in real-time. The smART+ Platform includes instructions for correct tube positioning (initially and during continuous use). When malposition is detected, the platform stops feeding. Dual feeding machines, compensation algorithms, and a mechanism for compensating feeding or fluid losses due to reflux events or feeding pauses are included to prevent malnutrition. Additionally, continuous metabolic monitoring and an algorithm to select the best formula according to ICU nutrition ESPEN guidelines are integrated. The smART+ feeding tube is part of the smART+ Platform (Fig. 14.1) (ART MEDICAL, Netanya, Israel. http://www.artmedical.com). The smART+ GRV drainage bag is intended for collecting residual gastric content expelled during reflux events, allowing gastric decompression per individual reflux event. Recently, this platform technology has been compared to the standard of care in a prospective randomized study involving 100 patients, showing a significant improvement in feeding efficacy ([66] in press). The smART+ platform was associated with a mean feeding efficiency of 89.4% ($n = 48$) versus 65.7% for the control group ($n = 50$). Maximal and daily GRV were significantly decreased in the smART + group. ICU length of stay (LOS) and length of ventilation days (LOV) were


New technologies

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smART+™ Console
A nutrition management system and optimal feeding plan to achieve 100% feeding efficiency

smART+™ Metabolism
Continuous Resting Energy Expenditure (REE) measurement

smART+™ Sensor - based feeding tube
Detection of gastric reflux and reduction of aspiration

smART+™ Hub
Dynamic, real-time micro-residual evacuation

smART+™ urineFlow
Real-time urine flow monitoring and trend prediction

smART+™ helps reduce VAP/VAE using automatic reflux detection, which reduces aspiration and related serious complications.

Fig. 14.1 Description of the smART platform in the intensive care setting decreased in the smART+ group versus control (mean LOS: 10.4 days versus 13.7; reduction of 3.3 days, adjusted HR 1.71, 95% CI: 1.13–2.60, $p = 0.012$; mean LOV: 9.5 days versus 12.8 days, reduction of 3.3 days, adjusted HR 1.64, 95% CI: 1.08–2.51, $p = 0.021$ in the adjusted analysis). No adverse events were related to treatment, and no serious adverse events occurred in either group. This technology can overcome enteral feeding complications related to large gastric residual volume. Additionally, the improvement in feeding efficiency will enable the provision of almost all targeted enteral nutrition to critically ill patients despite possible gastrointestinal disturbances.

Conclusions

Enteral nutrition is the most common route to feed ICU patients but is associated with complications. In addition to the recommended clinical protocols, new tools such as machine learning and advanced technologies are able to predict and to prevent these complications and may significantly reduce the complication rate of enteral nutrition.

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