Effects of enteral nutrition method using continuous feeding on patients in intensive care: A Systematic Review
Pengaruh pemberian nutrisi enteral dengan metode continuous feeding pada pasien kritis di unit perawatan intensif: Tinjauan Sistematik

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Abstract
Patients treated with intensive care are at risk of malnutrition. Enteral nutrition can help to maintain a patient's nutritional needs and digestive system function. However, some complications are associated with enteral feeding, including aspiration and refeeding syndromes. This study aimed to provide a comprehensive synthesis of the effects of enteral feeding methods in Intensive Care Unit (ICU) patients. Related literature was systematically retrieved from 2019 to 2023 using the ProQuest, PubMed, ClinicalKey, Science Direct, and Cochrane Library databases. Specific keyword combinations were applied when searching only for randomized controlled trials (RCT) on enteral feeding in critically ill patients. The results of this study found six articles were selected after screening based on the inclusion criteria. The continuous feeding method was found to improve the achievement of the target nutritional requirements and reduce the risk of aspiration. However, it is not always appropriate to consider circadian rhythm. In conclusion, there are important clinical factors to be considered before selecting the type of enteral access, including the patient's clinical condition, surgical history, length of anticipated feeding time, and potential risks.

Keywords: Continuous feeding, critical illness, enteral nutrition

Abstrak

Kata Kunci: Continuous feeding, nutrisi enteral, penyakit kritis
Introduction

A hospital’s intensive care unit (ICU) is important because it serves as a crucial area for the care and treatment of critically ill patients with acute health conditions (Marshall et al., 2017). According to the World Health Organization (WHO), intensive monitoring is generally required in cases, including but not limited to injuries to the head involving airway blockage in intubated patients, including those with tracheostomies. It is predominantly used in patients who require artificial airways and mechanical ventilation for survival (Fialkow et al., 2016).

Nutritional support is essential for nutritional wellbeing and immunological protection. The immune system plays a crucial role in protecting the body from infections, inflammation, and trauma. To function optimally, immune cells require an appropriate nutrient supply (Sharma et al., 2016). The significance of nutrition in critically ill patients is gaining recognition, particularly among patients with extended stay in the ICU, where prolonged life-sustaining assistance is often necessary (Preiser et al., 2021).

Nutritional support for critically ill patients can be provided through enteral or parenteral nutrition (PN). Enteral nutrition (EN) involves delivering nutrients and liquids directly into the gastrointestinal (GI) tract to facilitate digestion and absorption (Bendich, 2016). In contrast, parenteral nutrition is provided directly through the venous circulation without passing through the blood vessels. Parenteral nutrition is administered when the administration of nutrients through the digestive tract is either contraindicated or inadequate (Lambell et al., 2020).

In general, enteral nutrition is preferred over parenteral nutrition because of several advantages: (1) it serves as a physiological form of nutrition that preserves the functionality of the digestive organs, (2) it proves to be efficient in promoting weight gain, and (3) it presents fewer complications. It is significantly more cost-effective, costing 10-20 times less than parenteral nutrition (Selfie & Simadibrata, 2018).

Most critically ill patients in the ICU face high nutritional risks (Wang et al., 2021) because they have physiological dysfunctions and are prone to eating complications. Therefore, it is necessary to select the best method to provide nutrition by considering various factors.

There are various types of enteral nutrition options for patients, including continuous feeding, intermittent feeding, bolus feeding, cyclic feeding, and volume-based feeding, which can be used alone or in combination (Ichimaru, 2018). Continuous enteral feeding (CEF) is a commonly used method (Heffernan et al., 2022). Continuous feeding has a slower infusion rate, and is thus a safer enteral nutrition delivery approach in terms of feeding intolerance (Ichimaru & Amagai, 2014).

However, some journal articles mention several factors that make continuous feeding impractical. Intermittent feeding may be more advantageous than continuous feeding, especially in critically ill patients, in terms of muscle protein synthesis and gastrointestinal hormone secretion (McNelly et al., 2020). Moreover, patients undergoing continuous enteral nutrition experience a higher risk of constipation (Heffernan et al., 2022). Another reason is related to circadian rhythms because the normal condition of the body that requires pause for rest and recovery also needs to be considered (Kouw et al., 2022).

The novelty of this study lies in its comprehensive synthesis of the recent literature on the effects of enteral nutrition methods, specifically focusing on the continuous feeding approach in critically ill patients. While previous studies have examined various aspects of enteral nutrition in the ICU setting, this systematic review provides a specific emphasis on continuous feeding compared to other methods and its impact on nutritional outcomes and other potential risks.

Therefore, the current study aimed to describe the synthesis and interpretation of enteral feeding, especially the continuous feeding method, in patients treated in the ICU and can be considered in determining the feeding method for critically ill patients.

Methods

Design

This systematic review method was used to collect secondary data from various sources. This systematic literature review was based on
the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines for events evaluated by interventions and healthcare behaviors (Page et al., 2021).

To determine the eligibility of this study, the PICO approach comprising Population, Intervention, Comparison, and Outcome was employed. PICO is the most frequently used tool in quantitative cohort studies (Methley et al., 2014). The Population (P) of this study was critically ill patients, with Intervention (I) using intermittent enteral feeding, Comparison (C) was continuous enteral feeding, and Outcomes (O) were the effects of both methods on nutrition tolerance.

The data source for this study was the literature obtained via the Internet from five electronic journal search databases: ProQuest, PubMed, ClinicalKey, Science Direct, and Cochrane Library. These databases were chosen because they are reputable databases known for their extensive coverage of healthcare literature.

Search methods
To limit the search, the search method of this systematic literature review applied a single-line approach. The keywords used in the search were (Enteral Nutrition) AND (Continuous Feeding) AND (Nutrition in Critical Care).

Inclusion and exclusion criteria
The inclusion criteria for journal articles in this systematic literature review were full text, published within the last five years (2019-2023), applied randomized controlled trials (RCT) in the studies, provided information on nutrition for critical patients using the enteral feeding method, and written in English.

Data Extraction
The search results revealed 1,949 articles in ProQuest, 92 articles in PubMed, 933 articles in ClinicalKey, 725 articles in Science Direct, and 256 articles in the Cochrane Library. The 3,955 articles were subsequently defined according to the following inclusion criteria: 1) articles published in English and available in full text, 2) articles published within 2019-2023, 3) articles using randomized control trials, and 4) articles with main content regarding enteral nutrition in critically ill patients, especially in adults. Finally, 879 articles were excluded. The remaining 57 articles were assessed for their methodological quality and results. Finally, six studies passed the assessment. These studies included those by Seyyedi et al. (2020), Lee et al. (2022) and Anandika et al. (2022) and Ren et al. (2021), McNelly et al. (2020) and Zhu et al. (2020).

Quality Appraisal
A systematic review approach using the Joanna Briggs Institute (JBI) framework was used to systematically evaluate research results that assessed the effects of continuous feeding compared with other enteral feeding methods for patients in the ICU.

Data Analysis
A total of 3,955 journal articles were identified from the results of this study. Articles were selected based on the title, abstract, and keywords. After manual filtering, 11 similar articles and 19 articles that did not meet the inclusion criteria were excluded. Six articles were selected for the full-text review. Six articles met the qualification criteria for the final dataset. The PRISMA procedure used to select literature is shown in Figure 1.

**Figure 1.** PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)
Result and Discussion

Of the six selected articles, the research was conducted in Iran, South Korea, China, and India. Three articles discussed the continuous feeding method (n = 3) and compared it with the bolus, intermittent, and sequential feeding methods (n = 2). In addition, one article discusses nutritional therapy (n = 1). Table I provides an overview of the data synthesis for each study.

Table 1. Data Synthesis

<table>
<thead>
<tr>
<th>Authors, Year</th>
<th>Aim/Research Question</th>
<th>Methodology</th>
<th>Intervention</th>
<th>Main Findings</th>
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<tbody>
<tr>
<td>Seyyedi et al. (2020)</td>
<td>To assess the impact of both bolus and continuous enteral feeding approaches on the levels of serum phosphorus and glucose in mechanically ventilated patients.</td>
<td>Randomized Clinical Trial</td>
<td>34 patients in the ICU of Iran Hospital were randomly divided into control group (n=17) who received bolus feeding (BF) for seven days, and intervention groups (n=17) who received continuous feeding (CF) in October to February 2018.</td>
<td>Both bolus and continuous methods led to an elevation in serum phosphorus levels, highlighting the significance of the chosen nutritional approach in regulating phosphorus levels among critically ill patients. However, there were no significant distinctions in the impact of dietary methods on controlling blood glucose levels.</td>
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<tr>
<td>Lee et al. (2022)</td>
<td>To assess the effectiveness and safety of continuous enteral feeding (CEF) in critically ill patients in comparison to intermittent enteral feeding (IEF).</td>
<td>Randomized controlled trial</td>
<td>99 patients who were on mechanical ventilation in the ICU in Korea were divided into two groups: intermittent (n=49), and continuous (n=50), from May 2014 to December 2019.</td>
<td>The CEF group experienced a significantly higher frequency of achieving ≥80% of the target nutrition compared to the IEF group. However, there were no differences in terms of mortality or length of stay (LOS) in hospital and ICU, gastrointestinal intolerance, and organ support. The results of this study support the recommendation of continuous enteral feeding as the optimal strategy for enteral nutrition.</td>
</tr>
<tr>
<td>Anandika et al. (2022)</td>
<td>To compare the effectiveness of bolus versus feeding pump</td>
<td>Randomized Control Trial</td>
<td>70 patients in the ICU in India.</td>
<td>In the bolus method, as much as 5 ml is put through the NGT or OGT tube which is interrupted and gastric...</td>
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method of intermittent enteral feeding related to gastrointestinal problems such as diarrhea, abdominal distension, vomiting, and aspiration pneumonia in ICU in India.

These patients were then randomly grouped into: bolus feeding (n=35) and intermittent (n=35). Follow-up was carried out routinely every day for 7 days and on the 14th day during the study from July 2018 to January 2019.

Ren et al. (2021) To contrast the impact of sequential feeding (SF) and continuous feeding (CF) on the blood glucose levels in critically ill patients.

Randomized controlled trial A total of 62 patients in ICU in China were randomly divided into two groups: SF (n=32) and CF (n=30).

In the SF group, the enteral nutritional suspension was given by EF pump in three time periods a day within 2 h. Meanwhile in the CF group, patients received CF at a constant velocity throughout the study.

There were no significant differences found in demographic or physiological in both groups. The SF group did not exhibit a greater mean glucose level in comparison to the CF group. Hyperglycemia was observed to be more frequent in the CF group than in the SF group for each patient. The feeding intolerance observed in SF was comparable to that in CF. SF appears to be equally safe as CF for critically ill patients.

McNelly, et al. (2020) Does intermittent enteral feed decrease muscle wasting compared with continuous feed in critically ill patients?

Randomized controlled trial 121 adult patients who underwent mechanical ventilation in ICU in the UK

The patients were randomly divided into two groups: intervention group who received intermittent enteral feeding from six times in a day during 4 hours (n = 62), and control group who received standard continuous enteral feeding (n = 59).

Continuous tube feeding aspirate, in contrast to those utilizing the feeding pump method. However, there were no noteworthy distinctions in the occurrence rates of diarrhea, vomiting, abdominal distension, and aspiration pneumonia between the two groups.
Jiang and Li (2020) conducted a controlled trial with 78 neosurgery patients in China hospital in a year from January 2018 to 2019. The patients were randomly grouped into two groups: intermittent group (n = 40), and continuous group (n = 38) given enteral nutrition using a 100 cm long and 15-F nasogastric tube during 7 days. For the ITF group, the enteral nutrition was given four times at 6:00, 11:00, 17:00, and 21:00. For the CTF group, the enteral nutrition was given with a constant speed less than 100ml/h through the electric feeding pump for 24h. The continuous group exhibited a significantly reduced occurrence of diarrhea.

Nutritional support is important for ICU patients. Enteral nutrition in patients undergoing mechanical ventilation within 48 h of ICU admission is the standard of care established by all clinical guidelines (Lambell et al., 2020). However, most critically ill individuals have malfunctions in physiological processes and weak intestinal conditions that are intolerant and prone to eating complications (Ren et al., 2021).

There are several methods of providing nutrition to critically ill patients in the ICU. However, there is no definitive proof regarding the optimal approach for delivering nutrition to patients in critical conditions, because different methods are associated with specific complications. One of these is malnutrition. Malnutrition is associated with an elevated risk of complications including nosocomial infections and mortality (Lee et al., 2022).

Gastrointestinal Effects and Tolerance
Food intolerance affects the digestive system. It occurs when the digestive system is unable to properly process certain foods, resulting in unpleasant physical reactions, such as gas development, diarrhea, and other problems. Food intolerance is common among critically ill adult patients (Jenkins et al., 2022).

Zhu et al. (2020) demonstrated in their study that diarrhea and total intolerance were more prevalent in the intermittent feeding group compared to the continuous feeding group. The authors also noted no significant differences between the two groups in terms of vomiting, abdominal distension, constipation, gastric retention, and gastrointestinal bleeding.

Similarly, McNelly et al. (2020) emphasized that there was no notable difference in gastric tolerance between the two groups. In addition, Lee et al. (2022) demonstrated in their research that there were no noteworthy differences between the two groups regarding vomiting, diarrhea, constipation, regurgitation, aspiration, abdominal pain, and discomfort. This result indicated a lack of significant differences between the two feeding regimens in terms of gastric tolerance.

Bolus vs. Continuous Feeding Method
Seyyedi et al. (2020) conducted a study on 51 patients in Iran by dividing them into control and intervention group. This study aimed to examine the impact of both continuous and bolus feeding techniques on blood phosphate and glucose levels in patients with mechanical ventilation in the ICU. Enteral nutrition was carried out using two methods: continuous feeding for 16-24 hours, and bolus method for 4-6 times of feeding session per day.

In the continuous feeding method, nutritional intake is initiated via a pump, administered at a rate of 20–50 cc/h, and persisting throughout the day. This technique is frequently employed in patients experiencing respiratory failure as it diminishes the likelihood of aspiration. Additionally, it allows for enhanced absorption of micronutrients compared to alternative methods.
For the bolus method, nutrients are administered to the patient 4-6 times daily via a 50mL syringe at short intervals of 4-10 min. This approach is more economical and mirrors the typical dietary patterns. This method also reduces the duration of feeding sessions and is suitable for patients with proficient digestive functions. However, compared with alternative methods, the risk of aspiration is elevated due to gastroparesis.

On the first day of nutrition, 50% of the patient’s nutritional target was met, and the bolus volume was gradually increased hourly for the next two days to reach the final nutritional target of 25 kcal/kg/day. These dietary rules were maintained until the end of the study period.

Seyyedi et al. (2020) found that serum phosphorus levels increased significantly in both continuous and bolus feeding methods. The serum plays a crucial role in the weaning process of patients receiving mechanical ventilation.

**Continuous vs. Intermittent Feeding Method**

Lee et al. (2022) conducted a randomized trial to compare continuous enteral feeding and intermittent feeding among adult patients who underwent mechanical ventilation in the ICU. This study involved 99 patients admitted to the ICU of a hospital in South Korea who were randomly divided into two groups: continuous feeding (50 patients) and intermittent feeding (49 patients) between May 2014 and December 2019.

Patients on intermittent feeding received enteral feeding four times daily, each lasting one hour. Those on continuous feeding receive enteral nutrition through a nasogastric tube, administered continuously over a 24-hour period. The residual gastric volume was assessed every six hours using a 50 mL syringe.

Continuous enteral feeding has been shown to markedly enhance targeted nutritional requirements in patients receiving mechanical ventilation. Continuous feeding significantly increased the achievement of target nutritional needs by 80% compared with intermittent feeding. However, there was no difference in mortality or other significant secondary outcomes, such as the duration of hospital and ICU stay (LOS), gastrointestinal intolerance, and the need for organ support, between intermittent and continuous enteral feeding (Lee et al., 2022).

However, the use of feeding tubes for medication administration poses some challenges. The mixing of liquid medications with enteral formulas may result in incompatibilities, resulting in issues such as granulation, gel formation, and separation of the enteral product. These occurrences can lead to blockage of feeding tubes, disrupting the smooth delivery of nutrition to the patient (Mahan & Raymond, 2017).

**Blood Glucose**

Controlling glucose levels is crucial in the management of critically ill patients. Glycemic control should be treated well, especially in patients with diabetes mellitus during enteral feeding, as diabetes-specific formulas should have less carbohydrate content but more fat and fiber content compared to standard formulas (Sarfo-Adu et al., 2019).

Ren et al. (2021) conducted research that aims to compare blood glucose levels from the impacts of sequential feeding (SF) and continuous feeding (CF) in critically ill patients. In their study, 62 patients in China were given enteral nutrition via a gastric tube. After obtaining 80% of the daily caloric nutritional target through CF, patients were randomly separated into two groups that received different techniques: sequential feeding (SF) and continuous feeding (CF).

Hyperglycemia was less common in SF than in CF. There was no significant difference in the incidence of food intolerance between the SF and CF groups. Thus, SF and CF are considered to be equally safe for critically ill patients.

The CF method has been useful in reducing the complications associated with enteral feeding. Owing to the long infusion duration, critically ill patients are generally more tolerant of CF, offering improved blood glucose regulation and a reduced risk of feeding complications, such as diarrhea, vomiting, and aspiration (Ren et al., 2021).

**Feeding Pump Method on Intermittent Feeding**

Anandika et al. (2022) conducted a study that was aimed to assess the efficacy of the bolus method with feeding pump versus enteral intermittent feeding and its impact on the
occurrence of diarrhea, abdominal distention, increased gastric aspiration volume, vomiting, and aspiration pneumonia in ICU patients. The study involved 80 ICU patients at tertiary hospitals in India from July 2018 to January 2019 by dividing them into two groups: bolus method and pump feeding, with a total of 40 patients in each category.

This study found that patients who underwent bolus feeding experienced more interruptions in feeding and an elevated volume of gastric aspirate than those who utilized the feeding pump method. No significant differences were found in the occurrence of diarrhea, vomiting, abdominal distention, increased gastric aspiration volume, or aspiration pneumonia in either category.

Circadian Rhythms
While most ICUs prefer continuous feeding, there are concerns regarding circadian rhythms. Sleep-wake patterns and circadian rhythms may experience significant disturbances in the context of a critical illness.

Naturally, humans tend to have active metabolic activity and energy intake during the light phase, while adopting a resting and fasting state during the dark phase. Dietary intake that is not aligned with the natural patterns of the circadian clock has been shown to negatively impact human health (Kaczmarek et al., 2017). Thus, administering nutritional support at appropriate times can help preserve circadian rhythms and enhance the recovery process after treatment in the ICU.

Circadian rhythms are recurring oscillations in internal biological processes that govern metabolic processes, such as hormonal signaling, nutrient absorption, and xenobiotic detoxification (Kouw et al., 2022). Circadian rhythms are crucial for physiological, psychological, and behavioral processes.

Some studies have contended that disturbance of circadian rhythms not only plays a crucial role in triggering and promoting negative health consequences, intensifying the burden of symptoms, but also impedes the process of recovery (Sunderram et al., 2014). Complications such as disturbances in the immune system, long-term cardiovascular effects, and increased mortality are associated with circadian rhythm disruptions.

Meal timing serves as a potent training signal for peripheral clocks in numerous organs, and maintaining the circadian phase can affect glucose levels, gastrointestinal function, and muscle metabolism.

Promoting circadian well-being in critically ill patients could potentially enhance metabolism and reduce the risk of psychological health issues and delirium during the recovery phase after intensive care unit (ICU) treatment (Kouw et al., 2022).

Aligning the timing of nutrient consumption, physical activity, and/or medication with circadian rhythms offers potential approaches for resetting peripheral circadian rhythms and improving post-ICU stay. However, its actual benefits have not been conclusively proven. Consequently, the choice between intermittent and continuous feeding should be carefully considered, considering its advantages and disadvantages in clinical practice.

Nutrition Therapy
Therefore, nutritional therapy is important during critical care. An insufficient intake of essential nutrients can lead to malnutrition. Malnutrition is associated with elevated rates of illness and death. It is categorized as either non-severe (moderate) or severe, with three underlying causes: acute injury/illness, chronic illness, or social/environmental factors (such as limited access to food or beliefs/knowledge leading to reduced food intake) (Gropper et al., 2022).

One of the crucial parts of the information for the doctor to consider is that the patient did not receive the prescribed dose of energy and protein. Initiation of enteral feeding is recommended for ICU patients, as long as their gastrointestinal function permits (Ren et al., 2021). Considering that ICU patients exhibit clear signs of malnutrition due to significant loss of appetite, weight loss, or comorbidities, they often require nutritional support (Singer et al., 2019). Therefore, it is crucial to carefully plan and consider nutritional interventions at the same level as any other therapy that supports organ function in the ICU.

To prevent overfeeding, critically ill patients should not receive early full enteral nutrition (EN) or parenteral nutrition (PN); instead, these should be prescribed within a period ranging from three to seven days. (Singer et al., 2023). Minimizing malnutrition, along with avoiding overfeeding and complications during
hospital stay, should be the aim of every patient in the ICU.

In addition to nutrition, feeding method influences serum phosphorus and glucose levels, which are crucial in the weaning process of ventilators (Seyyedi et al., 2020).

Conclusion

Several studies have highlighted various methods of providing enteral nutrition for critically ill patients in the ICU, such as continuous feeding and intermittent feeding. It was found that intermittent enteral feeding offers greater benefits than continuous feeding, as it mirrors normal eating patterns, physiological fluctuations in gastric emptying, and gastrointestinal motility. This may promote improved gastrointestinal function, nutrient absorption, and patient comfort.

Nevertheless, there are still uncertainties surrounding enteral feeding methods for critically ill patients in terms of nutritional distribution, total caloric intake, and gastric tolerance. Each method has advantages and disadvantages, and is associated with certain complications.

Further research is recommended to provide information for medical personnel, especially nurses in the ICU, to provide enteral nutrition with the right method and to try to prevent complications due to enteral nutrition. Clinicians in the ICU must carefully weigh the benefits and challenges of continuous feeding against alternative methods, considering individual patient factors and the clinical context. Future research should focus on optimizing feeding protocols and exploring innovative strategies to enhance the delivery of enteral nutrition in the ICU setting.

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Effects of enteral nutrition method using continuous...


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