Continuous or intermittent feeding: pros and cons

Danielle E. Bear[a,b,c,d,e,*], Nicholas Hart[c,d,e], and Zudin Puthucheary[e,f,g,*]

Purpose of review
There has been a recent shift in the focus of providing nutrition support to critically ill adults towards enhancing recovery and promoting survivorship. With this has come an evaluation of our current approaches to nutrition support, which includes whether continuous feeding is optimal, particularly for reducing muscle wasting, but also for managing blood glucose levels and feeding intolerance and at the organizational level. This review will discuss the pros and cons of using intermittent and continuous feeding relating to several aspects of the management of critically ill adults.

Recent findings
Few studies have investigated the effect of intermittent feeding over continuous feeding. Overall, intermittent feeding has not been shown to increase glucose variability or gastrointestinal intolerance, two of the reasons continuous feeding is the preferred method. A current study investigating the effect of intermittent vs. continuous feeding is awaited to provide insight into the effect of muscle wasting.

Summary
Although there are limited studies investigating the safety and efficacy of an intermittent rather than continuous feeding regimen in critically ill adults, there are several theoretical advantages. Further studies should investigate these and in the meantime, feeding regimens should be devised based on individual patient factors.

Keywords
continuous feeding, critically ill, intermittent feeding, nutrition support

INTRODUCTION

Provision of nutrition support to the critically ill adult is undergoing a revolution. The reason for this is two-fold; first, several large clinical trials have not shown a benefit in terms of composition, dosing, timing and route of the delivery of nutrition support and, second, there has been a paradigm shift in our treatment targets with the significant focus now being on enhancing recovery and promoting survivorship [1■]. It is now generally accepted that nutrition alone will not influence mortality [2■■]. With this has come an evaluation of our current approach to nutrition support in the critically ill patient. Indeed, with enhanced understanding of the pathophysiological mechanisms of skeletal muscle wasting during early critical illness, we are moving from the current approach of nutrition delivery in critical care, which is based on general assumptions regarding the provision of nutrition support, to a strong evidence based approach based on detailing the mechanisms of skeletal muscle wasting and then developing interventions to prevent or reduce skeletal muscle wasting [1■]. One of the current assumptions is that of the method of feeding should being continuous over 24 h rather than intermittent or bolus feeding.

Over 20 years ago, the safety and feasibility of intermittent feeding in critically ill patients was demonstrated [3]. However, clinical trials of secondary infection prevention failed to show benefit [4–6] which led to this practice being abandoned in adult ICU. Furthermore, with the move to targeting glycaemic control and the widespread introduction of insulin as part of critical care management, continuous feeding has become a central component of internationally agreed feeding protocols. Although

[a]Department of Nutrition and Dietetics, [b]Department of Critical Care, [c]Lane Fox Clinical Respiratory Physiology Research Unit, Guy's and St Thomas' NHS Foundation Trust, [d]Centre for Human and Applied Physiological Sciences, King's College London, [e]Lane Fox Respiratory Unit, Guy's and St Thomas' NHS Foundation Trust, [f]Department of Medicine, Centre for Human Health and Performance, University College London and [g]Department of Intensive Care, The Royal Free London NHS Foundation Trust, London, UK

Correspondence to Danielle E. Bear, St Thomas' Hospital, Westminster Bridge Rd, London SE1 7EH, UK. Tel: +44 0207 188 5642; e-mail: Danielle.Bear@gstt.nhs.uk

*Danielle E. Bear and Zudin Puthucheary have contributed equally to the article.

Curr Opin Crit Care 2018, 24:000–000

DOI:10.1097/MCC.0000000000000513

KEY POINTS

- Investigating feeding methods that may enhance patient outcome in a multidimensional manner are a priority for clinicians and researchers.
- Continuous enteral feeding is currently the preferred feeding method in critically ill adults.
- Intermittent/bolus enteral feeding may theoretically provide metabolic and physiological benefits over continuous feeding in critically ill adults, but studies are limited.

there is limited data supporting the clinical effectiveness of a continuous feeding regimen, the rationale of maintaining glucose control whilst limiting glucose variability, combined with the presumed benefits of enhanced enteral feed tolerance has been given support to the continuous feeding approach. Indeed, the clinical support for this feeding method is reflected in both the American [7] and Canadian critical care nutrition guidelines [8], but these recommendations are based on expert opinion only.

In an era in which we are driven to enhance patient-centred care and outcomes, clinicians and researchers have increased interest in investigating feeding methods that may enhance patient outcome in a multidimensional manner. Intermittent, or bolus feeding, is one such method being considered with potential metabolic and physiological benefits. This review will discuss the pros and cons of both continuous and intermittent feeding in critically ill adults.

DEFINITIONS OF FEEDING METHODS

Before discussing the pros and cons of the different feeding schedules, it is important to understand the terminology and definitions. In dietetic clinical practice, several enteral feeding methods may be used depending on the patient's clinical condition and preference. These are continuous, cyclical, intermittent and bolus. Their definitions can be seen in Table 1. Although continuous and cyclical are simple in their definitions, the terms intermittent and bolus feeding are often used interchangeably. Intermittent feeding is most often provided 4–6 times/day and given over a period of 20–60 min, usually via a feeding pump. However, bolus feeding is most often provided using a syringe or gravity method over 5–10 min, also usually 4–6 times/day [9]. For the purpose of this review, the term intermittent feeding will be used, but we will specify timings of feed provision in which required as it is possible that both methods may lead to different outcomes.

Table 1. Definition of different feeding methods

Type of feeding	Definition
Continuous	Provided by an enteral feeding pump over 24 h
Cyclical	Provided by an enteral feeding pump for less than 24 h a day. E.g. overnight or daytime feeding only
Intermittent feeding[a]	Provided 4–6 times a day over 20–60 min with or without a feeding pump
Bolus feeding[a]	Provided 4–6 times a day over a short period of time (5–10 min) via syringe or gravity method

[a]Often the terms intermittent and bolus feeding are used interchangeably.

Parenteral nutrition on the ICU is generally provided over a 24-h period, but may be given over shorter periods of 12–18 h (cyclical) in those patients on long-term parenteral nutrition to reduce the negative effects on liver function. Bolus or intermittent parenteral nutrition is not seen as safe or optimal for the patient, although cyclical infusion of intravenous amino acids in critically ill patients, not just those requiring parenteral nutrition, is gaining popularity to meet the higher protein targets that have recently been recommended.

CONTINUOUS OR INTERMITTENT FEEDING: CURRENT STATE OF THE EVIDENCE

When considering the pros and cons of continuous and intermittent feeding (Table 2), several factors need to be considered. We will discuss these separately.

Blood glucose control

Although tight glucose control with intensive insulin therapy was a priority in the early 2000s, this practice has now shifted to an avoidance of glucose variability and hypoglycaemia as this has been shown to lead to negative outcome. It is the belief of many clinicians that continuous, rather than intermittent feeding helps to reduce this variability. However, in a recent study of 50 critically ill patients comparing bolus feeding given via a percutaneous endoscopic gastrostomy (PEG) tube with continuous feeding, no difference in glucose variability or insulin utilization was found [10]. Of note, participants in this study had to be suitable for PEG tube placement which means that they are likely to be a more stable population (mean APACHE II 14 in this study) in which glucose variability is either not common or not of primary concern. In addition, there are no details specified on how the bolus feeds

Table 2. Potential pros and cons of continuous and intermittent feeding in the critically ill adult

	Continuous feeding	Intermittent feeding
Pros	Better GRV management in some populations Better blood sugar control in early stages of critical illness Less labour intensive for nursing staff Wider choice of enteral feeds	May enhance muscle protein synthesis Ability to 'catch-up' on missed feeds Reduction in diarrhoea May be easier to determine NGT position using pH Allows freedom during rehabilitation and other procedures
Cons	Increased risk of diarrhoea More difficult to determine NGT position using pH Does not allow freedom during rehabilitation and procedures	May lead to higher GRVs in some populations May lead to erratic BGL control in the early stages of critical illness

BGL, blood sugar level; GRV, gastric residual volume; NGT, nasogastric tube.

were provided, or over what timeframe making the interpretation of these results difficult.

Although not comparing continuous to intermittent feeding, continuous feeding is certainly not without risks of hypoglycaemia. Both the CALORIES [11] and NUTRIREA-2 [12] Trials, comparing early parenteral nutrition with early enteral nutrition, reported more patients in the enteral feeding groups having episodes of hypoglycaemia (3.7 vs. 6.2% in CALORIES and 1 vs. 2% in NUTRIREA-2). Although speculative, this may be a result insulin infusions being left running when enteral nutrition is ceased for bedside or other procedures which must certainly be considered a risk. Current glucose control policies have been designed, implemented and audited for safety and compliance in the setting of continuous feeding. Further work is required to ascertain the difficulties in maintaining adequate and safe glucose control alongside the use of intermittent or bolus feeding protocols.

The 'muscle full effect'

In health, skeletal muscle mass is maintained through balanced muscle protein synthesis (MPS) and muscle protein breakdown (MPB) [13]. We have shown critical illness to both suppress MPS and provoke MPB and that this effect might partly relate to the mode of feeding utilized on the ICU [14]. Although starvation causes muscle wasting, protein ingestion normally stimulates MPS [15]. However, such effects rely upon intermittent 'pulse' elevations in amino acid concentrations. This process has been shown to be transient in healthy individuals with MPS returning to baseline levels after around 90-min after ingestion of amino acids [15,16]. This return to baseline levels occurs despite a continuous availability of amino acids in the plasma and muscle indicating that a continuous supply of amino acids does not stimulate MPS further. This concept has been termed 'the muscle-full effect'. Given that most ICU patients receive continuous enteral or parenteral feeding, it is not unreasonable to suggest that this may contribute to muscle wasting through the 'muscle full effect'. Our data suggest that this may indeed be happening, since loss of muscle mass was directly related to the quantity of protein delivered enterally [14].

Although the 'muscle full effect' has not been directly measured in critically ill patients, whole body protein balance was shown to increase due to protein synthesis when the equivalent of 1 g/kg/day was provided intravenously over a 3-h period. Importantly, amino acids were not oxidized indicating their utilization at this level of intake [17]. However, a direct relationship with MPS cannot be ascertained from this study as whole body protein turnover was measured. In addition, data in piglets, used as a model for neonates, indicates that bolus feeding stimulates MPS more than continuous feeding and also leads to a greater amount of protein deposition. This has been explained by the rapid and profound increase in circulating amino acids and insulin that occur with bolus feeding that allow activation of the intracellular signalling pathways leading to mRNA translation [18]. Although the response to amino acid ingestion is different between adults and neonates, these data are interesting and add to the hypothesis that intermittent feeding may in fact improve MPS in critically ill adult patients.

Conversely to the above, in a small study including patients with traumatic brain injury (TBI), intermittent feeding was not associated with improved nitrogen balance compared with continuous or combined (enteral and parenteral) feeding [19]. However, energy and protein targets were not met in either group and the definitions of continuous and intermittent feeding are not clear.

Although no data exists in critically ill adults, the above indicate that continuous feeding may not allow physiological stimulation of intermittent MPS and that intermittent (bolus) feeding (Fig. 1) may therefore restore a measure of anabolic function. However, a Phase IIb multicentre randomized controlled trial has been completed (NCT0235812; www.clinicaltrials.gov), and may offer some insight.

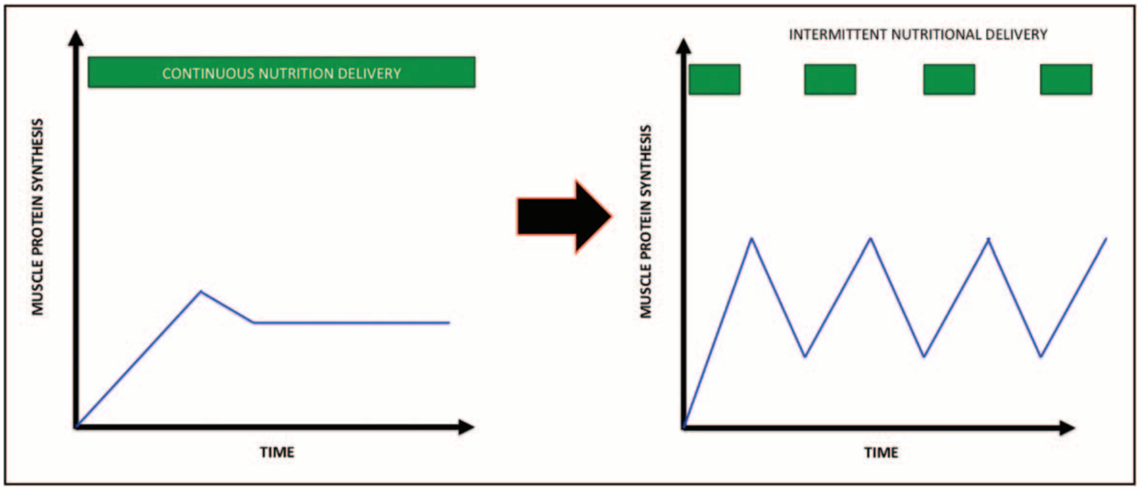

FIGURE 1. Visual representation of the 'muscle full effect' with continuous and intermittent feeding. The (left) shows the theoretical response of muscle protein synthesis to continuous feeding in critically ill adults. This is compared with the (right) in which muscle protein synthesis has been shown, in healthy individuals, to triple around 45 min after ingestion of oral protein and return to normal around 90 min later, despite a continued availability of amino acids in the plasma and muscle.

Gastrointestinal intolerance

More fundamental to the method of nutrition support is that each nutritional component needs to be delivered to the plasma from the gastrointestinal tract and then transported into cells to be utilized by the muscle – a variable and complex process.

Gastrointestinal intolerance is common in critically ill patients, especially in terms of delayed gastric emptying. It has been shown that both the rate and extent of nutrient absorption is impaired, even when postpyloric feeding is utilized as a feeding method. These impairments may then confound any potential to see a positive impact of nutrition in preventing muscle wasting. Intermittent feeding may increase gut motility by increasing cholecystokinin and peptide YY concentrations and by increasing superior mesenteric artery blood flow [20], although this has yet to be measured in the setting of critical illness. However, a three-arm trial [21] has been published comparing the effects of continuous enteral feeding vs. bolus administration using a syringe over 15–20 min and intermittent administration provided via a feeding pump over 18 h. Thirty-six critically ill septic patients were included and assessed for signs of gastrointestinal intolerance over a 3-day period. Results showed no differences between the two groups, but patient characteristics in this study are poorly reported and therefore firm conclusions cannot be made and further work is needed work is needed to establish the ability (or inability) of intermittent feeding to improve gastric motility.

Chrononutrition

Lipid, protein and energy homeostasis are affected to some degree by the circadian rhythm. This central clock regulation in turn regulates local clocks responsible for metabolism and cellular processes such as autophagy in peripheral tissues, including skeletal muscle. Specific to altered physiology and muscle wasting in the critically ill patient, the hepatic clock regulates glycaemic control and glucose clearance, the pancreatic clock regulates insulin secretion and sensitivity and the skeletal muscle clock regulates glucose uptake and metabolism. Adaptation to novel feeding patterns (e.g. continuous feeding while critically ill) is not immediate, taking from 3 (liver) to 7 days (cardiac) with adaptation times of skeletal muscle being unknown [22▪].

Circadian misalignment is detrimental to metabolism [22▪]. Continuous nutritional delivery alters circadian rhythms of intestinal hormones, and postprandial rhythms of ghrelin and insulin release in response to nutrition [20]. Disruption of the skeletal muscle autophagy process has been noted in the critically ill fed population, and may be risk factor for further muscle wasting [23]. These patterns of altered physiology might be avoided by preventing reprogramming of the circadian rhythm using an intermittent feeding regimen, but studies are needed to confirm this hypothesis.

Organizational factors

Critically ill patients regularly do not meet feeding targets for a variety of clinical reasons such as routine and emergency procedures, scheduled visits to the Operating Theatres or Imaging [24]. Intermittent feeding may be of benefit in these settings, allowing staff to bolus missed feeds, and therefore increase the chance of meeting feeding targets. This was not shown in the previously mentioned study undertaken in patients with TBI, but this may be due to local organizational factors which are discussed in the article by the authors [19].

Although no specific study has examined the effect of enteral nutrition delivery on mobilization of patients within the intensive care unit, intermittent feeding has two potential benefits here. First, patients can be mobilized without discontinuation of feed ensuring they are more likely to meet targets. Second, administration of a bolus feed postexercise allows the patient to take advantage of the postexercise period of enhanced MPS [25]. This window for increasing muscle mass is especially important in elderly patients, in which the response to feeding and exercise is blunted [26].

Lastly, there are patient safety factors that should be considered when deciding between intermittent and continuous feeding methods. In many countries, confirmation of nasogastric tubes (NGTs) is by pH. This becomes impossible to interpret in the setting on continuous feeding due to the influence of the alkaline enteral feed on the result. Many ICUs therefore choose to feed their patient over a 20 rather than 24-h period to allow the pH of the stomach to return to normal and therefore confirm the position of the tube. Intermittent feeding may allow this practice to more easily occur, but it should be balanced by the fact that other factors can contribute to an undesirable pH (e.g. the use of proton pump inhibitors and position of the NGT) and this may not negate the need for repeated chest radiograph confirmation and the risks associated with this.

Parenteral vs. enteral routes

Although all the above advantages and disadvantages are independent of route of nutritional delivery (with the exception of gastric motility), intermittent feeding may not be appropriate in patients with naso-jejunal feeding tubes. To date we are unaware of any studies pertaining to safety.

CONCLUSION

To date, there are limited studies investigating the potential benefits and safety of using intermittent feeding over continuous feeding, however there are several theoretical advantages. When considering successful intermittent feeding individual patient characteristics and organizational factors need to be considered. It is possible that the most appropriate and beneficial feeding method is one that considers these factors and is amended depending on the point of the individual patients admission and individual goals. These factors should be considered in future research.

Acknowledgements

None.

Financial support and sponsorship

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:
■ of special interest
■■ of outstanding interest

1. ■ Bear DE, Wandrag L, Merriweather JL, *et al.* The role of nutritional support in the physical and functional recovery of critically ill patients: a narrative review. Crit Care 2017; 21:226.

Comprehensive review of the literature surrounding the role of nutrition support in the recovery of critically ill patients.

2. ■■ Arabi YM, Casaer MP, Chapman M, *et al.* The intensive care medicine research agenda in nutrition and metabolism. Intensive Care Med 2017; 43:1239–1256.

Important agenda providing questions and rationale for the direction of research in critical care nutrition.

3. Bonten MJ, Gaillard CA, van der Hulst R, *et al.* Intermittent enteral feeding: the influence on respiratory and digestive tract colonization in mechanically ventilated intensive-care-unit patients. Am J Respir Crit Care Med 1996; 154(2 Pt 1):394–399.
4. Serpa LF, Kimura M, Faintuch J, *et al.* Effects of continuous versus bolus infusion of enteral nutrition in critical patients. Rev Hosp Clin Fac Med Sao Paulo 2003; 58:9–14.
5. Steevens EC, Lipscomb AF, Poole GV, *et al.* Comparison of continuous vs intermittent nasogastric enteral feeding in trauma patients: perceptions and practice. Nutr Clin Pract 2002; 17:118–122.
6. MacLeod JB, Lefton J, Houghton D, *et al.* Prospective randomized control trial of intermittent versus continuous gastric feeds for critically ill trauma patients. J Trauma 2007; 63:57–61.
7. McClave SA, Taylor BE, Martindale RG, *et al.* Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S. P. E. N.). J Parenter Enteral Nutr 2016; 40:159–211.
8. Canadian clinical practice guidelines for nutrition support in the mechanically ventilated, critically ill adult patient 2015 [Available from: https://www.criticalcarenutrition.com/docs/CPGs%202015/Summary%20CPGs%202015%20vs%202013.pdf. [Accessed 10 April 2018].
9. Ichimaru S, Amagai T. Intermittent and bolus methods of feeding in critical care. In: Rajendram R, Preedy VR, Patel VB, editors. Diet and nutrition in critical care. New York, NY: Springer New York; 2015. pp. 533–548.
10. Evans DC, Forbes R, Jones C, *et al.* Continuous versus bolus tube feeds: does the modality affect glycemic variability, tube feeding volume, caloric intake, or insulin utilization? Int J Crit Illn Inj Sci 2016; 6:9–15.
11. Harvey SE, Parrott F, Harrison DA, *et al.* Trial of the route of early nutritional support in critically ill adults. N Engl J Med 2014; 371:1673–1684.
12. Reignier J, Boisrame-Helms J, Brisard L, *et al.* Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2). Lancet 2018; 391:133–143.
13. Millward D. Protein turnover in cardiac and skeletal muscle during normal growth and hypertrophy. Wildenthal K, editor. Amsterdam: Elsevier/North Holland; 1980. pp. 161–200.
14. Puthucheary ZA, Rawal J, McPhail M, *et al.* Acute skeletal muscle wasting in critical illness. JAMA 2013; 310:1591–1600.

15. Atherton PJ, Etheridge T, Watt PW, *et al.* Muscle full effect after oral protein: time-dependent concordance and discordance between human muscle protein synthesis and mTORC1 signaling. Am J Clin Nutr 2010; 92:1080–1088.
16. Bohé J, Low JFA, Wolfe RR, *et al.* Latency and duration of stimulation of human muscle protein synthesis during continuous infusion of amino acids. J Physiol 2001; 532:575–579.
17. Liebau F, Sundstrom M, van Loon LJ, *et al.* Short-term amino acid infusion improves protein balance in critically ill patients. Crit Care 2015; 19:106.
18. Davis TA, Fiorotto ML, Suryawan A. Bolus vs. continuous feeding to optimize anabolism in neonates. Curr Opin Clin Nutr Metab Care 2015; 18:102–108.
19. Mazaherpur S, Khatony A, Abdi A, *et al.* The effect of continuous enteral nutrition on nutrition indices, compared to the intermittent and combination enteral nutrition in traumatic brain injury patients. J Clin Diagn Res 2016; 10: Jc01–Jc5.
20. Chowdhury AH, Murray K, Hoad CL, *et al.* Effects of bolus and continuous nasogastric feeding on gastric emptying, small bowel water content, superior mesenteric artery blood flow, and plasma hormone concentrations in healthy adults: a randomized crossover study. Ann Surg 2016; 263:450–457.
21. Nasiri M, Farsi Z, Ahangari M, *et al.* Comparison of intermittent and bolus enteral feeding methods on enteral feeding intolerance of patients with sepsis: a triple-blind controlled trial in intensive care units. Middle East J Dig Dis 2017; 9:218–227.
22. Johnston JD, Ordovas JM, Scheer FA, *et al.* Circadian rhythms, metabolism, ▪ and chrononutrition in rodents and humans. Adv Nutr 2016; 7:399–406.
Comprehensive review discussing the concept of chrononutrition.
23. Dos Santos C, Hussain SN, Mathur S, *et al.* Mechanisms of chronic muscle wasting and dysfunction after an intensive care unit stay: a pilot study. Am J Respir Crit Care Med 2016; 194:821–830.
24. Segaran E, Barker I, Hartle A. Optimising enteral nutrition in critically ill patients by reducing fasting times. J Intensive Care Soc 2016; 17:38–43.
25. Atherton PJ, Kumar V, Selby AL, *et al.* Enriching a protein drink with leucine augments muscle protein synthesis after resistance exercise in young and older men. Clin Nutr 2017; 36:888–895.
26. Phillips BE, Williams JP, Greenhaff PL, *et al.* Physiological adaptations to resistance exercise as a function of age. JCI Insight 2017; 2:. [Epub ahead of print]