Original article

Journal of the Intensive Care Society
2019, Vol. 20(4) 299–308
© The Intensive Care Society 2019
Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/1751143719847321
journals.sagepub.com/home/jics

Volume based feeding versus rate based feeding in the critically ill: A UK study

Mina Bharal[1], Sally Morgan[2], Tariq Husain[1], Katerina Hilari[2], Charlie Morawiec[1], Kirsty Harrison[2], Paul Bassett[1] and Alison Culkin[1]

Abstract

Background: Underfeeding in intensive care patients on enteral nutrition is commonplace and multifactorial. This can be exacerbated by interruptions caused by routine fasting for procedures and investigations. Our study aims to demonstrate that a volume based feeding protocol can overcome the barriers of underfeeding and safely increase energy and protein delivery in UK intensive care patients, potentially improving clinical outcomes.

Methods: In this single centre cohort study, data were collected from adult mechanically ventilated patients. We compared the standard care of rate based feeding, from an International Nutrition Survey (2014/15) to the new intervention of volume based feeding, in a mixed medical and surgical intensive care unit. The primary outcomes were the proportion of energy and protein daily targets delivered. Secondary outcomes compared the effects on gastrointestinal tolerance, glycaemic control, mortality, mechanical ventilation days, length of stay in intensive care unit and hospital.

Results: From a total of 82 patients (rate based feeding = 27, volume based feeding = 55), volume based feeding patients received significantly more prescribed energy (52% versus 81%; $p < 0.001$) and protein (40% versus 74%; $p < 0.001$). There was no significant difference in gastrointestinal symptoms such as gastric residual volumes ($p = 0.62$), glycaemic control ($p = 0.94$) or insulin usage ($p = 0.75$). Although there was an improvement in energy and protein delivery, there were no differences in mechanical ventilation days ($p = 0.12$), mortality ($p = 0.06$), length of stay in intensive care unit ($p = 0.93$) and hospital ($p = 0.72$) between the groups.

Conclusion: Compared to rate based feeding, volume based feeding significantly improved energy and protein provision with no adverse effects on glycaemic control or gastrointestinal tolerance, clinical outcomes were not affected.

Keywords

Underfeeding, enteral nutrition, volume based feeding, rate based feeding, intensive care, clinical outcome

Introduction

Nutrition support is an essential part of treatment in patients requiring intensive care. Timely provision of greater energy and protein intake is associated with lower mortality and a faster time to discharge alive.[1,2] However, underfeeding in intensive care patients is commonplace and multifactorial.[3] In response to stress, underfeeding can lead to malnutrition and poor clinical outcomes, including increased mechanical ventilation days, infectious complications, length of stay (LOS) in the intensive care unit (ICU) and in hospital, with an increase in associated healthcare costs.[4–8]

Enteral nutrition (EN) remains the preferred route of feeding in ICUs, providing both nutritional and non-nutritional benefits.[9–12] However, there is currently insufficient evidence for the optimal EN delivery method in the literature for intensive care patients, with options including rate based feeding (RBF) or bolus feeding.[13,14] Frequent interruptions to EN including routine fasting for procedures and investigations exacerbate underfeeding in ICU patients[15,16] and recent studies have demonstrated that RBF is ineffective in addressing this issue.[17–20] Despite this, RBF remains the most common method of EN delivery throughout ICUs in Europe. The recent International Nutrition Survey (INS, 2014/15)

[1]London North West University Healthcare NHS Trust, London, UK
[2]Centre for Language and Communication Science Research, School of Health Sciences, City, University of London, London, UK

Corresponding author:
Mina Bharal, London North West University Healthcare NHS Trust, Watford Road, Harrow, London, Middlesex HA1 3UJ, UK.
Email: m.bharal@nhs.net

demonstrated that adequacy of energy and protein in enterally fed ICU patients in Europe was 58 and 54%, respectively (unpublished data; Darren Heyland, 2017, personal communication).

A volume based feeding (VBF) approach has been recommended to address the challenges of frequent interruptions and optimise the delivery of EN,[12,14] designed to adjust the infusion rate to make up for daily interruptions in delivery, enabling a greater volume of EN to be delivered compared to a fixed hourly RBF.[18] This recommendation for VBF is based on studies in North America.[18–21] To date there are no studies evaluating VBF alone and its effect on EN delivery or clinical outcomes outside of North American healthcare institutes. Although the practice of intensive care medicine is universal in most countries, there can be significant differences in healthcare and populations in this already heterogeneous patient group; these previous VBF studies may not be generalisable to other intensive care populations where differing health systems, barriers, patient characteristics and priorities towards nutrition might present.[22]

So far there has been no study in the United Kingdom (UK) that addresses whether VBF is a safe and more effective method than RBF in improving energy and protein delivery in mechanically ventilated ICU patients. We hypothesised that VBF would improve energy and protein delivery without deleterious effects on glycaemic control or gastrointestinal tolerance and subsequently, may improve clinical outcome.

Methodology

Study design and setting

We conducted a single centre study in an adult, mixed medical and surgical ICU in England, UK between January 2015 and March 2017. This is a cohort study, comparing the usual RBF protocol (cohort 1) to a newly implemented VBF Protocol (cohort 2). Retrospective data were used for RBF participants and prospective data were collected for VBF participants, before and after VBF was introduced. An application to both City, University of London's Senate Research Ethics Committee (Reference number MRes/15-16/40) and UK's Health Research Authority advised that ethical approval was not required for this service evaluation, in that these patients would not undergo any additional intrusive procedure to their normal attention, the data collected were part of their routine care and further patient consent was not required.

Participants

Eligible patients were mechanically ventilated adults (>18 years), requiring EN for >48 h at any point during their first 12 days of stay. Consecutive patients were assessed and selected by a registered dietitian for both cohorts. Patients were excluded for the following reasons: contraindications to EN including bowel obstruction, complex bowel surgery (not including post-operative, uncomplicated colonic resections), proximal enterocutaneous fistula, short bowel, bowel ischaemia or paralytic ileus; pre-existing or onset of GI intolerance including profuse diarrhoea (five stools or >750 ml/24 h), nausea, vomiting, abdominal distension (based on nursing assessment), one episode or more of gastric residual volume (GRV) > 250 ml; receiving parenteral nutrition; aspiration of feed within 48 h; pregnancy.

Figure 1 outlines the feeding protocol for our study. GRVs were monitored every 4–6 h and in the absence of a GRV > 250 ml, feed rates were advanced every 4–6 h. If there was one or more GRV >250 ml, feeds were initially reduced to a previously tolerated rate or subsequently reduced to 10–25 ml/h and prokinetic agents were prescribed. EN was stopped if GRVs were excessive (>500 ml).

Recruitment of RBF patients (cohort 1)

Data for RBF patients were collected retrospectively between January and April 2015 as part of an INS (Critical Care Nutrition, INS Study Protocol, 2014/15). Of the 48 participants recruited for the INS, 27 met the inclusion criteria for this study.

Recruitment of VBF patients (cohort 2)

Consecutive patient data were collected prospectively between March 2016 and March 2017. Patients that were established on the standard EN protocol or RBF regimen were assessed by the dietitian for VBF.

A previously reported VBF protocol[18] was modified and adopted for this study, including using a maximum rate of 150 ml/h[17] and the pre-calculated algorithm in which the remaining volume has been rounded to 100 ml volumes (instead of 50 ml) to simplify calculations (Figure 2). Education before, during and after the implementation of VBF protocol was provided for ICU staff by the unit dietitian.

If patients subsequently developed a poor tolerance to EN, presenting with a single GRV > 250 ml, vomiting, blood glucose concentration (>18 mmol/l) or profuse diarrhoea (defined as five stools or 750 ml/24 h period), the nurses were permitted to reduce the rate back to a previously tolerated rate or to 25 ml/h, after the accepted treatments such as prokinetics for high GRV, change of enteral formula for diarrhoea or insulin treatment were unsuccessful.

Data collection

Patient characteristics, demographics, anthropometry, Acute Physiology and Chronic Health

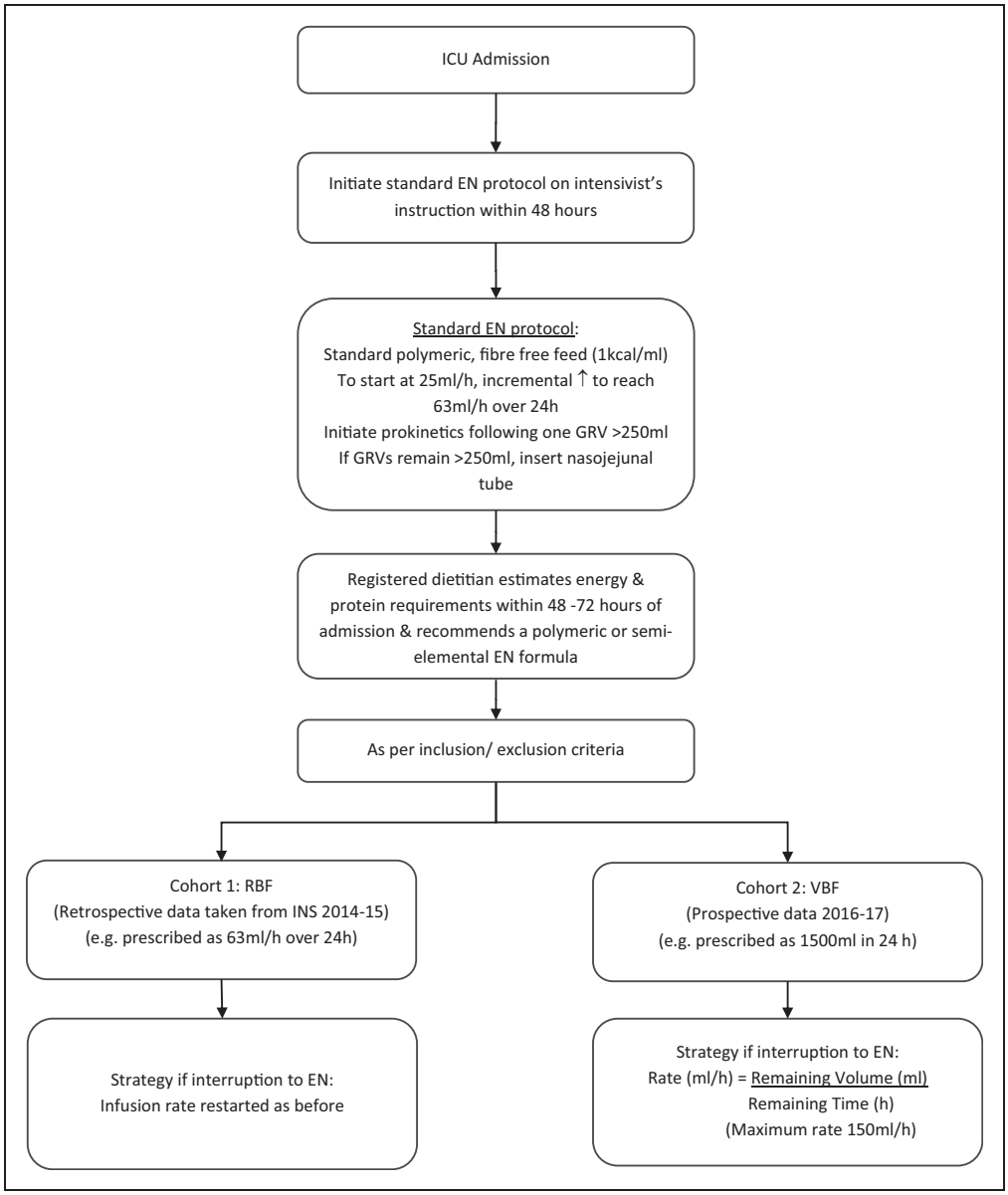

Figure 1. Feeding protocol.
EN: enteral nutrition; GRV: gastric residual volume; ICU: intensive care unit; RBF: rate based feeding; VBF: volume based feeding.

Evaluation II (APACHE II)[23] score and admission details (date and type of admission, i.e. medical/surgical and aetiology) were recorded on ICU admission. The goals for requirements were determined by the unit dietitian using predictive formulas such as 25 kcal/kg and 1.2–1.5 g/kg for protein[10] or Penn State equation.[24]

The primary outcome measures were the percentage of energy and protein requirements delivered over the patients' ICU stay and included non-nutritious energy from medications such as Propofol. Data were collected until ICU discharge, death or for a maximum of 12 days, whichever came first.

Secondary outcome measures included the number of vomiting episodes, GRV >250 ml, prokinetic use, morning and highest daily blood glucose concentrations in addition to insulin usage. Mechanical ventilation days, ICU and hospital LOS, ICU and hospital mortality were also collected for 60 days during and post ICU admission or until discharge/death.

Statistical analysis

Statistical analysis was completed using IBM SPSS version 22.0 (UK version). The power calculation was based on a similar study[18] which demonstrated improvement in the delivery of EN on percentage means of energy delivered for RBF (n = 20) at 80.9% (SD = 18.9%) and VBF (n = 37) 92.9% (SD = 16.8%) of goal energy requirements ($P < 0.01$), with a medium to high effect size of 0.67. A priori analysis with G*Power for a two-tailed t test of the difference between these independent means (RBF versus VBF), using this effect size, and α error level of 0.05 with 80% power resulted in a sample size of 36 patients per group (total 72). The tests used to

Goal total mL formula per 24h	Hours remaining in the day to feed 24h volume																							
	24	23	22	21	20	19	18	17	16	15	14	13	12	11	10	9	8	7	6	5	4	3	2	1
2400	100	104	109	114	120	126	133	141	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150
2300	96	100	105	110	115	121	128	135	144	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150
2200	92	96	100	105	110	116	122	129	138	147	150	150	150	150	150	150	150	150	150	150	150	150	150	150
2100	88	91	95	100	105	111	117	124	131	140	150	150	150	150	150	150	150	150	150	150	150	150	150	150
2000	83	87	91	95	100	105	111	118	125	133	143	150	150	150	150	150	150	150	150	150	150	150	150	150
1900	79	83	86	90	95	100	106	112	119	127	136	146	150	150	150	150	150	150	150	150	150	150	150	150
1800	75	78	82	86	90	95	100	106	113	120	129	138	150	150	150	150	150	150	150	150	150	150	150	150
1700	71	74	77	81	85	89	94	100	106	113	121	131	142	150	150	150	150	150	150	150	150	150	150	150
1600	67	70	73	76	80	84	89	94	100	107	114	123	133	145	150	150	150	150	150	150	150	150	150	150
1500	63	65	68	71	75	79	83	88	94	100	107	115	125	136	150	150	150	150	150	150	150	150	150	150
1400	58	61	64	67	70	74	78	82	88	93	100	108	117	127	140	150	150	150	150	150	150	150	150	150
1300	54	57	59	62	65	68	72	76	81	87	93	100	108	118	130	144	150	150	150	150	150	150	150	150
1200	50	52	55	57	60	63	67	71	75	80	86	92	100	109	120	133	150	150	150	150	150	150	150	150
1100	46	48	50	52	55	58	61	65	69	73	79	85	92	100	110	122	138	150	150	150	150	150	150	150
1000	42	43	45	48	50	53	56	59	63	67	71	77	83	91	100	111	125	143	150	150	150	150	150	150
900	38	39	41	43	45	47	50	53	56	60	64	69	75	82	90	100	113	129	150	150	150	150	150	150
800	33	35	36	38	40	42	44	47	50	53	57	62	67	73	80	89	100	114	133	150	150	150	150	150
700	29	30	32	33	35	37	39	41	44	47	50	54	58	64	70	78	88	100	117	140	150	150	150	150
600	25	26	27	29	30	32	33	35	38	40	43	46	50	55	60	67	75	86	100	120	150	150	150	150
500	21	22	23	24	25	26	28	29	31	33	36	38	42	45	50	56	63	71	83	100	125	150	150	150

Figure 2. Volume based feeding schedule.

compare cohort 1 (RBF) and cohort 2 (VBF) were Mann–Whitney U for continuous variables with skewed distributions and independent t tests for normally distributed variables. Chi Square test or Fisher's Exact test were used for the categorical data as appropriate. Some differences in patient characteristics between groups were adjusted for using regression methods. Continuous outcomes were analysed using linear regression, with a log transformation performed before analysis for those outcomes with positively skewed distributions. Logistic regression was used to analyse binary outcomes. Subsequently, multiple regression was used to adjust for factors found to vary between the two groups from the initial analyses.

Results

Recruitment and demographics

A total of 82 patients met the eligibility criteria and were enrolled into the study. Twenty-seven from 48 patients were enrolled pre-VBF implementation from the INS study for the RBF group. Of the 21 patients excluded from the study, 15 required parenteral nutrition and 6 received no nutrition prior to extubation. Fifty-five out of 56 patients were enrolled for the VBF group. One patient was excluded from the VBF group after enrolment due to the development of a gastrointestinal disorder which required parenteral nutrition.

There was a significant difference in APACHE II score (RBF 23.4 versus VBF 19.4; $p = 0.02$), type of admission ($p = 0.02$) and reason for admission diagnoses ($p = 0.04$) between the groups (see Table 1). Surgical admissions were less common in the VBF group (9% versus 30%; $p = 0.02$). The majority of patients were admitted for respiratory conditions in both RBF (22.2%) and VBF (59.3%) groups. The VBF group ($n = 31$, 56%) had a higher number of patients with a medical respiratory diagnosis than the RBF group ($p = 0.004$).

Gastric feeding occurred in most patients; only two patients had post pyloric feeding, both in the VBF group. Enteral feeding was interrupted at least once in 96% of patients for both cohorts. The primary reason for these interruptions was fasting for endotracheal intubation or extubation. The mean hours of all daily interruptions between the RBF and VBF was 2.7 versus 2.2 h per day, respectively ($p = 0.233$). The average time to start EN was significantly different with a median of two days (interquartile range (IQR) 1, 2) for RBF and one day (IQR 1, 2) for VBF ($p = 0.01$). The number of days in which patients started VBF from date of admission was 4.5 ± 2.5 days.

Primary outcome

Delivery of energy and protein. Table 2 reports the difference in energy and protein delivered between the groups. The VBF patients received a significantly

Table 1. Demographics and other baseline characteristics.

Characteristics	Rate based feeding (n=27)	Volume based feeding (n=55)	*P*-value
Male sex, no. (%)	15 (56%)	31 (56%)	0.95
Age, median [IQR], years	63 [51, 75]	63 [43, 75]	0.57
APACHE II score, mean ±SD	23.4 ± 6.4	19.4 ± 6.7	0.02
Weight, median [IQR], kg	76 [57, 90]	68 [58, 85]	0.37
BMI, median [IQR], kg/m^2	26.2 [24.0, 28.4]	25.0 [21.3, 29.1]	0.34
Type of admission			
Medical, no. (%)	19 (70%)	50 (91%)	0.02
Surgical, no. (%)	8 (30%)	5 (9%)	
Admission diagnosis			0.04
Medical, no. (%)			
Cardiovascular/vascular	5 (19%)	7 (13%)	0.48
Respiratory	6 (22%)	31 (56%)	0.004
Neurological	5 (19%)	8 (15%)	0.65
Sepsis	0 (0%)	2 (4%)	N/A
Other	3 (11%)	2 (4%)	0.22
Surgical			
Respiratory	1 (4%)	1 (2%)	0.59
Gastrointestinal	1 (4%)	1 (2%)	0.59
Head and neck	4 (15%)	2 (4%)	0.79
Other	2 (7%)	1 (2%)	0.26
Estimated energy requirements mean ± SD, kcal	1645 ± 255	1702 ± 279	0.38
Estimated protein requirements median [IQR], g	90 [76, 97]	90 [73, 104]	0.66
Start of EN median [IQR], days	2 [1, 2]	1 [1, 2]	0.01
Start of VBF mean ±SD, days		4.5 ± 2.5	
Patients with interruptions to feed, no. (%)	26 (96%)	53 (96%)	1.00
Interruptions to feed (h/day)	2.7	2.2	0.77

APACHE II: Acute Physiology and Chronic Health Evaluation II; BMI: body mass index; EN: enteral nutrition; IQR: interquartile range; N/A: not applicable; no.: number; VBF: volume based feeding.
Data are reported as mean ± standard deviation (SD), or median and interquartile range (IQR).

Table 2. Mean daily delivery of energy and protein from rate based and volume based feeding.

Outcome	Analysis	Rate based feeding (n = 27)	Volume based feeding (n = 55)	Difference Mean (95% CI)	P value
Energy (kcal)	Unadjusted	737 ± 282	1308 ± 239	570 (452, 689)	<0.001
received	Adjusted[a]	–	–	488 (318, 629)	<0.001
% Energy	Unadjusted	46.1 ± 19.7	77.8 ± 13.4	31.7 (24.4, 39.1)	<0.001
requirements	Adjusted[a]	–	–	25.2 (15.0, 35.5)	<0.001
Energy (kcal)	Unadjusted	826 ± 256	1383 ± 245	557 (441, 674)	<0.001
received[b]	Adjusted[a]	–	–	492 (327, 666)	<0.001
% Energy	Unadjusted	51.6 ± 18.6	82.2 ± 13.8	30.6 (23.3, 37.9)	<0.001
requirements[b]	Adjusted[a]	–	–	26.2 (16.1, 36.2)	<0.001
Protein (g) received	Unadjusted	33.4 ± 14.1	64.7 ± 15.0	31.2 (24.4, 38.1)	<0.001
	Adjusted[a]	–	–	25.3 (15.7, 34.9)	<0.001
% Protein requirements	Unadjusted	40.1 ± 18.9	72.9 ± 15.0	32.8 (25.2, 40.5)	<0.001
	Adjusted[a]	–	–	25.2 (14.5, 35.9)	<0.001
Energy delivered (kcal/kg)		10.8	20.3		
Protein delivered (g/kg)		0.44	0.95		

Summary statistics are mean ± standard deviation or number (percentage) in each category.
[a]Adjusted for APACHE II score, admission type, method of estimated energy requirement, time to start enteral nutrition.
[b]Including energy from Propofol.

greater percentage of prescribed energy, including non-nutritious energy from Propofol (82% versus 52%, $p < 0.001$) and protein (73% versus 40%, $p < 0.001$) compared to RBF patients. There was also a significant difference in percentage energy delivery from EN alone (78% versus 46%, $p < 0.001$). The daily mean energy and protein calculated over $\leqslant 12$ days indicated that the RBF group received 11 kcal/kg and 0.4 g protein/kg in contrast to 20 kcal/kg and 1.0 g protein/kg for the VBF group.

Secondary outcomes

Safety outcomes. After adjusting for the differences in patient characteristics, there was no significant difference in glycaemic control, units of insulin administered, episodes of GRV >250 ml and prokinetic use between the two groups (Table 3). Vomiting was higher in the RBF group, but this difference was non-significant after adjusting for confounding factors, such as APACHE II score, admission type, time to start EN and method of estimated energy requirements ($p = 0.08$).

Patient outcomes. The results demonstrated a significant difference between groups in the number of days of mechanical ventilation in the unadjusted analysis ($p = 0.002$), which was no longer statistically significant ($p = 0.12$) after controlling for APACHE II score, type of admission and time to start EN. There was no significant difference in both ICU and hospital LOS or ICU and hospital mortality.

Rates of EN infusion during VBF

The mean 'average' rate of infusion for VBF was 54 ml/h ± 9.0 and the mean 'maximum' rate was 85 ml/h ± 32.6. However, in six cases, rates were increased up to a maximum 150 ml/h with no complications observed.

Table 3. Safety and patient outcomes.

Outcome	Analysis	Rate based feeding (n = 27)	Volume based feeding (n = 55)	Difference[a] (95% CI)	P value
Glycaemic control					
Hypoglycaemic event	Unadjusted	1 (4%)	3 (5%)	–	1.00
Highest blood glucose	Unadjusted	11.7 ± 3.2	11.6 ± 2.8	−0.2 (−1.5, 1.2)	0.80
concentrations (mmol/l)	Adjusted[b]	–	–	0.1 (−1.9, 2.0)	0.94
Morning blood glucose	Unadjusted	8.4 ± 1.9	8.6 ± 1.3	0.2 (−0.5, 0.9)	0.57
concentrations (mmol/l)	Adjusted[b]	–	–	0.5 (−0.5, 1.6)	0.33
Insulin (daily units)	Unadjusted	4 [0, 52]	18 [0, 53]	1.83 (0.78, 4.34)	0.17
	Adjusted[b]	–	–	1.21 (0.36, 4.10)	0.75
Gastrointestinal tolerance					
Vomiting	Unadjusted	7 (26%)	5 (9%)	0.29 (0.08, 1.01)	0.05
	Adjusted[b]	–	–	0.21 (0.04, 1.21)	0.08
⩾1 GRVs > 250 ml	Unadjusted	2 (7%)	7 (13%)	1.82 (0.35, 9.44)	0.47
	Adjusted[b]	–	–	1.82 (0.18, 18.7)	0.62
Prokinetic use	Unadjusted	5 (19%)	5 (9%)	0.44 (0.12, 1.67)	0.23
	Adjusted[b]			0.39 (0.05, 3.04)	0.37
Mechanical ventilation	Unadjusted	6 [4, 10]	9 [6, 15]	1.76 (1.23, 2.51)	0.002
days	Adjusted[b]			1.46 (0.91, 2.35)	0.12
Length of ICU stay	Unadjusted	10 [6, 15]	11 [7, 19]	1.24 (0.88, 1.75)	0.22
(days)	Adjusted[b]	–	–	1.02 (0.63, 1.66)	0.93
Length of hospital stay	Unadjusted	13 [10, 44]	23 [11, 48]	1.14 (0.75, 1.73)	0.52
(days)	Adjusted[b]	–	–	0.90 (0.49, 1.64)	0.72
Mortality					
ICU mortality	Unadjusted	3 (11%)	10 (18%)	1.78 (0.45, 7.08)	0.42
	Adjusted[b]	–	–	8.67 (0.95, 79.4)	0.06
Hospital mortality	Unadjusted	6 (22%)	12 (22%)	0.98 (0.32, 2.96)	0.97
	Adjusted[b]	–	–	3.64 (0.66, 20.1)	0.14

GRV: gastric residual volumes; ICU: intensive care unit.
Summary statistics are mean ± standard deviation, median [interquartile range] or number (%) in each category
[a]Difference between groups reported as mean difference (normally distributed continuous variables), ratios (skewed continuous variables) or odds ratios (binary variables).
[b]Adjusted for APACHE II score, admission type, method of estimated energy requirement, time to start enteral nutrition.

Discussion

This study established that VBF can significantly increase energy and protein delivery in the first 12 days of ICU admission. These findings offer further evidence that VBF is a safe, alternative strategy in achieving target energy and protein goals in both clinical and research settings in spite of frequent interruptions to EN, intending to minimise nutritional deficits which have been associated with improving clinical outcomes.[1,4,6,7] VBF has previously been used as part of a multi-strategy protocol[17,20,21] and has shown to increase energy and protein delivery but it is difficult to determine if this increase was attributed entirely to VBF. Other contributing components from these studies include the routine use of protein supplementation ($\geqslant$24 g protein) at initiation of EN, use of a semi-elemental or peptide feed (1.0–1.5 kcal/ml), initiation of EN at target rate, use of prophylactic prokinetics on initiation of EN and higher GRV threshold.[17,20,21] While other VBF studies have also successfully improved the delivery of percentage goal energy,[18,19] this is the first study to demonstrate an increase in protein delivery from VBF alone.

Previous work has demonstrated that during interrupted EN days, there was a statistically significant difference in goal energy delivered between VBF (78%) and RBF (62%) ($p = 0.001$).[18] Our study epitomises the perpetual interruptions to EN, where 96% ($n = 79$) of patients experienced routine interruptions of 2.7 h per day (RBF) and 2.2 h per day (VBF), with no significant difference between the two groups. We identified various reasons for interruptions to EN during our study, primarily fasting for endotracheal intubation or extubation, in addition to medical investigations or procedures, drug administration, an inaccessible gastrointestinal tract or enteral tube displacement. The delays in extubation or possible re-intubation, resulted in EN being held for long periods and on consecutive days, leading to difficulties making up for the entirety of EN hours missed.

Observational studies on mechanically ventilated patients have demonstrated that providing at least 80% of energy[25] and protein[26] target was associated with improved clinical outcomes, in particular patients with a higher nutritional risk.[2] However, there is currently debate on the most efficacious dose of energy and protein to optimise patient outcomes, especially in the early phase of critical illness. Current guidelines recommend 20–25 kcal/kg and 1.2–2.0 g protein per day.[10,12] Although our VBF group succeeded in meeting 80% of goal energy, this did not translate into improved clinical outcomes, with the study insufficiently powered for such aspects. In addition, despite a significant increase in protein delivery, it fell short at 73% of goal protein. The barriers in providing adequate protein can be related to the additional provision of energy from non-nutritious sources such as Propofol, glucose containing infusions and citrate anticoagulation used in continuous venovenous haemofiltration,[27] which often requires a reduction in energy from EN, subsequently reducing protein provision. Patients will benefit from EN formulas modified to avoid overfeeding exogenous energy and using higher protein formulas or protein supplementation together with VBF.[17]

This is a study exploring the delivery of energy and protein, safety and clinical outcomes of VBF, which is a relatively novel approach to EN delivery in Europe. It measures the impact of VBF on both gastrointestinal tolerance and glycaemic control. Our results suggest that VBF was delivered safely, with no significant difference in gastrointestinal tolerance, including GRV, vomiting, prokinetic use, glycaemic control and insulin use compared to RBF. The intensive monitoring of GRVs for EN tolerance is currently under question but was included as another measure of safety for this study. Holding or reducing EN is common after a GRV >250 ml, contributing to further interruptions and resulting in a reduction in the volume of EN received and an energy deficit.[5] Recent research findings[28,29] of patients predominantly with medical diagnoses indicate that monitoring GRVs may be unnecessary and that this, in turn, may assist in further reducing EN interruptions. This study found that GRVs were unaffected by VBF despite being perceived as more aggressive and less likely to be tolerated with potentially faster rates than RBF. Similar studies comparing VBF with RBF demonstrated no difference in gastrointestinal tolerance and pulmonary aspiration,[18] ventilator acquired pneumonia and urinary tract infections.[19] The anticipated concerns relating to the implementation of VBF in ICUs are the higher rates of hourly EN delivery, leading to vomiting and aspiration of EN resulting in an increase in mechanical ventilation days. Our study demonstrated that irrespective of higher respiratory diagnoses in our VBF group ($n = 31$, 56%) than the RBF group ($n = 6$, 22.2%) which also might account for the higher number of mechanically ventilated days, VBF strategy had no significant effect ($p = 0.12$). Our findings together with several studies[17–21] suggest vomiting was also not increased ($p = 0.08$). This is presumably related to VBF patients in this study being selected based on having good gastrointestinal function and previously tolerating EN.

Data relating to nutritional intake and tolerance were collected from day 1 of admission up to day 12 or until discharge from ICU. We recognise that EN delivery in the early acute phase is often difficult and it remains uncertain whether VBF is a suitable strategy at admission.[13] However, it is conceivable that VBF may be beneficial when patients are established on EN post-acute phase and in their recovery phase, over a longer ICU stay. The average number of days from admission to start of VBF in this study was 4.5 ± 2.5.

Our study was conducted in a mixed medical and surgical adult ICU in England, UK. The characteristics of patients were broadly representative and, as a pragmatic effectiveness study, probably represent the reality of current nutritional practice in critical care in the UK. It is notable that the mean APACHE II score for VBF and RBF patients recruited to this study was 23.4 ± 6.4 and 19.4 ± 6.7, respectively, similar to the mean APACHE II (20.5 ± 8.5) of intensive care patients in the UK.[22] A similar study investigated VBF in intensive care patients in North America with median APACHE II scores of 10 (IQR 8, 16) and 17 (IQR 12, 19) for RBF and VBF groups, respectively.[19] The original single centre VBF study by McClave et al.[18] confirmed safe and improved energy delivery in patients with a mean Simplified Acute Physiology Score score of 21.7 ± 9.0 19.5 ± 9.3. Our UK study demonstrated that VBF can be tolerated in patients with a higher disease severity. While the practice of critical care medicine is universal in most countries, there can be differences in disease severity and populations in this already heterogeneous patient group[22] and these previous VBF studies[18,19] might not be generalisable to critical care populations outside North America.

Strengths of this study include a heterogeneous, adult population in a UK single centre ICU that had pre-existing, established protocols and guidelines for managing nutritional support, raised GRVs and glycaemic control, reflecting good mainstream practice.[9,10,12] Despite using a convenience sample from the INS data for cohort 1, the same inclusion and exclusion criteria were used for selection for both cohorts.

The non-randomised controlled design, single centre population that had a greater representation of medical rather than surgical patients may limit generalisability. Recent studies using a multi-strategy EN protocol including VBF have demonstrated an improvement of nutrition delivery in medical patients[3,17,21] but did not have the same effect in surgical patients.[30] The low frequency of gastrointestinal complications for our VBF group could be due to the selection of patients that were already established on EN. Comorbidities and Nutrition Risk in Critically ill (NUTRIC) or other nutrition screening scores were not collected but might have influenced secondary outcomes such as lower mortality and faster time to discharge alive, in that patients with higher nutritional risk may benefit more from optimal provision of energy and protein compared with those with lower risk.[2,31,32]

Other limitations include, the small sample size and therefore, underpowered to determine statistical significance for secondary outcomes. The regular education sessions held on VBF for ICU nurses and doctors possibly heightened awareness of nutrition on the unit, contributing to better EN delivery in the VBF cohort. The patients for the two cohorts were recruited over a year apart. During that time the ICU updated its GRV threshold to 350 ml (from 250 ml) before VBF was implemented, therefore, to avoid bias, GRVs recorded by nurses at 250 ml or above were considered as 'high' for both groups. Protein supplementation was also introduced during this period; however, it was not routine practice. When protein supplementation was prescribed in 19% of the intervention group, nurses did not routinely administer it, therefore having little effect on total protein intake. Finally, indirect calorimetry was not available and predictive equations were used which are less reliable.[33,34]

In future, a more robust, adequately powered randomised controlled trial, including more surgical patients is recommended to investigate the impact of the VBF protocol on nutrition delivery. The use of body composition analysis, functional or health related quality of life measures as primary outcomes to evaluate nutrition intervention may be more suitable than mortality and infectious complications.[35]

In conclusion, this study described an alternative strategy to the RBF protocol. It confirmed that compared to RBF, VBF protocol can be successfully implemented to significantly enhance the delivery of EN safely, with no adverse effect on glycaemic control and gastrointestinal tolerance. However, despite this improvement, there was no beneficial effect observed on clinical outcomes, as it was underpowered to do so. This study's findings should encourage the development of a robust, adequately powered randomised controlled trial to investigate the impact of this safe VBF protocol on nutrition delivery and appropriate clinical outcomes.

Acknowledgements

We would like to thank all the staff on the intensive care unit for their support.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: We would like to thank Health Education England/National Institute of Health Research for funding this project.

References

1. Alberda C, Gramlich L, Jones N, 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: 1728–1737.

2. Compher C, Chittams J, Sammarco T, et al. Greater protein and energy intake may be associated with improved mortality in higher risk critically ill patients: a multicenter, multinational observational study. *Crit Care Med* 2017; 45: 156–163.
3. Heyland DK, Dhaliwal R, Wang M, et al. The prevalence of iatrogenic underfeeding in the nutritionally 'at-risk' critically ill patient: results of an international, multicentre, prospective study. *Clin Nutr* 2015; 34: 659–666.
4. Villet S, Chiolero RL, Bollmann MD, et al. Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients. *Clin Nutr* 2005; 24: 502–509.
5. Dvir D, Cohen J, and Singer P. Computerized energy balance and complications in critically ill patients: an observational study. *Clin Nutr* 2006; 25: 37–44.
6. Tsai J-R, Chang W-T, Sheu C-C, et al. Inadequate energy delivery during early critical illness correlates with increased risk of mortality in patients who survive at least seven days: a retrospective study. *Clin Nutr* 2011; 30: 209–214.
7. Mault J. Energy balance and outcome in critically ill patients: results of a multi-centre, prospective, randomised trial by the ICU Nutrition Study Group. *J Parenter Enteral Nutr* 2000; 24: S4.
8. Barker LA, Gout BS, and Crowe TC. Hospital malnutrition: prevalence, identification and impact on patients and the healthcare system. *Int J Environ Res Public Health* 2011; 8: 514–527.
9. Reintam Blaser A, Starkopf J, Alhazzani W, et al. Early enteral nutrition in critically ill patients: ESICM clinical practice guidelines. *Intensive Care Med* 2017; 43: 380–398.
10. Kreymann KG, Berger MM, Deutz NEP, et al. ESPEN Guidelines on enteral nutrition: intensive care. *Clin Nutr* 2006; 25: 210–223.
11. Dhaliwal R, Cahill N, Lemieux M, et al. The Canadian Critical Care Nutrition Guidelines in 2013. *Nutr Clin Pract* 2014; 29: 29–43.
12. McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient. *J Parenter Enteral Nutr* 2016; 40: 159–211.
13. 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.
14. Critical Care Nutrition. Canadian Clinical Practice Guidelines. Summary of Revisions to the Recommendations, https://www.criticalcarenutrition.com/docs/CPGs%202015/Summary%20CPGs%202015%20vs%202013.pdf (2015, accessed 28 March 2017).
15. McClave SA, Sexton LK, Spain DA, et al. Enteral tube feeding in the intensive care unit: factors impeding adequate delivery. *Crit Care Med* 1999; 27: 1252–1256.
16. Peev MP, Yeh DD, Quraishi SA, et al. Causes and consequences of interrupted enteral nutrition. *J Parenter Enteral Nutr* 2015; 39: 21–27.
17. Heyland DK, Cahill NE, Dhaliwal R, et al. Enhanced protein-energy provision via the enteral route in critically ill patients: a single center feasibility trial of the PEP uP protocol. *Crit Care* 2010; 14: R78.
18. McClave SA, Saad MA, Esterle M, et al. Volume-based feeding in the critically ill patient. *J Parenter Enteral Nutr* 2015; 39: 707–712.
19. Haskins IN, Baginsky M, Gamsky N, et al. Volume-based enteral nutrition support regimen improves caloric delivery but may not affect clinical outcomes in critically ill patients. *J Parenter Enteral Nutr* 2017; 41: 607–611.
20. Taylor B, Brody R, Denmark R, et al. Improving enteral delivery through the adoption of the 'feed early enteral diet adequately for maximum effect (FEED ME)' protocol in a surgical trauma ICU. *Nutr Clin Pract* 2014; 29: 639–648.
21. Heyland DK, Murch L, Cahill N, et al. Enhanced protein-energy provision via the enteral route feeding protocol in critically ill patients: results of a cluster randomized trial. *Crit Care Med* 2013; 41: 2743–2753.
22. Wunsch H, Angus DC, Harrison DA, et al. Comparison of medical admissions to intensive care units in the United States and United Kingdom. *Am J Respir Crit Care Med* 2011; 183: 1666–1673.
23. Knaus WA, Draper EA, Wagner DP, et al. APACHE II: a severity of disease classification system. *Crit Care Med* 1985; 13: 818–829.
24. Frankenfield DC, Coleman A, Alam S, et al. Analysis of estimation methods for resting metabolic rate in critically ill adults. *J Parenter Enteral Nutr* 2009; 33: 27–36.
25. Heyland DK, Cahill N, and Day AG. Optimal amount of calories for critically ill patients: depends on how you slice the cake! *Crit Care Med* 2011; 39: 2619–2626.
26. Nicolo M, Heyland DK, Chittams J, et al. Clinical outcomes related to protein delivery in a critically ill population. *J Parenter Enteral Nutr* 2016; 40: 45–51.
27. New AM, Nystrom EM, Frazee E, et al. Continuous renal replacement therapy: a potential source of calories in the critically ill. *Am J Clin Nutr* 2017; 105: 1559–1563.
28. Reignier J, Mercier E, Le Gouge A, et al. Effect of not monitoring residual gastric volume on risk of ventilator-associated pneumonia in adults receiving mechanical ventilation and early enteral feeding: a randomized controlled trial. *JAMA* 2013; 309: 249–256.
29. Montejo JC, Miñambres E, Bordejé L, et al. Gastric residual volume during enteral nutrition in ICU patients: the REGANE study. *Intensive Care Med* 2010; 36: 1386–1393.
30. Declercq B, Deane AM, Wang M, et al. Enhanced protein-energy provision via the enteral route feeding (PEPuP) protocol in critically ill surgical patients: a multicentre prospective evaluation. *Anaesth Intensive Care* 2016; 44: 93–98.
31. Heyland DK, Dhaliwal R, Jiang X, et al. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. *Crit Care* 2011; 15: R268.
32. Rahman A, Hasan RM, Agarwala R, et al. Identifying critically-ill patients who will benefit most from nutritional therapy: further validation of the "modified NUTRIC" nutritional risk assessment tool. *Clin Nutr* 2015; 35: 158–162.
33. Walker RN, and Heuberger RA. Predictive equations for energy needs for the critically ill. *Respir Care* 2009; 54: 509–521.

34. Tatucu-Babet OA, Ridley EJ, and Tierney AC. Prevalence of underprescription or overprescription of energy needs in critically ill mechanically ventilated adults as determined by indirect calorimetry. *J Parenter Enteral Nutr* 2016; 40: 212–225.

35. 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.