The effect of continuous versus intermittent enteral nutrition on metabolic outcomes in critically ill patients.

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Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal signs and symptoms
Study type	Interventional

Summary

ID

NL-OMON57591

Source
ToetsingOnline

Brief title
CONVEnIENT

Condition

- Gastrointestinal signs and symptoms
- Glucose metabolism disorders (incl diabetes mellitus)
- Muscle disorders

Synonym
Critical illness, severly ill

Research involving
Human

Sponsors and support

Primary sponsor: Ziekenhuisvoorzieningen Gelderse Vallei
Source(s) of monetary or material Support: NWO

Intervention

Keyword: Chrononutrition, Critical care, Glycemic control, Tube feeding

Outcome measures

Primary outcome

The primary outcome is the between-group difference in glycaemic variability during ICU admission measured with Continuous Glucose Monitoring (CGM) expressed as Coefficient of Variation (COV). This COV is calculated by dividing the standard deviation by the mean blood glucose level and multiplying by 100. It gives a relative measure of variability, which is helpful in comparing variability between individuals or groups with different mean glucose levels.

Secondary outcome

1.Glycaemic control (assessed by CGM and blood samples):

- Mean interstitial glucose concentrations per day (mmol/L)

- SD of mean interstitial glucose concentrations per 24 h

- Mean insulin dose (IU/day)

- Mean Amplitude of Glucose Excursions (MAGE)

- Mean plasma insulin concentrations (*µU/mL/24h)

- HbA1c at admission (%)

- Hypoglycaemic events per day (blood glucose level below 4.0 mmol/L)

- Hyperglycaemic events per day (blood glucose level above 10.0 mmol/L)

2. Gastrointestinal tolerance/function (assessed as part of clinical practice, extracted from patient records):

- Gastric residual volumes (mL), total per 24h and largest volume per 24h (assessed as part of clinical practice)

- Incidence of vomiting, diarrhoea, constipation, and regurgitation per 24 h

3. Marker of inflammation (extracted from patient records)

- CRP at admission ((mg/L)

4. Sleep quality and circadian rhythm (assessed from blood and saliva samples at the start and end of the intervention and extracted from patient records):

- Melatonin and cortisol levels obtained at 6 time points in saliva (06:00, 10:00, 14:00, 18:00, 22:00, 02:00)

- mRNA expression of essential clock genes (BMAL, CLOCK, Cry1 and, Per2) obtained at 6 time points in blood (06:00, 10:00, 14:00, 18:00, 22:00, 02:00)

- Core body temperature per day (°C, mean, highest and lowest value/24h)

- Mean, highest and lowest Richmond Agitation Sedation Scale (RASS) score per 24 h

- Glasgow Coma Scale (GCS) score per 24 h

- Delerium Observation Screening (DOS) scale per calendar day

- Confusion Assessment Method for the ICU (CAM-ICU) scores per calendar day

- Sleep quality measured with the Pittsburgh Sleep Quality Index (PSQI) at T=3

5. Muscle mass and body composition (assessed by BIA and muscle ultrasound at the start and end of intervention), only in centers with available equipment for these measurements:

- Cross-sectional area and muscle layer thickness of quadriceps muscle by ultrasonography

- Fat-free mass (FFM), fat mass (FM), skeletal muscle mass (SMM), intracellular water (ICW), extracellular water (ECW), body fat percentage (BF%), total body water (TBW), ECW/TBW-ratio by bio-electrical impendence analysis

6. Nutrition intake (extracted from patient records):

- Total nutritional intake per day (energy in kJ/24h, protein in g/24 h, fat in g/24 h and carbohydrate in g/24h and % of total intake)

7. Quality of life

- Health-related quality of life measured with SF-36

Study description

Background summary

Optimal timing of nutritional therapy has the potential to reduce metabolic complications in intensive care unit (ICU) patients, including improving glycemic control, restoring circadian rhythm and reducing loss of muscle mass during critical illness. This could potentially reduce long-term consequences such as post intensive care syndrome. This effect is expected because intermittent tube feeding, unlike continuous feeding, improves insulin sensitivity, increases the rate of muscle protein synthesis (MPS), activates fasting-induced autophagy and ketogenesis, and maintains circadian rhythm in studies in healthy humans and animals. However, studies in critically ill humans show conflicting results regarding these metabolic outcomes, and therefore, in the current study, we want to investigate these outcomes simultaneously in intensive care patients. If the results show that intermittent tube feeding during the day is better for the metabolic outcomes studied compared to continuous tube feeding, international guidelines for nutrition in the ICU can potentially be improved.

Study objective

The primary objective of the CONVEnIENT trial is to investigate the effect of daytime intermittent enteral tube feeding, compared to a standard continuous tube feeding pattern (24-hour/day), on glycaemic control, gastrointestinal function, circadian rhythms, and muscle mass in critically ill patients.

Study design

Multicentre, randomised controlled trial, with two parallel groups.

Intervention

Patients will be randomised to receive either intermittent tube feeding during the day (4 times delivered in 1 hour, e.g. at 08:00, 12:00, 16:00, and 20:00h; INT) or continuous for 24 h (total needed volume spread evenly per hour over 24 h e.g. 50 mL/hr for 24 h; CON). The amount of nutrition patients will receive is based on their requirements according to standard nutritional practices.

Study burden and risks

This study will include invasively mechanically ventilated patients admitted to the ICU. This is a vulnerable patient group that, due to the nature of their condition, will not be able to give informed consent before the start of the study. However, alternative models or patients are not able to answer our

research question, as it is specific to this patient group. Critical illness (for which mechanical ventilation is necessary for an undetermined period) is a severe, life-threatening disease with unique and detrimental metabolic derangements. Previous work on intermittent nutrition administration and metabolic outcomes in healthy or less severe disease conditions cannot simply be extrapolated to ICU patients. The study's findings will inform clinical practice to optimise nutritional care for critically ill patients. The proposed study is believed to pose no significant ethical issues. Screening eligible patients involves accessing medical records to assess in- and exclusion criteria, and, with appropriate measures in place to preserve privacy and confidentiality, it is a negligible-risk procedure. The care provided to patients will be unaffected by participation in the study. All measurements performed during the study are non-invasive (glycaemic control assessed by continuous glucose monitoring, circadian rhythms assessed by clock genes in blood samples (in total 44 mL), melatonin, and cortisol in saliva samples and body composition and muscle mass by BIA and ultrasound), or part of standard clinical care (gastrointestinal function assessed by gastric residual volumes).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Age >=18 years
2. Receiving or eligible to receive exclusively gastric tube feeding
3. Expected ICU stay >=48 hours
4. Receiving invasive mechanical ventilation upon initiation of the study

Exclusion criteria

1. The treating clinician considers participation in the study clinically contraindicated (e.g., change in feeding regimen, no possibility for placement of CGM on arms, not able to receive exclusive gastric tube feeding)
2. Death is deemed to be imminent or inevitable during admission, and the attending doctor, patient, or substitute decision-maker is not committed to active treatment
3. Pregnancy
4. Expected fasting in the next 12 hours, for example, due to surgery
5. Readmission in last 14 days
6. Patients with burn injuries

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2025
Enrollment:	124
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	28-05-2025
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL88158.091.24