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ClinicalTrials.gov ID: [Not yet assigned]

Study Identification

Unique Protocol ID:	NL73247.068.20
Brief Title:	Proteins and RECovery in Critical IllneSs (PRECISe)
Official Title:	The Impact of High Versus Standard Enteral Protein Provision on Functional Recovery Following Intensive Care Admission: a Randomized Controlled, Multicenter, Parallel Group Trial in Mechanically Ventilated, Critically Ill Patients
Secondary IDs:	80-85200-98-18574 [Grantor or Funder: KCE-ZonMW (BeNeFIT)]

Study Status

Record Verification:	March 2020
Overall Status:	Not yet recruiting
Study Start:	November 2020 [Anticipated]
Primary Completion:	November 2022 [Anticipated]
Study Completion:	February 2023 [Anticipated]

Sponsor/Collaborators

Sponsor:	Maastricht University Medical Center
Responsible Party:	Sponsor
Collaborators:	Ziekenhuis Oost-Limburg Zuyderland Medisch Centrum Gelderse Vallei Hospital Medisch Spectrum Twente Centre Hospitalier Universitaire Liège Centre Hospitalier Régional de la Citadelle Universitair Ziekenhuis Brussel General Hospital Groeninge NOTE : "Centre Hospitalier Universitaire Liège" has been asserted to be a valid organization name by MaastrichtUMC.

Oversight

U.S. FDA-regulated Drug:	No
U.S. FDA-regulated Device:	No
U.S. FDA IND/IDE:	No
Human Subjects Review:	Board Status: Approved Approval Number: METC20-039

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Data Monitoring: Yes

FDA Regulated Intervention: No

Study Description

Brief Summary: Rapid skeletal muscle wasting during critical illness had a detrimental impact on both short and long term outcomes following ICU admission. Increased dietary protein delivery might attenuate skeletal muscle wasting and its subsequent effects on post-ICU function.

The investigators will conduct a 824 patient, randomised controlled, quadruple blinded parallel group trial to determine whether enteral nutrition with increased protein content in mechanically ventilated, critically ill patients is able to improve functional recovery.

Detailed Description: Every year, more than 92.000 patients are acutely admitted to an intensive care unit (ICU) across Belgium and the Netherlands. 25-30% of these patients require more than 3 days of invasive ventilation, with an average ICU stay of 10 days.

It has become evident that many of these patients are faced with prolonged recovery periods and persistent debilitating health problems that remain after critical illness. Collectively termed the ‘Post-Intensive Care Syndrome’ (PICS), the enormous impact of an ICU admission on patient’s health and quality of life has now been clearly established.

The key determinant of poor post-ICU health status is the development of ICU acquired weakness (ICU-AW). ICU-AW is the consequence of the body’s reserves being depleted during critical illness and results in severe skeletal muscle wasting during the first week of ICU admission.Therefore, measures aimed at preserving muscle mass during critical illness and improving recovery after ICU discharge are urgently needed.

Retrospective observational cohort studies suggest that the administration of high protein nutrition is associated with improved survival and outcome. The provision of dietary protein is a well-known anabolic stimulus able to promote and maintain muscle mass in both healthy and various clinical settings. In this light, optimising nutritional support and protein provision during ICU stay is a promising, easily applicable tool to preserve muscle mass and improve functional outcomes after ICU discharge. Daily protein requirements for the healthy are approximately 0.8 g/kg/day. Current ICU guidelines recommend dietary protein delivery at 1.3 g/kg/day (ESPEN), or even up to 2.0 g/kg/day (ASPEN).

However, strong clinical evidence of the effectiveness and safety of high enteral protein delivery is lacking and urgently awaited. Therefore, the aim of the present study is to investigate the effect of high versus standard protein provision on the functional recovery of critically ill patients.

The focus on functional, patient-centered outcomes rather than traditional clinical endpoints like mortality is an important aspect and strength of the study. Previous nutritional intervention studies focusing primarily on improving mortality have repeatedly shown no effect. Therefore, it is nowadays increasingly recognized to move primary ICU trial endpoints away from classical outcomes, such as survival or length of stay, towards more functional outcomes, in line with the underlying pathophysiology.

Conditions

Conditions: Critical Illness

Keywords: Enteral Nutrition
Dietary Proteins
Respiratory failure
Catabolism

Study Design

Study Type: Interventional

Primary Purpose: Treatment

Study Phase: N/A

Interventional Study Model: Parallel Assignment

Number of Arms: 2

Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)
Study feeds will be blinded. Dosing of intervention will be volume based, with the same volume targets for both groups. Differences in composition of study feeds will result in differences in protein intake when the same volume targets are reached.

Allocation: Randomized

Enrollment: 824 [Anticipated]

Arms and Interventions

Arms	Assigned Interventions
Experimental: PRECISe protocol EN (8g protein/100kcal) Enteral (EN) feed with 8 grams protein per 100 kcal (2.0 g/kg/day protein when on target). The goal rate for administration of PRECISe protocol EN is 25 kcal/kg/day to be reached on day 4 of ICU admission.	Dietary Supplement: PRECISe protocol EN 8g protein/100kcal Enteral feed containing 8g protein/100kcal
Active Comparator: PRECISe protocol EN (5g protein/100kcal) Enteral (EN) feed with 5 grams protein per 100 kcal (1.2 g/kg/day protein when on target). The goal rate for administration of PRECISe protocol EN is 25 kcal/kg/day to be reached on day 4 of ICU admission.	Dietary Supplement: PRECISe protocol EN 5g protein/100kcal Enteral feed containing 5g protein/100kcal

Outcome Measures

Primary Outcome Measure:

1. Health-related Quality of Life

EQ-5D single summary index

[Time Frame: Day 30, 90 and 180 after ICU admission]

2. Primary and Secondary Outcomes will be assessed based on a Core Outcome Measures Set (COMS) for Acute Respiratory Failure Survivors.
Core Outcome Measures in Acute Respiratory Failure Survivors (Needham et al. AJRCCM 2017)

[Time Frame: Day 30, 90 and 180 after ICU admission]

Secondary Outcome Measure:

3. Overall survival
Overall survival

[Time Frame: Day 30, 90 and 180 after ICU admission]

4. Changes in Health-related Quality of Life
Short Form 36 (SF-36)

[Time Frame: Day 30, 90 and 180 after ICU admission]

5. Changes in mental health status
Assessed by:

- Hospital Anxiety and Depression Scale (HADS)
- EQ-5D-5L pain question (VAS score)
- Impact of Event Scale Revised (IES-R)

[Time Frame: Day 30, 90 and 180 after ICU admission]

6. Changes in physical function
Assessed by 6-minute walk test

[Time Frame: Day 30, 90 and 180 after ICU admission]

7. Changes in muscle and nerve function
Assessed by:

- MRC-SUM score
- Handgrip strength (Dynamometer)

[Time Frame: Day 30, 90 and 180 after ICU admission]

Other Pre-specified Outcome Measures:

8. Duration of mechanical ventilation
Number of days on invasive mechanical ventilation

[Time Frame: during index ICU stay]

9. Incidence of ICU-acquired infections
Incidence of ICU-acquired infections (including ventilator associated pneumonia, line sepsis etc.)

[Time Frame: during ICU stay]

10. Incidence of acute kidney injury
AKI; serum creatinine level higher than 2 times baseline level

[Time Frame: during index ICU stay]

11. Days on renal replacement therapy
Number of days on renal replacement therapy

[Time Frame: during index ICU stay]

12. Incidence of hepatic dysfunction
bilirubin level > 3mg/dl

[Time Frame: during index ICU stay]

13. Maximum and mean SOFA score

Sequential Organ Faillure Assessment score

[Time Frame: every other day (1, 3, 5 etc) for the first 14 days of index ICU stay]

14. Difference in frailty
Rockwood Clinical Frailty Scale

[Time Frame: baseline and 180 days after ICU admission]

15. Number of days on prokinetics
Collected daily during ICU admission

[Time Frame: during index ICU stay]

16. Difference in mobilization treatment
Daily mobilization treatement (passive/active, bedcycling etc) are collected

[Time Frame: during index ICU stay]

17. Length of index ICU stay
Number of days in ICU

[Time Frame: during index ICU stay]

18. Length of index hospitalisation
Number of days in hospital

[Time Frame: during index hospitalisation]

19. Incidence of ICU-readmissions
Number of patients readmitted to the ICU after previous discharge

[Time Frame: during index hospital stay]

20. Destination of hospital discharge
Destination of hospital discharge (home, rehabilitation center, care facility etc).

[Time Frame: Following index hospital stay]

21. Length of stay at rehabilitation facility
Number of days at rehabilitation center

[Time Frame: after index hospitalisation]

22. Time to return to work
Returned to precvious work en how many days after ICU admission?

[Time Frame: follow-up until 180 days after ICU admission]

23. Incidence of gastrointestinal intolerance/symptoms
i.e. vomiting, ischemia, diarrhea, abdominal distention, gastric paresis, bleeding/ulcer

[Time Frame: during index ICU stay]

Eligibility

Minimum Age:	18 Years
Maximum Age:	
Sex:	All
Gender Based:	No
Accepts Healthy Volunteers:	No
Criteria:	Inclusion Criteria:

- Adult (18 years or above) patient admitted to the ICU
- Unplanned ICU admission

- Invasive mechanical ventilation initiated <24 hours of ICU admission
- Expected ICU stay on ventilator support of 3 days or more

Exclusion Criteria:

- Contraindication for enteral nutrition
- Moribund or expected witholding of treatment
- Kidney failure AND 'no-dialysis'-code on admission
- Hepatic encephalopathy
- Body-mass index < 18 kg/m2

Contacts/Locations

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Study Principal Investigator
Maastricht UMC+

Locations:

IPDSharing

Plan to Share IPD:

References

Citations: Needham DM, Sepulveda KA, Dinglas VD, Chessare CM, Friedman LA, Bingham CO 3rd, Turnbull AE. Core Outcome Measures for Clinical Research in Acute Respiratory Failure Survivors. An International Modified Delphi Consensus Study. Am J Respir Crit Care Med. 2017 Nov 1;196(9):1122-1130. doi: 10.1164/rccm.201702-0372OC. PubMed 28537429

Links:

Available IPD/Information: