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Skeletal muscle metabolism and Critical Illness Myopathy (CIM) during early course of systemic inflammation

Submission date	Recruitment status	[_] Prospectively registered
21/10/2007	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
13/02/2008	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
04/08/2022	Signs and Symptoms	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
No. 192/0, WE 4386/1-1

Study information

Scientific Title
Skeletal muscle metabolism and Critical Illness Myopathy (CIM) during early course of systemic inflammation

Study objectives
Amended 15/11/10:
Hypothesis 2: Electrical muscle stimulation has been demonstrated to improve the muscle insulin sensitivity and might thereby prevent the development of CIM
Test: To investigate the safety and efficacy of electrical muscle stimulation in critically ill patients during early systemic inflammation or sepsis as a potential therapeutic approach to prevent CIM
Hypothesis 2 will be tested by an intraindividual interventional study (Phase 2).

Initial information at time of registration:
Hypothesis 1: Impaired insulin sensitivity may be involved in the development of CIM secondary to systemic inflammation or sepsis and may lead to skeletal muscle protein breakdown
Test 1: To identify metabolic and/or inflammatory parameters in patients, which allow identification of individuals who develop CIM during early course of systemic inflammation and /or sepsis
Test 2: To investigate histomorphological changes during early course of systemic inflammation or sepsis in patients who develop CIM
Hypothesis 1 will be tested by an observational pilot study (Phase 1).

Hypothesis 2: Low frequency electrical muscle stimulation has been demonstrated to improve the muscle insulin sensitivity and might thereby prevent the development of CIM
Test: To investigate the safety and efficacy of low frequency electrical muscle stimulation in critically ill patients during early systemic inflammation or sepsis as a potential therapeutic approach to prevent CIM
Hypothesis 2 will be tested by an interventional study (Phase 2).

Please note that as of 15/11/10 this record has been updated to include amendments to the protocol relating to the replacement of the parallel-group intervention with an intraindivdual intervention. All updates may be found in the relevant field with the above update date.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved by the Charite - Berlin Medical University (Charite - Universitätsmedizin Berlin) Ethics Committee on 8th of June 2006 (ref: EA2/061/06). Amendment to the protocol approved on the 10th of December 2009.

Study design
Phase 1: Observational. Phase 2: Interventional (randomly assigned side of intervention)

Primary study design
Interventional

Secondary study design

Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Critical illness myopathy (CIM)

Interventions
Current intervention as of 15/10/2021:
The following will be carried out in the Phase 1 observational pilot study:
1. Severity of illness, organ failure:
1.1. Sequential Organ Failure Assessment (SOFA) score, assessed daily until discharge from ICU or for 28 days
1.2. Acute Physiology and Chronic Health Evaluation (APACHE) II, assessed daily until discharge from ICU or for 28 days
1.3. Acute Physiology Score (SAPS) -II, III, assessed daily until discharge from ICU or for 28 days
2. Nursing workload: Therapeutic Interventions Scoring System-28 (TISS-28), assessed daily until discharge from ICU or for 28 days
3. Clinical neurological assessment:
3.1. Richmond Agitation Sedation Scale (RASS), assessed daily until discharge from ICU or for 28 days
3.2. Delirium Detection Score (DDS), assessed daily until discharge from ICU or for 28 days
3.3. The Medical Research Council (MRC) score (measures motor strength), assessed daily until discharge from ICU or for 28 days
3.4. Daily questionnaire of 5 standardized questions to assess comprehension
4. Clinical sepsis parameters:
4.1. Predisposition, Infection, Host response, Organ dysfunction (PIRO), assessed daily (day 1 - 14)
4.2. Hemodynamics, assessed daily (day 1 - 14)
5. Nutritional support and insulin/glucose adjustments:
5.1. Feeding protocol, assessed daily (day 1 - 14)
5.2. Insulin protocol, assessed daily (day 1 - 14)
5.3. Glucose monitoring, assessed daily (day 1 - 14)
6. Medication from charts, filled by the nurse daily (day 1 - 14)
7. Blood sample:
7.1. Nutritional markers (insulin, insulin like growth factors and binding proteins [IgF's, IGFBP's and TGF-beta]), assessed daily (day 1 - 14)
7.2. Inflammatory markers (flow cytometry), assessed daily (day 1 - 14)
8. Electrophysiology (ElectroMyoGraphy [EMG]/ElectroNystagmoGraphy ENG, Direct Muscle Stimulation [DMS]), carried out on Day 4 and 12, and at day of discharge from ICU
9. Hyperinsulinemic-euglycemic clamp:
9.1. Microdialysis, carried out on Day 4 and Day 12
9.2. Spectrophotometry, carried out on Day 4 and Day 12

9.3. Indirect calorimetry, carried out on Day 4 and Day 12
10. Muscle biopsies (Surgical biopsy), carried out on Day 4 and Day 12
11. Daily bioimpedance measurements

Phase 2 interventional study:
Phase 2 intraindividual intervention study: Side of unilateral electrical muscle stimulation (EMS) will be randomly assigned and treated with twice daily EMS of tibial anterior and vastus lateral muscles.

Control group will receive usual care only.

Gender-specific sub-analysis will be performed to investigate potential differences in skeletal muscle metabolism and CIM and account for gender bias.

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Previous intervention:
Amended 15/11/10:
Phase 2 intraindividual intervention study: Side of unilateral electrical muscle stimulation (EMS) will be randomly assigned and treated with twice daily EMS of tibial anterior and vastus lateral muscles.

Initial information at time of registration:
The following will be carried out in the Phase 1 observational pilot study:
1. Severity of illness, organ failure:
1.1. Sequential Organ Failure Assessment (SOFA) score, assessed daily until discharge from ICU or for 28 days
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1.3. Acute Physiology Score (SAPS) -II, III, assessed daily until discharge from ICU or for 28 days

2. Nursing workload: Therapeutic Interventions Scoring System-28 (TISS-28), assessed daily until discharge from ICU or for 28 days

3. Clinical neurological assessment:
3.1. Richmond Agitation Sedation Scale (RASS), assessed daily until discharge from ICU or for 28 days
3.2. Delirium Detection Score (DDS), assessed daily until discharge from ICU or for 28 days
3.3. The Medical Research Council (MRC) score (measures motor strength), assessed daily until discharge from ICU or for 28 days
3.4. Daily questionnaire of 5 standardized questions to assess comprehension

4. Clinical sepsis parameters:
4.1. Predisposition, Infection, Host response, Organ dysfunction (PIRO), assessed daily (day 1 - 14)
4.2. Hemodynamics, assessed daily (day 1 - 14)

5. Nutritional support and insulin/glucose adjustments:
5.1. Feeding protocol, assessed daily (day 1 - 14)
5.2. Insulin protocol, assessed daily (day 1 - 14)
5.3. Glucose monitoring, assessed daily (day 1 - 14)

6. Medication from charts, filled by the nurse daily (day 1 - 14)

7. Blood sample:
7.1. Nutritional markers (insulin, insulin like growth factors and binding proteins [IgF's, IGFBP's and TGF-beta]), assessed daily (day 1 - 14)

7.2. Inflammatory markers (flow cytometry), assessed daily (day 1 - 14)

8. Electrophysiology (ElectroMyoGraphy [EMG]/ElectroNystagmoGraphy ENG, Direct Muscle Stimulation [DMS]), carried out on Day 4 and 12, and at day of discharge from ICU

9. Hyperinsulinemic-euglycemic clamp:
9.1. Microdialysis, carried out on Day 4 and Day 12
9.2. Spectrophotometry, carried out on Day 4 and Day 12
9.3. Indirect calorimetry, carried out on Day 4 and Day 12

10. Muscle biopsies (Surgical biopsy), carried out on Day 4 and Day 12

11. Daily bioimpedance measurements

Phase 2 interventional study:
After an observational pilot phase of the study, patients will be randomized into two groups. Those who are allocated to the intervention group will receive Electrical Muscle Stimulation (EMS) daily (day 1 - 14).

Control group will receive usual care only.

Scientific contact/ Co-investigator:
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Intervention Type
Other

Phase
Not Applicable

Primary outcome measure
Primary outcome measures for both observational and interventional studies:

Insulin sensitivity:
1. Studies of the insulin receptor pathways such as IRS, PI3K, AKT and Glut4 will be performed
2. Glucose uptake as well as Insulin-Receptor kinase and PI3Kinase-activities will be determined
3. Hyperinsulinemic-euglycemic clamp will be performed

Histopathology on muscle biopsies: Type II myosin loss will be investigated

Secondary outcome measures
Secondary outcome measure for both observational and interventional studies:

Electrophysiology: Measurement of membrane excitability

Overall study start date
01/10/2007

Completion date
30/09/2010

Eligibility

Key inclusion criteria
Critically ill patients with the Sequential Organ Failure Assessment (SOFA) score greater than or equal to 8 on 3 of the 5 successive days within 7 days after admission to ICU.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
80

Key exclusion criteria
1. Patients under age of 18
2. Missing written informed consent from a legal proxy
3. Pretreatment in ICU >7 days

Date of first enrolment
01/10/2007

Date of final enrolment
30/09/2010

Locations

Countries of recruitment
Germany

Study participating centre

Augustenburger Platz 1
Berlin
Germany
13353

Sponsor information

Organisation
Charité - University Medicine Berlin (Charité - Universitätsmedizin Berlin) (Germany)

Sponsor details
c/o Prof Friedrich Luft
European Clinical Research Center
Charite Campus Buch
Max-Delbrück-Centrum für Molekulare Medizin (MDC)
Berlin-Buch
Robert-Rössle-Str. 10
Berlin
Germany
13092

Sponsor type
University/education

ROR
https://ror.org/001w7jn25

Funder(s)

Funder type
Research organisation

Funder Name
Charité - University Medicine Berlin (Charité - Universitätsmedizin Berlin) (Germany)

Funder Name
German Research Foundation (DFG) (ref: No.192/1, WE 4386/1-1)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	15/02/2013		Yes	No
Results article	results	20/03/2014		Yes	No
Results article	results	01/04/2014		Yes	No
Results article	results	29/09/2014		Yes	No
Results article	Retrospective analysis	01/02/2020	01/06/2021	Yes	No
Results article		03/08/2022	04/08/2022	Yes	No