

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

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

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
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 intraindividual 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.

Primary study design

Interventional

Study design

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

Study type(s)

Prevention

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.

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

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:

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(s)

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

Key secondary outcome(s)

Secondary outcome measure for both observational and interventional studies:

Electrophysiology: Measurement of membrane excitability

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

Healthy volunteers allowed

No

Age group

Adult

Sex

All

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

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Sponsor information**Organisation**

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

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

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		01/02/2020	01/06/2021	Yes	No
Results article	Retrospective analysis	03/08/2022	04/08/2022	Yes	No