

Recovery From Severe Cardio-Respiratory Failure: The Trajectory of Muscle Mass, Strength, Function and Health Related Quality of Life (CLEVERER)

The CLEVERER study (**NCT03753412**). 1st Recipient of Barts Charity PhD fellowship and sponsored by Queen Mary University of London (QMUL)

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Introduction and Background (Intensive Care Unit-Acquired Weakness: ICUAW)

- **Definition:** *The American Thoracic Society (ATS) has formally defined ICUAW as, “a syndrome of generalised limb weakness that develops while the patient is critically ill for which there is no alternative explanation other than the critical illness itself”.*
- **Prevalence:** 7-100%
- **Cost:** 1.6 Billion Euros annually
- **Morbidity:** 49% unable to return to work
- **Literature:** Significant muscle loss exacerbated by ECMO (between 15 and 30% in 7 days)
- **Molecular Mediators:** GDF-15 and IGF-1 correlated with muscle atrophy



Hypothesis and Aims

Patients would lose considerable **skeletal muscle mass**, muscle strength, and physical function in the initial periods of severe critical illness (**between day 0 and day 7**) and then **recover** between **ICU discharge**, hospital discharge and **outpatient follow up**.

Aims

The overarching aim is to understand the effects of critical illness requiring ECMO on muscle atrophy and how this is recovered at follow-up. The aim was also to explore, strength, function, bio-electrical impedance, HRQoL.

- (i) The **initial** muscle loss in the first seven days post-ECMO
- (ii) The **recovery** period from ICU discharge to follow up

To understand how the indices of muscle mass and strength correlate with parameters reflecting HRQoL

To investigate the profiles of selected, circulating, potential biomarkers and modulators of muscle homeostasis with muscle-related and other clinical outcomes.

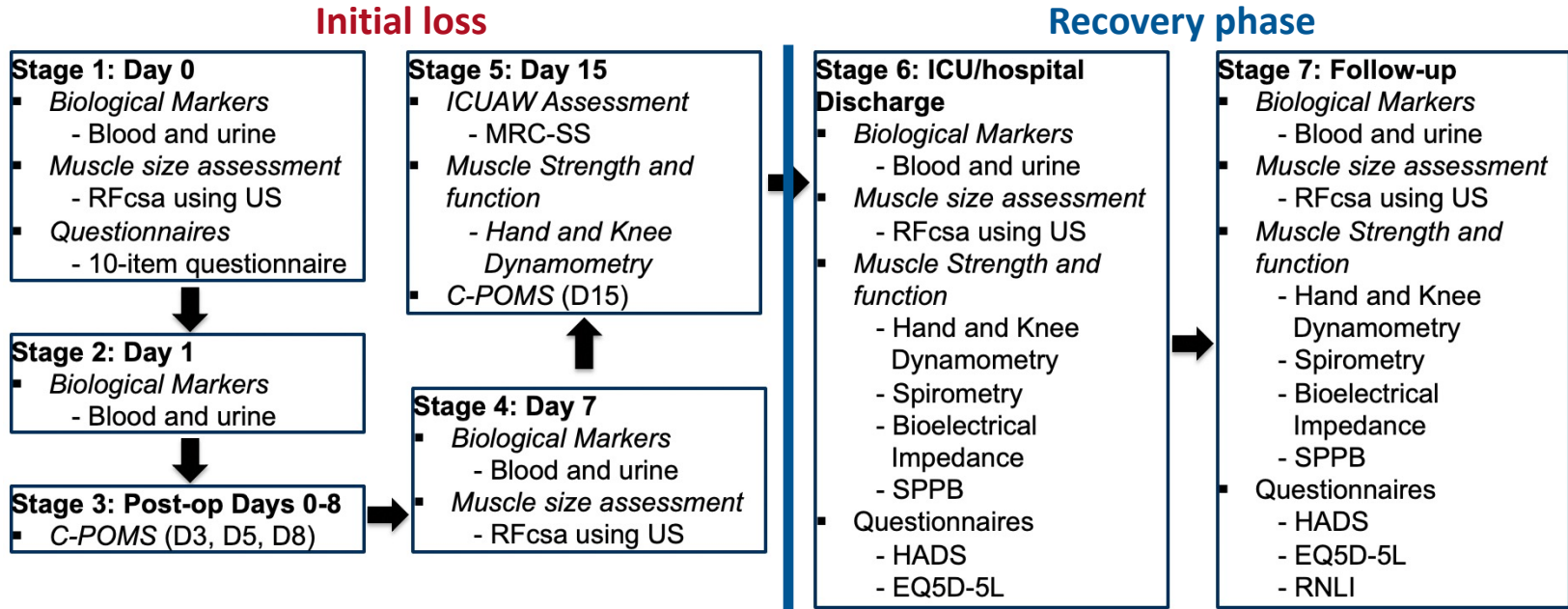
The primary outcome Rectus Femoris Cross Sectional Area (RF_{csa})

The secondary outcomes included strength, function, HRQoL and biological markers

Methods

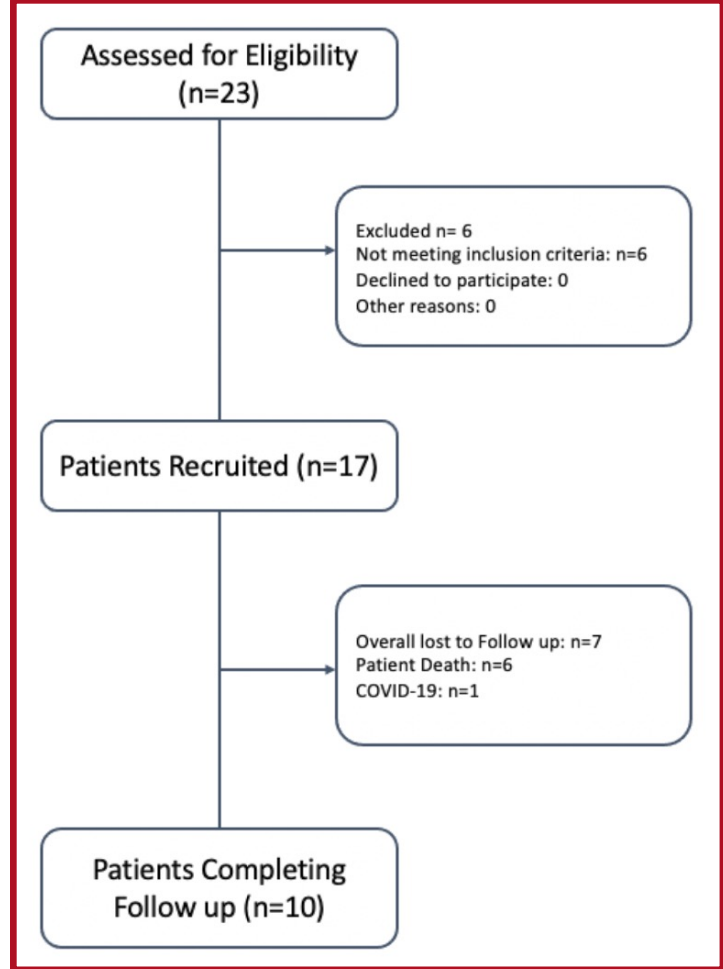
Inclusion: Adults needing ECMO related to severe cardiac or respiratory failure or is suffering from cardiogenic shock.

Exclusion: Adults with pre-existing causes of severe muscle weakness or wasting e.g previous stroke, neuromuscular disease or malignancy were excluded. This included bone defects or unresolved muscle injuries.



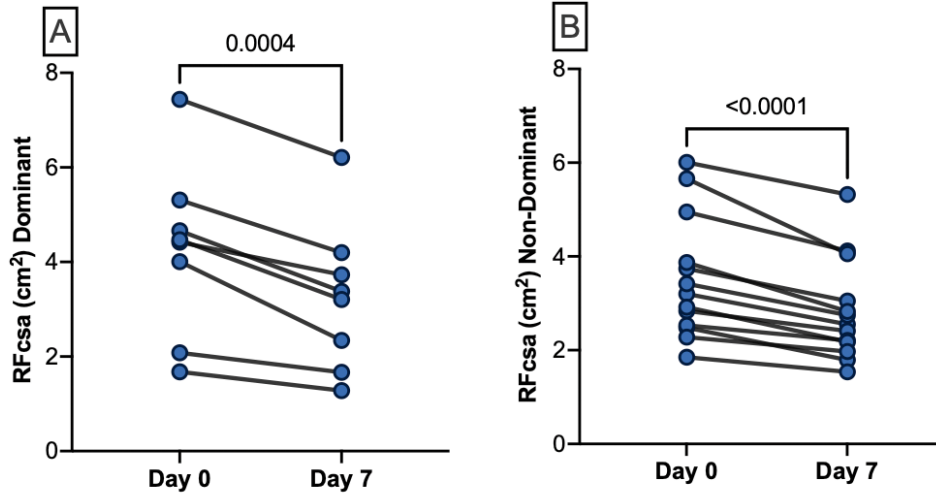
Results

Sex (M):	n=9 (52.9%)
Ethnicity Caucasian:	n=6 (35.2%)
Ethnicity Asian:	n=5 (29.4%)
Ethnicity Black:	n=6 35.2%
Age:	49.1 years (25-65)
VV ECMO:	52.9%
VA ECMO:	41.1%
Peripherally cannulated:	70.5%
ECMO duration:	6.77 days
MV duration:	14.05 days.
ICU length of stay:	20.76 days
Hospital length of stay:	36.41 days
Mortality:	n=6 (35.29%)



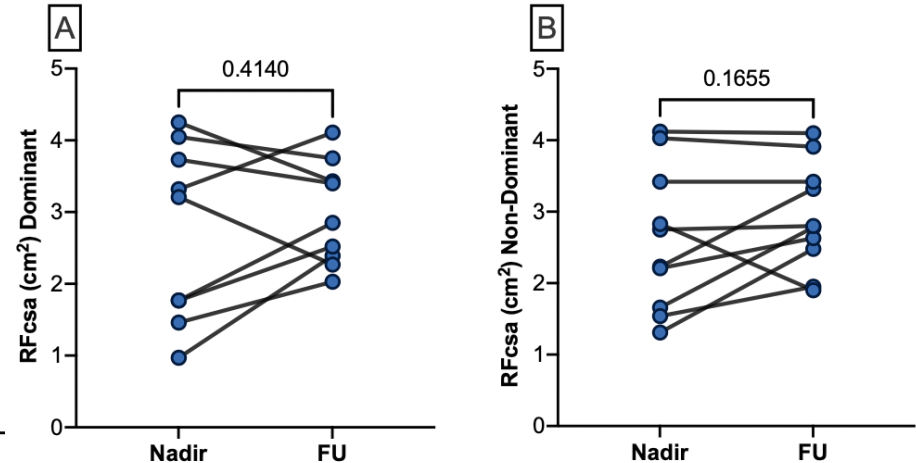
Results – Muscle Mass

Muscle loss between day 0 and 7



A **loss of 24.24%** (1.006cm² [1.670 – 0.400cm²]) in seven days continuing to ICU discharge. (1.53cm² [95% CI 0.1109 to 2.954cm²]).

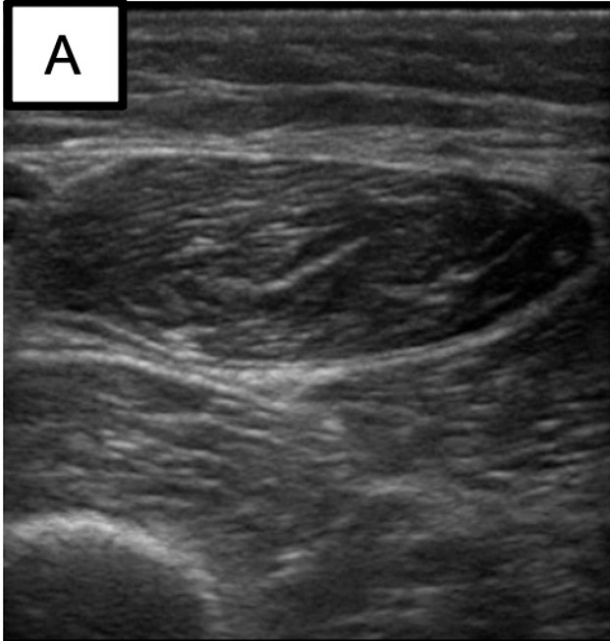
Muscle Recovery between nadir and FU



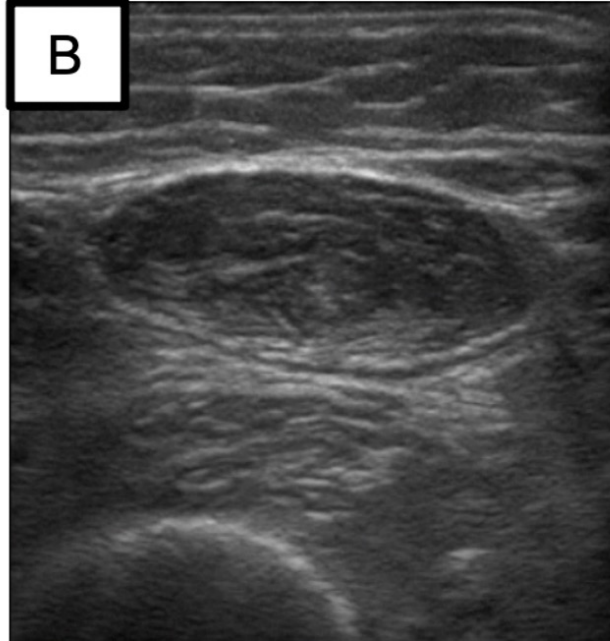
The Initial **muscle loss had not recovered** at follow up, with only **50%** of the group recovering.

Results - Ultrasound

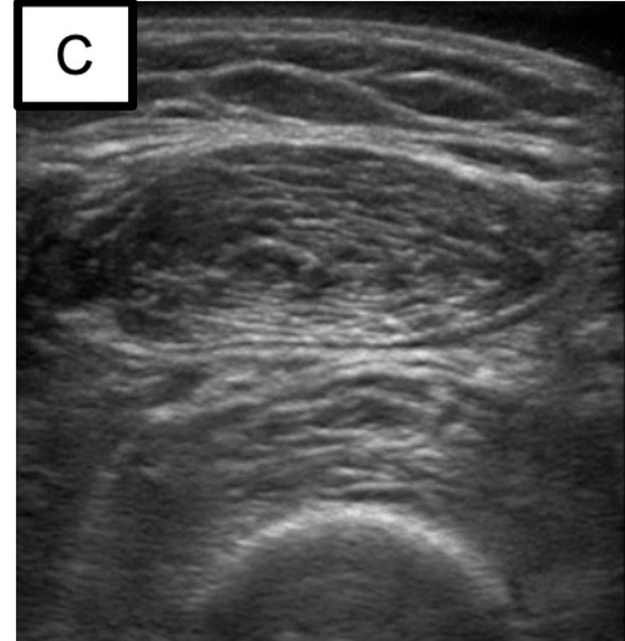
A: Day 0



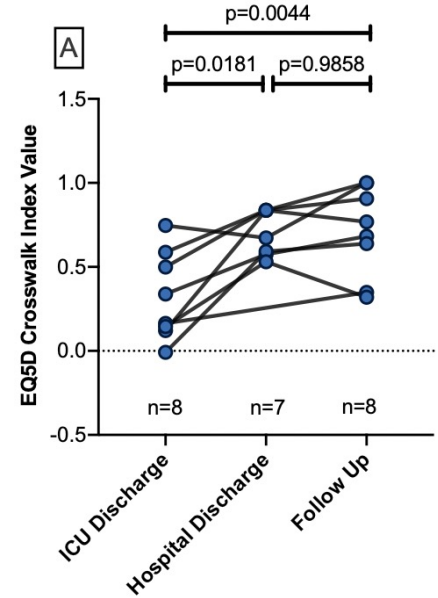
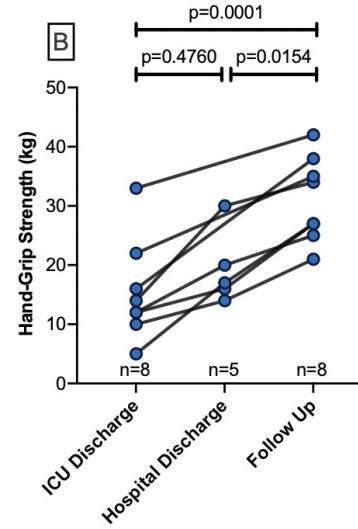
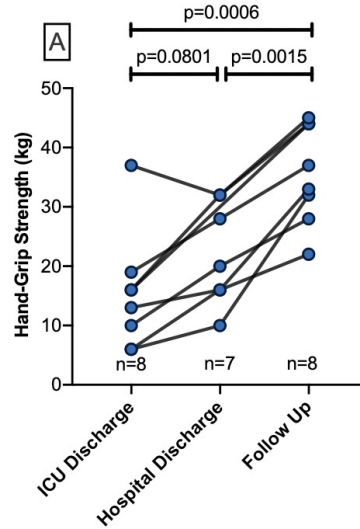
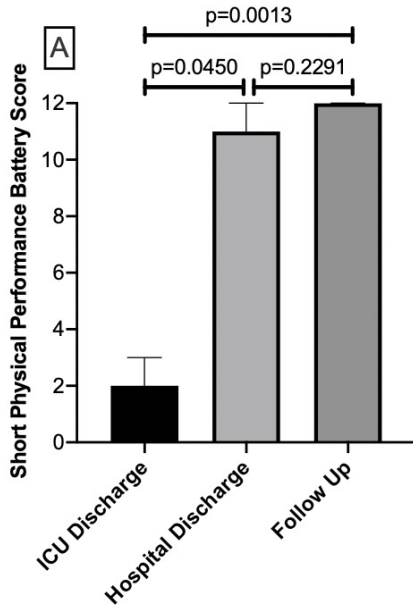
B: Day 7



C: Follow-Up



Results- Strength and Function

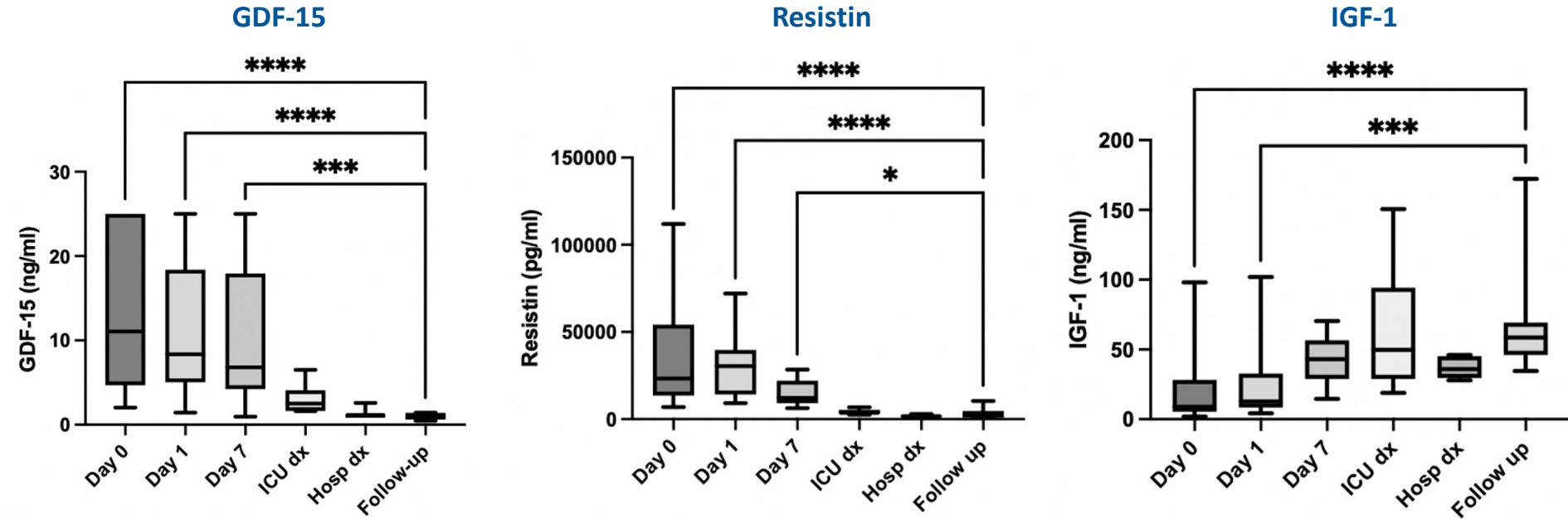


- Function **recovered** significantly between ICU discharge and FU

- Hand-held grip strength **recovered significantly** between ICU discharge and FU



- EQ5D-5L **recovered** significantly between ICU discharge and FU

Results

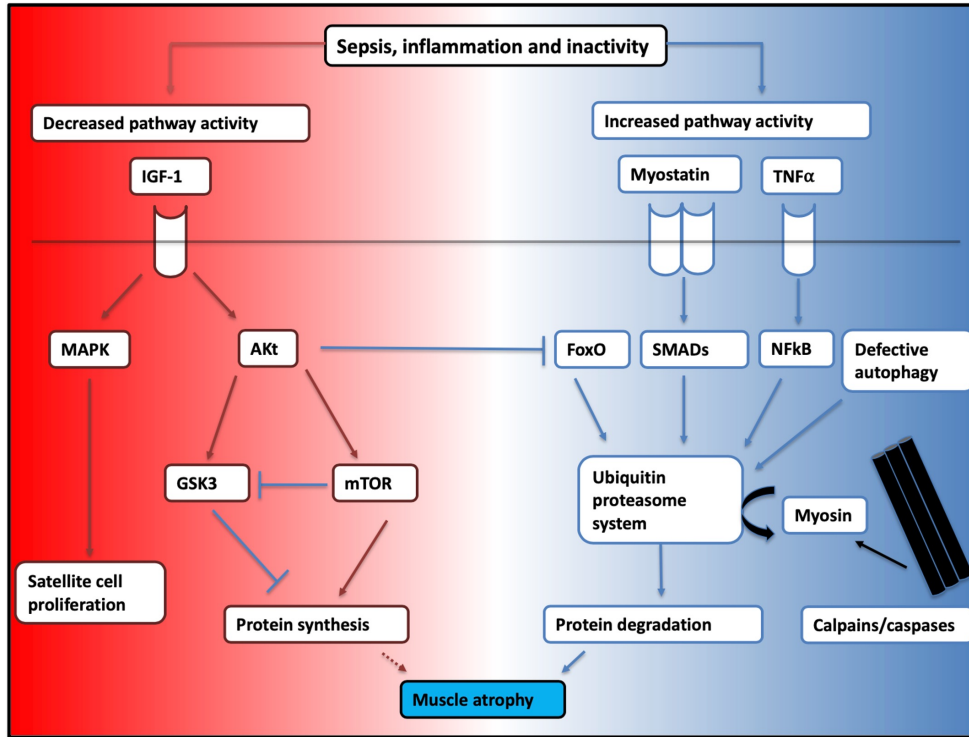


- The pattern of mediator release was as expected, most were elevated within days of maximum insult declining to baseline at outpatient follow-up (**GDF-15 Resistin, STC-1, NGAL, IL-18**).
- The injurious and pro-inflammatory nature of the insult suffered by the CLEVERER patients was severe with **IGF-1 being low** at maximum insult and returning to normal levels by outpatient follow up.

Conclusion

Aims	Conclusion
<p>To understand the effects of critical illness and ECMO on muscle atrophy</p> <ul style="list-style-type: none">• Initial muscle loss• Recovery period	<ul style="list-style-type: none">• Muscle mass was lost in the first 7 days and continued to ICU discharge• This muscle appeared unrecoverable with only 50% recovering any mass
<p>To understand how the indices of muscle mass and strength correlate with parameters reflecting HRQoL</p>	<ul style="list-style-type: none">• Significant improvement of the patient EQ5D-5L cross-walk index was noted between ICU discharge and FU• This correlated with muscle mass and strength which also improved from ICU discharge and FU
<p>To investigate the profiles of selected, circulating, potential biomarkers and modulators of muscle homeostasis with muscle-related and other clinical outcomes.</p>	<ul style="list-style-type: none">• The pattern of mediator release was as expected, most were elevated within days of maximum insult declining to baseline at outpatient follow-up <p> IGF-1  GDF-15, Resistin, Stanniocalcin, IL-18, NGAL</p>

Strengths and Limitations



- Day 0 and its definition
- Heterogeneity
- RFcsa in peripheral ECMO cannulation
- Patient recruitment
- COVID

The PhD and its Clinical Relevance

- This study along with my other PhD study **VARIANCE** both contribute to the literature of muscle atrophy and recovery after critical illness.

The clinical relevance

- Aftermath of critical illness and ECMO
- Early identification
- Pharmaceutical therapy and interventions
- Predicting patients of high risk of wasting muscle mass for better targeted interventions
- Nursing practice
- Prehabilitation and rehabilitation

Recovery from intensive care unit acquired muscle weakness
(ICUAW): molecular determinants and consequences for
physical recovery and quality of life in patients after aortic
cardiac surgery and severe cardio-respiratory failure.

Submitted in partial fulfillment of the requirements of the Degree of

Doctor of Philosophy

Queen Mary University of London

2017-2022

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Barts Health
NHS Trust

Thank you for Listening

Any Questions

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Special thanks to:

My PhD supervisors Professors Mark Griffiths and Julie Sanders

My PhD Examiners Professors Stephen Wort and Ian Jones

Barts Charity and QMUL

ACCU St Bartholomew's Hospital specifically 6A

