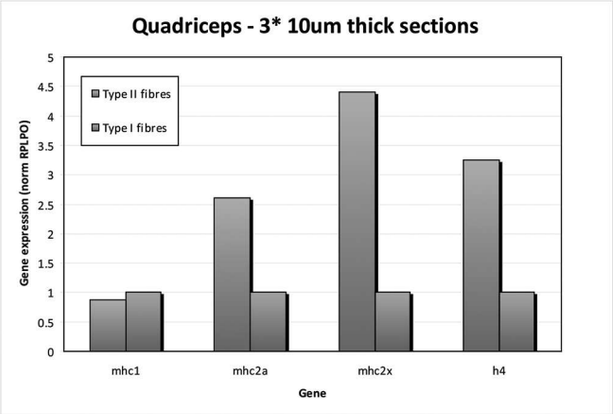
qPCR was performed on fibre populations for target genes MHC I, MHC IIa, MHC IIx, HDAC-4 and RPLPO.

Results Preliminary results from three 10micron slices indicate that this technique is feasible to study fibre-specific signalling in COPD. LCM following immunostaining captures distinct fibre populations (Figure 1) confirmed by a higher MHC I content in 'type I fibres', with 'type II' fibres containing more MHC IIa, MHC IIx and HDAC-4 as would be expected. Gene expression is normalised against RPLPO.

Conclusion LCM can be used to study fibre specific inflammatory signalling in the skeletal muscle of COPD patients and immunostaining with MHC antibodies is a feasible way to distinguish between fibre types when capturing composite fibre populations.



Abstract S53 Figure 1. Gene expression (normalised for RPLPO) for Type I (red) and Type II (blue) quadriceps muscle fibres in COPD using three 10 micron sections for Laser Capture Micro-Dissection. Fold difference compared to type I fibres shown

S54 PRESERVATION OF MITOCHONDRIAL OXIDATIVE CAPACITY IN CRITICALLY ILL PATIENTS BALANCES REDUCTION IN MITOCHONDRIAL BIOGENESIS

R Astin[1], Z Puthucheary[1], S Saeed[2], C Velloso[3], M McPhail[4], J Rawal[1], J Skipworth[1], M Singer[2], S Harridge[3], H Montgomery[1], N Hart[5].; Institute for Human Health and Performance, University College London,, London, United Kingdom[1]; Bloomsbury Institute for Intensive Care Medicine, University College London, London, United Kingdom[2]; Centre of Human and Aerospace Physiological Sciences, King's College London, London, United Kingdom[3]; Department of Medicine, Imperial College London, London, United Kingdom[4]; Lane Fox Clinical Respiratory Physiology Research Centre, Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom[5]

10.1136/thoraxjnl-2013-204457.61

Background and Aims In severe sepsis, early mitochondrial dysfunction in skeletal muscle is associated with decreased biogenesis and adverse patient outcome. We hypothesised that reduction in mitochondrial content during critical illness would be balanced by enhanced capacity to produce ATP achieved by switching from glucose to fatty acid oxidation as the preferred metabolic substrate.

Methods 30 critically ill patients (70% male, age 56.4 ± 19.7 years, APACHE II score 22.4 ± 6.6) were prospectively recruited <24 hours following intensive care admission from August 2009 to April 2011. Quadriceps vastus lateralis muscle biopsies were taken on day 1 and 7 and concentrations of mitochondrial respiratory complex proteins and key proteins of the -oxidation pathway were determined using a Luminex assay normalised to an internal control (NNT). Mitochondrial DNA content (mtDNA), PGC1- , and PPRC mRNA concentrations were determined contemporaneously by RT-qPCR.

Results There were reduction in both skeletal muscle mtDNA ($p = 0.04$) and PGC1- ($p = 0.02$) from day 1 to day 7, with fold change in PGC1 correlated with the fold change in mtDNA ($r^2 = 0.65$, $p < 0.001$, $n = 19$). PGC1- and PPRC did not change. In ICU survivors, neither PGC1- or mtDNA fold change predicted hospital or 18 month mortality ($p > 0.1$). Protein levels of mitochondrial respiratory complexes I-V did not change significantly from day 1 to day 7 and mtDNA fold change did not correlate with fold change in complex I-V ($p > 0.1$). There was a weak positive correlation between feeding (protein delivered) and fold change in complex I ($r^2 = 0.20$, $p = 0.014$) and complex III protein level ($r^2 = 0.20$, $p = 0.016$). Overall levels of mitochondrial -oxidation pathway proteins (CPT1, MCAD, ETF, DecR1) did not change whilst peroxisomal MEFII increased significantly ($p < 0.01$).

Conclusion These data suggest decreased mitochondrial biogenesis over the first week of critical illness. The increase in -oxidation proteins combined with the lack of change in respiratory chain complex concentrations during the first week suggests that the oxidative capacity of the remaining mitochondria was enhanced with increased capacity to metabolise fatty acids. These data support our hypothesis that the decreased cellular energy utilisation accompanying decreased mitochondrial biogenesis is offset by increased capacity to produce ATP through the -oxidation of fats.

S55 MIR-181: A POTENTIAL BIOMARKER OF ACUTE MUSCLE WASTING?

[1]SAA Bloch, [1]PR Kemp, [2]MJD Griffiths, [2]MI Polkey; *[1]NHLI, Imperial College, London, UK; [2]Royal Brompton and Harefield NHS Trust, London, UK*

10.1136/thoraxjnl-2013-204457.62

Introduction and Objectives Acute muscle wasting in the critically ill is common and associated with significant morbidity and mortality. Although some aetiological risk factors are recognised it is difficult to predict those who will develop muscle wasting. The ability to predict who will go on to develop muscle wasting or to detect muscle wasting prior to it becoming clinically significant would provide the opportunity to intervene at an early stage with strength training or anabolic agents.

MicroRNAs are small non coding RNA that are thought to modulate post transcriptional regulation of translation. Since we have previously found that microRNA expression in skeletal muscle relates to muscle weakness in COPD (*Thorax* 2012;67:26–34) and in blood are associated with skeletal muscle phenotype (*Thorax* in press PMID 23814167) we hypothesised that plasma microRNAs could be biomarkers of ICU acquired muscle weakness.

Methods In a prospective observational study (*Crit Care Med* 2013;41:982–989) of 42 patients undergoing elective high-risk cardiothoracic surgery plasma levels of selected microRNAs were assayed pre-operatively and over the first week post operatively. Those who developed muscle wasting were identified by ultrasound.

Main Results 55% (23 of the 42) of patients developed muscle atrophy. Rise in mir-181 was significantly higher at day 2 post surgery in those who developed muscle wasting compared to those who did not ($p = 0.03$, figure 1). A rise in mir-181 of greater than 1.7 times baseline at day 2 post surgery has a 90%