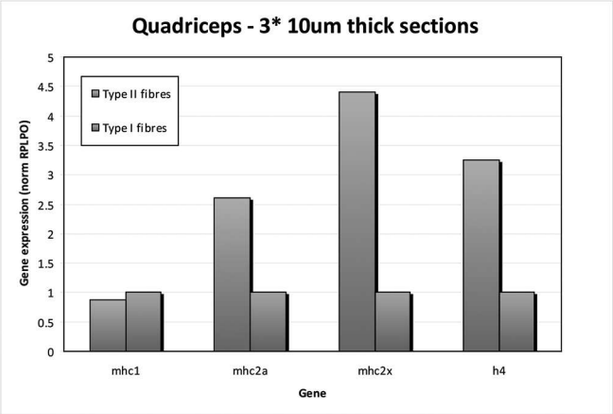
qPCR was performed on fibre populations for target genes MHC I, MHC IIa, MHC IIx, HDAC-4 and RPLPO.

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

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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?

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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%

specificity for muscle wasting, (with 55% sensitivity). Other microRNAs did not show significant differences between the groups.

Conclusion Mir-181 has been shown to be involved in both regulation of inflammation and muscle regeneration and differentiation. Mir-181 provides a potential biomarker of developing muscle wasting and with further development in the future may prove to be useful in directing treatment.

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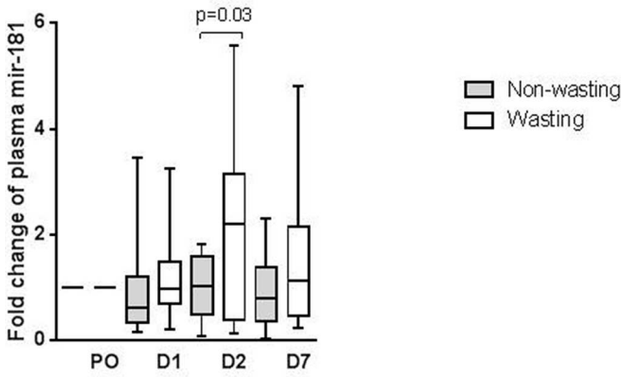

Abstract S55 Figure 1. Relative plasma mir-181 concentration in non-wasting (n = 19) and wasting patients(those with >9.24% muscle loss: n = 23) pre-operatively (PO), on day1 (D1), day 2 (D2) and on day 7 (D7). Data presented as box and whisker plots with median, interquartile ranges and 5–95% percentiles. P = 0.03 at day 2 for comparison between groups with Kolmogorov-Smirnov test.

TB: predicting disease occurrence and severity

S56 DOES TIME SINCE ARRIVAL AFFECT SITE OF TB DISEASE IN UK MIGRANTS?

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Background In contrast to global tuberculosis (TB) epidemiology, the UK and many low incidence countries have a high proportion of cases with extra-pulmonary tuberculosis (ETB). Almost 70% of reported cases in the UK are non-UK born, and many of these develop TB within the first five years after entry to the UK. The aim of the study was to analyse whether time since entry to the UK was associated with site of disease among migrants.

Methods All TB cases (n = 95,427) reported to national enhanced TB surveillance system in the UK from 2000–2011 were included. In univariable analysis we explored associations between site of disease and place of birth, ethnic group, gender, age and previous TB diagnosis, using proportions and unadjusted odds ratios. Logistic regression was used to assess the association between site of disease and time since entry to the UK, adjusted for significant confounders.

Results A total of 86,754 cases had complete information for site of disease and place of birth. Of these, 46,284 (53%) cases had ETB increasing from 47% in 2000 to 58% in 2011. ETB was more common amongst the non-UK born (61%) compared with UK-born TB cases (36%). Cases who entered the UK more than one year ago were almost 3 times more likely to have ETB compared to UK born cases after adjusting for sex, age, ethnicity and previous TB diagnosis (aOR 2.98, 95% CI 2.89–3.07). Females (OR 1.22 95% CI 1.18–1.26), adults aged 30–60 years and individuals of black African/Indian subcontinent ethnicities were significantly more likely to have ETB.

Conclusions ETB was associated with being non-UK born, having entered the UK more than a year before diagnosis, female gender, age 30–60 years, and ethnic group. Conveying our findings to healthcare workers in the UK may improve awareness of ETB in specific populations, which could help lead to earlier diagnosis.

S57 DIABETES AND LATENT TUBERCULOSIS INFECTION: NESTED CASE-CONTROL STUDY WITHIN THE PREDICT COHORT

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10.1136/thoraxjnl-2013-204457.64

Background Diabetes is associated with an increased risk of tuberculosis disease, but it is unclear whether a similar association exists between diabetes and latent tuberculosis infection (LTBI).

Methods The ongoing UK PREDICT (Prognostic Evaluation of Diagnostic IGRAs Consortium) cohort study aims to recruit 10,000 participants to assess the predictive values of interferon gamma release assays (IGRAs) for the development of active TB in recent entrants to the UK and contacts of active TB cases. We used a nested case-control design within the first 5000 recruits in this cohort, to investigate the association between diabetes and LTBI. Participants in PREDICT provide demographic, medical and social information, including any history of diabetes. LTBI is detected using the two commercially available IGRAs, Quantiferon Gold In-Tube and TSpot.*TB*. Cases were individuals who tested positive on either or both IGRAs; controls were negative on both assays (or negative on one and indeterminate on the other). Logistic regression was used to estimate odds ratios and adjust for potential confounders. Assuming a 5% diabetes prevalence, 1084 cases and 3252 controls would allow the detection of a 1.5-fold increase of LTBI with 80% power and 5% error.

Results Overall, 1388/4730 (29%) had a positive IGRA. 286/4730 (6%) reported a history of diabetes. Amongst diabetic participants, 168 used insulin and/or oral hypoglycaemic medications and 25 reported control through diet alone (1 participant was being monitored only and for 92 the level of control was unknown). Univariate analysis found an association between diabetes and LTBI (OR = 1.45 [95% CI 1.13–1.86], p = 0.003). After adjustment for age, this association was no longer apparent (OR = 1.15 [95% CI 0.88–1.50], p = 0.30). Adjustment for other variables in addition to age (sex, ethnicity, birthplace outside the UK, previous contact with a TB case, or previous TB diagnosis) did not substantially change the estimated age-adjusted