syndecan-1 expression. These questions are the subject of ongoing studies into the role of RAGE activation in endothelial dysfunction in SIRS.

S73 CIRCULATING REGULATORS OF ACUTE MUSCLE WASTING IN THE CRITICALLY ILL: GDF-15 A POTENTIAL NOVEL DRIVER OF ACUTE MUSCLE WASTING

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Introduction Acute muscle wasting in the critically ill manifesting as intensive care unit acquired paresis (ICUAP) is common, and causes significant morbidity and mortality. The pathological mechanisms underlying ICUAP are poorly understood and, other than rehabilitation, no therapeutic interventions exist. It was hypothesised that known or potential circulating modulators of muscle mass: insulin-like growth factor-1 (IGF-1), myostatin and growth and differentiation factor-15 (GDF-15) would have distinct dynamic profiles in patients who develop acute muscle wasting in a novel human model of ICUAP.

Methods In a prospective observational study of 42 patients undergoing elective high-risk cardiothoracic surgery (at the Royal Brompton Hospital, London, UK) those who developed muscle wasting were identified by ultrasound. Circulating IGF-1, myostatin and GDF-15 were assayed pre-operatively and over the first week post-operatively. The ability of GDF-15 to cause muscle wasting in vitro was determined in cultured C2C12 myotubes.

Main results 23 of 42 patients (55%) developed quadriceps atrophy. Plasma concentrations of IGF-1 and unexpectedly myostatin, known mediators of muscle hypertrophy and atrophy respectively, both decreased from baseline in the first post operative days. By contrast, plasma GDF-15 concentrations increased in all patients. This increase in GDF-15 was higher ($535\% \pm 308\%$ versus $495\% \pm 247\%$) and sustained at day 7 in those who developed muscle wasting (day 7 compared with baseline, $p < 0.01$), but recovered in the non-wasting group ($p > 0.05$). Furthermore IGF-1 also did not recover in those who developed muscle wasting (day 7 compared with baseline, $p < 0.01$) but did in the non-wasting group ($p > 0.05$).

Myostatin recovered to baseline in both groups. Finally, we demonstrated that GDF-15 caused atrophy of myotubes in vitro (average control myotube diameter was $26.3 \pm 9.0 \mu\text{m}$ versus $22.3 \pm 7.5 \mu\text{m}$ for GDF-15 treated myotubes, equating to 15% myotube atrophy, $p = 0.011$).

Conclusion This data supports the hypothesis that acute muscle loss occurs as a result of an imbalance between drivers of muscle atrophy and hypertrophy. GDF-15 is a potential novel mediator of muscle atrophy in ICUAP, which may become a therapeutic target in patients with ICUAP and other forms of acute muscle wasting.

S74 INCIDENCE AND ANALYSIS OF RISK FACTORS FOR THROMBOCYTOPENIA IN CRITICALLY ILL PATIENTS

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Introduction Thrombocytopenia occurs in 15% to 58% of intensive care unit patients. Up to 25% of acutely ill patients develop drug-induced thrombocytopenia. Establishing the etiology of secondary thrombocytopenia is challenging, since many medications and co morbidities have been implicated.

Objective To define the incidence and severity of thrombocytopenia in critically ill patients and to examine risk factors that may be related to the development of thrombocytopenia.

Method This is a retrospective chart review of 328 critically ill patients with thrombocytopenia requiring at least 72 hours of critical care. 30 suspected risk factors, including patient characteristics, drug effects, and associated diseases were identified from the literature and further evaluated using a multiple logistic regression. Mild Thrombocytopenia defined as platelet count less than $200 \times 10^9/\text{L}$ was observed frequently, but only 9 percent had severe thrombocytopenia defined as less than $20 \times 10^9/\text{L}$.

Results Demographic characteristics of patients predisposed to thrombocytopenia are males, older than 55, and Hispanic population. Hemodynamic instability and/or heparin exposure appear to be the strongest identifiable correlates with thrombocytopenia. Sepsis, acute kidney injury and respiratory failure were strongly correlated ($p < 0.0001$) with thrombocytopenia. Patients with severe thrombocytopenia were found to have concurrent alterations in

Plasma GDF-15 concentration (pg/ml) in non-wasting (n=19) and wasting patients (those with $>9.24\%$ muscle loss: n=23) pre-operatively (PO), on day 1 (D1), day 2 (D2) and on day 7 (D7). Data presented as mean $\pm$ SD. ** $p < 0.01$, *** $p < 0.001$, repeated measures ANOVA with Bonferroni correction for comparison with pre-operative baseline.

Abstract S73 Figure 1