vitro. Thus, we provide important insights into the changes occurring after prolonged *in vitro* expansion, underlining the importance of using low passage MSCs in clinical trials for ARDS. In agreement with published data, we also found that MSCs do not induce cellular proliferation in the absence of stimulation.

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S12 PLASMA SYNDECAN-1 LEVEL AS A PREDICTIVE MARKER OF VASOPLEGIA ASSOCIATED WITH SURGERY REQUIRING CARDIOPULMONARY BYPASS AND POSSIBLE INVOLVEMENT OF OXIDATIVE STRESS

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Background Vasoplegic syndrome (severe refractory hypotension) is associated with oxidative stress leading to endothelial dysfunction and complicates 10 to 40% of surgery requiring cardiopulmonary bypass (CPB). Whilst operative mortality is low, recovery is often prolonged in patients developing vasoplegia. There are, as yet, no validated biomarkers for vasoplegia that could be used to identify 'at risk' patients. We hypothesised that plasma levels of the endothelial surface layer (glycocalyx) protein, syndecan-1, shed during CPB, will be higher in patients who develop vasoplegia and that leukocyte responses to oxidative stress will be altered.

Methods Patients (n = 48) undergoing cardiac surgery requiring CPB were, prospectively, enrolled; blood collected and indices of outcome recorded. A surrogate index of vasoplegia was adopted: requirement for infusion of vasoconstrictor agents for longer than 48h. An enzyme-linked immunosorbent assay was used to measure plasma levels of syndecan-1 at four time-points: after induction of anaesthesia but before CPB (T1); within 30 min of CPB ending (T2); 2h (T3) and 24h (T4) post-CPB. Real time qPCR was used to determine, in patient leukocytes (n = 20), relative expression (to house-keeping gene18*S*) of mRNA for markers of oxidative stress; NQO1 and SOD2, cytoplasmic and mitochondrial enzymes, respectively; and for comparison, TNFα.

Results Syndecan-1 levels at T2 were significantly higher in vasoplegic patients (110.7 ng/mL, IQR 65.46–155.2) than non-vasoplegic patients (53.8 ng/mL, IQR 40.67–102.2; $p < 0.001$). ROC curve analysis showed syndecan-1 had significant ($p = 0.009$) predictive power for onset of vasoplegia, with an area under the curve of 0.766 (95% CI: 0.6019–0.9301); and a cut-off of 63.33 ng/mL (83.33% sensitivity, 69.23% specificity). Syndecan-1 levels were higher in patients whose intensive care unit length of stay (LOS) and hospital LOS were above corresponding medians for the cohort ($p = 0.0061$ and $p = 0.0148$, respectively). NQO1 relative expression was significantly higher ($p = 0.022$) in vasoplegic patients (3.779 ± 1.036) than non-vasoplegic patients (1.3 ± 0.302); whereas, neither SOD2 nor TNFα expression were significantly altered.

Conclusion Plasma syndecan-1 measured immediately post-CPB had good predictive power for patients at risk of vasoplegia. Greater relative expression of leukocyte NQO1 in vasoplegic patients indicates activation of antioxidant defence mechanisms in response to oxidative stress, which could contribute to syndecan-1 shedding.

S13 PHARMACOKINETICS AND PHARMACODYNAMICS OF ANTIMICROBIALS IN CRITICALLY ILL PATIENTS WITH LOWER RESPIRATORY TRACT INFECTIONS. ARE 'ONE SIZE FITS ALL' DOSES APPROPRIATE?

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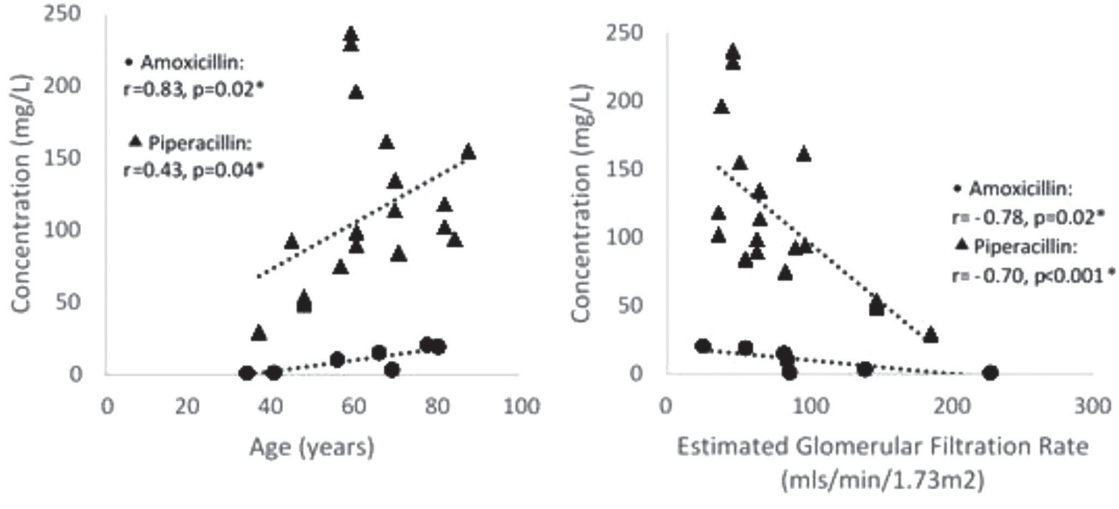
Introduction Respiratory infection is a common cause of severe sepsis.[1] Current therapeutic guidelines emphasise the importance of early initiation of antibiotic therapy, but make no



Abstract S13 Figure 1 Antimicrobial concentration measured at 50% of the dosing interval plotted against age (left) and eGFR (right). Line of best fir and associated coefficients suggest correlation with age and negative correlation with eGFR