

## Royal Society of Medicine, Colt Foundation Research & Clinical Innovation Meeting 2022

### 1 PLATELET DYSFUNCTION IN A MODEL OF COMPLEX MILITARY TRAUMA

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**Background** Haemorrhage is a principal contributory factor in trauma-related deaths in military (battlefield) and civilian settings. A significant proportion of severely injured casualties develop an early trauma-induced coagulopathy (TIC), which is an independent predictor of death. One aspect of TIC is an alteration in platelet function. In vivo trauma models are often essential to develop new treatments. The aim of this study was to evaluate whether an established model of trauma incorporates platelet dysfunction.

**Method** The study was conducted in accordance with the Animals (Scientific Procedures) Act, 1986. Blood was collected from terminally anaesthetised pigs before (Baseline) and 30 minutes after the induction of trauma/haemorrhagic shock (S30), and again after 90 minutes of hypotensive resuscitation (R90) with either 0.9% saline, 1:1 packed red cells and plasma (PRBC:FFP) or whole blood (WB). Platelet function was assessed by aggregometry in response to ADP and TRAP (Multiplate®). Platelet count was obtained using a haematology analyser, and shock was quantified by measuring Actual Base Excess (ABE) of arterial blood.

**Results** ABE fell significantly from Baseline to S30 and remained negative ( $-7 \pm 1$  mM) until R90 in all groups ( $P < 0.001$ ), without significant difference between groups ( $P = 0.4747$ ). Injury, shock and resuscitation were associated with a significant fall in platelet aggregation in response to ADP ( $P < 0.0001$ ) and TRAP ( $P = 0.0006$ ), but no difference between treatment groups ( $P = 0.9388$  ADP;  $P = 0.06385$  TRAP). The response to TRAP was markedly less than that to ADP. Platelet count fell significantly ( $P < 0.0001$ ), again without significant difference between treatment groups ( $P = 0.8574$ ). After 90 minutes of resuscitation, the response to ADP had fallen to 62% of the baseline response while platelet numbers had only fallen to 85% of baseline over the same period.

**Conclusions** Our model of trauma results in an attenuation of platelet function that, in the early phase, is independent of resuscitation strategy.

### 2 DEVELOPING A MILITARILY RELEVANT EX-VIVO MODEL OF TRAUMATIC INJURY AND HAEMORRHAGIC SHOCK

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**Background** Traumatic injury is a leading cause of death worldwide. There is a crucial need to develop therapies that

improve critically injured patient outcomes. Current trauma research models are ethically and financially challenging, with poor translation. However, traumatic injury and haemorrhagic shock can be modelled using ex-vivo normothermic perfusion (EVNP), a methodology adapted from transplantation. The aim of this study was to develop a 24hr EVNP dual porcine limb and kidney model.

**Method** Eight porcine forelimbs, bilateral kidneys and blood were retrieved via standard protocols. Following <4hrs cold storage, the kidneys were connected to a bespoke Ex-Vivo Research Centre circuit via the renal artery, and a mean arterial pressure (MAP) of 80mmHg was maintained. The perfusate consisted of leukocyte-deplete blood and Ringer's solution. Once the kidney was haemodynamically stable, the limb was connected via the brachial and radial collateral arteries. Haemodynamic parameters were continuously monitored, biochemical perfusate assessment performed hourly and histopathology baseline and end timepoints samples taken.

**Results** Perfusion was maintained for 24hrs in all limbs, with blood flows of 345.03mls/min ( $\pm 54.78$  SD) and MAP of 77.57mmHg ( $\pm 3.82$  SD). Three kidneys achieved 24hr perfusion, with flows of 214.53mls/min ( $\pm 41.6$  SD) and MAP of 80.58mmHg ( $\pm 0.51$  SD). Biochemical analysis showed a statistically significant potassium elevation at 24hrs compared to baseline,  $p = 0.0078$ . A further three kidneys were disconnected from the circuit at 7, 11 and 12hrs, and two kidneys showed decline in flow >15 hrs due to declining haemodynamics. Compared to baseline, evidence of cell death was observed in 24hr muscle samples. In the end-point kidney samples, tubular degeneration, protein loss and necrosis extended along the nephron.

**Conclusions** Limb EVNP can be successfully achieved for 24hrs, but further protocol improvements are required to sustain renal perfusion for 24hrs alongside adjustments to reduce the ischaemic insult and cell death.

### 3 CARDIOPULMONARY, FUNCTIONAL, COGNITIVE AND MENTAL HEALTH OUTCOMES POST COVID, ACROSS THE RANGE OF SEVERITY OF ACUTE ILLNESS, IN A PHYSICALLY ACTIVE WORKING AGE POPULATION: BASELINE FINDINGS FROM THE MCOVID STUDY

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**Background** The medium-long impact of coronavirus disease 2019 (COVID-19) on active populations is yet to be fully understood, with potential individual and operational impact on military service personnel (SP). The M-COVID study was established to investigate cardiopulmonary, functional, cognitive, and mental health post-COVID-19 SP outcomes, across the spectrum of acute COVID-19 severity.

**Method** Observational four-cohort study; hospitalised, community-based illness with on-going symptoms (community-symptomatic), community-based illness now recovered (community-recovered) and age, sex, job-role matched control. Participants underwent extensive clinical assessment involving