Developing a Pragmatic Murine Injury Model for Polytrauma Research

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Purpose: Fractures are the most common injury in polytraumatized patients and they are often accompanied by hemorrhagic shock (HS). Accordingly, animal preparations that model fractures and HS are important research tools. Murine models are typically suited for foundational investigations to survey pathophysiologic mechanisms and potential therapies as they are relatively inexpensive and can homogenize genetic variability. Murine polytrauma models that include fractures and shock typically require sophisticated vascular access, are time- consuming, and are costly. We have developed a novel simple, reproducible murine polytrauma that includes a femoral fracture, quadriceps muscle crush, and HS achieved through retroorbital puncture that requires no vascular access or invasive monitoring.

Methods: Sixty 12-week-old, C57BL/6 female mice were used in this study. Mice sustained a femur fracture stabilized with an intramedullary wire, manual muscle crush, volume-controlled HS (40% blood volume) via retro-orbital puncture and saline resuscitation. Splenocytes were isolated at euthanasia in an uninjured control group and at 0, 1, 4, and 24 hours post-trauma (n = 12/group). Changes in hemoglobin and lactate were assessed in an additional 39 mice.

Results: Overall operative time was 10.1 min/mouse with 96% survival. Hemorrhage was completed with an average time of 1.33 ± 1.10 min (range <1-9 min). Post-injury splenocyte changes were consistent with other trauma models. Splenic neutrophil percentages significantly increased ($P<0.05$) at 4 hours compared to control. The percentage of natural killer (NK) cells significantly increased at 24 hours compared to control and all time points ($P<0.05$). Hemoglobin decreased from 14.7 ± 0.6 g/dL at baseline to 7.0 ± 0.8 g/dL at 24 hours (<0.0001). Unexpectedly, serum lactate decreased from 3.9 ± 1.2 mmol/L at baseline to 1.6 ± 0.5 mmol/L ($P<0.001$) 4 hours after injury.

Conclusion: Our model offers a less expensive and more expedient model to study polytrauma without the need for sophisticated vascular access and invasive monitoring. Retro-orbital puncture was universally well tolerated by all mice. This model emulates non-fatal, polytraumatic injuries, with excellent survival rates. The decrease in lactate was unanticipated as lactate is an accepted biomarker reflecting the magnitude of HS in humans, suggesting mice accommodate hypoperfusion with alternative metabolic compensation.