Lipidomic Analysis Reveals Global Lipid Profile Changes in a Porcine Model with Hemorrhagic Shock and Multiple Injuries

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Purpose: The role of lipid mediators in the posttraumatic response has been hypothesized but not yet proven. With vast advances in analytic technology, lipid profile changes can be characterized on a molecular level. The aim of this study was to characterize the lipididomic response to trauma in a translational large animal model.

Methods: 54 male pigs (50 ± 5 kg) were randomized for 3 conditions: Sham, Monotrauma, and Polytrauma. All animals were anesthetized for 6 hours. Monotrauma group received a femoral shaft fracture only and polytrauma received additional blunt chest trauma liver laceration and a pressure controlled hemorrhagic shock for 60 min. Resuscitation was performed with crystalloid fluids and fractures were stabilized by intramedullary nailing. Venous samples were collected at 6 time points (baseline, trauma, resuscitation, 2 h, 4 h, and 6 h). Lipidomic analysis was performed via liquid chromatography mass spectrometry (LC-MS). Lipid profiles were characterized using bioinformatic approaches and dimensionality reduction. Linear mixed models were programmed to analyze profile changes over time.

Results: Overall, 307 individual lipids were identified. Principal component analysis (PCA) revealed clustering of lipids with similar molecular characteristics and lipids were organized into 18 functional subgroups. Polytrauma showed a significantly different lipid profile compared to Sham and Monotrauma. These differences were most pronounced after resuscitation and at 6 h post-injury. PCA confirmed strong variation between Polytrauma and the other groups at these time points. Lipid subgroups involved in energy metabolism showed significant ($P < 0.05$) decrease over time in polytrauma. In contrast, acylcarnitines (AcCas) showed a highly significant ($P < 0.001$) twofold increase after resuscitation in polytrauma only.

Conclusion: Our data suggest that lipidomic profile changes align with injury severity. Causal inferences can be drawn based on the lipids' functional characteristics: While the strong decrease of "energy lipids" points to a hypercatabolic response to polytrauma, acylcarnitines (a lipid specific to the mitochondrial membrane) show high potential as a marker for oxidative stress.