Circulating Markers of Immune Function and Tissue Damage Are Associated with Operative Delay and Mortality Among Severely Injured Orthopaedic Polytrauma Patients

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Purpose: Optimizing surgical timing for severely injured orthopaedic polytrauma patients is challenging, and the decision to delay surgical fixation may impact outcomes. ISS often fails to predict survival, and markers of immune function and tissue damage may better reflect the underlying physiology or response to interventions. We sought to evaluate the association between inflammatory mediators, orthopaedic fixation time, and mortality among severely injured polytrauma patients. We hypothesized that inflammatory mediators would not differ based on time of definitive orthopaedic fixation.

Methods: We included severely injured polytrauma patients enrolled in the Prehospital Air Medical Plasma Trial who sustained orthopaedic fractures and were transported to the University of Pittsburgh Medical Center. We sampled circulating markers of immune function and tissue damage at hospital admission and 24 and 72 hours after admission. We assessed patient and injury characteristics, surgical procedures, and marker values among patients who received orthopaedic fixation and those who died prior to definitive orthopaedic surgery. We modeled the association between inflammatory mediator trends over 72 hours and orthopaedic fixation time using linear mixed effects models controlling for injury characteristics and operative procedures.

Results: 40 patients met inclusion criteria: 23 received early fixation (<72 hours), 11 received delayed fixation (>72 hours), and 6 died prior to definitive orthopaedic surgical intervention. These patients were mostly male (78%) with blunt injuries (100%) and a median ISS of 22. Although ISS was similar between surgical patients and nonsurvivors (22 [17, 30] vs 22 [17, 33], $P = 0.98$), several markers of immune function and tissue damage measured upon hospital admission stratified patients who died before orthopaedic fixation. Compared to similarly injured patients who received orthopaedic fixation, patients with pelvis or femur fractures who died prior to definitive surgery had significantly higher levels of interleukin (IL)-6, IL-8, monocyte chemoattractant protein-1, syndecan-1, and vascular endothelial growth factor and significantly lower levels of IL-2 and IL-7. Among patients who received early orthopaedic fixation, every hour delay in definitive surgery was associated with a 5.2 pg/mL decrease in IL-6 ($P = 0.04$) even after controlling for injury and surgical characteristics, suggesting that delayed surgical intervention may mediate the impact of surgery following trauma.

Conclusion: Among severely injured orthopaedic polytrauma patients, circulating immune and tissue damage markers measured upon admission were associated with mortality prior to definitive surgery. These markers may inform the appropriate timing of operative interventions or further reveal the burden of a "second hit" to the body incurred by surgery following traumatic injury.