Deficient Epithelial and Adaptive Immunologic Mediators Predict Organ Dysfunction in Patients Treated With Early Total Care (ETC)

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Purpose: Optimizing timing for orthopaedic interventions in patients with polytrauma improves outcomes. This study quantified differences in immunologic mediators in patients who were physiologically stable and treated with early total care (ETC) (definitive fixation <36 hours post-injury) in whom organ dysfunction did or did not develop.

Methods: This is a secondary analysis of 322 prospectively enrolled patients with polytrauma with surgical fractures of the pelvis, acetabulum, femur, or tibia. Injury severity scores (ISS), maximum lactate, and transfusion volumes were quantified on injury day 1 (D1). Daily organ dysfunction was quantified using Marshall Organ Dysfunction Scores (MODS). Patients with an average MODS of 3 or greater from post-injury D2 to D5 (aMODSD2-D5) had greater ventilation days and complications; therefore, they were defined as having high-magnitude organ dysfunction, while aMODSD2-D5 of 2.75 or less indicated low-magnitude organ dysfunction. In total, 33 immunologically active mediators were quantified at five timepoints from admission to 48-hours post-admission. We identified 122 of 322 patients who met criteria for ETC (ISS < 24, maximum lactate < 3.9, transfusion volume < 3000 mL, GCS > 8) of whom 77 had ETC. We compared temporal changes in immunologic mediator concentrations between patients treated with ETC in whom high-magnitude (aMODSD2-D5 > 3; n = 7) developed versus low-magnitude organ dysfunction (aMODSD2-D5 < 2.75; n = 70).

Results: Hierarchical clustering delineated three mediator clusters in the entire population (n = 322), including an inflammation-, adaptive-, and epithelial-based cluster. Inflammatory mediators demonstrated minimal differences between the low- and high-magnitude organ dysfunction groups. In contrast, the epithelial mediators interleukin (IL)-9 and IL-21 were 2.5 to 3 times lower at all timepoints ($p<0.001$) in patients with high-magnitude organ dysfunction, with 2.0 to 3.0 times decreases in other epithelial cytokines (IL-23, IL-33) at 24- and 48-hours post-injury ($p<0.01$). Adaptive mediators (IL-7, IL-1β, IL-2, interferon gamma and interferon alpha) were decreased beginning 12 hours post-injury ($p<0.01$) in patients with high-magnitude organ dysfunction.

Conclusion: Deficient epithelial and adaptive mediators were associated with risk of organ dysfunction development in patients who met criteria for ETC, while excessive inflammatory mediators were not observed. This finding needs further investigation to identify patients at risk for organ dysfunction after ETC.