Distinct Inflammatory Networks are Associated with Organ Dysfunction in Orthopaedic Trauma Patients

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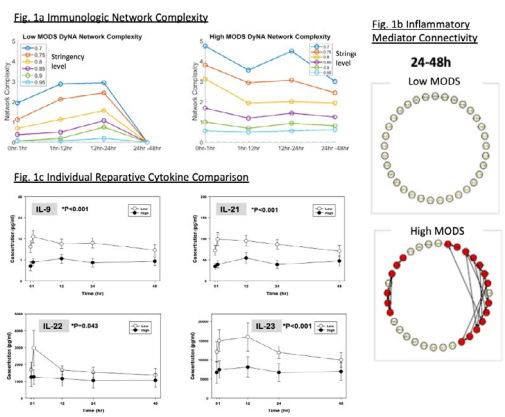
Purpose: Pathologic inflammation has been implicated in adverse outcomes for trauma patients. However, there are limited data on the post-injury immunologic response in orthopaedic trauma patients. We hypothesized differential inflammatory networks in multiply injured patients with fractures would correspond with organ dysfunction.

Methods: Polytrauma patients aged 18 to 55 years admitted to a higher level of care with operative pelvis, acetabular, femur, and / or tibia fractures (OTA / AO 61B-C,62A-C,31,32,33A-C,42A-C) were enrolled in the prospective observational PRECISE study from 2018 to 2022. Blood was collected at 0, 1, 12, 24, and 48 hours post-injury. A panel of 33 trauma-relevant immunologic mediators were quantified using a multiplex platform. The primary outcome was the Marshall Multiple Organ Dysfunction Score (without neurologic) averaged over days 2-5 (aMODS2-5). As a secondary analysis of the PRECISE study, inflammatory networks were compared in patients with higher versus lower organ dysfunction (aMODS2-5 >1.5; "high MODS", n = 39 vs aMODS2-5 <1.5; "ow MODS", n = 50) using dynamic network analysis (DyNA); Pearson correlation coefficient 0.7 to 0.95 between any 2 mediators. Two-way analysis of variance compared individual mediator concentrations. Groups were otherwise matched based on age, 24-hour hypoperfusion, and ISS.

Results: DyNA revealed a greater degree of immunologic biomarker network complexity in high MODS versus low MODS (Fig. 1a). High MODS networks were formed primarily with lymphoid-based cytokines, including interleukin (IL)-2, IL-4, IL-5, and IL-7 (Fig. 1b). A reparative cluster of tissue-protective cytokines, including IL-9, IL-21, IL-22, IL-23, IL-25, IL-27, and IL-33 were significantly elevated in low MODS compared to high MODS (Fig. 1c).



Conclusion: Multiply injured patients with fractures who developed higher levels of organ dysfunction had lower circulating levels of tissue protective cytokines and displayed a distinct immunologic response from those with lower levels of organ dysfunction. Immunologic profiles may inform clinical decisions surrounding timing of fracture interventions.