Early Immunotypes Identify Trauma-Tolerant and Trauma-Sensitive Patients with Orthopaedic Injuries

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Purpose: Multiply injured patients (MIPs) frequently sustain skeletal trauma. These patients are at risk to develop acute (infections, organ failure) and long-term (nonunion, osteomyelitis) complications. There are anecdotal trauma-tolerant (TT) MIPs who are severely injured but recover without complications in contrast to trauma-sensitive (TS) MIPs who are less injured but develop complications and poor long-term outcomes.

Recent work has demonstrated that early immunologic response to injury may identify patients who are TT or TS. The objective of this study was to compare the early immunologic response between 2 subsets of MIPs with orthopaedic injuries who were phenotypically TT or TS.

Methods: 100 MIPs (admitted to ICU; SS >18), 18-55 years old, were included. Initial hemorrhage was measured by temporal integration of elevated serial shock index values (HR/SBP > 0.9) over the first 6 hours after injury (6-hour shock volume [6hr SHVL]). Organ dysfunction was quantified by averaging Marshall Organ Dysfunction scores from day 2-5 after injury (aMOD). Regression analysis showed close correspondence between aMOD and 6hr SHVL. We identified a subcohort of 13 patients with similar demographics, orthopaedic injuries, and ISS who either had high 6hr SHVL (>60 units) and low aMOD (< 4) (6 patients TT), or who had low 6hr SHVL (< 20 units) and high aMOD (>4) (7 patients TS). We compared serial serum cytokines measured at 0, 8, 24, and 48 hours after injury between TT and TS patients.

Results: ISS (TT = 32.7; TS = 36.6; P = 0.53) and age (TT = 35.7 years; TS = 35.9 years; P = 0.98) were equal between groups. TT patients had high-magnitude initial hemorrhage (6hr SHVL TT = 88.1 units; TS = 8.9 units; P <0.0001) and low organ dysfunction (aMOD TT = 2.4; aMOD TS = 5.2; P = 0.0016) compared to TS patients. TS patients had more days in ICU (16.0 vs 5.3 days; P = 0.012) and more ventilator days (14.1 vs 2.5 days; P = 0.022). There were no cytokine differences between TT and TS patients at 0 hours. By 8 hours after injury, levels of protective, reparative cytokines interleukin (IL)-9, 21, 22, 23, 33, and IL-17E/IL-25 were reduced and MIG and sIL2RA increased (P <0.05) in TT patients compared to TS patients. At 24 hours, significant reductions in IL-9, 21, 22, and 33 remained along with reductions in HMGB1 and increases in IL-10 in TT patients. No differences were measured at 48 hours.

Conclusion: There were distinct immunotypes identified that discriminated TT and TS patients in cohorts of MIPs who were otherwise similar in age and injury severity. Differences were primarily in tissue-protective cytokines. Information that could risk-stratify response to injury was evident by 8 hours after injury. Such information could be useful to inform initial and staged orthopaedic intervention decisions.