

Inflammatory Cytokines Provide Unique Predictive Value Beyond Injury Severity: A Prospective Cohort Study of Orthopaedic Trauma Patients

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Purpose: Elevated cytokines are associated with worsened posttraumatic outcomes. It is unknown whether this elevation simply mirrors trauma severity or holds predictive value. We hypothesized cytokine levels would be associated with unique variation in outcomes.

Methods: A prospective cohort study with patients presenting to a Level-I trauma center with orthopaedic injuries and new injury severity score (NISS) >5 was undertaken. Within 24 hours of presentation, interleukin (IL)-6, IL-8, IL-10, and macrophage migration inhibitory factor (MIF) levels were measured. Clinical and demographic covariates and outcomes including pulmonary complication, acute kidney injury (AKI), days in the ICU, length of stay (LOS), and death were abstracted from the medical record. Nested linear regression was used to estimate the unique predictive value of cytokines beyond NISS.

Results: 58 patients (83% male, mean age 40 years) were included. Median ICU and hospital stays were 3 and 14 days, respectively. Six patients suffered pulmonary complications, 5 had AKI, and no deaths occurred. The addition of IL-6 to baseline models including NISS significantly improved the prediction of pulmonary complication (likelihood ratio [LR] = 6.21, P = 0.01), ICU (change in R² = 0.31, P <0.01) and hospital LOS (change in R² = 0.16, P <0.01), while the addition of IL-8 significantly improved the prediction of AKI (LR = 9.15, P <0.01). Addition of IL-10 and MIF to baseline models with NISS did not significantly improve the prediction of outcome.

Conclusion: The addition of post-injury IL-6 level to the baseline NISS model is better able to predict occurrence of pulmonary complications as well as prolonged ICU and hospital LOS. This suggests that inflammatory cytokines, a measure of the internal physiologic inflammatory response, elucidate more information about a patient's outcome than the NISS alone.

Table 1: Hierarchical Regression results for outcomes		
Linear Regression model	Change in R-squared	P-Value
For ICU Stay		
1: NISS	Ref	
2: NISS + IL-6	0.308	0.003
3: NISS + IL-8	0.071	0.140
4: NISS + IL-10	0.003	0.781
5: NISS + MIF	0.003	0.7982
For hospital stay		
1: NISS	Ref	
2: NISS + IL-6	0.162	0.005
3: NISS + IL-8	0.039	0.149
4: NISS + IL-10	0.001	0.902
5: NISS + MIF	0.001	0.969
Logistic regression model	Likelihood ratio	P Value
For pulmonary complications		
1: NISS	Ref	
2: NISS + IL-6	6.21	0.013
3: NISS + IL-8	2.47	0.116
4: NISS + IL-10	0.02	0.900
5: NISS + MIF	3.31	0.069
For acute kidney injury		
1: NISS	Ref	
2: NISS + IL-6	0.49	0.483
3: NISS + IL-8	9.15	0.003
4: NISS + IL-10	2.98	0.085
5: NISS + MIF	0.00	0.961