Using Cellular Measures of Immunocoagulopathy as a Predictor of Mortality in Necrotizing Fasciitis

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INTRODUCTION:

When it comes to orthopaedic infections, few confer greater severity than necrotizing fasciitis (NF), a rapid and progressive infection of the musculoskeletal system with a mortality rate of 20-30%. Given the low incidence and high mortality rate, NF is difficult to study clinically; thus, current management recommendations and therapeutic interventions are largely based on historical practice patterns of rapid identification, early antibiotic administration, and surgical debridement. Determining the severity of musculoskeletal infections and a patient's risk for precipitous deterioration, thereby requiring more intensive care, can greatly aid the physician caring for the patient. Given that few prognostic labs have been examined in patients with NF, the goal of this study was to use cellular measures of inflammation and coagulation dysfunction, together termed immunocoagulopathy, on admission to prognosticate for mortality in adult patients with NF.

Specifically, this study examined if measures from a complete blood count with differential (CBC with Diff) could be utilized to efficiently measure immunocoagulopathy in patients with NF; Coagulation will be assessed by platelet count while the neutrophil to lymphocyte ratio (NLR) will be examined as a measure of inflammation. While NLR has been demonstrated to be an excellent prognostic marker in conditions such as sepsis and COVID-19, its use in orthopaedic conditions is less established.

METHODS:

A retrospective review was conducted to identify confirmed cases of NF at a single tertiary care center over a 10+ year period. The protocol used to identify cases was modeled after past large retrospective cohort studies on NF. Patients were excluded if they were ≤18 years of age, no operation was performed, or operative findings were inconsistent with NF. Demographics, infection characteristics, and laboratory values were analyzed. A multivariable logistic regression model was built on immunocoagulopathy measures (absolute neutrophil count [ANC], absolute lymphocyte count [ALC], NLR, platelet count) and patient age to predict in-hospital mortality in NF.

RESULTS:

This retrospective review identified 389 verified cases of NF infections cared for at a single tertiary care center. Amongst 389 NF cases, there were 312 survivors (80.2%) and 77 non-survivors (19.8%). The study cohort was 55.0% male (N=214) with a median age of 51 years (range: 19-85y). The pelvis (N=170) and extremities (N=136) were the most common infection locations, accounting for 78.7% of all cases. Infected wounds (N=131, 33.7%), idiopathic (N=130, 33.4%), and trauma (N=32, 8.2%) were the most common mechanisms by which patients contracted their infections. Patient age was significantly different between survivors and non-survivors ($p<0.05$). There were 261 patients (67.1%) with complete immunocoagulopathy measures on admission (CBC with Diff). Platelet count, ANC, and the NLR were significantly different between survivors and non-survivors ($p<0.05$). There was no difference in total WBC and ALC. A multivariable logistic regression model was built using NLR at admission, platelet count at admission, and patient age to predict in-hospital mortality. The model discriminated between survivors and non-survivors well with an original C-index of 0.829 (Figure 1).

DISCUSSION AND CONCLUSION:

This retrospective study determined that in patients with NF, patient age and measures of immunocoagulopathy at admission, specifically NLR and platelet count, effectively prognosticated patient in-hospital mortality risk. Platelet count was an effective surrogate for coagulation dysfunction as thrombocytopenia was significantly associated with mortality. To assess inflammation, the total WBC is often utilized clinically to identify the presence and/or severity of an infection. Without looking at the parts of a total WBC that make up the whole, this measure can predispose to an inaccurate representation of the patient's inflammatory status. While the total WBC can be non-specific, analysis of specific leukocyte subtypes, such as neutrophils and lymphocytes, was demonstrated to assess the severity of NF in this study. Given the accessibility of immunocoagulopathy measures in a CBC with Diff, future studies examining the utility of this measure in cases of NF and other severe orthopedic infections are warranted.

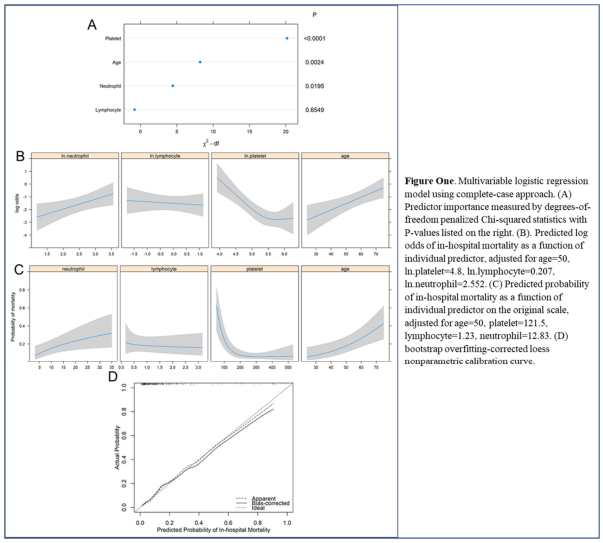

Figure One. Multivariable logistic regression model using complete-case approach. (A) Predictor importance measured by degrees-of-freedom penalized Chi-squared statistics with P-values listed on the right. (B). Predicted log odds of in-hospital mortality as a function of individual predictor, adjusted for age=50, ln.platelet=4.8, ln.lymphocyte=0.207, ln.neutrophil=2.552. (C) Predicted probability of in-hospital mortality as a function of individual predictor on the original scale, adjusted for age=50, platelet=121.5, lymphocyte=1.23, neutrophil=12.83. (D) bootstrap overfitting-corrected loess nonparametric calibration curve.