The Role of Novel Immunologic Biomarkers in Predicting Outcome in Severe Sepsis/Septic Shock Patients

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Background: Innate immune response is one of the important host responses to infection. However, the role of neutrophil chemotaxis activity, CD11b expression on neutrophil, and monocyte HLA-DR (mHLA-DR) expression as novel prognostic biomarkers in patients with severe sepsis/septic shock is still unknown.

Objective: The purpose of this study was to evaluate the discriminatory characteristics on mortality outcome of these biomarkers.

Methods: A prospective cohort study was conducted at ICU, King Chulalongkorn Memorial Hospital. Patients with severe sepsis or septic shock were enrolled. We collected blood samples at the time of enrollment to test immunologic biomarkers. Neutrophil function was evaluated by measurement of neutrophil chemotaxis activity and CD11b expression. Monocyte function was assessed by measurement of mHLA-DR expression, a key marker of immunoparalysis state, and presepsin level. The primary end point was 28-day mortality.

Results: A total of 136 participants were enrolled. Patients were classified by mortality at day 28 into 2 groups as survivor group (n=59, 43%) and non-survivor group (n=77, 57%). Neutrophil chemotaxis activity was significantly higher in the survivor group than the non-survivor group (46.7\% vs 41.4\%, \textit{p}=0.027). There was significantly lower CD11b expression on neutrophil in the survivors than the non-survivors (10.3\% vs 14.8\%, \textit{p}=0.012). There was no significant difference in mHLA-DR expression and presepsin level between both groups. Neutrophil chemotaxis activity alone predicted 28-day mortality with an area under the receiver operating characteristic curve (AUC-ROC) of 0.76 (95\%CI 0.67-0.85). Neutrophil chemotaxis activity at the cutoff of 49\% showed the sensitivity of 0.51, and specificity of 0.71. By stepwise analysis, combining neutrophil chemotaxis activity with mHLA-DR, CD11b expression, presepsin, and APACHE II score provided the highest AUC-ROC of 0.84 (0.77-0.91) in predicting 28-day mortality.

Conclusion: Neutrophil chemotaxis activity appears to be the promising novel immunologic biomarkers in predicting clinical outcome in patients with severe sepsis or septic shock.

Keywords: Sepsis, Septic shock, Neutrophil chemotaxis activity, CD11b, mHLA-DR, Presepsin, Prognosis, Mortality, ICU