Use of a Combination Biomarker Algorithm to Identify Intensive Care Unit Patients with Suspected Sepsis at Very Low Likelihood of Bacterial Infection

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ABSTRACT

Background: Sepsis remains a diagnostic challenge in the intensive care unit (ICU), and the use of biomarkers may help in differentiating bacterial sepsis from other causes of systemic inflammatory syndrome (SIRS). The goal of this study was to assess test characteristics of a number of biomarkers for identifying ICU patients with a very low likelihood of bacterial sepsis.

Methods: A prospective cohort study was conducted in a medical ICU of a university hospital. Patients with presumed bacterial sepsis were consecutively enrolled from January 2012 to May 2013. Concentrations of nine biomarkers (α-haptoglobin, C-reactive protein [CRP], ferritin, fibrinogen, haptoglobin, procalcitonin [PCT], serum amyloid A, serum amyloid P, and tissue plasminogen activator) were determined at baseline, 24 hours, 48 hours, and 72 hours after enrollment. Performance characteristics were calculated for varying combinations of biomarkers for discrimination of bacterial sepsis from other causes of SIRS.

Results: Seventy patients were included during the study period; 31 (44%) had documented bacterial sepsis and 39 (56%) had other causes of SIRS. PCT and CRP values were significantly higher at all measured timepoints in patients with bacterial sepsis (Fig. 1). The use of combinations of CRP and PCT demonstrated high discriminatory ability (AUC of the ROC curve of 0.810 for the 24 hour timepoint), and was superior to that of the individual biomarkers.

Conclusions: The combination of biomarkers, particularly procalcitonin (PCT), has been shown to help with diagnosis of bacterial sepsis in the intensive care unit (ICU).

Background: Sepsis remains a diagnostic challenge in the critically ill patient population.

Empirical broad-spectrum antibiotics are frequently initiated with systemic inflammatory response syndrome (SIRS) and continued for prolonged courses.

Biomarkers, particularly procalcitonin (PCT), have been shown to help with diagnosis of bacterial sepsis in the intensive care unit (ICU).

The use of a combination of biomarkers may help inform safe discontinuation of antibiotics in the ICU in patients with SIRS who do not have a bacterial infection.

To assess test characteristics of a number of biomarkers for identifying medical ICU (MICU) patients with a very low likelihood of bacterial sepsis.

Methods: Prospective cohort study in the 24-bed MICU at the Hospital of the University of Pennsylvania (HUP)

Patients with presumed bacterial sepsis were consecutively enrolled from January 2012 to May 2013

Levels of nine biomarkers were determined at baseline, 24 hours, 48 hours, and 72 hours after enrollment

Biomarkers included n-2 macroglobulin, C-reactive protein (CRP), ferritin, fibrinogen, haptoglobin, procalcitonin (PCT), serum amyloid A, serum amyloid P, and tissue plasminogen activator.

The definitive diagnosis of bacterial infection was determined by the investigators using established CDC criteria.

Performance characteristics were calculated for varying combinations of biomarkers for discrimination of bacterial sepsis from other causes of SIRS.

The goal was to maximize the negative predictive value (NPV) in order to identify patients at low likelihood of bacterial infection in whom empiric antibiotics could be safely discontinued.

Performance of combinations of PCT and CRP in identifying patients at low likelihood of bacterial infection

<table>
<thead>
<tr>
<th>Combination</th>
<th>NPV (95% CI)</th>
<th>Specificity (95% CI)</th>
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<tbody>
<tr>
<td>24 hr PCT ≥ 0.2 and 24 hr CRP ≥ 40</td>
<td>85.7 (72.7-89.7)</td>
<td>93.7 (84.3-98.7)</td>
</tr>
<tr>
<td>48 hr PCT ≥ 0.5 and 48 hr CRP ≥ 50</td>
<td>83.3 (68.5-95.4)</td>
<td>93.7 (84.3-98.7)</td>
</tr>
<tr>
<td>24 hr PCT ≥ 1.5 and 24 hr CRP ≥ 40</td>
<td>81.1 (68.5-93.7)</td>
<td>93.7 (84.3-98.7)</td>
</tr>
<tr>
<td>48 hr PCT ≥ 2.0 and 48 hr CRP ≥ 40</td>
<td>81.1 (68.5-93.7)</td>
<td>93.7 (84.3-98.7)</td>
</tr>
</tbody>
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NPV: negative predictive value; PCT in μg/mL, CRP in mg/L

Conclusions:

- Combinations of PCT and CRP demonstrated high ability to discriminate bacterial sepsis from other causes of SIRS in medical ICU patients.
- These biomarkers may be an important adjunct to clinical and laboratory assessments for diagnosing bacterial infection in this population, as well as safe discontinuation of antibiotics in patients with a low likelihood of bacterial infection.
- Future studies should focus on the use of these algorithms in antibiotic stewardship interventions in the ICU setting.

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