ABSTRACT

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Title: Use of Clinical Criteria for Prediction of Invasive Bacterial Infection in Febrile Infants: Evaluation of the PROS Criteria
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Background: In a 2004 study, the American Academy of Pediatrics Pediatric Research in Office Settings (PROS) network developed clinical criteria that had a sensitivity of 93.6% for identification of febrile infants at low-risk for invasive bacterial infection (IBI). Although application of the PROS criteria would reduce routine testing and emergency department (ED) evaluation for febrile infants in outpatient settings without readily available access to laboratory testing, these criteria have not been externally validated in a contemporary cohort.

Objective: To evaluate the sensitivity of the PROS criteria for IBI in febrile infants ≤60 days old.

Design/Methods: We performed a secondary analysis of a retrospective cohort study of febrile infants ≤60 days old with IBI who presented to 11 EDs between 7/1/2011-6/30/2016. Infants were included if 1) they had a temperature of ≥38°C at home, in the office, or at triage in the ED; 2) had a bacterial pathogen isolated in blood and/or cerebrospinal fluid (CSF); and 3) were treated for IBI. We calculated the sensitivity of the PROS criteria (age <25 days, ill-appearance, maximum temperature ≥38.6°C) for identification of IBI.

Results: Among 313 febrile infants ≤60 days old with IBI, 249 infants (79.6%) had bacteremia without meningitis and 64 (20.5%) had bacterial meningitis. The sensitivity of the PROS criteria for IBI overall was 87.9% (95% confidence interval [CI] 83.7-91.3), and was 90.6% (95% CI 80.7-96.5) for bacterial meningitis. Overall, 38 infants with IBI (12.1% of the cohort) were misclassified as low-risk, including 6 infants with bacterial meningitis (Table 1).
**Conclusions:** The sensitivity of the PROS criteria for identification of IBI was lower in our multicenter ED cohort than in the original PROS study. Although the PROS criteria may help inform management of febrile infants in settings with limited access to laboratory testing, newer low-risk prediction rules for IBI are preferable when laboratory testing is available.

**Table 1.** Febrile infants with bacterial meningitis misclassified as low-risk by the PROS criteria

<table>
<thead>
<tr>
<th>Age, d</th>
<th>Maximum temperature (℃)</th>
<th>Ill-Appearing Y/N</th>
<th>Peripheral WBC (cells/µL)</th>
<th>CSF WBC (cells/µL)</th>
<th>Blood culture</th>
<th>CSF culture</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>38.4</td>
<td>N</td>
<td>9,670</td>
<td>91</td>
<td><em>K. pneumoniae</em></td>
<td>No growth²</td>
</tr>
<tr>
<td>25</td>
<td>38.0</td>
<td>N</td>
<td>4,600</td>
<td>820</td>
<td><em>S. gallolyticus</em></td>
<td><em>S. gallolyticus</em></td>
</tr>
<tr>
<td>26</td>
<td>38.3</td>
<td>N</td>
<td>11,450</td>
<td>Not performed</td>
<td>No growth</td>
<td><em>E. coli</em></td>
</tr>
<tr>
<td>36</td>
<td>38.2</td>
<td>N</td>
<td>5,630</td>
<td>3</td>
<td>GBS</td>
<td>GBS</td>
</tr>
<tr>
<td>39</td>
<td>38.3</td>
<td>N</td>
<td>14,800</td>
<td>102</td>
<td><em>E. coli</em></td>
<td>No growth²</td>
</tr>
<tr>
<td>54</td>
<td>38.3</td>
<td>N</td>
<td>4,300</td>
<td>432</td>
<td>GBS</td>
<td>GBS</td>
</tr>
</tbody>
</table>

1PROS criteria for classification as low-risk for IBI: age ≥25 days, non-ill-appearing, and maximum temperature ≤38.6℃

2CSF culture obtained >11 hours after antimicrobial administration; treated as bacterial meningitis

**Word Count: 304**