Sepsis Diagnostics

A fast and accurate diagnostic test for severe sepsis using kernel classifiers

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Problem: Treat sepsis within 6 hours

SEPSIS = ORGAN FAILURE + INFLAMMATION + INFECTION

Brain
Lungs
Heart
Liver
Kidney
Blood

ICU:
11–15% incidence
30–60% mortality
$17B USD annual cost

Cause of death:
2nd in the ICU
10th in the USA
Aim: Insulin sensitivity (SI) may be a useful real-time sepsis biomarker.
Method: Develop a classifier using joint real-time retrospective data

<table>
<thead>
<tr>
<th>patients</th>
<th>sepsis</th>
<th>non-sepsis</th>
<th>prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>36</td>
<td>213 hours</td>
<td>5858 hours</td>
<td>3.5%</td>
</tr>
</tbody>
</table>

Temperature (C) decreases

RR decreases

HR increases

Mean arterial pressure (mm Hg) increases

Respiratory rate (breaths/min) decreases
Classification: What is the probability the data is sepsis?

Predictors increase discrimination

Greater

Less

log temperature

kernel probability density

joint probability

x1 x2 x3
### Results: The test identifies the majority of sepsis and non-sepsis hours

<table>
<thead>
<tr>
<th></th>
<th>negative test</th>
<th>positive test</th>
<th>cutoff 0.32</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>sepsis</strong></td>
<td>FN = 13</td>
<td>TP = 200</td>
<td>94% SENSITIVITY</td>
</tr>
<tr>
<td>213 (3.5%)</td>
<td>(0.2%)</td>
<td>(3.3%)</td>
<td></td>
</tr>
<tr>
<td><strong>non-sepsis</strong></td>
<td>TN = 5531</td>
<td>FP = 327</td>
<td>94% SPECIFICITY</td>
</tr>
<tr>
<td>58589 (96.5%)</td>
<td>(91.1%)</td>
<td>(5.4%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>100% NPV</td>
<td>38% PPV</td>
<td></td>
</tr>
</tbody>
</table>
Results: Likelihood ratios show the test often provides useful information.

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>LHR+ (&gt; 5)</th>
<th>LHR- (&lt;0.2)</th>
<th>DOR (&gt;20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Out-of-sample</td>
<td>69%</td>
<td>75%</td>
<td>3</td>
<td>0.4</td>
<td>7</td>
</tr>
<tr>
<td>In-sample</td>
<td>94%</td>
<td>94%</td>
<td>17</td>
<td>0.06</td>
<td>260</td>
</tr>
</tbody>
</table>

Best: Alter clinical decisions

Worst: Better than useless
Results: The AUC shows the test performs with good to high accuracy.

AUC = 0.78–0.99
Comparison: The test is faster and more accurate than existing sepsis tests

<table>
<thead>
<tr>
<th></th>
<th>clinical biomarker</th>
<th>standard culture</th>
<th>molecular biomarker</th>
</tr>
</thead>
<tbody>
<tr>
<td>time to results</td>
<td>hour-to-hour</td>
<td>48 hours</td>
<td>&lt; 6 hours</td>
</tr>
<tr>
<td>accuracy</td>
<td>good–high</td>
<td>high?</td>
<td>low</td>
</tr>
</tbody>
</table>
Conclusions: Drowning in data and searching for knowledge

Novel biomarker
Real-time diagnostics
Good to high accuracy