INTRODUCTION

- Value of blood cultures (BCx) for confirming the clinical diagnosis of sepsis is low:
  - 30% of patients with bacterial lung or GI infections had +BCx
  - Only 50% of patients with septic shock have + BCx
  - Only 5 to 15% of BCx drawn for any reason are +
- Timely administration of appropriate antibiotics improves outcomes
- Blood culture (BCx) is considered the gold standard for diagnosing BSI, but is limited by
  - Suboptimal sensitivity (10% in suspected bacteremia)
  - Slow turnaround time (average: 84 hours)
  - Several nucleic acid amplification tests (NAATs) for detection of bacteria directly from blood have been developed
- Given the poor sensitivity of BCx, it may be more accurate to use composite microbiologic and clinical criteria in evaluating the performance of these non-cultural diagnostic tests
- T2Bacteria Panel (T2B) is an automated, rapid, culture-independent diagnostic test that identifies microbes directly from whole blood
- T2B identifies 5 target organisms responsible for ≥50% of BSI
- T2B can detect bacteria at a density as low as 2 CFU/mL of whole blood

METHODS

- Prospective study with sample collections from Dec 2015 – Aug 2017
- 11 centers throughout the US
- Inclusion criteria: Patients (18-95 years of age) with a diagnostic BCx ordered per standard of care
- Samples T2B were run on a fully automated T20v Instrument
- Data analysis:
  - T2B performance versus paired BCx
  - T2B performance versus composite clinical/microbiologic criteria

RESULTS

A. Descriptive data
- Paired samples from 1,427 unique patients were obtained
- 6% (82) of BCx were positive
- 4% (39) were due to 5 T2B targets
- Mean time to BCx+: 51 ± 43 h (7.1 - 171 h)
- Mean time to BCx speciation: 83.7 ± 47.6 h (22.8-243.8 h)
- Mean time to T2B result: 5.4 ± 1.6 h (3.6 - 10 h)

B. Summary of results

<table>
<thead>
<tr>
<th>T2B Target</th>
<th>LoD (CFU/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enterococcus faecium</td>
<td>5</td>
</tr>
<tr>
<td>Escherichia coli</td>
<td>11</td>
</tr>
<tr>
<td>Klebsiella pneumoniae</td>
<td>2</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>5</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>2</td>
</tr>
</tbody>
</table>

C. Sensitivity of T2B compared with BCx

<table>
<thead>
<tr>
<th>T2B Target</th>
<th>Sensitivity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>91% (10/11)</td>
<td>62-98%</td>
</tr>
<tr>
<td>E. faecium</td>
<td>100% (1/1)</td>
<td>21-100%</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>100% (6/6)</td>
<td>61-100%</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>100% (5/5)</td>
<td>57-100%</td>
</tr>
<tr>
<td>S. aureus</td>
<td>81% (13/16)</td>
<td>57-93%</td>
</tr>
</tbody>
</table>

D. Receipt of in vitro effective antibacterial agents on the day of paired BCx+/T2B+ drawn.

<table>
<thead>
<tr>
<th>T2B Target</th>
<th>Receipt of in vitro effective antibacterial on the day of paired BCx+/T2B+ draw</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. coli</td>
<td>20% (2/10)</td>
</tr>
<tr>
<td>E. faecium</td>
<td>0% (0/1)</td>
</tr>
<tr>
<td>K. pneumoniae</td>
<td>17% (1/6)</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>20% (1/5)</td>
</tr>
<tr>
<td>S. aureus</td>
<td>46% (6/13)</td>
</tr>
</tbody>
</table>

CONCLUSIONS

- T2B demonstrates excellent performance in detecting BSI
  - Overall sensitivity: 90%
  - Detects 5 bacteria accounting for ~50% of BSI
  - Use T2B in conjunction with BCx
- The specificity of T2B was:
  - 96-99% when BCx was used as gold standard comparator
  - 98-100% when composite clinical/microbiologic criteria was used
- Our data clearly demonstrate the limitations of BCx as gold standard for both diagnostic and study design purposes
- Among the patients with discordant BCx+/T2B+ samples, evidence of infection was identified in 70%
- T2B+ matched the bacteria recovered from blood or non-blood site cultures
- T2B+ patients had clinical pictures that fit infection syndromes caused by bacteria identified by T2B
- Of note, 52% of patients had received antecedent antibiotics
- Potential advantages of T2B over BCx:
  - Detect bacteremia several days before BCx (3-5 hours versus 2-3 days)
  - Diagnose infections missed by BCx
  - Patients with antecedent antibiotics
  - Patients with extra-blood site infections
  - Inform appropriate therapy within hours of blood draw
  - 66% of patients with BCx+/T2B+ would have benefited from earlier appropriate antibiotics if T2B was performed.

Definitions

- Proven: Paired BCx+ and T2B+ for same organism
- Probable: BCx+/T2B+ but with positive culture for T2B organism in 1) blood or 2) extra-blood site within 14 days of paired sample
- Possible: BCx+/T2B+ associated with infectious syndromes that fit clinical scenario of T2B+ result, but cultures were either not performed or negative