Development of a new diagnostic tool for rapid detection of bloodstream infections in patients on home parenteral nutrition using ‘droplet digital PCR’ (ddPCR)

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June 22, 2019
No disclosures
Diagnosis of bloodstream infections

- **Bloodstream infections:**
  - 1 episode every 1–5 years

- **Diagnosis with blood cultures (‘gold standard’):**
  - Slow (1-2 days bacteria, 1-5 days fungi)
  - False-negative results (antibiotics)

37°C
Molecular techniques

• Advantages:
  – Culture-independent
    • Detection of pathogen DNA (dead or alive)
  – Rapid diagnosis (4-8 hours)
    • Rapid tailoring of treatment
  – Decreased morbidity and mortality
  – Shorter hospital stay

• Disadvantage:
  • Moderate sensitivity (65-85%) to detect pathogens
Droplet digital PCR

• Novel molecular technique
• Innovative
• Developed to increase sensitivity
Two studies in one

- Feasibility study (does it work?)
- Diagnostic accuracy study (sensitivity?)
Feasibility of ddPCR

- Can we detect pathogen DNA with ddPCR?
- What is the ‘detection limit’ of the ddPCR?
- How fast can we detect pathogen DNA?
Can we detect pathogen DNA with ddPCR?

• Both bacteria and fungi
Detection limit of ddPCR

1 pathogen DNA strand in 40,000 human DNA strands
How fast can we detect pathogen DNA?

Detection time: **4 hours**

Collecting blood  →  Detection pathogen DNA

**FAST**
Diagnostic accuracy of ddPCR

- Retrospective cohort of adult intestinal failure patients
- Suspicion of a bloodstream infection
- Admitted to the Radboudumc between 2008-2010
Design diagnostic accuracy study
45 patients suspected of a bloodstream infection:
- 15 had positive blood cultures

<table>
<thead>
<tr>
<th>ddPCR</th>
<th>Blood cultures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
</tr>
<tr>
<td>Positive</td>
<td>12</td>
</tr>
<tr>
<td>Negative</td>
<td>3</td>
</tr>
<tr>
<td>Total:</td>
<td>15</td>
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</tbody>
</table>

12/15 correct: Sensitivity = 80%
Discussion and conclusions

• Novel diagnostic tool for pathogen DNA detection
• Detection of pathogen DNA is possible within 4 hours
• Extremely low detection limit (1 in 40,000)
• Acceptable sensitivity (80%):
  • Further optimization is required
  • Larger (prospective) studies is needed

More information: Breakout Session 3
Sunday 4:20 PM - 5:05 PM
Questions?
Development of a new diagnostic tool for rapid detection of bloodstream infections using ‘droplet digital PCR’ (ddPCR) in patients on home parenteral nutrition

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Results diagnostic accuracy study

• 45 patients suspected of a bloodstream infection:
  • 15 had positive blood cultures
  • 30 had negative blood cultures

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12/15 correct: Sensitivity = 80%
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<thead>
<tr>
<th></th>
<th>Bloodstream infection</th>
<th>Bacteria</th>
<th>Gram-positive bacteria</th>
<th>Gram-negative bacteria</th>
<th>Fungi</th>
</tr>
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<tbody>
<tr>
<td><strong>Sensitivity (95%CI)</strong></td>
<td>80 (52–96)</td>
<td>83 (52–98)</td>
<td>71 (29–96)</td>
<td>67 (22–96)</td>
<td>60 (15–95)</td>
</tr>
<tr>
<td><strong>Specificity (95%CI)</strong></td>
<td>87 (69–96)</td>
<td>82 (65–93)</td>
<td>89 (75–97)</td>
<td>92 (79–98)</td>
<td>100 (91–100)</td>
</tr>
<tr>
<td><strong>LR+ (95%CI)</strong></td>
<td>6.00 (2.33–15.46)</td>
<td>4.58 (2.13–9.87)</td>
<td>6.79 (2.40–19.17)</td>
<td>8.67 (2.54–29.52)</td>
<td>NA</td>
</tr>
<tr>
<td><strong>LR− (95%CI)</strong></td>
<td>0.23 (0.08–0.64)</td>
<td>0.20 (0.06–0.73)</td>
<td>0.32 (0.10–1.04)</td>
<td>0.36 (0.12–1.12)</td>
<td>0.40 (0.14–1.17)</td>
</tr>
<tr>
<td><strong>PPV (95%CI)</strong></td>
<td>75 (54–89)</td>
<td>63 (44–78)</td>
<td>56 (31–78)</td>
<td>57 (28–82)</td>
<td>NA</td>
</tr>
<tr>
<td><strong>NPV (95%CI)</strong></td>
<td>90 (76–96)</td>
<td>93 (79–98)</td>
<td>94 (84–98)</td>
<td>95 (85–98)</td>
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