Implementation of T2 Magnetic Resonance into the Antimicrobial Stewardship Program Improves Management of Candidemia at HFHS

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Background

- **Candidemia** represents a clinically important diagnosis and treatment challenge in hospitalized patients, and is associated with significant patient morbidity and mortality. Prompt identification and early treatment is the most important modifiable factor to improve patient outcomes.
- Blood culture has poor sensitivity (false negative tests) to detect candidemia. Microbiology previously implemented 1,3 beta-D-glucan send out testing as a quality improvement over blood culture for candidemia diagnosis, incorporated into institutional antimicrobial stewardship program (ASP) candidemia guideline. Despite microbiology quality improvements to improve turn around time, 1,3 beta-D-glucan has been limited by suboptimal turn around time and poor specificity (false positive tests).
- **T2MR** is a new rapid diagnostic test that combines magnetic resonance and polymerase chain reaction. The test detects the five most common species of Candida directly from whole blood. Results are obtained within 3 to 5 hours on the instrument, and has strong sensitivity and specificity compared to other diagnostic methods.
- **T2MR** was identified as a way to further improve the diagnosis and management of patients with candidemia.

Do

**Interventions Implemented**

- **Rapid Diagnostic Testing:** The HFHS clinical microbiology laboratory implemented T2MR in November 2015 as a further improvement over the previous standard of care 1,3 beta-D-glucan and blood culture.
- **Guidelines:** The T2MR was incorporated into the HFHS ASP guidelines for candidemia, replacing 1,3 beta-D-glucan.
- **Education:** The HFHS ASP team, comprised of staff from microbiology, pharmacy, and the Division of Infectious Diseases, performed significant education of key stakeholders (ICU prescribers, pharmacists, and nurses) to ensure successful implementation of T2MR. Key educational messages included:
  - When the test is clinically indicated
  - How to properly collect the specimen
  - Clinical implications of positive and negative tests
- **Real Time Alerts:** T2MR test results trigger Theradoc alerts and prompt intervention by the ASP pharmacists.
  - Negative tests generally result in a recommendation to discontinue unnecessary antifungal therapy.
  - Positive test results in recommendations to optimize management of candidemia, including infectious diseases consultation.

Example T2MR Result

- **TheraDoc** notifies the ASP pharmacist in real time for prompt intervention.

Test Performance at HFHS

- **Based upon an evaluation of 120 patients, the positive predictive value and negative predictive value of T2MR was demonstrated to be 60% and 95%, respectively.**
- **Reasons identified to explain situations where blood culture was positive and T2MR was negative (11 patients) included:**
  - Different dates of blood collection (5 patients)
  - T2 sample obtained by peripheral stick but blood culture obtained from an IV catheter (3 patients)
  - Antifungal therapy administered before T2MR collection (2 patients)
- **Candida sp. identified was not of the five detected by T2MR (1 patient)**

Impact on Management and Outcomes of Patients with Candidemia

- **Between April 2016 and May 2016, 115 patients diagnosed by the standard of care were compared to 27 patients diagnosed by T2MR**

<table>
<thead>
<tr>
<th>T2MR is Associated with Significantly Reduced Time to Identify Candidemia</th>
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<tbody>
<tr>
<td>Median Time to Candidemia Diagnosis in Hours</td>
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<tr>
<td>Standard of care</td>
</tr>
<tr>
<td>10</td>
</tr>
</tbody>
</table>

- **T2MR is Associated with Significantly Reduced Time to Antifungals**

| Median Time to Antifungals in Hours |
| Standard of care | T2MR |
| 10 | 15 | 20 | 25 | 30 | 35 | 40 |

- **Anidulafungin** was the most common antifungal received in both groups, consistent with HFHS ASP guidelines.

**Patient Outcomes**

- **T2MR diagnosis** was associated with clinically significant improvements in important patient-focused outcomes:
  - Endocarditis was diagnosed in 18 (24.7%) in the standard of care group compared to 1 (5%) patients in the T2MR group.
  - Intensive care unit length of stay after candidemia onset was 12 days for the standard of care group versus 8 days with T2MR diagnosis.
  - No difference was detected between groups for in hospital crude mortality: 39 (33.9%) in standard of care group compared to 10 (38.5%) in the T2MR group.

- **70 HFHS patients who were receiving antifungal therapy at the time of a negative T2MR result were evaluated.**
  - 53 (76%) were receiving anidulafungin.
  - 21/70 pts had an indication for antifungals other than suspected candidemia, resulting in 49 clinically evaluable patients:
    - Median days of antifungal therapy: 1 (0.3-3) days.
    - Response to T2: discontinue antifungal therapy in 35 patients (71%), narrow the spectrum of antifungal therapy from anidulafungin to fluconazole: 2 (4%).

Annualized Costs, Return on Investment

<table>
<thead>
<tr>
<th>Cost Domain</th>
<th>Expenditures</th>
<th>Savings</th>
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</thead>
<tbody>
<tr>
<td>Laboratory Testing</td>
<td>$303,328</td>
<td>$45,706</td>
</tr>
<tr>
<td>Antifungal Drugs</td>
<td>$35,515</td>
<td></td>
</tr>
<tr>
<td>Length of Stay</td>
<td>$2,112,000</td>
<td>$4,800 per ICU day x 4 days x 110 candidemia patients per year</td>
</tr>
<tr>
<td>Subtotal</td>
<td>$303,328 annually</td>
<td>$1,293,212 annually</td>
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Return on investment = $1.99 million per year

Act

- After evaluating the results of T2MR implementation, system-wide Epic enhancements were performed:
  - The T2MR orderable was enhanced to facilitate improved quality of specimen collection by nursing staff.
  - The anidulafungin 200mg loading dose was defaulted to stat to first dose of antifungal therapy.
- The ASP continues to evaluate further methods to improve the outcomes of patients with candidemia and reduce unnecessary antifungal use.

Debrief

- **Microbiology, the Division of Infectious Diseases, and the ASP have a history of quality improvement related to candidemia and antifungal stewardship.** Previous efforts included implementation of 1,3 beta-D-glucan and institutional guidelines for candidemia.
- **Implementation of the T2MR assay in combination with ASP intervention was an important improvement over the previous method, positively impacting patient treatment and outcomes.** The strong negative predictive value continues to help the ASP reduce unnecessary antifungals.
- Among patients with candidemia, T2MR significantly reduced the time to diagnosis and time to antifungal therapy. T2MR was also associated with reduced ICU length of stay.
- Among patients with a negative T2MR, antifungal therapy was rapidly discontinued after only a single dose in most patients.
- Pathology and laboratory medicine was willing to take on the significant capital and annual expense for T2MR testing, resulting in substantial return on investment to HFHS.

**Strong teamwork, open communication, and prompt feedback between microbiology, pharmacy, infectious diseases, nursing, and the ICU prescribers was essential to the success of T2MR implementation.