T2Bacteria® Panel: Impact on Diagnosis and Clinical Outcomes in Sepsis and Bloodstream Infections

Summary of clinical literature evaluating the performance and clinical outcomes of the T2Bacteria Panel for the diagnosis of bloodstream infections

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Background

Bloodstream infections (BSI) are a major cause of global morbidity and mortality and are increasing in incidence[1,2]. When left untreated, bloodstream infections can progress to sepsis, an inflammatory response to infection that can result in organ system failure and death. Sepsis contributes to >35% of inpatient deaths and is the most expensive US hospital-treated conditions, representing a total cost of sepsis care for inpatient and SNF admissions conservatively estimated at more than $62 billion as of 2019[3,4]. Because of the high burden of an untreated infection, clinicians administer antimicrobials in patients suspected of BSI at rates of 50%–70%[5-7], far exceeding the actual BSI infection rate of 10%–15%[8-12]. A consequence of over-prescribing antibiotics is the emergence and spread of antibiotic resistance.

Early appropriate antimicrobial treatment is associated with reduced mortality in patients with sepsis and BSIs. For every hour delay in time to appropriate therapy survival decreases by 7.6% during septic shock[13] and the relative odds of death increase by 4.0% during bacteremia[14]. Blood cultures (BC), the gold standard for diagnosing BSI, detect bacteremia in only about 50% of patients who are clinically suspected of having sepsis, and that value may decrease after antimicrobial administration[15,16]. A recent retrospective analysis of 13 U.S. hospitals with more than 150,000 cultures found a median BC time to species identification of 43 hours[11]. Therefore, patients are commonly treated empirically with broad spectrum therapy for up to 2 days or longer until diagnostic information is available to allow species-directed therapy to be initiated. Magnetic resonance technology from T2Biosystems (T2MR) employs culture-independent testing, providing species identification directly from whole blood samples in 3 to 5 hours without the wait for a positive blood culture. The T2Bacteria Panel is the only FDA cleared, commercially available assay for direct-from-blood identification of the five most common implicated organisms known to commonly cause bloodstream infections: *Enterococcus faecium, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa*, and *Staphylococcus aureus*. Rapid detection and identification of these organisms in the bloodstream may aid clinicians in making appropriate treatment decisions earlier in the course of therapy.

T2Bacteria Panel Targets ESKAPE Pathogens Commonly Causing Sepsis and BSI

The T2Bacteria Panel is designed for the detection of the ESKAPE pathogens[17], which are a group of infectious bacteria that have garnered particular attention for their ability to escape or evade common therapies through antimicrobial resistance. The ESKAPE pathogens were first defined in 2008 and consist of *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Enterobacter species*[18]. ESKAPE pathogens remain a major health care burden, and recent studies suggest upward trends of ESKAPE prevalence[19], economic cost[20], and resistance[21,22]. A recent study found that ESKAPE pathogens represented 42.2% of species isolated from bloodstream infections, and compared with non-ESKAPE pathogens, were associated with a 3.3-day increase in length of stay, a $5500 increase in cost of care, and a 2.1% absolute increase in mortality (P < 1e-99)[23]. ESKAPE pathogens were not universally more resistant to antibiotics, but only to select antibiotics (P < 5e-6), particularly against common empiric therapies[23]. Throughout the world ESKAPE pathogens are the major cause of life-threatening nosocomial or hospital-acquired infections in immunocompromised and critically ill patients who are most at risk.

T2Bacteria Panel Provides Rapid and Accurate Diagnosis of Bloodstream Infections

The T2Bacteria Panel clinical trial evaluated the performance of the T2Bacteria Panel for diagnosing BSIs as compared to blood culture. The prospective trial included 1,427 adult patients who were suspected of BSIs and had a diagnostic blood culture ordered per standard of care at 11 U.S. medical centers. Paired blood culture and T2Bacteria Panel blood samples were drawn from each patient, with the blood culture samples drawn first. In the clinical trial, the mean time to species identification for T2Bacteria Panel was 5.4 hours, 66.3 hours faster than blood culture for identification of on-panel pathogens. During the clinical trial, the positivity rate was 2.7% by paired blood culture for target organisms versus 13.3% (190/1427) by T2Bacteria Panel. Compared to the paired blood culture, T2Bacteria Panel demonstrated a positive percent agreement (PPA) that ranged from 81.3% to 100% depending on target organism and a negative percent agreement (NPA) that ranged from 95.0% to 99.4%. Evaluation of the patients with discordant T2Bacteria-positive/blood culture-negative (T2+/BC-) results revealed that 59% (92/155) were proved to be associated with evidence of true infection. A total of 914, or 64% of patients were on at least one antibiotic at the time of blood draw, which could have affected the sensitivity of the blood culture and explained some of the discordant T2+/BC- results. T2Bacteria Panel results are not influenced by antecedent antibiotics in the blood.

The T2Bacteria Panel clinical trial demonstrated the distinct advantages of T2Bacteria Panel over culture-based methodologies, including: faster time to result, improved sensitivity, and freedom from antimicrobial interference. These advantages have also been demonstrated in several other published studies which are summarized in Table 1[24-27].

T2Bacteria Panel Provides Opportunity for Improved Patient Outcomes

Appropriate and rapid delivery of targeted antibiotics is critical for surviving sepsis and improving patient outcomes. The time savings provided by T2Bacteria for patients infected with panel-targeted organisms, compared to current conventional methods, represents a significant opportunity to positively impact patient outcomes and help to optimize antimicrobial stewardship.

Providing T2Bacteria Panel-enabled species-directed therapy in hours instead of days, is an opportunity to substantially reduce length of stay and improve patient outcomes for 50 - 70% of all patients suffering from a bloodstream infection[26,28]. Additionally, the T2Bacteria Panel represents an opportunity to de-escalate antimicrobial therapy in patients with sepsis that are on unnecessary therapy, helping address the problem of overuse of antibiotics and support the reduction of antibiotic resistance. Studies evaluating the clinical impact and antimicrobial stewardship opportunities of early diagnosis with T2Bacteria Panel are summarized in Table 1 [27,29,30].

Conclusion

The T2Bacteria Panel is a useful diagnostic tool to aid in the early diagnosis of bloodstream infections in various patient populations such as those admitted to the intensive care unit or emergency department with sepsis and suspected bloodstream infections or patients with malignancies and suspected bloodstream infections. The T2Bacteria Panel detects the five most common and deadly sepsis-causing bacteria species accounting for more than 50% of BSIs with an overall PPA of 90% and NPA of 98%[28] as compared to blood culture. Further, the T2Bacteria Panel detects infections that may be missed by blood culture. Unlike culture-based methodologies, T2Bacteria Panel results are not influenced by antecedent antibiotics in the blood. Taken together, the data suggest that T2Bacteria Panel may improve management of bloodstream infections and sepsis by providing results more rapidly than blood cultures and identifying some pathogens that are missed by blood cultures. The ability to access clinically relevant results within hours offers an opportunity to improve patient outcomes and the quality of care.

Table 1.

T2Bacteria Clinical Literature Summary

Reference	Objective(s)	Study Design	Setting	Study Population	Results
DeAngelis 2018 [24]	To assess performance of research version of T2Bacteria compared to blood cultures (BC) in diagnosing bloodstream infection (BSI)	Prospective, observational	Tertiary-care teaching hospital in Rome, Italy	N=140 samples from 129 patients admitted to Emergency Medicine Department, Infectious Diseases Unit and ICU for whom blood cultures were ordered	• Sensitivity 83.3% (CI 51.6%-97.9%) • Specificity 97.6% (CI 96.3%-98.5%) • NPV 99.8% • Mean time to species ID was significantly shorter for T2Bacteria compared to BC: 5.5 hrs (SD, 1.4) vs 25.3 hrs (SD, 15.2), (p<0.001) • T2Bacteria covered 50% of all species detected by BC
Nguyen 2019 [28]	To assess performance of the T2Bacteria compared to blood cultures in diagnosing suspected BSI or sepsis in adults	Prospective, observational	11 US hospitals	N=1427; Patients for whom blood cultures were ordered as standard of care	• Sensitivity 90% (CI, 76% to 96%) • Per-patient Specificity 90% (CI, 88% to 91%) • Per-assay Specificity 98% (CI, 97% to 98% • NPV 99.7% • T2Bacteria detected more pathogens than BC: 13% (181 of 1427) vs 3% (39 of 1427) • T2Bacteria provided faster species ID [3.61 (SD, 0.2) to 7.7 (SD, 1.38) hrs] compared to BC [71.7 (SD, 39.3) hrs]

Table 1. (Continued)

Reference	Objective(s)	Study Design	Setting	Study Population	Results
Voigt 2020 [26]	To evaluate T2Bacteria performance compared to blood culture and potential to affect patient care	Prospective, observational	Subset of patients from 2 US hospitals enrolled in the T2Bacteria Panel clinical study	N=137; Emergency Department patients for whom blood cultures were ordered as standard of care	• PPA 100% (CI, 75.7%-100%) • NPA 98.4% (CI, 97.1%-99.1%) • T2Bacteria detected 25% more positives, and provided species ID on average 56.6 hrs faster • T2Bacteria covered 70.5% of all species detected by BC • T2Bacteria could have potentially focused therapy in 8 patients, reduced time to a species-directed therapy in 4 patients, and reduced time to effective therapy in 4 patients
Kalligeros 2020 [25]	To evaluate significance of discordant T2Bacteria-positive/blood culture-negative (T2+/BC-) results	Retrospective case series	Subset of patients from 2 US hospitals enrolled in the T2Bacteria Panel clinical study	N=20 patients with 21 discordant T2B+/BC- results	• Probable BSI (52.5%), possible BSI (19%), presumptive false positives (28.5%) • Possible/probable BSI were often associated with closed space and localized infections [pyelonephritis (n=7), abscess (n=4), pneumonia (n=1), infected hematoma (n=1), and osteomyelitis (n=1)] • 80% of patients received at least 1 dose of active antibiotic prior to sample collection
Walsh 2019 [27]	To evaluate clinical impact of T2Bacteria compared to blood culture	Prospective, observational	Academic medical center in New York, NY, US	N=94 patients with hematological malignancies and hematopoietic stem cell transplant (HSCT) with suspected bacteremia	• PPA 75% (CI, 30.1% to 95.4%) • NPA 98.1% (CE, 96.2%) to 99% • Median time to species ID faster with T2Bacteria (3.7 hrs) vs BC (12.5 hr), difference of 8.8 hrs (p=0.002)
Seitz 2019 [30]	To evaluate clinical impact of T2Bacteria compared to blood cultures for diagnosing BSI	Prospective cohort	Single center hospital in Vienna, Austria	N=44; Patients admitted to the Infectious Diseases Department	• T2Bacteria detected more pathogens than BC alone: 41% (9 of 22) vs 14% (3 of 22) • T2Bacteria provided species ID significantly faster [59.3 hrs (p 0.01] than BC • T2Bacteria provided faster time to targeted antibiotic therapy (median 6.6. hrs) compared to BC (77.7 hrs) Length of stay was shorter in the T2Bacteria group (10.6 days) vs BC alone group (13 days)
Horowitz 2020 [29]	To assess impact of T2Bacteria on antibiotic therapy changes	Prospective cohort	Large community hospital in San Antonio, TX, US	N=59 samples from 39 patients with HSCT and febrile neutropenia	• T2Bacteria prompted early de-escalation of empiric anti-pseudomonal therapy in 29 patients • Total of 124 days of anti-pseudomonal therapy saved (5.2 days per patient)

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