



# Novel T2 Magnetic Resonance Assay Compared to Standard Blood Cultures for Detection of Candidemia.

Shamik Dwivedi D.O., Eloy Ordaya M.D., Brie Kezlarian M.D., Rachel Kenny PharmD, Robert Tibbetts PhD, Linoj Samuel PhD, George Alangaden M.D.



## Abstract (revised)

**Introduction:** Poor outcomes due to candidemia are improved by rapid diagnosis and treatment. Blood culture (BC), the current gold standard for detection of candidemia, has a turn-around-time (TAT) of 2-5 days. T2 magnetic resonance (T2) assay is a novel nano-diagnostic test that detects: *C.albicans/C.tropicalis* (Ca/Ct), *C.krusei/C.glabrata* (Ck/Cg) and *C.parapsilosis* (Cp) in blood. Early clinical trials demonstrated good sensitivity and specificity with NPV of 99% and TAT of 4-5 hours. T2 was implemented for use at our institution in patients (pts) with suspected candidemia (sepsis like syndrome and unresponsive to broad spectrum antibiotic therapy after >72 hours) and Candida Score of  $\geq 3$  (Leon, et al. Crit Care Med 2009;37:1624). We evaluated the use and performance characteristics of T2 in detecting candidemia during routine clinical practice.

**Methods:** Observational, retrospective, cross-sectional evaluation of pts with suspected candidemia who had T2 performed from 11/2015 - 06/2016 at Henry Ford Health System, a large healthcare system in Detroit, MI. Candida Score of  $\geq 3$  was defined as high risk for candidemia. Discordant results of T2 and BC were assessed. PPV and NPV were calculated for specimens collected within 24 hours vs. overall.

**Results:** Fifty (25%) patients had positive T2 and/or BC: 11/50 (22%) had both positive results and 39/50 (78%) had discordant results. Overall, possible reasons for discordance were: different dates of blood collection (54%), antifungal therapy before blood collection (52%) and Candida sp. not detected by T2 (4%). 17/50 patients had only positive BC: 7-*C.glabrata*, 5-*C.albicans*, 2-*C.lusitaniae*, 3-*C.parapsilosis*. The average Candida Score was 2.1 (range 0-4) and 2/17 patients had no clinical features of candidemia. Of the 17 BC+/T2- cases, possible reasons for discordance were: 6-T2 peripheral blood/BC central-line blood; 5-T2 blood drawn  $\geq 1$  day after BC; 4-antifungal therapy before blood collected; 2-*C.lusitaniae*. 22/50 had only positive T2: 10-Ca/Ct, 4-Cp, 8-Cg/Ck. The average candida score was 2.1 (range 0-4) and 8/22 had no clinical features of candidemia. The average TAT for T2 was 11 hours (range 3-41 hours) and for BC was 51 hours (range 3-120 hours) to preliminary result and 6 days (range 3-13 days) to final results. The positive and negative predictive values for T2 were 22% and 96% for specimens collected within 24 hours vs. 33% and 90% overall.

**Conclusions:** Performance characteristics of T2 in routine clinical practice differs from that reported in clinical trials. Targeted use of T2 in only high-risk patients and uniformity in sample collection will be important for accurate interpretation of this test. The rapid TAT and good NPV of T2 should help support antimicrobial stewardship efforts.

## Introduction

Poor outcomes associated with candidemia are improved with rapid diagnosis and treatment. Blood cultures (BC), the current "gold standard" for detection of candidemia have a turn-around-time (TAT) of 2-5 days. T2 magnetic resonance (T2) assay is a novel nano-diagnostic test that detects five Candida species: *C.albicans/C.tropicalis* (Ca/Ct), *C.krusei/C.glabrata* (Ck/Cg) and *C.parapsilosis* (Cp) in blood. Clinical trials of T2 have demonstrated good sensitivity and specificity, NPV of 99% and TAT of 4-5 hours. T2 was implemented at HFHS for use in patients with suspected candidemia.

The objective of this study was to evaluate the use and performance characteristics of T2 in detecting candidemia in routine clinical practice.

## T2MR Assay

- The T2 magnetic resonance assay (T2MR) is a novel rapid diagnostic assay that identifies candidemia directly from whole blood specimen. The cartridge based assay uses polymerase chain reaction (PCR) to amplify the target organism which is then detected by magnetic resonance using organism specific nanoparticles. The T2MR identifies the five most common types of candida species: *C. albicans/C. tropicalis*, *C. glabrata/C. krusei* and *C. parapsilosis* with TAT of 4-5 hours.

## Methods

Observational, retrospective, cross-sectional evaluation of patients with suspected candidemia who had T2 performed from 11/2015 - 6/2016 at Henry Ford Health System, a large healthcare system in Detroit, MI. TAT, discordant results of T2 and BC, and PPV/NPV were assessed.

## Results

- Of the first 200 patients, 50 (25%) had positive T2 and/or BC:
  - 11/50 (22%) had dual positive results and 39/50 (78%) had discordant results
- Overall, possible reasons for discordance were:
  - Different dates of blood collection (69%), antifungal therapy before blood collection (57%), and Candida sp. not detected by T2 (4%)
- The average TAT:
  - T2  $\rightarrow$  11 hours (range 3-41 hours) vs. BC  $\rightarrow$  51 hours (range 3-120 hours) to preliminary result ( $p < 0.0001$ ) and 6 days (range 3-13 days) to final results.
- The positive and negative predictive values for T2 were 22% and 96% for specimens collected within 24 hours vs. 33% and 90% overall.

**Table 1. Characteristics of patients with positive T2 and/or blood culture as compared to negative control patients.**

Characteristics	T2MR and/or BC positive (+) (n = 50)	T2MR and BC negative (-) (n = 150)
<b>Demographic</b>		
- Male Sex	25 (50%)	81 (54%)
- Age, mean (range)	59 (19 – 87)	58 (20 – 85)
<b>Immune-compromised</b>	23 (46%)	63 (42%)
- Malignancy (solid organ or hematologic)	12 (52%)	27 (43%)
- Chemotherapy	7 (30%)	18 (29%)
- Solid organ transplant	7 (30%)	24 (38%)
- Glucocorticoid use	6 (26%)	22 (35%)
- Stem cell transplant	2 (9%)	7 (11%)
<b>Immune-competent</b>	27 (54%)	87 (58%)
- Renal failure (requiring dialysis)	9 (33%)	16 (18%)
- Diabetes mellitus	8 (30%)	35 (40%)
- TPN	8 (30%)	14 (16%)
- Central Venous Catheter	22 (81%)	70 (80%)
- Prolonged ICU stay (>10 days)	19 (70%)	54 (62%)
- Abdominal Surgery	4 (15%)	21 (24%)
<b>Clinical features</b>		
- Fever*	34 (68%)	72 (48%)
- Hypotension*	24 (48%)	48 (32%)
- Endocarditis	1 (2%)	1 (0.66%)
- Chorioretinitis	1 (2%)	0
<b>Laboratory data</b>		
- Leukocytosis	25 (50%)	93 (62%)
- Neutropenia	6 (12%)	15 (10%)
<b>Mean Candida score</b>	2.1	2.1
- Greater than or equal to 3	18 (36%)	49 (33%)
- Less than 3	32 (64%)	101 (67%)

\*Denotes  $p$  value <0.05

**Table 2. Characteristics of patients with discordant T2 and blood culture results.**

Characteristics	T2 + / BC – ( 22 patients )	T2 – / BC + ( 17 patients )	$p$ value
<b>Demographic</b>			NS
- Male sex	11 (50%)	6 (35%)	
- Age, mean (range)	58.5 (19 – 87)	58.7 (22 – 80)	
<b>Medical history</b>			NS
- Immuno-compromised	11 (50%)	9 (53%)	
- Diabetes mellitus	5 (23%)	7 (41%)	
- Renal failure (requiring dialysis)	4 (18%)	4 (24%)	
- TPN	8 (36%)	5 (29%)	
- Central Venous Catheter	19 (86%)	13 (77%)	
- Prolonged ICU stay (>10 days)	15 (68%)	11 (65%)	
- Abdominal surgery	5 (23%)	3 (18%)	
<b>Clinical presentation</b>			NS
- Fever	15 (68%)	13 (77%)	
- Hypotension	12 (55%)	9 (53%)	
- Chorioretinitis	0	1 (6%)	
- Deep seated infection	3 (14%)	1 (6%)	
- Colonization	3 (14%)	7 (41%)	
- Prior positive blood cultures	1	--	
<b>Laboratory</b>			NS
- Leukocytosis	14 (64%)	6 (35%)	
- Neutropenia	4 (18%)	1 (6%)	
<b>Blood culture positive</b>			
- <i>C. albicans</i>	--	5 (29%)	--
- <i>C. glabrata</i>	--	7 (41%)	--
- <i>C. lusitaniae</i>	--	2 (12%)	--
- <i>C. parapsilosis</i>	--	3 (18%)	--
<b>T2MR positive*</b>			
- <i>C. albicans/C. tropicalis</i>	10 (46%)	--	--
- <i>C. parapsilosis</i>	4 (18%)	--	--
- <i>C. glabrata/C. krusei</i>	8 (36%)	--	--
<b>Candida score (range)</b>	2.1 (0 – 4)	2.2 (0 – 4)	NS
<b>Candidemia presentation</b>	14 (64%)	15 (88%)	NS
<b>Treatment</b>	21 (96%)	16 (94%)	NS
<b>Average length of treatment (range)</b>	10.8 (2 – 20)	11 (1 – 25)	NS
<b>Death</b>	8 (36%)	10 (59%)	NS

## Conclusion

- Performance characteristics of T2 in routine clinical practice differ from those reported in clinical trials.
- Targeted use of T2 in only high-risk pts and uniformity in sample collection will be important for accurate interpretation of this test.
- The low PPV differs from that noted in early clinical trials and requires further investigation.
- The rapid TAT and good NPV of T2 will support future antimicrobial stewardship efforts.

## Bibliography

- Mylonakis E., Clancy C.J., Ostrosky-Zeichner, L. Garey K.W., Alangaden, G.J. Vazquez, et al (2015). T2 Magnetic Resonance Assay for the Rapid Diagnosis of Candidemia in Whole Blood: A Clinical Trial. *Clinical infectious diseases* 2015;60, 892 – 899.
- Pfaller, M.A., Wolk, D.M., Lowery, T.J. (2015). T2MR and T2Candida: novel technology for the rapid diagnosis of candidemia and invasive candidiasis. *Future microbiology* 2015; 11(1), 103 – 107.
- León C, Ruiz-Santana S, Saavedra P, Galván B, Blanco A, Castro C, Balasini C, Utande-Vázquez A, González de Molina FJ, Blasco-Navalproto MA, López MJ, Charles PE, Martín E, Hernández-Viera MA; Cava Study Group. Usefulness of the "Candida score" for discriminating between Candida colonization and invasive candidiasis in non-neutropenic critically ill patients: a prospective multicenter study. *Crit Care Med.* 2009 May;37(5):1624-33.