T2 *Candida* Panel: A Game Changer in Diagnosis of Fungal Infections

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Abstract

In invasive fungal infections, early initiation of treatment within the day of symptom onset is related with a significantly reduced mortality. Early initiation of treatment and specifically treatment initiation within the day of symptom onset and blood culture draw is related to a significantly reduced mortality. However, automated blood culture methodologies, which are routinely used for the diagnosis of candidemia, take up to 2–5 days to grow and lead to a crucial delay in treatment initiation. Therefore, a highly sensitive, specific, and rapid diagnostic method is expected to allow early initiation of antifungal therapy and subsequently improve outcomes. Rapid diagnostic methods for fungal infections are long-awaited and are expected to improve outcomes through early initiation of targeted antifungal therapy. T2 *Candida* panel is a novel qualitative diagnostic platform that was recently approved by the US Food and Drug Administration (FDA) for diagnosis of candidemia with a mean time to species identification of <5 hours. Technological advances in the field of nanotechnology coupled with the proven applications of magnetic resonance have recently presented a rapid, fully automated, qualitative, sensitive, and specific diagnostic platform, the "T2 *Candida* panel". The introduction of this technology in diagnostic algorithms will increase the cost per patient tested, but it is expected to provide an economically self-supporting policy if savings from shorter hospital stays and termination of excess empiric antifungal treatment are taken into account. Expected benefits in terms of morbidity, mortality, and costs remain to be confirmed in clinical practice. The T2 Magnetic Resonance (T2MR) assay can detect and speciate the five most common *Candida* spp.; namely, *Candida albicans*, *Candida glabrata*, *Candida parapsilosis*, *Candida tropicalis*, and *Candida krusei*, in approximately 5 hours. The five detectable *Candida* spp. are responsible for >95% of the total *Candida* infections. T2 Magnetic Resonance demonstrated a sensitivity and specificity of 91.1 and 98.1%, respectively. The utility of T2MR in candidemia depends on the prevalence of the disease in each clinical setting. In intensive care units and other high-prevalence settings, the incorporation of T2MR in diagnostic algorithms is very appealing. T2 Magnetic Resonance is expected to allow timely initiation of antifungal therapy and help with antifungal stewardship. In low-prevalence settings, the positive predictive value of T2MR might not be enough to justify the initiation of antifungal treatment in itself.

Keywords: *Candida*, Investigation, T2 *Candida* panel.

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Introduction

Consequent to the increase of immunocompromised patients, an increase in the incidence of invasive fungal infections has been documented.[1] Early initiation of treatment and treatment initiation within the day of symptom onset and blood culture draw is related with a significantly reduced mortality.[2,3] However, automated blood culture methodologies, which are routinely used for the diagnosis of candidemia, take up to 2–5 days to grow and lead to a crucial delay in treatment initiation.

Therefore, a highly sensitive, specific, and rapid diagnostic method is expected to allow early initiation of antifungal therapy and subsequently improve outcomes.[4] Moreover, a rapid diagnostic method has the potential to reduce the administration of empiric antifungal treatment to patients who test negative, reducing this way the adverse effects of antifungal therapy,[5] as well as the antimicrobial pressure that is associated with the development of resistance to antifungal agents.[6–8]

Rapid diagnostic methods for fungal infections are long-awaited and are expected to improve outcomes through the early initiation of targeted antifungal therapy. T2 *Candida* panel is a novel qualitative diagnostic platform that was recently approved by the US Food and Drug Administration (FDA) for diagnosis of candidemia with a mean time to species identification of <5 hours. Technological advances in the field of nanotechnology coupled with the proven applications of magnetic resonance have recently presented a rapid, fully automated, qualitative, sensitive, and specific diagnostic platform, the "T2 *Candida* panel".[9] T2 *Candida* panel combines nuclear magnetic resonance and PCR molecular assays to directly detect and identify *Candida* spp. from whole blood samples.[9]

The introduction of this technology in diagnostic algorithms will increase the cost per patient tested, but it is expected to provide an economically self-supporting policy if savings from shorter hospital stays and termination of excess empiric antifungal treatment are taken into account.[7,9] Expected benefits in terms of morbidity, mortality, and costs remain to be confirmed in clinical practice. This new technology may represent a paradigm shift in the field of infectious diseases diagnostics.

Invasive candidiasis is a common healthcare-associated infection with a high mortality rate that can exceed 60% in cases

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of septic shock. Blood culture performance is far from ideal, due to a long time of positivity and suppression by antifungal agents. The T2 Magnetic Resonance (T2MR) assay can detect and speciate the five most common *Candida* spp.; namely, *Candida albicans*, *Candida glabrata*, *Candida parapsilosis*, *Candida tropicalis*, and *Candida krusei*, in approximately 5 hours. The five detectable *Candida* spp. are responsible for >95% of the total *Candida* infections.[10] It should be noted that the T2 *Candida* panel does not estimate the resistance profile of the isolated *Candida* spp. Using quantified spiked samples, the limit of detection of T2 *Candida* panel was estimated to be 1 CFU/mL for *C. tropicalis* and *C. krusei*, 2 CFU/mL for *C. albicans* and *C. glabrata*, and 3 CFU/mL for *C. parapsilosis*. In a multicenter clinical trial that included both a prospective and a contrived arm to represent the full range of clinically relevant concentrations of *Candida* spp., T2MR demonstrated a sensitivity and specificity of 91.1 and 98.1%, respectively. The utility of T2MR in candidemia depends on the prevalence of the disease in each clinical setting. In intensive care units and other high-prevalence settings, the incorporation of T2MR in diagnostic algorithms is very appealing. T2 Magnetic Resonance is expected to allow timely initiation of antifungal therapy and help with antifungal stewardship. In low-prevalence settings, the positive predictive value of T2MR might not be enough to justify the initiation of antifungal treatment in itself. The performance of T2MR has not been studied in cases of deep-seated candidiasis. Despite some promising evidence in published clinical trials, further studies are needed to determine the performance of T2MR in invasive candidiasis without candidemia.

The T2 *Candida* panel can identify five *Candida* spp. and the following three results can be reported:[5]

- *Candida albicans*/*Candida tropicalis*.
- *Candida parapsilosis*.
- *Candida glabrata*/*Candida krusei*.

Conclusion

Upcoming T2 Magnetic Resonance for Fungal Diagnosis panel can be a gamechanger in the management of invasive fungal infections. It can identify five important *Candida* species in 3 hours with 100% sensitivity and 98% specificity and helps decide antifungal medication early. Although it cannot replace old age gold standard investigation—blood culture for drug sensitivity pattern, but it is cost-effective in the management of *Candida* infection and will help in reducing morbidity and mortality due to invasive candidemia.

T2 Magnetic Resonance represents a highly promising molecular diagnostic method that allows the rapid, accurate, and species-specific diagnosis of candidemia. The positive T2MR results should be interpreted in the context of the expected prevalence of the disease in the specific clinical setting. We should note the paucity of data regarding the cases with culture-negative invasive candidiasis and the evolving everyday clinical experience with this new technology. Future studies remain to determine the performance of T2MR in patients diagnosed with deep-seated infections by following those patients with T2MR, blood cultures, and fungal markers.

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