AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology®

MYCOLOGY

Evaluation of a Rapid Fungal Detection Panel for Identification of Candidemia at an Academic Medical Center

John P. Bomkamp,[a]* Rand Sulaiman,[a]* Jennifer L. Hartwell,[b] Armisha Desai,[a] Vera C. Winn,[c] Justin Wrin,[a] Michelle L. Kussin,[a] Jon J. Hiles[a]

[a]Indiana University Health, Adult Academic Health Center, Department of Pharmacy, Indianapolis, Indiana, USA
[b]Indiana University School of Medicine, IU Health Methodist Hospital, Indianapolis, Indiana, USA
[c]Indiana University Health, Pathology Laboratory, Indianapolis, Indiana, USA

ABSTRACT This study was conducted to assess the utility of the T2Candida panel across an academic health center and identify potential areas for diagnostic optimization. A retrospective chart review was conducted on patients with a T2Candida panel and mycolytic/fungal (myco/f lytic) blood culture collected simultaneously during hospitalizations from February 2017 to March 2018. The primary outcome of this study was to determine the sensitivity, specificity, and positive and negative predictive values of the panel compared to myco/f lytic blood culture. Secondary outcomes included *Candida* species isolated from culture or detected on the panel, source of infection, days of therapy (DOT) of antifungals in patients with discordant results, and overall antifungal DOT/1,000 patient days. A total of 433 paired T2Candida panel and myco/f lytic blood cultures were identified. The pretest likelihood of candidemia was 4.4%. The sensitivity and specificity were 64.7% and 95.6%, respectively. The positive and negative predictive values were 40.7% and 98.5%, respectively. There were 16 patients with T2Candida panel positive and myco/f lytic blood culture negative results, while 6 patients had T2Candida panel negative and myco/f blood culture positive results. The overall antifungal DOT/1,000 patient days was improved after implementation of the T2Candida panel; however, the use of micafungin continued to decline after the panel was removed. We found that the T2Candida panel is a highly specific diagnostic tool; however, the sensitivity and positive predictive value may be lower than previously reported when employed in clinical practice. Clinicians should use this panel as an adjunct to blood cultures when making a definitive diagnosis of candidemia.

KEYWORDS candidemia, invasive candidiasis, microbiology, rapid diagnostic, T2Candida

Candida species represent one of the most common pathogens associated with nosocomial bloodstream infections (1). Candidemia is also associated with excess mortality, prolonged length of stay, and increased health care costs (2). These poor outcomes remain relevant in today's clinical practice due to the lack of streamlined diagnostic modalities for candidemia. Currently, blood cultures are the gold standard for detection of *Candida* species in the bloodstream. However, blood cultures are slow, stemming from the time *Candida* requires to grow to a detectable limit. Depending upon the *Candida* species present, it may take 1 to 3 days for detection, thus increasing the time for a patient to be without antifungal therapy (3).

In addition to time delays, another limitation of blood culture is the variable concentrations of *Candida* in the blood for patients with invasive disease. Studies have shown that the sensitivity of blood culture for the detection of candidemia is approximately 50% (4). This poor sensitivity is thought to be primarily due to the absence of

Citation Bomkamp JP, Sulaiman R, Hartwell JL, Desai A, Winn VC, Wrin J, Kussin ML, Hiles JJ. 2020. Evaluation of a rapid fungal detection panel for identification of candidemia at an academic medical center. J Clin Microbiol 58:e01408-19. https://doi.org/10.1128/JCM.01408-19.

Editor Kimberly E. Hanson, University of Utah

Address correspondence to Jon J. Hiles, jhiles@iuhealth.org.

* Present address: John P. Bomkamp, Indiana University Health Arnett Hospital, Department of Pharmacy, Lafayette, Indiana, USA; Rand Sulaiman, Ascension Health, St. Louis, Missouri, USA.

Received 28 August 2019
Returned for modification 14 October 2019
Accepted 14 December 2019
Accepted manuscript posted online 18 December 2019
Published 24 February 2020

organism circulating when patients initially present with invasive disease. Commonly, the inoculum of *Candida* at detection is low, with a median of 1 CFU/ml in the first positive blood culture (5). Therefore, *Candida* may or may not grow, depending upon the number of viable cells present in the blood when the culture is obtained. This further underscores the need for not only timely but also consistent methods for the detection of candidemia.

In 2014, the FDA approved a novel fungal rapid diagnostic panel. The T2Candida panel developed by T2 Biosystems utilizes magnetic resonance technology to detect molecular targets in *Candida* (6). This rapid diagnostic test utilizes whole blood directly from patients without the need to wait for growth in culture medium. Five of the common *Candida* species are detected on the T2Candida panel, *C. albicans*, *C. tropicalis*, *C. parapsilosis*, *C. krusei*, and *C. glabrata* (7). Additional advantages of this panel include a turnaround time of 3 to 5 hours and a 1 CFU/ml level of detection (4, 8). In one trial, the sensitivity and specificity of the T2Candida panel was reported as 91% and 98%, respectively, compared in blood cultures inoculated with various concentrations of these 5 *Candida* species (9).

In February 2017, the Indiana University Health Adult Academic Health Center (IUH-AAHC) implemented the T2Candida panel as part of a candidemia diagnostic method named the candidemia screen. The candidemia screen consisted of an order for the simultaneous collection of the T2Candida panel and a Bactec mycolytic/fungal (myco/f lytic) blood culture bottle. The myco/f lytic bottles introduce unique proteins and carbohydrates, promoting faster growth of *Candida* (10, 11). The panel and myco/f lytic blood cultures were obtained at the same time from the same site to increase the probability of growing the organism on culture medium for susceptibility testing when *Candida* was detected by the T2Candida panel. Additionally, this allowed for evaluation of the T2Candida panel compared to the myco/f lytic blood culture in clinical practice.

The candidemia screen was recommended at IUH-AAHC for patients with a high likelihood of candidemia. This included patients who were septic as a result of intra-abdominal infections and those with persistent fever despite broad-spectrum antimicrobial therapy, parenteral nutrition, *Candida* colonization, and presence of a chronic central line. These risk factors were originally based on published candidemia risk factors but were then internally validated (12). Ultimately, the decision to order the test was left to the prescriber.

The primary outcome of this study was to determine the sensitivity, specificity, and positive and negative predictive values of the T2Candida panel compared to the myco/f lytic blood culture when drawn concomitantly. Secondary objectives included the *Candida* species identified by the panel, possible sources of infection for patients with discordant panel and blood culture results (e.g., T2Candida panel positive but blood culture negative), days-of-therapy (DOT) of antifungals in patients with these discordant results, and overall antifungal DOT/1,000 patient days in our hospitals.

MATERIALS AND METHODS

This Institutional Review Board (IRB)-approved study was a retrospective review of electronic health records of patients admitted to IUH-AAHC hospitals with a candidemia screen collected during admissions from February 2017 to March 2018. In the primary analysis, patients were included if they were age ≥18 years and had a T2Candida panel and myco/f lytic blood culture drawn simultaneously. Patients were excluded if there was an invalid result with the T2Candida panel as part of their candidemia screen. When invalid results occurred, prescribers could reorder the test at their discretion.

In patients with discordant results (either T2Candida panel positive and myco/f lytic blood culture negative, or panel negative and culture positive), a more in-depth electronic health record review was performed. This included specific *Candida* species detected by either the panel or blood culture, possible source of infection, and if any interfering substances were administered around the time of T2Candida panel collection. Per the T2Candida panel instructions for use, the following are substances that could interfere with results of the instrument: calcium hypochlorite (20 mg/ml), K2EDTA (≥3.0 mg/ml), ferumoxytol (≥76.5 mg/ml), Magnevist (≥1.7 mg/dl), Ablavar (≥0.39 mg/ml), and Intralipid (≥1.6 mg/ml) to represent lipemia (13). Additionally, patients with T2Candida panel positive and myco/f lytic blood culture negative results were further reviewed to determine if they had possible, probable, or proven invasive fungal disease as outlined by the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group (14). Antifungal DOT was evaluated to

TABLE 1 Primary analysis for the T2Candida panel[a]

Result	Result for myco/f lytic blood culture (no. of patients):	
	Positive	Negative
Positive	11	16
Negative	6	350

[a]The positive predictive value and negative predictive value for the T2Candida panel were 40.7% and 98.5%, respectively, and the sensitivity and specificity values for the myco/f lytic blood culture were 64.7% and 95.6%, respectively.

determine how clinicians interpreted the discordant results. DOT was defined as receiving any number of doses of an antifungal agent during a calendar day. Additionally, patients' charts were reviewed to determine if any antifungals had been administered prior to the T2Candida panel and myco/f lytic blood culture being collected.

Total antifungal utilization data in DOT/1,000 patient days at IUH-AAHC were collected before, during, and after availability of the T2Candida panel. The "before" period is from April 2015 to January 2017 prior to the availability of the panel. The "during" time period is from February 2017 to April 2019. In May 2019, the use of the T2Candida panel was suspended. The "after" period is from May 2019 to November 2019.

DOT/1,000 patient days was compiled on a monthly basis and considered a continuous variable, and time periods were compared utilizing the Mann-Whitney U-test with statistical significance set to be $P = 0.05$. Descriptive statistics were used to compare the remainder of the data.

RESULTS

In the primary analysis, a total of 433 candidemia screens were collected from February 2017 to March 2018. There were 50 (11.5%) invalid T2Candida panels, resulting in a total of 383 candidemia screens for review. The pretest likelihood of candidemia defined as a positive myco/f lytic blood culture was 4.4%. Concordant T2Candida panel and myco/f lytic blood culture results occurred in 361 (94.3%) patients, 11 (2.9%) with T2Candida panel positive, myco/f lytic blood culture positive and 350 (91.4%) with T2Candida panel negative, myco/f lytic blood culture negative results. In 6 (1.6%) patients, the T2Candida panel was negative and the myco/f lytic blood culture was positive for *Candida* growth. Additionally, there were 16 (4.2%) patients with positive T2Candida panel results and negative myco/f lytic blood cultures, for a total of 22 (5.7%) patients with discordant results (Table 1). This resulted in a sensitivity of 64.7% and a specificity of 95.6% when the T2Candida panel was compared to myco/f lytic blood cultures drawn simultaneously. The positive predictive value was 40.7%, while the negative predictive value was 98.5%, again using the myco/f lytic blood culture as the standard.

In the 16 patients with a positive T2Candida panel and negative myco/f lytic blood culture, the T2Candida panel detected 7 (44%) *Candida parapsilosis*, 7 (44%) *Candida albicans*/*C. tropicalis*, and 2 (12%) *Candida glabrata*/*C. krusei* strains. For the 6 patients with a negative T2Candida panel and a positive myco/f lytic blood culture, the myco/f lytic blood culture grew 3 (50%) *Candida glabrata*, 2 (33%) *Candida albicans*, and 1 (17%) *Candida parapsilosis* strain. There were no cases of candidemia due to organisms not represented on the T2Candida panel. In the 16 patients with a positive T2Candida panel and negative myco/f lytic blood culture, 14 patients had a documented suspected source of infection in the electronic health record. The suspected sources of infection were central-line associated ($n = 5$; 31%), intra-abdominal ($n = 5$; 31%), empyema ($n = 2$; 13%), skin/soft tissue ($n = 1$; 6%), and central nervous system ($n = 1$; 6%). Two patients in the T2Candida panel positive and myco/f lytic blood culture negative group had no documented source of infection. Table 2 lists the determination of possible, probable, or proven invasive fungal disease. In the T2Candida panel negative and myco/f lytic blood culture positive group, the suspected sources of infection were intra-abdominal ($n = 5$; 83%) and central-line associated ($n = 1$; 17%). All of these patients met criteria for proven invasive fungal disease due to their positive blood culture. No patients with discordant T2Candida panel and myco/f lytic blood culture results received a substance known to interfere with the results of the panel.

TABLE 2 Determination of invasive fungal disease in T2Candida panel positive and myco/f lytic blood culture negative results

Case	*Candida* sp. detected	Potential source of infection	Determination of invasive fungal disease	Criteria[a]
1	*C. albicans/C. tropicalis*	Unknown	Proven	Positive blood culture 12 days prior to T2Candida panel
2	*C. albicans/C. tropicalis*	Unknown	No criteria met	None
3	*C. glabrata/C. krusei*	Central venous catheter	Proven	Positive blood culture 21 days prior to T2Candida panel
4	*C. parapsilosis*	Central venous catheter	No criteria met	None
5	*C. albicans/C. tropicalis*	Central venous catheter	No criteria met	None
6	*C. albicans/C. tropicalis*	Central venous catheter	No criteria met	None
7	*C. parapsilosis*	Central venous catheter	No criteria met	None
8	*C. parapsilosis*	Intra-abdominal	Possible	Allogeneic HSCT Abscesses on liver
9	*C. parapsilosis*	Intra-abdominal	No criteria met	None
10	*C. parapsilosis*	Intra-abdominal	No criteria met	None
11	*C. parapsilosis*	Intra-abdominal	No criteria met	None
12	*C. albicans/C. tropicalis*	Intra-abdominal	No criteria met	None
13	*C. albicans/C. tropicalis*	Empyema	Possible	Allogeneic HSCT Retinal exudates on exam
14	*C. glabrata/C. krusei*	Empyema	No criteria met	None
15	*C. parapsilosis*	Skin/soft tissue	No criteria met	None
16	*C. albicans/C. tropicalis*	Central nervous system	Probable	TNF-α administration within 90 days Focal lesions on CT BAL culture with fungal elements

[a]HSCT, hematopoietic stem cell transplantation; TFN-α, tumor necrosis factor-α; CT, computerized tomography; BAL, bronchoalveolar lavage.

In patients with a discordant result, the antifungals prescribed consisted of fluconazole, micafungin, and amphotericin B. In the T2Candida panel positive and myco/f lytic blood culture negative group, patients received a median antifungal DOT of 11 days (range, 1 to 76 days), 4.5 days (range, 2 to 12 days), and 39 days (range, 8 to 55 days) for fluconazole, micafungin, and amphotericin B, respectively. Amphotericin B was used in only three patients of the 16 in this category. In the T2Candida panel negative and myco/f lytic blood culture positive group, the median antifungal DOT was 10 days (range, 2 to 45 days) and 5.5 days (range, 1 to 15 days) for fluconazole and micafungin, respectively. No patients in this group received amphotericin B.

In the T2Candida panel positive and myco/f lytic blood culture negative group, 1 patient had received fluconazole for 7 days, and another patient had received amphotericin B for 27 days prior to collection. In the T2Candida panel negative and myco/f lytic blood culture positive group, 1 patient received one dose of fluconazole prior to collection.

The mean (standard deviation) of fluconazole DOT/1,000 patient days at IUH-AAHC before, during, after implementation of the candidemia screen was 45.3 (5.4), 41.6 (5.2), and 47.8 (5.5), respectively ($P = 0.017$ before versus during and $P = 0.012$ during versus after). The mean (standard deviation) of micafungin DOT/1,000 patient days before, during, after implementation was 14.2 (2.3), 9.9 (2.3), and 8.8 (2.0), respectively ($P < 0.001$ before versus during and $P = 0.252$ during versus after).

DISCUSSION

The objective of this study was to determine the sensitivity, specificity, positive predictive value, and negative predictive value of the T2Candida panel compared to myco/f lytic blood cultures when both were drawn simultaneously. Prior to implementation, the concern with the T2Candida panel in clinical practice was the previously described high sensitivity reported by studies using spiked blood cultures. This level of sensitivity could potentially increase the risk of false positives due to detecting low-level contamination resulting in low specificity. The Detecting Infections Rapidly and Easily for Candidemia Trial part 2 (DIRECT2) study evaluated the T2Candida panel in comparison to blood cultures in patients with known candidemia (15). In that study, there were 37 instances in which the T2Candida panel was positive and companion blood cultures were negative. The authors concluded that there may be an advantage to the panel, as it can detect *Candida* species down to 1 CFU/ml and *Candida* that is

nonviable or unable to grow, which may be especially important if the patient has received antifungals prior to screening. The DIRECT2 study suggested that the T2Candida panel may identify cases of candidemia or invasive candidiasis missed by conventional blood culture.

In the present study, the T2Candida panel detected 16 potential candidemia patients when the myco/f lytic blood cultures were negative. The specificity remained high because of the low incidence of candidemia (4.4%) identified, even in this high-risk population. It appears that clinicians at the IUH-AAHC continued antifungal therapy in patients with a positive T2Candida panel and negative myco/f lytic blood culture as evident with an antifungal of any type DOT of 14 days. This approach seems reasonable considering the positive T2Candida panel result and the presence of risk factors for candidemia. However, more concerning are the patients in which the T2Candida panel was negative and the myco/f lytic blood culture was positive.

Another prior study reviewed the implementation of the T2Candida panel within a community health system (16). This study specifically evaluated the utility of the panel in a clinical practice setting. The findings revealed that the implementation of the T2Candida panel led to a reduction in time to initiation of appropriate antifungal therapy and a reduction in micafungin DOT in patients with a negative T2Candida panel result. Patients in the study commonly had blood cultures obtained as well. Based on the results of this study, comparing the T2Candida panel with blood cultures resulted in a sensitivity of 73%, specificity of 96%, positive predictive value of 40%, and negative predictive value of 99%. A total of 325 patients were evaluated, and 12 had a positive T2Candida panel and a negative blood culture, while 3 had a negative T2Candida panel and a positive blood culture. The authors theorized that the discordant panel and blood culture results were due to the panel and blood culture being drawn at separate times. Therefore, the authors concluded that these patients may have had intermittent candidemia, and the separate collection times may explain the reasoning behind the resulting sensitivity.

In the present study, we evaluated the simultaneous collection of the T2Candida panel and myco/f lytic lytic blood cultures to determine if this strategy would improve the sensitivity, specificity, positive predictive value, and negative predictive value in clinical practice. Despite the pairing of the T2Candida panel and myco/f lytic blood culture at the IUH-AAHC, we did not observe an improvement in these reliability markers. Surprisingly, we found a lower sensitivity when pairing the two tests together. Our study suggests that discordant results between the panel and myco/f lytic blood cultures can likely not be explained by intermittent candidemia.

Previously, Mylonakis et al. observed similar sensitivity to our present study when the T2Candida panel was employed in clinical practice (9). This study found 2 patients with T2Candida panel negative and blood culture positive results and 29 patients with T2Candida panel positive and blood culture negative results. This equates to a sensitivity of approximately 67%, similar to that observed in our study.

Both the present study and past studies have had T2Candida panel positive and blood culture negative discordant results. Previous authors concluded that this could be explained by the high sensitivity of the T2Candida panel (9, 16). However, failure of the T2Candida panel in this study to detect candidemia in 6 cases out of 17 where myco/f lytic blood culture did detect candidemia brings that supposed high sensitivity into question.

Despite recommending the candidemia screen only for patients at high risk for candidemia, it was not routine practice at IUH-AAHC to start empirical antifungal therapy for all of them, but rather, was at the providers' discretion. When the T2Candida panel was implemented at the IUH-AAHC, the antimicrobial stewardship team began using this diagnostic tool to limit empirical antifungal therapy, specifically recommending discontinuation in those patients who had been started on antifungals and had a T2Candida panel negative result. Patients that had panel negative and myco/f lytic blood culture positive results may have had their empirical antifungal discontinued. The panel's results are available within 3 to 5 hours, compared to the myco/f lytic blood

culture taking 1 to 3 days for first detection of growth. This has the potential to delay antifungal therapy for up to 1 to 3 days. At our institution, the observed sensitivity and negative predictive value suggest that approximately 40% of candidemia events will be missed, thus resulting in 1 in 20 patients receiving delayed therapy. Accounting for the pretest probability of not having candidemia (95.6%), the observed sensitivity of the T2Candida panel added little clinically when excluding disease. This is confirmed by a positive likelihood ratio of 14.7 and negative likelihood ratio of 0.37. Our results are concerning because previous research has shown increased risk for in-hospital mortality with delay in antifungal therapy (17).

In response to the data reported in this study, IUH-AAHC stopped offering the T2Candida panel. This provided us with the opportunity to assess the impact on antifungal utilization. We observed a decrease in fluconazole and micafungin use after implementation and then an increase in fluconazole and a continued decrease in micafungin after removal of the panel. Fluconazole use at our institution is largely driven by prophylaxis in immunocompromised populations and targeted therapy to susceptible *Candida* species. Micafungin is more commonly utilized as an empirical option for suspected candidemia. There may have been other factors contributing to the initial and continued reduction in micafungin use other than the T2Candida panel. There was a simultaneous increase in stewardship resources around the implementation of the T2Candida panel. Two more infectious disease pharmacists began actively auditing and giving feedback on antimicrobial use. Another factor may be the clinicians' realization that the incidence is low even in high-risk patients, at 4.4%, with the T2Candida PANEL serving to start therapy sooner in only 2.9% of our population tested. Ideally, a test like this could be used in combination with blood cultures to hold antifungal therapy until confirmed. However, this would require 35 T2Candida tests to start antifungal therapy earlier for one patient with eventually confirmed candidemia.

The strengths of this study include the coupling of the T2Candida panel and myco/f lytic blood culture collection. Additionally, we did not have any cases in which interfering substances were administered near the time of testing. Our study sought to reduce and identify possible confounders that might result in lower sensitivity compared to previous research. The process of simultaneous T2Candida panel and myco/f lytic blood culture collection reduced the possibility of intermittent candidemia playing a role in the resulting sensitivity. Finally, only 3 of the 22 patients with discordant results had received prior antifungal therapy.

There are also several limitations of this observational study. Patient outcome data were not collected as part of this study. Patients were reviewed retrospectively, and only descriptive statistics were able to be used to evaluate the primary endpoints of the study. After the study period, an update to the T2Candida panel was implemented by T2 Biosystems, aimed at reducing the number of invalid panel results. Although this update was not expected to affect valid results of the panel, it is not known if this would have impacted the results of this study. Another potential limitation is the lack of control for the volume of blood obtained. This introduces the possibility of some samples not containing the recommended amount of blood for accurate testing. However, this represents realistic implementation of a new diagnostic test. Lastly, it is important to recognize the limitations of blood cultures as the current gold standard. As reviewed above, blood cultures have a poor sensitivity themselves when detecting *Candida* in the blood.

Based on previously published *in vitro* studies, the T2Candida panel showed promise as being a highly sensitive test for detecting candidemia. Our study represented use in clinical practice and showed a low sensitivity, which was inconsistent with *in vitro* studies. This has now been shown to be similarly low in two separate studies (16). There is a risk of delayed antifungal therapy with a negative panel when the blood culture may later become positive. One benefit the T2Candida panel may offer clinicians is the ability to hold off on initiation of antifungal therapy until results of this or the blood culture are available. However, the low prevalence of disease, low rate of detection by the panel, and cost of the panel should be considered by health systems before offering

such testing. In conclusion, invasive candidemia remains difficult to diagnose, and further improvements in rapid diagnostics for this infection are needed.

ACKNOWLEDGMENTS

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

All of the authors declare no conflict of interest related to this study.

REFERENCES

1. Morgan J, Meltzer MI, Plikaytis BD, Sofair AN, Huie-White S, Wilcox S, Harrison LH, Seaberg EC, Hajjeh RA, Teutsch SM. 2005. Excess mortality, hospital stay, and cost due to candidemia: a case-control study using data from population-based candidemia surveillance. Infect Control Hosp Epidemiol 26:540–547. https://doi.org/10.1086/502581.
2. Benedict K, Jackson BR, Chiller T, Beer KD. 2019. Estimation of Direct Healthcare Costs of Fungal Diseases in the United States. Clin Infect Dis 68:1791–1797. https://doi.org/10.1093/cid/ciy776.
3. Fernandez J, Erstad BL, Petty W, Nix DE. 2009. Time to positive culture and identification for Candida bloodstream infections. Diagn Microbiol Infect Dis 64:402–407. https://doi.org/10.1016/j.diagmicrobio.2009.04.002.
4. Clancy CJ, Nguyen MH. 2013. Finding the "missing 50%" of invasive candidiasis: how nonculture diagnostics will improve understanding the disease spectrum and transform patient care. Clin Infect Dis 56:1284–1292. https://doi.org/10.1093/cid/cit006.
5. Pfeiffer CD, Samsa GP, Schell WA, Reller LB, Perfect JR, Alexander BD. 2011. Quantitation of Candida CFU in initial positive blood cultures. J Clin Microbiol 49:2879–2883. https://doi.org/10.1128/JCM.00609-11.
6. Pfaller MA, Wolk DM, Lowery TJ. 2016. T2MR and T2Candida: novel technology for the rapid diagnosis of candidemia and invasive candidiasis. Future Microbiol 11:103–117. https://doi.org/10.2217/fmb.15.111.
7. Zacharioudakis IM, Zervou FN, Mylonakis E. 2018. T2 magnetic resonance assay: overview of available data and clinical implications. J Fungi (Basel) 4:e45. https://doi.org/10.3390/jof4020045.
8. T2 Biosystems. 2019. T2Candida panel: faster targeted therapy and reduction in empiric antifungal costs. https://www.t2biosystems.com/products-technology/t2candida-panel/. T2 Biosystems, Lexington, MA.
9. Mylonakis E, Clancy CJ, Ostrosky-Zeichner L, Garey KW, Alangaden GJ, Vazquez JA, Groeger JS, Judson MA, Vinagre YM, Heard SO, Zervou FN, Zacharioudakis IM, Kontoyiannis DP, Pappas PG. 2015. T2 magnetic resonance assay for the rapid diagnosis of candidemia in whole blood: a clinical trial. Clin Infect Dis 60:892–899. https://doi.org/10.1093/cid/ciu959.
10. Becton Dickinson. 2016. BD BACTECTM myco/F lytic culture vials [package insert]. Becton Dickinson. Franklin Lakes, NJ.
11. Fuller DD, Davis TE, Jr, Denys GA, York MK. 2001. Evaluation of BACTEC MYCO/F lytic medium recovery of mycobacteria, fungi, and bacteria from blood. J Clin Microbiol 39:2933–2936. https://doi.org/10.1128/JCM.39.8.2933-2936.2001.
12. Leon C, Ruiz-Santana S, Saavedra P, Almirante B, Nolla-Salas J, Alvarez-Lerma F, Garnacho-Montero J, León MA, EPCAN Study Group. 2006. A bedside scoring system ("Candida score") for early antifungal treatment in nonneutropenic critically ill patients with Candida colonization. Crit Care Med 34:730–737. https://doi.org/10.1097/01.CCM.0000202208.37364.7D.
13. Virotech Diagnostics. 2019. T2Candida panel instructions for use. http://www.virotechdiagnostics.com/fileadmin/user_upload/Doc/AL/AL_HW90-01794.pdf. Virotech Diagnostics, Rüsselsheim, Germany.
14. De Pauw B, Walsh TJ, Donnelly JP, Stevens DA, Edwards JE, Calandra T, Pappas PG, Maertens J, Lortholary O, Kauffman CA, Denning DW, Patterson TF, Maschmeyer G, Bille J, Dismukes WE, Herbrecht R, Hope WW, Kibbler CC, Kullberg BJ, Marr KA, Muñoz P, Odds FC, Perfect JR, Restrepo A, Ruhnke M, Segal BH, Sobel JD, Sorrell TC, Viscoli C, Wingard JR, Zaoutis T, Bennett JE, National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group. 2008. Revised definitions of invasive fungal diseases from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group. Clin Infect Dis 46:1813–1821. https://doi.org/10.1086/588660.
15. Clancy CJ, Pappas PG, Vazquez J, Judson MA, Kontoyiannis DP, Thompson GR, 3rd, Garey KW, Reboli A, Greenberg RN, Apewokin S, Lyon GM, 3rd, Ostrosky-Zeichner L, Wu AHB, Tobin E, Nguyen MH, Caliendo AM. 2018. Detecting Infections Rapidly and Easily for Candidemia Trial, part 2 (DIRECT2): a prospective, multicenter study of the T2Candida panel. Clin Infect Dis 66:1678–1686. https://doi.org/10.1093/cid/cix1095.
16. Patch ME, Weisz E, Cubillos A, Estrada SJ, Pfaller MA. 2018. Impact of rapid, culture-independent diagnosis of candidaemia and invasive candidiasis in a community health system. J Antimicrob Chemother 73:iv27–iv30. https://doi.org/10.1093/jac/dky046.
17. Morrell M, Fraser VJ, Kollef MH. 2005. Delaying the empiric treatment of candida bloodstream infection until positive blood culture results are obtained: a potential risk factor for hospital mortality. Antimicrob Agents Chemother 49:3640–3645. https://doi.org/10.1128/AAC.49.9.3640-3645.2005.