254. National Trends in the Japanese Distribution of Major Candida Species Causing Candidemia During 2003–2017: A Report by the Epidemiological Investigation Committee for Human Mycoses in Japan

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Background. Candida species are a common cause of nosocomial bloodstream infections, and candidemia is associated with high mortality rates among adults and neonates. There is limited epidemiological data regarding candidemia in Japan. Therefore, the Epidemiological Investigation Committee for Human Mycoses in Japan performed a retrospective epidemiological survey of candidemia and causative Candida species.

Methods. Blood culture results from 2003 to 2017 were retrospectively evaluated. The data included the center-specific numbers of annual blood cultures, bacterial isolates that included fungi, numbers of fungi, and Candida species. Data were collected from 10 Japanese university hospitals located on all over Japan.

Results. A total of 433,961 blood cultures were included. The prevalence of fungi in all cultures and in positive cultures were 0.53 ± 0.07% and 3.78 ± 0.47%, respectively. Among the results that were positive for Candida species (N = 2,270), C. albicans was the most common species (39.2%) and was followed by *C. parapsilosis* (22.8%), *C. glabrata* (15.6%), *C. tropicalis* (9.7%), *C. krusei* (2.2%), and others. And the temporal changes in the five major Candida species' distributions were analyzed. The frequency of *C. albicans* was 48% in 2003 and 2004, approximately 40% during 2005–2011, approximately 30% in 2012 and 2014, and 40% in 2015–2017. The next most common species were *C. parapsilosis* and *C. glabrata*. The frequency of *C. parapsilosis* was approximately 16% in 2003, approximately 28% during 2005–2009 and 21.7% during 2010–2017. There was a significant difference in the *C. parapsilosis* rates for the first and second halves of the study period (24.8% vs. 21.7%, $P = 0.03$). The frequency of *C. glabrata* was <10% during 2004–2006, and approximately 17% after 2010. *C. glabrata* was significantly more common in the second half of the study period, compared with in the first half (12.0% vs. 17.3%, $P = 0.004$). The frequency of *C. tropicalis* remains stable, and *C. krusei* was significantly less common in the second half of the study period, compared with in the first half (4.3% vs. 1.6%, $P < 0.001$).

Conclusion. The frequency of C. albicans has varied in each year in Japan, while that of C. glabrata has increased. Additional surveys are needed to continuously monitor the trends in the distribution of candidemia in Japan.

Disclosures. **All authors:** No reported disclosures.

255. Breakthrough Mucormycosis (BT-MCR) on Antifungals Having Mucorales Activity Portrays Worse Prognosis compared with BT-MCR on Mold-Active Antifungals with no Mucorales Activity

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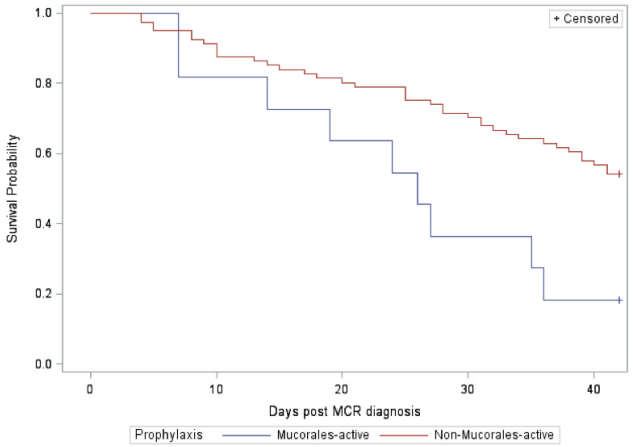
Background. BT-MCR is known to develop in the setting of agents having *Aspergillus* but no Mucorales activity. However, BT-MCR can occur even with the use of antifungals having with Mucorales activity in patients with hematologic malignancies and or stem cell transplant (HM).

Methods. We reviewed the records of HM patients treated for MCR (1994 to 2019) at MD Anderson Cancer Center. We identified patients with BT-MCR on antifungals having Mucorales activity: posaconazole (POSA), isavuconazole (ISA), and amphotericin B (AMB) (group A), and patients with BT-MCR on agents having *Aspergillus* but no Mucorales activity: voriconazole (VRC), itraconazole (ITZ), echinocandins (group B). BT-MCR was defined as MCR diagnosis (dx) after ≥7days (d) of antifungal use. The primary outcome was 42d mortality after the BT-MCR dx. Chi-square or Fisher's exact test was used for categorical variables and Wilcoxon rank-sum test used for continuous variables. Cox regression model was used to evaluate the independent variables on outcome.

Results. We identified 11 patients in group A (3 POSA, 5 ISA, 3 AMB) and 81 patients in group B (61 VRC, 13 echinocandins, 7 ITZ). Both groups were not different in terms of age, sex, underlying HM (AML/MDS in 100% vs. 88% in groups A and B, respectively), status of HM (active disease in 82% vs. 67%), prior stem cell transplant (45% vs. 54%) or GvHD (80% vs. 84%), neutropenia at dx (55% vs. 42%), prior receipt of >600 mg of prednisone (45% vs. 41%) or ICU at MCR dx (36% vs. 26%). Similarly, Mucorales species (*Rhizopus* spp. in 55% vs. 49%) and type of infection (sino-pulmonary in 73% vs. 68%) were no different between the groups. However, both d42 (82% vs. 46%, $P = 0.025$) and d84 (100% vs. 60%, $P = 0.007$) mortality was worse in group A. Similarly, median time to death was faster in patients in group A (26d, range 7-80d), vs. group B (42d, range 4–3146d, $P = 0.031$). Kaplan–Meier analysis showed a similar difference (Figure 1). In multivariate analysis, neutropenia ($P = 0.038$) and ICU at dx ($P = 0.002$) were independent factors on day 42d mortality in all 92 patients with prior Mucorales–active antifungals showing a trend associated with poor outcome ($P = 0.17$).

Conclusion. BT-MCR on agents having Mucorales activity is a marker of poor prognosis in HM patients. Early use of investigational immunotherapy and salvage antifungal chemotherapy studies is needed in that subgroup of patients.

Figure 1. Kaplan-Meier survival curves of MCR patients with different antifungal prophylactic treatment (within 42 days of diagnosis) (p=0.007).



Disclosures. **All authors:** No reported disclosures.

256. Optimizing the Clinical Utilization of T2 Rapid Candida Panel at a Large Community Hospital

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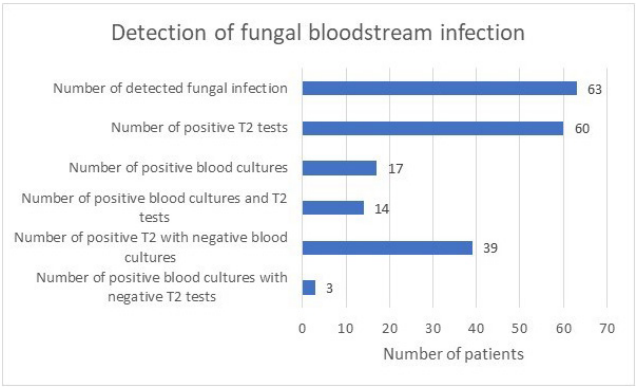
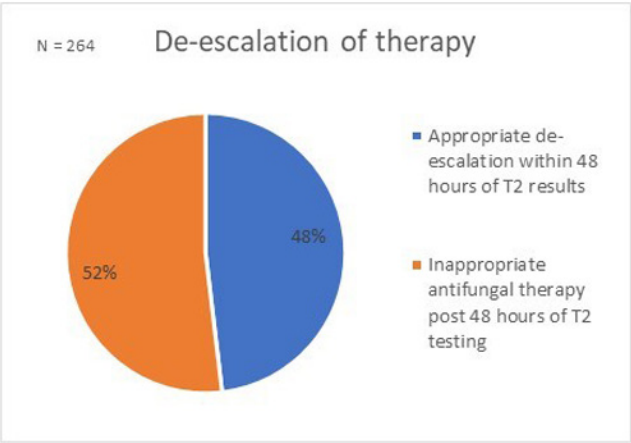
Background. Candidemia is the fourth leading hospital-acquired bloodstream infection with an estimated mortality rate of 35%. Fungal blood cultures result in at least five days and fail to identify 40% of Candida infections. The T2 Candida Panel is a diagnostic test which utilizes whole blood to provide rapid detection of five Candida varieties. It has a 91% sensitivity and 99% specificity rate and enables physicians to initiate or de-escalate therapy rapidly, possibly decreasing mortality. However, practical utilization clinically has not been studied. Our aim is to evaluate the appropriate utilization of the T2 Candida Panel in a large community hospital.

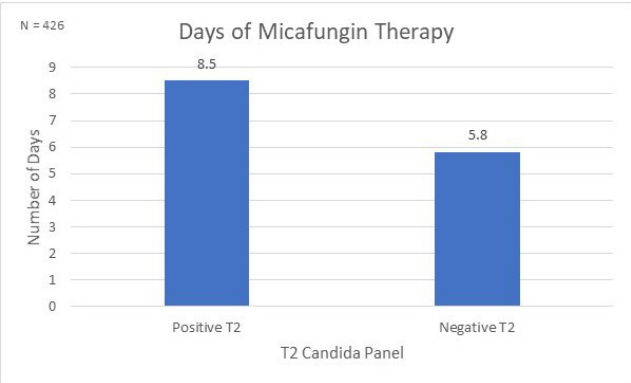
Methods. A retrospective chart review of hospitalized with a T2 Candida Panel result from December 2015 to June 2018 was performed. The panel was restricted and could only be ordered by two specialties, Infectious Disease and Oncology. Baseline demographics and patient characteristics were collected. Endpoints assessed included patient outcomes, antifungal medication use, T2 Candida panel results, corresponding blood culture results, time to appropriate therapy and duration of therapy.

Results. A total of 628 T2 Candida panels resulted during the study period with 56.6% involving the intensive care setting. The average age was 59.5 years with 52.5% of the population being male. Of the total, 8.1% ($n = 60$) were positive. Only three patients had a positive fungal blood culture result with a negative T2 panel collected at the same time (sensitivity 94.3%, 95% CI 80.8–99.3; specificity 94.2%, 95% CI 91.4–96.3). 264 (42%) were ordered with concomitant antifungal therapy and 48.1% underwent de-escalation of therapy based on T2 result. The average time to de-escalation was 137 hours. Of the positive results, 40 (66.7%) had an antifungal ordered when the T2 panel was ordered and 30 (50%) were switched to appropriate therapy after T2 resulted in an average time of 11 hours.

Conclusion. Our data shows that while the T2 Candida Panel demonstrated faster and more sensitive results, there was still a considerable delay in achieving appropriate therapy. The variation in utilization of the T2 Candida Panel indicates that further intervention regarding appropriate use of the panel is required.







Disclosures. **All authors:** No reported disclosures.

257. Aspergillus Galactomannan Lateral Flow Assay for Rapid Diagnosis of Invasive Aspergillosis in Bronchoalveolar Lavage

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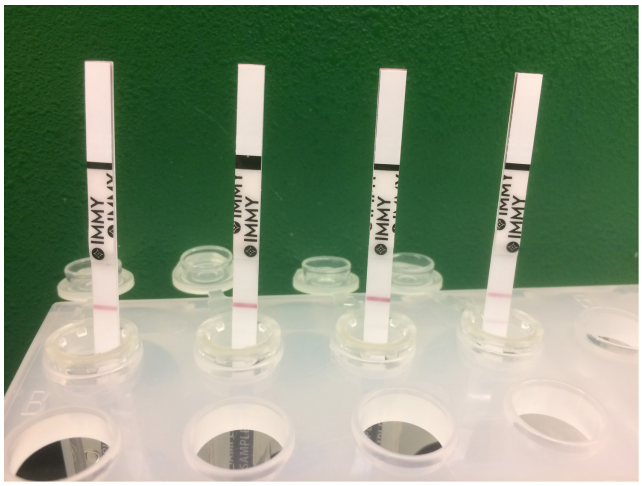
Background. Early diagnosis and treatment of invasive pulmonary aspergillosis (IPA) remain the most important factor to reduce mortality. Diagnosis remains a challenge, however, due to unspecific clinical presentation and radiological findings. Only very recently rapid tests for IPA have been developed. The objective of this study was to evaluate the performance of the new CE-marked Aspergillus Galactomannan Lateral Flow Assay (LFA; IMMY, Oklahoma, USA; figure) for IPA in patients with and without hematological malignancies.

Methods. The Aspergillus Galactomannan LFA was retrospectively performed according to the manufacturer's instructions in 106 previously frozen bronchoalveolar lavage fluid (BAL) samples from 106 patients at risk for IPA (23% with underlying hematological malignancies). Samples were collected between September 2016 and September 2018 at the University of California, San Diego. Performance of the LFA was compared with Galactomannan, BAL culture and the Aspergillus-specific LFD (another rapid test for IPA). IPA was classified according to revised EORTC/MSG criteria.

Results. Overall, 22 patients met criteria of probable or proven IPA, 9 possible IPA, while 75 patients did not fulfill criteria of IPA. Sensitivity of the Apergilllus Galactomanann LFA for probable/proven IPA was 77% (17/22). Sensitivity was similar to BAL GM (77% with a cutoff of 1.0 ODI), but higher compared with the Aspergillus-specific LFD (59%), and BAL culture (23%). The LFA resulted negative in 7/9 cases with possible IPA and 47/73 cases without IPA (overall specificity 66%, 54/82). The less than perfect specificity was driven particularly by non-neutropenic patients (specificity 62%, 43/69), while specificity was 85% among patients with underlying hematological malignancies. Lower specificity among non-neutropenic patients was also observed for the BAL GM (overall 77%, non-neutropenic patients 72%), the Aspergillus-specific LFD (overall 70%, non-neutropenic patients 67%) and BAL culture (overall 90%, non-neutropenic 88%).

Conclusion. Our study indicates that the LFA may be useful for rapid diagnosis of IPA in BALF when IPA is clinically suspected. The lower specificity in non-neutropenic patients may be explained by limited applicability of the EORTC/MSG criteria in those patients.



Disclosures. **All authors:** No reported disclosures.

258. False Negative Rate of T2Candida Assay in Blood Culture Positive Candidemia

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Background. The T2Candida (T2C) assay is an FDA-approved, non-culture-based rapid diagnostic that utilizes PCR and magnetic resonance technology to detect candidemia in a whole blood specimen. T2C can detect the 5 most common pathogenic species: *C. albicans*, *C. tropicalis*, *C. parapsilosis*, *C. krusei*, and *C. glabrata*. The sensitivity of T2C is reported to be 88–94%, varying by the species, based on the original clinical trial from 2015. Only 6 patients with candidemia were included in the study, so it was supplemented with samples spiked with known quantities of *Candida spp*. In this study, we sought to evaluate the sensitivity of T2C with routine usage in a tertiary-care academic hospital.

Methods. All patients with a blood culture (BC) positive for *Candida spp*. during the years 2016 through 2018 were identified. Repeat positive cultures of the same species within 30 days of the initial culture were excluded. We then reviewed the medical records of those patients with a T2C collected ±12 hours from the time of the BC collection. Data collection included demographics, time to antifungal therapy, time to culture reported positive, impact of false negative T2C on antifungal therapy, and 30-day mortality.

Results. There were 281 episodes of candidemia (designated as a positive blood culture) in the study period. Forty-four of these episodes had a T2C collected within the specified timeframe (Figure 1). Overall, there were 17 false-negative T2C, reflecting a sensitivity of 61% (27/44). Excluding species not detected by T2C, the sensitivity was 71% (21/38). Of the false-negative group, antifungal therapy was impacted in 8 patients: delayed initiation in 6 patients (1–4 days) and treatment interruption in 2 patients (1 dose each). Demographics, time to treatment, time to culture positivity, and 30-day mortality were similar in the two groups (Table 1).

Conclusion. In spite of the test being readily available and increasingly used, only 44/281 (16%) of patients with a positive BC had a T2C ordered concurrently. Our experience shows a much lower sensitivity than the clinical trial, in part due to species not detected by T2C. Considering only those organisms on the T2C panel, the false-negative rate was 29%. Impact on treatment was limited to half of the false-negative patients with no difference in mortality.

Table 1: Concordance of T2 negative testing with blood culture positivity (N = 44).

	Total N = 44	Concordant (T2 + /Blood culture +) N = 27	Discordant (T2 -/ Blood culture +) N = 17	P-value
Male, N (%)	28 (64)	16 (59)	12 (71)	0.53
Ethnicity • White • Black • Hispanic	 • 21 (48) • 22 (50) • 1 (2)	 • 12 (44) • 14 (52) • 1 (4)	 • 9 (53) • 8 (47) • 0 (0)	0.66
Age • Mean (SD) • Median (IQR)	 • 54 (14) • 55.5 (21)	 • 56 (14.5) • 60 (20)	 • 50.2 (13) • 51.5 (21)	0.17
Time to positive cultures, hours • Mean (SD) • Median (IQR)	 • 42.7h (19.2) • 36 h (17)	 • 45.1h (22.5) • 36h (23)	 • 38.8h (12.1) • 36h (16)	0.79
Time to antifungals, hours • Mean (SD) • Median (IQR)	 • 0.44 (0.82) • 0 (1)	 • 0.27 (0.45) • 0 (1)	 • 0.71 (1.16) • 0 (2)	0.32
30 day mortality, n (%)	14 (32)	9 (33)	5 (29)	0.79