2857. A Statistical Model to Predict Invasive Fungal Disease in Pediatric Cancer and Hematopoietic Stem Cell Transplantation Patients

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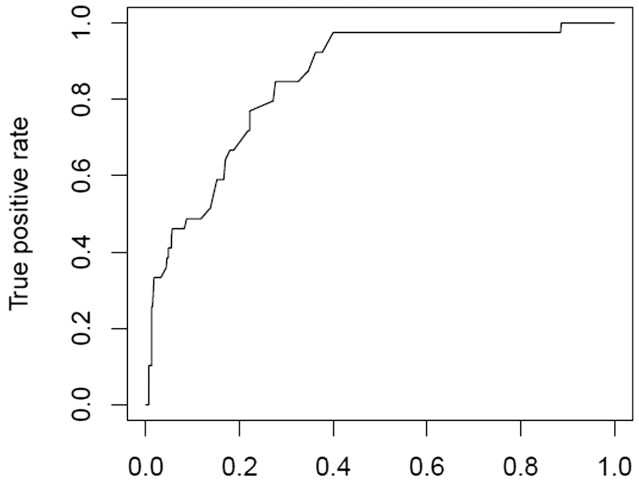
Session: 297. Pediatric Viral and Fungal Diseases
Saturday, October 5, 2019: 2:45 PM

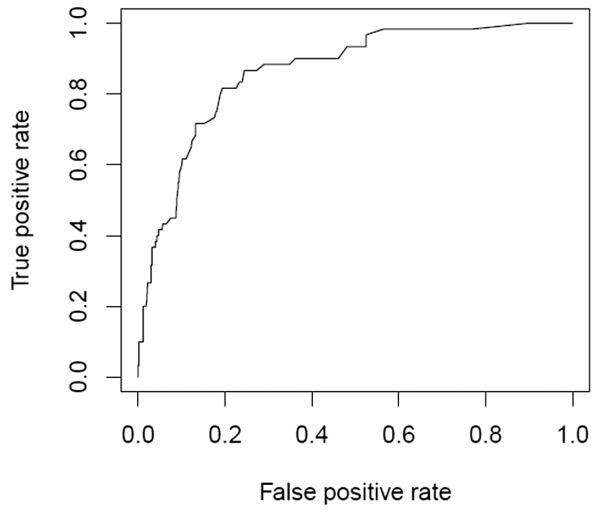
Background. Invasive fungal diseases (IFDs) are devastating opportunistic infections that result in significant morbidity and death in pediatric cancer and hematopoietic stem cell transplantation (SCT) patients. Identification of risk factors for IFD will help clinical decisions relevant to the diagnosis and management of IFD in a timely manner. Despite this, data evaluating prediction risk tools for IFD in pediatric cancer are limited.

Methods. We conducted a retrospective review of pediatric oncology patients with a diagnosis of febrile neutropenia (FN) at UChicago Comer Children's Hospital from July 2009 to December 2016. We analyzed 13 clinical, laboratory, and treatment-related risk factors for IFD including (age, gender, underlying diagnosis, SCT status, graft vs. host disease, chemotherapy in the last 2 weeks, temperature, height, fever duration, presence of hypotension, absolute neutrophil count, duration of neutropenia, absolute monocyte count, and the absolute lymphocyte count (ALC)). IFD was stratified as possible, probable, and proven according to the latest EORTC/MSG criteria (2008). Multivariable logistic regression risk prediction models were developed with separate analyses for all suspected IFD cases and only proven and probable cases.

Results. A total of 667 FN episodes (FNEs) were identified in 265 patients. IFD was diagnosed in 62 episodes (9.2%) of which 13 (1.9%) were proven, 27 (4%) probable, and 22 (3.3%) possible. Five variables obtained were significantly more common in IFD. Patients presenting with hypotension and fever >5 days were highly associated with IFD ($P < 0.001$). SCT receipts ($P < 0.01$), neutropenia longer than 10 days ($P = 0.02$), and ALC <300 mm^3 at time of presentation ($P = 0.03$) were additional risk factors. The final model performs very well compared with other published models with a receiver operating characteristic–area under the curve (ROC-AUC) of 86.5 for all IFD cases and ROC-AUC of 84.5 for proven, probable IFD cases.

Conclusion. Our findings showed important clinical markers for the development of IFD in pediatric oncology patients. A predictive regression model including identified significant factors has been created. Risk stratification with prospective external validation using this model can be used to refine the clinical approach.





Disclosures. **All Authors:** No reported Disclosures.

2885. A Host Transcriptional Signature for Accurate Diagnosis of Candidemia in the Hospital Setting

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Session: 308. Fungi: Blood, Sweat, and Genes
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Background. Candidemia is one of the most common nosocomial bloodstream infections in the United States and causes significant morbidity and mortality in hospitalized patients. Improved rapid diagnostics capable of differentiating candidemia from other causes of febrile illness in the hospitalized patient are of paramount importance. Pathogen class-specific biomarker-based diagnostics such as those focusing on host gene expression patterns in circulating leukocytes may offer a promising alternative.

Methods. RNA sequencing was performed on peripheral blood samples from 27 hospitalized patients with blood culture positive invasive candidiasis. Samples from healthy controls as well as at-risk subjects with acute febrile illness and similar clinical backgrounds but other infectious or noninfectious etiologies were used as comparator phenotypes (35 subjects with culture-proven bacterial infection, 49 with confirmed viral infection, and 17 with acute noninfectious illness). Bayesian techniques were utilized to develop infection-specific classifiers and leave one out cross-validation was used to estimate the predictive probability of each pathogen class.

Results. Candidemia triggers a unique, robust and conserved transcriptomic response in human hosts with 1,170 genes differentially upregulated compared with healthy controls. Based on this strength of signal, we developed a transcriptomic classifier that was capable of identifying candidemia, viral, or bacterial infection with a high degree of accuracy (auROC for Candida 0.93, Bacterial 0.98, Viral 0.99). The *Candida* component of this classifier (29-genes) was able to diagnose candidemia with a sensitivity of 88% and specificity of 100%.

Conclusion. The host transcriptomic response during candidemia in hospitalized adults is highly conserved and unique from the genomic responses to acute viral and bacterial infection. This approach shows promise for the development of host response-based classifiers capable of differentiating multiple types of clinical illnesses at once in at-risk febrile patients.

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2886. Retrospective Case–Control Study of the Performance of the Karius Test, a Plasma Microbial Cell-free DNA Next-generation Sequencing test, to Detect Invasive Mold Infections in Hematopoietic Cell Transplant Recipients with Pneumonia

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Session: 308. Fungi: Blood, Sweat, and Genes
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Background. Pulmonary invasive mold infections (IMI) cause significant morbidity and mortality after hematopoietic cell transplant (HCT). Noninvasive diagnostic options are limited, particularly for non-*Aspergillus* (non-Asp) molds. Given differences in activity and toxicities of antifungals, early diagnosis and targeting of specific IMI is important. We evaluated the performance of the Karius Test, a plasma microbial cell-free DNA next-generation sequencing (NGS) test, for detecting IMI in HCT recipients.

Methods. We conducted a retrospective case–control study of 24 HCT recipients with proven non-Asp pulmonary IMI, 51 probable/proven *Aspergillus* pulmonary IMI, and 20 controls with nonfungal pulmonary infections. All subjects had plasma obtained within 14 days of diagnosis. Workup included bronchoalveolar lavage (BAL) and/or biopsy, with fungal stains/culture and galactomannan testing of BAL and serum. Plasma cell-free DNA was extracted and NGS performed (Karius, Redwood City, CA). Human reads were removed and remaining sequences aligned to a curated database including over 300 fungi. Organisms present above a predefined significance threshold were reported. A higher sensitivity research-use only pipeline was also used. Analysis of sequencing data was blinded to all clinical data.

Results. We identified pathogenic molds in 19/24 (79%) of subjects with proven non-Asp IMI, including *Mucor, Rhizomucor, Scedosporium, Rhizopus,* and *Cunninghamella* spp. In *Aspergillus* proven/probable IMI, *A. fumigatus* was identified in 13.7% (7/51) of subjects. In 3 other subjects with proven/probable aspergillosis, we also identified *Rhizomucor miehei* and *R.pusillus*, and *Cunninghamella*, consistent with clinical findings. The use of an optimal-sensitivity pipeline identified an additional 9 subjects with *Aspergillus* spp. and other pathogenic molds, increasing detection of molds to 37.3% (19/51). Specificity for molds in negative samples was 100% (20/20).