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Transplantation and invasive fungal infections

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Most fungal infections are opportunistic infections. When people's immune system is weakened, fungi can cause severe infection. For solid organ transplant (SOT) recipients, their immunity is weakened because they are taking immunosuppressive drugs. In actual, invasive candidiasis is most common in solid organ transplant patients. Especially, for lung transplant recipients, aspergillosis is most common. The incidence of invasive candidiasis and invasive aspergillosis has been estimated at around 2% and 0.1%~2.4%, respectively. Time to development of invasive fungal infection after transplantation varies according to type of fungal infection, type of transplant, and the use/duration of antifungal prophylaxis. Complicated operative courses, environmental exposures and state of immunosuppression all increase the risk for invasive fungal infection in SOT recipients. Depending on the type of transplant, main risk factors for invasive candidiasis and aspergillosis included the following: graft rejection/dysfunction, enhances immunosuppression, anastomotic disruption, post transplantation renal failure, and Aspergillus colonization (especially for lung transplantation). The overall mortality rates vary depending on the type of transplant and variations in entire follow up period in the different studies. In clinical microbiology laboratories, identification of fungal species is important. According to the revised EORTC/MSG guidelines for the diagnosis of invasive fungal disease, three diagnostic criteria were established to define proven, probable, or possible infection: (1) host factors (newly added receipt of a solid organ transplant), (2) clinical feature, and (3) mycological evidence (any mold recovered by culture, galactomannan antigen and *Aspergillus* PCR for *Aspergillosis* only). Methods for the identification of fungi include culture-based and non-cultured assays. Culture-based methods include microscopic examination, MALDI-TOF MS analysis, PCR, and sequencing. Non-culture-based tests include galactomannan, beta-D-glucan, lateral flow technology using an *Aspergillus* monoclonal antibody and Aspergillus PCR which has been extensively validated for standardized methodologies and is now included in the recent EORTC/MSG definition updates. Resistance to antifungal agents is an increasing problem in *Candida* spp. and *Aspergillus* spp.. As a phenotypic antifungal susceptibility testing (AST) method, EUCAST and CLSI broth microdilution method can de used for determination of minimum inhibitory concentration. In addition, many clinical laboratories use commercial AST methods; (1) Sensititre YeastOne (commercial broth microdilution assay for *Candida* spp. and *Aspergillus*

spp.), and (2) Vitek 2 system (fully automated system for *Candida* spp.). Based on the underlying mechanisms of antifungal resistance, molecular assays can be used for detection of resistance associated mutations; (1) azole resistance in *Candida* spp. (*ERG11 and ERG3*), (2) echinocandin resistance in *C. glabrata* (*FKS*), and (3) azole resistance in *Aspergillus* spp. (*CYP51A*). For molecular-based resistance detection assay, cultured fungi or original specimens (respiratory specimen or blood) can be used for analysis. Here, I will discuss about the clinical utility of several identification assays and antifungal susceptibility testing for invasive fungal infection in SOT recipients. In addition, I will introduce our clinical laboratory's experience to explain the importance of rapid identification of cryptic species and the implementation of AST for fungi including *Candida* spp. and *Aspergillus* spp..