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Paper Poster Session
Update in fungal resistance and susceptibility

Rapid detection of fluconazole and anidulafungin resistance in Candida glabrata isolates using a MALDI-TOF MS-based assay

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Background: *Candida glabrata* is an important cause of bloodstream infection. This infection is very difficult to treat due to its tendency to easily develop azole (e.g., fluconazole [FLC]) resistance. Although echinocandins (e.g., anidulafungin [AND]) are recommended as a first-line therapy, resistance also emerged against this drug. So, early detection of azole- or echinocandin- resistant isolates of *C. glabrata* has become an essential prerequisite for establishing appropriate antifungal therapy. For this reason we sought to use of MALDI-TOF analysis for mass spectrometry (ms)-based antifungal susceptibility testing (AFST) to the *C. glabrata* and rapid detection of FLC- or AND- resistant isolates.

Material/methods: We studied 98 *C. glabrata* isolates, 69 molecularly well-characterized strains and 19 freshly collected routine clinical isolates. For all the isolates, conventional AFST assay was performed by the broth microdilution method in accordance with the Clinical and Laboratory Standards Institute (CLSI) document M27-A3. For the ms-AFST assay, yeasts were grown in RPMI medium with intermediate (16 mg/L for FLC and 0.06 mg/L for AND), maximum (256 mg/L for FLC and 32 mg/L for AND) drug concentrations or with RPMI alone, for 3 h at 37°C. After protein extraction, MALDI-TOF analysis was performed .Spectra at the null (0 mg/L), intermediate, or maximum concentration of drug were used to create individual composite correlation index (CCI) matrices for each isolate; then, the isolate was classified as susceptible or resistant to FLC (or AND) if the CCI value obtained by matching the spectra at intermediate and maximum concentrations was respectively higher or lower than the CCI value obtained by matching the spectra at intermediate and null concentrations

Results: Results obtained with ms-AFST and conventional AFST assays were compared to reference molecular-based analyses. Among 66 isolates tested against FLC, 36 of 38 isolates were correctly classified as FLC-resistant and 28 of 28 isolates as FLC-susceptible by ms-AFST. Among 32 isolates tested against AND, 24 of 25 isolates were correctly identified as AND-susceptible and 6 of 7 isolates as AND-resistant by ms-AFST. With regards to the conventional AFST, FLC results were fully concordant with the molecular analyses, whereas one wild-type isolate was classified as AND-

resistant (also in accordance with ms-AFST) and one *fks1* mutant was categorized as AND-intermediate (this isolate was classified as susceptible with ms-AFST).

Conclusions: Our MALDI-TOF MS-based AFST method seems to be very promising for the rapid and accurate detection of antifungal resistance in relevant pathogenic yeasts.