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Risk Factors for Micafungin non-susceptible *Candida* isolates

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Abstract

Background: Echinocandins (EC) are the agents of choice for candidiasis in patients with risk factors for fluconazole resistant *Candida*. With the emergence of EC non-susceptibility, identifying patients at risk is of utility to ensure optimal selection of empiric antifungal therapy.

Methods: Adult inpatients with a *Candida* isolate in any culture were included. Micafungin susceptibility was based on current CLSI standards.[1] Isolates with micafungin (Mica) intermediate sensitivity or resistance between 5/1/2012 – 4/30/2016 were included in the Mica non-susceptible group (MicaNS), while isolates that were susceptible to Mica between 5/1/2015-4/30/2016 were included in the Mica susceptible group (MicaS). Patients in the MicaS group were randomized for inclusion in the risk factor analysis for comparison. We also evaluated length of stay (LOS), and 30 day all-cause mortality.

Results: 12 patients had MicaNS *Candida*, while 238 patients had MicaS *Candida* (20 patients were randomized for the risk factor analysis). Baseline characteristics and the univariate analysis are shown in Table 1. On multivariate analysis, previous hospitalization within 90 days (p=0.02) and ICU admission (p=0.04) were independently associated with MicaNS. All-cause 30-day mortality (33% vs 10%, p= 0.17) and LOS (48.2d vs 18.8d, p= 0.04) were higher in the MicaNS group.

Conclusion: ICU admission and prior hospitalization were found to be independent predictors for MicaNS *Candida*. Solid organ transplant, ESRD, and days admitted prior to culture may also contribute to the risk. Patients with MicaNS *Candida* exhibited worse clinical outcomes with increased mortality and prolonged LOS. Further studies are needed to fully elucidate clinical characteristics associated with MicaNS.

Background

- Clinical practice guidelines for the management of Candidiasis recommend echinocandins as first-line therapy for non-neutropenic and neutropenic patients with candidemia, resulting in an increase in echinocandin use[2]
- While overall, echinocandin non-susceptible *Candida* is rare, reports of non-susceptibility have been increasing over the years[3-5]
  - Studies show a rate of echinocandin non-susceptibility of 2-3% for *Candida albicans* and other non-*glabrata* isolates, and 8->13% for *Candida glabrata*
- A previous study evaluated risk factors for specifically echinocandin non-susceptible *Candida glabrata* blood stream isolates, identifying prior echinocandin exposure, previous candidemia episode, hospitalization in previous 90days, and fluconazole resistance as predictors[6]
- We sought to evaluate all echinocandin non-susceptible *Candida* isolates, including all *Candida* isolates and culture sites to identify predictors for non-susceptibility

Methods

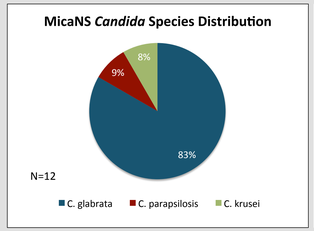
Study Design
- Retrospective, observational, single-center study
- Analysis period: 5/1/2012 – 4/30/2016 (MicaNS), 5/1/2015-4/30/2016 (MicaS)
- Patients with multiple cultures were included in the risk factor analysis only once, using their initial culture date to assess presence of risk factors

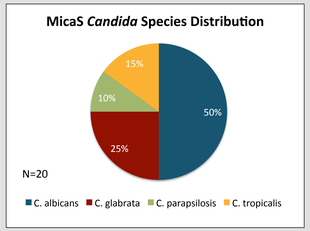
Study Population
- Adult patients ≥ 18 years with any culture growing *Candida* species with susceptibilities reported

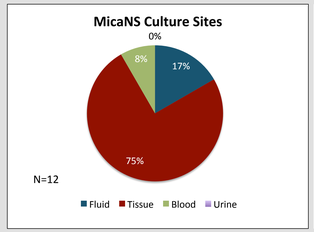
Primary Endpoint
- Risk factors for micafungin non-susceptibility

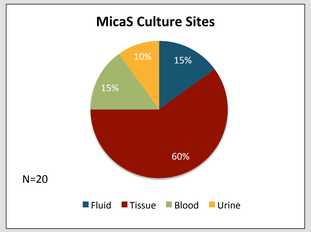
Statistical Analysis
- Baseline demographics, susceptibility, outcomes: Chi^2 test or Fishers exact (categorical variables), Student's t-test/Mann-Whitney U test (continuous variables)
- Risk factors: Univariate and multivariate regression analysis

Results

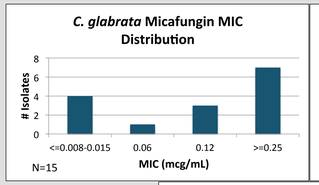


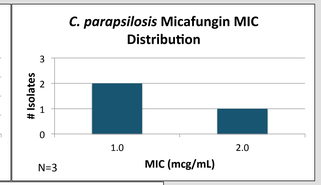


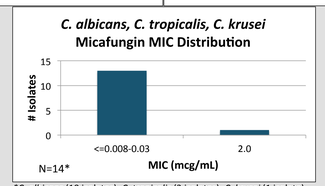




Results *(cont'd)*







**C. albicans* (10 isolates), *C. tropicalis* (3 isolates), *C. krusei* (1 isolate)

Table 1: Univariate analysis

Parameter	MicaNS (N = 12)	MicaS (N = 20)	p-Value
Age (mean)	52.4	61.6	0.07
Gender, Male (%)	6 (50)	14 (70)	0.26
Previous hospitalization, 90d (%)	10 (83)	8 (40)	0.03
Diabetes (%)	4 (33)	3 (15)	0.38
End stage renal disease (ESRD) (%)	5 (42)	2 (10)	0.07
Solid organ transplant (%)	2 (17)	0 (0)	0.13
Oncology diagnosis (%)	2 (17)	11 (55)	0.06
ICU at time of culture (%)	8 (67)	6 (30)	0.07
TPN w/in 14 days (%)	2 (17)	1 (5)	0.54
Previous abdominal surgery, 90d (%)	3 (25)	2 (10)	0.34
Previous *Candida* infection (%)	5 (42)	7 (35)	0.72
Previous echinocandin exposure (%)	6 (50)	3 (15)	0.05
Fluconazole Resistance (%)	3 (25)	3 (15)	0.65
Days admitted prior to culture (days, mean)	22	12.6	0.32

Table 2: Multivariate Analysis – Risk Factors for MicaNS Candida

	OR (95% CI)	p-Value
Previous hospitalization, 90 d	10.9 (1.4 – 82.6)	0.02
ICU at time of culture	7.1 (1.1 – 45.4)	0.04

Results *(cont'd)*

Table 3: Clinical Outcomes

Parameter	MicaNS (N = 12)	MicaS (N = 20)	p-Value
All-cause 30day mortality	33%	10%	0.17
Length of stay	48.2	18.8	0.04

Conclusion

- On multivariate analysis, ICU admission at time of culture and prior hospitalization (90d) were independent predictors for micafungin non-susceptibility.
- Patients with micafungin non-susceptible Candida had significantly longer lengths of stay and also had higher all-cause 30d mortality.
- Due to the small sample size the ability to detect additional potential risk factors is limited.
- ESRD, solid organ transplant, diabetes, TPN initiated within 14 days prior to culture, previous abdominal surgery (90d), previous echinocandin therapy at any time prior to culture, previous candida infection were all more common in the MicaNS group, but not to a statistically significant degree.
- Patients in the MicaNS group were also hospitalized for a longer duration (~10 days) prior to culture.

References

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Disclosure

The authors of this presentation have no financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation