



# Elderly Age, Underlying Malignancy and Diabetes are Not Significant Risk Factors for Candidemia with *Candida glabrata*

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## Abstract (revised)

**Background:** The 2016 update of the clinical practice guideline for the management of candidiasis recommends an echinocandin as initial therapy for treatment of candidemia in neutropenic and non-neutropenic patients. Fluconazole is acceptable as initial therapy only in patients who are hemodynamically stable, without prior azole exposure, and are not at increased risk for *Candida glabrata* (CG) infections. Elderly patients or those with underlying malignancy or diabetes (DM) are defined as groups at high risk for CG infections. These risk factors include a wide range of patients, may lead to increased echinocandin use, and have not been consistently proven in prior studies. We sought to evaluate if elderly age ( $\geq 65$  years), underlying malignancy and DM are risk factors for candidemia with CG at our institution.

**Methods:** Adult patients with at least one positive blood culture for *Candida* species between 1/1/2013-12/31/2015 were included. Only the first episode of candidemia was included for patients with recurrent candidemia. Risk factors were analyzed using regression analysis.

**Results:** A total of 147 patients were reviewed. CG: 47; non-CG: 100 (*C. albicans*: 52; *C. parapsilosis*: 25; *C. dubliniensis*: 6; *C. tropicalis*: 5; *C. krusei*: 5; other: 7). Demographics and outcomes are summarized in table 2. Risk factors and their association with CG candidemia are shown in table 3. Elderly age, DM, prior azole exposure and vasoactive support met *a priori*  $p < 0.2$  for inclusion in multivariate (MV) analysis. Neither elderly age nor DM was found to be an independent predictor for CG candidemia in MV analysis (elderly age:  $p = 0.19$ ; DM:  $p = 0.06$ ).

**Conclusion:** Contrary to recommendations in the candidiasis guideline, elderly age, underlying malignancy and DM were not significant risk factors of CG candidemia in our patients. Presence of these patient characteristics alone should not preclude the use of fluconazole as initial therapy.

## Background

- The 2016 clinical practice guideline for the management of invasive candidiasis recommends an echinocandin as first-line initial therapy for treatment of candidemia in neutropenic and non-neutropenic patients.<sup>1</sup>
- Fluconazole is an acceptable alternative in selected patients:<sup>2</sup>
  - Not critically ill
  - No previous azole exposure
  - Unlikely to have fluconazole-resistant *Candida* species [e.g. *Candida glabrata* (CG)]
- The guideline defines elderly age, underlying malignancy and DM as risk factors for CG infections.<sup>1</sup>
- These risk factors include a wide range of patients and have not been consistently proven in prior studies.<sup>2-6</sup>
- We sought to evaluate if elderly age ( $\geq 65$  years), underlying malignancy and DM are risk factors for candidemia with CG at our institution.

## Methods

### Study Design

- Retrospective, observational, single-center study
- Analysis period: 1/1/2013-12/31/2015

### Study Population

- Adult patients  $\geq 18$  years with  $\geq 1$  blood culture positive for *Candida* species
- Only the 1<sup>st</sup> episode of candidemia in patients with recurrence(s) was included

### Endpoint

- Risk factors for candidemia with CG

### Statistical Analysis

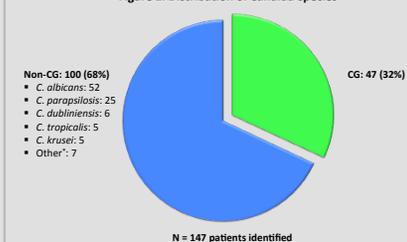
- Baseline demographics, susceptibility, outcomes: Chi<sup>2</sup> test (categorical variables), Student's t-test/Mann-Whitney U test (continuous variables)
- Risk factors: regression analysis

### Definitions

- Prior azole exposure: use of any azole antifungal within 30 days prior to date of first positive blood culture for *Candida* species
- Vasoactive support: use of  $\geq 1$  vasoactive agent (norepinephrine, vasopressin, dopamine, phenylephrine, epinephrine) during the same admission prior to or on the date of the first positive blood culture for *Candida* species
- Fluconazole susceptibility: per breakpoints recommended by Clinical and Laboratory Standards Institute<sup>7</sup>

## Results

Figure 1. Distribution of *Candida* species



<sup>7</sup>*C. lusitanae*: 2; *C. utilis*: 1; *C. pelliculosa*: 1; *C. kefyr*: 1; Species not identified: 2  
Fluconazole Susceptibility: CG 84% versus Non-CG 89%,  $p = 0.42$

## Results (cont'd)

Table 1: Fluconazole Minimum Inhibitory Concentration (MIC, mg/dL) \*

	$\leq 0.25$	0.5	1	2	4	8	16	32	64	$\geq 128$
<i>C. albicans</i>	14	22	3	1			1			
<i>C. glabrata</i>	1	2	12	12	5	1	2			7
<i>C. parapsilosis</i>	5	6	9	1						
<i>C. dubliniensis</i>	4	2								
<i>C. tropicalis</i>			3	2						
<i>C. kefyr</i>	1									
<i>C. pelliculosa</i>				1						
<i>C. utilis</i>				1						
Other species				1		1				

Table 2: Patient Demographics and Outcomes

Parameter	CG (N = 47)	Non-CG (N = 100)	p-Value
Gender (male)	21 (45%)	46 (46%)	0.79
Age (mean $\pm$ SD, years)	60.1 $\pm$ 14.1	56.9 $\pm$ 16.0	0.24
Elderly (age $\geq 65$ years)	20 (43%)	30 (30%)	0.13
Malignancy			
Solid	19 (40%)	31 (31%)	0.32
Hematologic	14	21	
All-Cause Inpatient Mortality	10 (21%)	44 (44%)	0.01
Length of Stay [median (IQR), days]	16 (4 – 98)	19.5 (2 – 122)	0.21

Table 3: Univariate Analysis – Risk Factors for CG Candidemia

	OR (95% CI)	p-Value
Elderly Age ( $\geq 65$ years)	1.7 (0.8 – 3.5)	0.14
Underlying Malignancy	1.4 (0.7 – 3.0)	0.32
DM	2.3 (1.0 – 5.1)	0.04
Prior Azole Exposure	2.6 (1.1 – 6.1)	0.03
Vasoactive Support	2.1 (0.9 – 4.5)	0.07

## Results (cont'd)

### Multivariate Analysis

- Risk factors which met *a priori*  $p < 0.2$  in univariate analysis were included in multivariate analysis:
  - 1) Elderly age
  - 2) DM
  - 3) Prior azole exposure
  - 4) Vasoactive Support

Table 4: Multivariate Analysis – Risk Factors for CG Candidemia

	OR (95% CI)	p-Value
Elderly Age ( $\geq 65$ years)	1.7 (0.8 – 3.6)	0.19
DM	2.4 (1.0 – 5.7)	0.06
Prior Azole Exposure	3.7 (1.5 – 9.1)	0.01
Vasoactive Support	2.0 (0.9 – 4.6)	0.10

## Conclusion

- Elderly age, underlying malignancy and diabetes were not found to be significant risk factors for candidemia with CG.
- Presence of these patient characteristics alone should not preclude the use of fluconazole as initial therapy.

## 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

\*Data shown as number of isolates; IDSA = Infectious Diseases Society of America; SD = standard deviation; IQR = interquartile range; OR = odds ratio; CI = confidence interval