

Comparison of costs, length of stay, and mortality associated with *Candida glabrata* and *Candida albicans* bloodstream infections

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We compared costs, length of stay, and mortality between adults with *Candida albicans* and *Candida glabrata* bloodstream infections. Early evidence of *C glabrata*, as defined by a positive culture within 2 days of admission, was associated with higher costs (\$56,026 vs \$32,810; $P = .04$) and longer hospital stays (19.7 vs 14.5 days; $P = .05$) compared with early evidence of *C albicans*. Mortality was similar between the groups.

Key Words: *Candida albicans*; *Candida glabrata*; cross infection; health care costs; length of stay; mortality.

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Candida bloodstream infections lead to prolonged hospital stays, significant costs, and high mortality.^{1,2} Prompt diagnosis is critical, because patients treated more than 48 hours after diagnosis have a lower probability of survival.³ The most frequently isolated *Candida* species is *C albicans*; however, non-*C albicans* infections are increasing in frequency.⁴⁻⁶ One emerging species, *C glabrata*, is more resistant than *C albicans* to antifungal therapy and may be associated with higher mortality.⁴ We previously reported that adults with *Candida* bloodstream infections have shorter lengths of stay and lower inpatient costs compared with children.⁷ In the present study, limited to adults, we compared inpatient costs, length of stay, and mortality associated with *C glabrata* and *C albicans* bloodstream infections. We separated patients into those with early infections (occurring within 2 days after admission) and late infections (occurring more than 2 days after admission), given the difference in mortality for patients with delayed diagnosis and treatment.

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METHODS

We conducted a retrospective cohort study of patients over age 18 years who were admitted to Duke University Hospital between February 1996 and July 2007 with a blood culture positive for *C glabrata* or *C albicans*. Bact/ALERT (bioMerieux, Marcy l'Etoile, France) or BACTEC (BD, Franklin Lakes, NJ) automated blood culture systems were used, and isolates were identified by standard microbiological methods. The primary outcome measures were length of hospital stay, total inpatient costs, and inpatient mortality over the hospitalization period. Outcomes were calculated from the date of first positive blood culture to the date of death or discharge. Patients were stratified according to whether the first reported positive culture occurred early (on the day of or the day after admission) or late (2 or more days after admission).

Detailed cost data were available for patients hospitalized since December 2002. The Consumer Price Index for Medical Care was used to update costs to 2007 values. Generalized linear models with gamma distributions and log links were used to compare costs, negative binomial distributions and log links were used to compare length of stay, and the χ^2 test was used to compare inpatient mortality. Duke University Health System's Institutional Review Board approved the study.

RESULTS

There were 887 patients with at least 1 blood culture positive for *Candida*, of whom 600 had at least 1 blood culture positive for *C albicans* or *C glabrata*. Forty-eight patients (5%) had a blood culture positive for more

Table 1. Length of stay, inpatient costs, and mortality associated with early and late evidence of candidemia

Variable	Early evidence of candidemia		P [†]	Late evidence of candidemia*		P [†]
	<i>C glabrata</i> (n = 45)	<i>C albicans</i> (n = 80)		<i>C glabrata</i> (n = 186)	<i>C albicans</i> (n = 289)	
Length of stay, days			.05			.31
Number	44	80		185	285	
Mean (SD)	19.7 (19.0)	14.5 (13.3)		21.9 (21.8)	20.0 (23.8)	
Median (IQR)	13.5 (8.5 to 25.0)	11.5 (6.0 to 19.0)		17.0 (7.0 to 29.0)	12.0 (6.0 to 24.0)	
Costs, \$.04			.09
Number	25	30		76	96	
Mean (SD)	56,026 (56,186)	32,810 (34,947)		67,793 (80,421)	52,112 (74,044)	
Median (IQR)	31,782 (17,325 to 88,586)	20,501 (8,252 to 39,252)		39,865 (19,629 to 93,429)	25,324 (10,567 to 64,323)	
Mortality, n (%)			.96			.36
Number	45	80		186	289	
Deaths, n (%)	15 (33.3)	27 (33.8)		89 (47.8)	126 (43.6)	

IQR, interquartile range; SD, standard deviation.

*More than 2 days from admission.

†Reported P values are 2-tailed.

than 1 *Candida* species. Among the patients with a single species, 38.5% (231/600) had a positive blood culture for *C glabrata* and 61.5% (369/600) had a positive blood culture for *C albicans*. Mean patient age was 59 years in those positive for *C glabrata* and 56 years in those positive for *C albicans*. Males composed approximately 55% of each group.

Data on length of stay were available for 99% of the patients, and cost data were available for 37.8%. Approximately 21% had a positive blood culture during the first 2 days of admission (19.5% [45/231] for *C glabrata* and 21.7% [80/369] for *C albicans*). In this early infection cohort, *C glabrata* was associated with a longer mean length of stay than *C albicans* (19.7 days vs 14.5 days; $P = .05$), higher costs (\$56,026 vs \$32,810; $P = .04$), and comparable mortality (33.3% vs 33.8%; $P = .96$) (Table 1). For patients with a first positive culture more than 2 days after admission ($n = 186$ for *C glabrata* and $n = 289$ for *C albicans*), the mean cost for *C glabrata* bloodstream infection was higher, although the difference was not statistically significant (\$67,793 vs \$52,112; $P = .09$). Length of stay (21.9 days vs 20.0 days; $P = .31$) and inpatient mortality (47.8% vs 43.6%; $P = .36$) were similar in the 2 groups.

DISCUSSION

Candida is responsible for approximately 10% of nosocomial bloodstream infections.⁵ The most common species isolated include *C albicans*, *C glabrata*, *C parapsilosis*, and *C tropicalis*. Risk factors for *C albicans* infection include broad-spectrum antibiotic use, presence of a central venous catheter, gastrointestinal procedures, and parenteral nutrition.⁶ Risk factors for *C glabrata* infection include organ transplantation, renal insufficiency, solid tumors, antifungal

(fluconazole) prophylaxis, and the intensive care unit setting.⁴

Hospitalized adults with *Candida* bloodstream infections have longer hospital stays and higher costs of care compared with those without candidemia.² Rentz et al⁸ reported that candidemia results in approximately 1-month longer hospital stays and up to \$45,000 in additional costs. Our unadjusted comparisons revealed longer inpatient stays and higher costs with *C glabrata* compared with *C albicans* in patients with early evidence of infection, in whom costs and length of hospital stay before the development of infection did not influence comparisons.

Mortality estimates for patients with candidemia vary. A recent analysis found the mortality associated with *C albicans* and *C glabrata* bloodstream infections to be 44% and 41%, respectively.⁹ Our data also show no mortality difference. Although our study was limited to patients with *C albicans* or *C glabrata*, patients with multiple infections had higher mortality (58%).

Our study is limited by its single-institution experience and retrospective design, as well as by the absence of clinical data on underlying illnesses, duration of antifungal therapy, presence of a central venous catheter, blood culture data, and cause of death. Limiting the study to patients with positive cultures obtained within 2 days of admission may have led to underrepresentation of patients with early infection. Although time to positive blood culture varies with the culture system used and the *Candida* species isolated, it can take up to 4 days for *Candida* to grow from a blood culture. But the average time for a positive culture across infection sites has been reported to be 33.9 ± 3 hours, within our 2-day window.¹⁰ Because growth of *C glabrata* can take even longer,¹⁰ more early infections may have been classified as late infections.

Cost data were available for only 38% of patients. Major strengths of our study include the large cohort of all patients with positive *Candida* cultures over approximately 10 years and the availability of patient-level cost data for the most recent 4.5-year period.

This study demonstrates that patients with early evidence of *C glabrata* have higher costs and longer hospital stays compared with those with *C albicans*. There were no differences in outcomes for late infections in the 2 groups.

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