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# Comparison of Costs, Length of Stay, and Mortality Associated with *Candida glabrata* and *Candida albicans* Bloodstream Infections

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## Abstract

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 ($56026 vs $32810; $P = .04$) 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.

## Introduction

*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-*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 when compared to children.[7] In this 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 (within 2 days after admission) and late infections (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 older than 18 years 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, Inc) or BACTEC (Becton Dickinson) 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. We stratified patients 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. We used the Consumer Price Index for Medical Care 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 to compare length of stay, and $\chi^2$ tests to compare inpatient mortality. The institutional review board of the Duke University Health System 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 than 1 *Candida* species. Among patients with a single species, 38.5% (231/600) had a blood culture positive for *C glabrata* and 61.5% (369/600) for *C albicans.* Mean patient age was 59 years and 56 years for *C glabrata* and *C albicans*, respectively. Approximately 55% in each group were men.

Data on length of stay were available for 99% and cost data for 37.8% of patients. Approximately 21% had a positive blood culture during the first 2 days of admission (19.5% [45/231] for *C glabrata*; 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 ($56026 vs $32810; $P = .04$), and comparable mortality (33.3% vs 33.8%; $P = .96$). For patients with a first positive culture more than 2 days after admission (n=186 for *C glabrata*; n=289 for *C albicans*), the mean cost for *C glabrata* bloodstream infection was higher, though the difference was not significant ($67793 vs $52112; $P = .09$). Length of stay (21.9 days vs 20.0 days; $P = .31$) and inpatient mortality (47.8% vs 43.6%; $P = .36$) were similar.

## 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* include broad-spectrum antibiotic use, presence of a central venous catheter, gastrointestinal procedures, and parenteral nutrition.[6] Risks for *C glabrata* include organ transplantation, renal insufficiency, solid tumors, antifungal (fluconazole) prophylaxis, and the intensive care unit setting.[4]

*Candida* bloodstream infections in adults are associated with longer hospital stays and higher costs compared to hospitalized adults without candidemia.[2] Rentz et al[8] reported candidemia resulted in approximately 1 month longer hospital stays and up to $45000 in additional costs. Our unadjusted comparisons revealed longer inpatient stays and higher costs with *C glabrata* compared to *C albicans* among patients with early evidence of infection, where costs and hospital days prior to infection did not influence comparisons.

Mortality for patients with candidemia can be as high as 40%.[5] A recent analysis found that mortality associated with *C albicans* and *C glabrata* bloodstream infections are similar (44% and 41%, respectively).[9] Similarly, our data do not show a 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 a single institution experience, retrospective design, and absence of clinical data regarding underlying illnesses, duration of antifungal therapy, presence of a central venous catheter, blood culture draw data, or cause of death. Limiting the study to patients with positive cultures 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. However, the average time for a positive culture across sites of infection has been reported to be 33.9 ± 3 hours, within our 2-day window.[10] Because growth can take even longer for *C glabrata*,[10] more early infections may have been classified as late infections. Cost data were available for only 38%. 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 years.

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

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**Table 1**

Length of Stay, Inpatient Costs, and Mortality Associated with Early and Late Evidence of Candidemia

| Variable | Early Evidence of Candidemia | | | Late Evidence of Candidemia* | | |
|---|---|---|---|---|---|---|
| | *C glabrata* (n = 45) | *C albicans* (n = 80) | *p*† | *C glabrata* (n = 186) | *C albicans* (n = 289) | *p*† |
| Length of stay, d | | | .05 | | | .31 |
| No. | 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 (8.5–25.0) | 11.5 (6.0–19.0) | | 17.0 (7.0–29.0) | 12.0 (6.0–24.0) | |
| Costs, $ | | | .04 | | | .09 |
| No. | 25 | 30 | | 76 | 96 | |
| Mean (SD) | 56,026 (56,186) | 32,810 (34,947) | | 67793 (80421) | 52112 (74044) | |
| Median (IQR) | 31,782 (17325–88586) | 20501 (8252–39252) | | 39865 (19629–93429) | 25324 (10567–64323) | |
| Mortality, No. (%) | | | .96 | | | .36 |
| No. | 45 | 80 | | 186 | 289 | |
| Deaths, No. (%) | 15 (33.3) | 27 (33.8) | | 89 (47.8) | 126 (43.6) | |

Abbreviation: IQR, interquartile range.

*Greater than 2 days from admission.

†Reported *P* values are 2-tailed.