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Comparing central line-associated bloodstream infections caused by *Candida* to bacteria in hospitalized patients at two university hospitals

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Comparing central line-associated bloodstream infections caused by *Candida* to bacteria in hospitalized patients at two university hospitals

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An abstract submitted to the Faculty of the James T. Laney School of Graduate Studies of Emory University in partial fulfillment of requirements for the degree of Masters of Science in Clinical Research 2015

Abstract

Background:

While central line-associated blood stream infection (CLABSI) rates have decreased nationally, the proportion of CLABSIs due to *Candida* has increased. We sought to determine risk factors for CLABSI due to *Candida* when compared to bacteria, and assess the impact on mortality. We hypothesized that having multiple central lines were an independent risk factor for CLABSI due to *Candida*.

Methods:

Data on patients with CLABSI at two 500-bed hospitals from 12/1/2009 to 6/30/2011 were extracted from an existing database and a supplemental chart review was performed. Patients with neutropenia, lymphoma, or leukemia were excluded due to significant clinical differences in this group. Chi square, Fisher's exact test, and multiple logistic regression were used to determine the strengths of association of variables on CLABSI with *Candida* compared with bacteria. We examined the impact on 30 day mortality of CLABSI due to *Candida* compared to bacteria by performing a Kaplan-Meier curve and utilizing Cox proportional hazard models.

Results:

Univariate analysis revealed no significant difference in odds of having multiple central lines when comparing CLABSI due to *Candida* and bacteria, however, adjusted odds of multiple central lines was significant in multivariate analysis. Significant predictors in multivariate analysis include: Broad spectrum antibiotics (aOR 8.15 CI 3.11 - 21.37), pulmonary disease (aOR 4.71 CI 1.51 - 14 .66), non-tunneled dialysis catheters (aOR 3.60 CI 1.01 - 12.82), mechanical ventilation (aOR 2.90 CI 1.15 - 7.32), blood transfusion (aOR 2.70 CI 1.18 - 6.54), silver coated needleless connectors (aOR 2.65 CI 1.09 - 6.49), and TPN (aOR 2.47 CI 1.00 – 6.10). Thirty day mortality was higher for patients with CLABSI due to *Candida* but not significant when accounting for prior ICU stay.

Conclusions:

Multiple central lines may be more predictive of CLABSI due to bacteria rather than *Candida* spp. when accounting for other significant risk factors. Further studies examining the effect that antibiotic stewardship programs have on CLABSI due to *Candida* are warranted.

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INTRODUCTION

Central line-associated bloodstream infections (CLABSIs) are a significant cause of morbidity and mortality (1-3). CLABSIs are caused by two broad categories of organisms: yeast and bacteria. Nearly all yeast causing CLABSI are *Candida* spp. (4, 5). CLABSI rates have been steadily declining over the past fifteen years but *Candida* species have decreased at a lower rate than other bacteria spp. (6). Thus the proportion of CLABSI due to *Candida* spp. have increased and these organisms are now the second leading cause of CLABSIs in the United States (1).

Candida spp. bloodstream infections are associated with increased mortality, hospital length of stay, and patient expense (7, 8), and most are associated with central lines (9, 10). While risk factors for CLABSIs have been explored extensively, no study has compared CLABSIs due to *Candida* spp. to those caused by bacteria, nor directly assessed the impact of multiple central lines on CLABSI due to *Candida spp*.

We therefore seek to determine the magnitude of association of having multiple central lines on CLABSI with *Candida* spp. compared to bacteria. We also sought to discover other determinants of CLABSI when compared to bacteria with the hope of discovering potential interventions at lowering their rate and compared mortality among patients with CLABSI due to *Candida* spp. to bacteria.

BACKGROUND

In the inpatient setting it is estimated that one in 20 patients will have a healthcare-associated infection (HAI) (1). CLABSIs are associated with a mortality rate of 12-25%, among the highest of HAIs (11). CLABSI can be separated into two broad categories of organisms: yeast and bacteria (4). Nearly all CLABSIs caused by yeast can be attributed to *Candida* spp. with the most common being *Candida albicans* (5).

CLABSIs have consistently decreased over the past fifteen years, however, the proportion of CLABSIs caused by *Candida* spp. has increased from 11.8% in 2006-2007 to 14.6% in 2009-2010, making *Candida* spp. the second leading cause in the United States (1, 6). Approximately 56 to 87 percent of all episodes of bloodstream infections due to *Candida* spp. (also known as candidemia) are estimated to be CLABSIs (9, 10). Candidemia has been associated with a 10.1 day increase in hospital length of stay, approximately $39,000 increase in charges per patient, and a 14.5% increase in attributable mortality in adult patients (7). However, the harm of CLABSIs due to candidemia is not as well described. A case control study performed among pediatric patients from 2000 to 2010 found a threefold increase in mortality among patients with CLABSI due to *Candida* compared to uninfected controls (12). No study has compared mortality among patients with CLABSI due to *Candida* to those with bacteria.

Risk factors for candidemia include having a central line, antibiotic use, *Candida* infection at another site, total parenteral nutrition (TPN), blood product transfusion, pulmonary disease, cirrhosis, kidney disease, and shock (9, 13-16). A case to case study was performed comparing candidemia to bacteremia at a tertiary care medical center from 2002 and 2004 (17). Logistic regression revealed the following significant

predictors for candidemia when compared to bacteremia: ICU stay within 14 days of bloodstream infection (OR 6.24), receiving TPN (OR 4.69), history of pulmonary disease (OR 0.15), and history of cardiac disease (OR 0.21). The study size is relatively large for candidemia evens with 82 cases of candidemia and 82 cases of bacteremia. The study did not perform matching between candidemia and bacteremia cases and the study was not limited to patients with central lines. No mortality comparison was performed and the presence of multiple central lines was not assessed.

Concannon et al. have shown that multiple central lines are an independent risk factor for CLABSIs in hospitalized patients (18). They examined data from 197 cases and 201 controls between January 2008 and December 2010. Patients were identified as having more than one central line if at any time during admission more than one central line was present. Significant risk factors for CLABSI in univariate analysis included multiple central lines, TPN, hemodialysis, chemotherapy, ICU stay, hospital length of stay before event, days with a central line in place before event, and Apache II score. Multiple central lines remained an independent risk factor for CLABSI in multivariate analysis. Other studies have also shown an increase risk of CLABSI due to multiple central lines (19, 20). However, none of these studies have assessed the impact of multiple central lines on type of CLABSI (candidemia vs. bacteremia).

The majority of patients with multiple central lines are located in the ICU due to a combination of factors including need for monitoring of central venous pressure, monitoring right heart and pulmonary wedge pressure, hemodialysis, and need to rapidly, continuously and/or simultaneously infuse several medications, fluid volume, or blood products. Given that a higher proportion of patients with candidemia have been

previously admitted to an ICU it is possible that having multiple central lines increases the risk of CLABSI due to *Candida* to a greater extent than bacteria.

METHODS

We hypothesized that the increase in risk attributable to multiple central lines versus a single central line is greater for CLABSI due to *Candida* compared to bacteria among hospitalized patients. We have three specific aims:

1. Estimate the magnitude of association of having multiple central lines and CLABSI with *Candida* spp. compared to bacteria
2. Determine other predictors of CLABSI with *Candida* spp. compared to bacteria
3. Compare the difference in 30 day in-hospital mortality between CLABSI with *Candida* spp. and with bacteria

We performed a case to case analysis utilizing an existing database containing all patients at two 500 bed tertiary care medical centers in Atlanta from December 1st 2009 to June 30th 2011. This database includes 279 potential CLABSIs among 18,533 admissions attributed to 8,875 unique patients. This database includes date of birth, date of admission, date of discharge, sex, ethnicity, date of death (if applicable), facility, date of admission to ICU, date of discharge from ICU, CLABSI organisms, neutropenia on day of CLABSI, and central venous catheter attributes including: type, site, lumens, use of silver coated needleless connector, start date, and end date. CLABSIs were determined by the hospital epidemiologist using the standard surveillance definition.

CLABSI cases where cultures grew only *Candida* spp. were classified as *Candida* cases and cultures growing only bacterial spp. were classified as bacteria cases. We excluded CLABSI events where cultures were mixed, growing both *Candida* and bacteria. Subsequent CLABSI events during the same hospital admission or repeat admissions

were excluded. Patients having a history of lymphoma, leukemia, or neutropenia were also excluded as these patients were frequently taking concurrent prophylactic antifungals making their CLABSI more likely to be caused by bacteria.

Manual chart reviews were performed on all patients with CLABSI to obtain clinical data including date of abdominal surgery, and start and stop dates for mechanical ventilation, TPN, and dialysis. We also recorded the following comorbidities: rheumatologic disease, hypertension, congestive heart failure (CHF), atherosclerosis, myocardial infarction, peripheral vascular disease, diabetes mellitus, insulin use at home, end organ complications due to diabetes, chronic hepatitis, viral hepatitis, cirrhosis, portal hypertension, human immunodeficiency virus (HIV), AIDS status, cerebral vascular disease, hemiplegia, dementia, chronic obstructive pulmonary disease (COPD), asthma, pulmonary fibrosis, interstitial lung disease, bronchiectasis, bronchiolitis, pulmonary hypertension, end stage renal disease (ESRD), uremia, organ transplant, solid tumor, metastases, leukemia, lymphoma, and peptic ulcer disease. A Charlson Co-morbidity Index was calculated for each patient.

We obtained lab values during admission including serum creatinine, aspartate aminotransferase (AST), alanine aminotransferase (ALT), along with receipt of blood products including platelets and packed red blood cells, broad spectrum antibiotics, antifungals, and corticosteroids. Broad spectrum antibiotics included systemic 2nd, 3rd and 4th generation cephalosporins, anti-pseudomonal penicllins, carbapenems, intravenous polymixin E, and fluoroquinolones. Antifungals included systemic micafungin, amphotericin B, fluconazole, voriconazole, itraconazole, and posaconazole. Receipt of corticosteroids was counted if a systemic dose of a prednisone equivalent of 10mg or

higher within a 24 hour period. Corticosteroids included hydrocortisone, methylprednisolone, dexamethasone, and prednisone.

Central line types were separated into seven distinct categories: Peripherally inserted central catheter (PICC), tunneled PICC, multilumen (includes non-tunneled triple or quadruple lumen catheters), tunneled multilumen catheters, non-tunneled dialysis catheter, tunneled dialysis catheter, introducer, and port. We assessed for the presence of any of these central lines within seven days of CLABSI. We also created a category for any dialysis catheter or any tunneled catheter. Central line location was determined as arm, chest, femoral vein, internal jugular vein, subclavian vein, or hepatic vein.

We used chi square analysis or Fisher's exact test when appropriate comparing *Candida* CLABSI to bacteria for the following: sex, race, age, facility, days with a central line in place prior to event, hospital days prior to event, abdominal surgery within 30 days of event, cardiovascular disease, hepatic disease, pulmonary disease, kidney disease, diabetes, HIV, and organ transplant. We also assessed the following variables within seven days of CLABSI: multiple central lines, ICU stay, central line type, femoral line location, dialysis, mechanical ventilation, TPN, corticosteroids, broad spectrum antibiotics, antifungal medications, blood transfusion, silver coated needleless connectors. We created dichotomous variables for age (greater than 55), race (black versus white and other), hospital days (greater than 14), central line days (greater than 10), and Charlson Comorbidity Index (greater than 3). Multiple central lines was defined as having more than one central line present for at least one day within seven days prior to CLABSI. We specifically accounted for days where one central line was removed and another was

placed and this was not counted as having more than one central line unless an additional central line was present.

Since these central lines may have been in combination with other central line types we compared patients with a particular central line within seven days prior to CLABSI with those who did not have that type of central line. We also compared patients with at least one central line inserted in the femoral vein within seven days of CLABSI to those who did not have a central line inserted in the femoral vein.

Cardiovascular disease was defined as having any one of the following: hypertension, CHF, atherosclerosis, myocardial infarction, peripheral vascular disease, or heart transplant. Kidney disease was defined as having any one of the following: a serum creatinine ≥ 2, creatinine increase of at least twice the nadir value, dialysis requirement, or kidney transplant. Pulmonary disease was defined as having any one of the following: COPD, asthma, pulmonary fibrosis, interstitial lung disease, bronchiectasis, bronchiolitis, pulmonary hypertension, and lung transplant. Hepatic disease was defined as having viral hepatitis, other chronic hepatitis, cirrhosis, AST greater or equal to three times the upper limit of normal (120), or ALT greater or equal to three times the upper limit of normal (150), or liver transplant.

Multiple central lines and variables having a p value ≤ 0.1 in univariate analysis were included in our multiple logistic regression model. We used backwards selection to determine the final multivariate model. 30 day in-Hospital mortality was defined as death recorded while inpatient within a 30 day period after CLABSI event. We did not determine whether or not patients survived following discharge. 30 day mortality was compared between CLABSI due to *Candida* spp. and bacteria using a Kaplan-Meier

curve, censoring patients who were discharged prior to 30 days. We then used a Cox proportional hazard model to estimate the significance of CLABSI organism type on mortality accounting for either a Charlson Comorbidity Index > 3 or ICU stay seven days prior to CLABSI.

RESULTS

Among 279 cases initially classified as CLABSI, three did not meet CLABSI criteria after review (one patient had endocarditis and two had a central line in place for less than two days), 15 were subsequent events (five were subsequent admissions and 10 were subsequent events during the same admission), 10 were mixed infections with both *Candida* and bacteria, and 79 had either leukemia, lymphoma, or neutropenia on the day of CLABSI, this left 172 patients with CLABSI for our analysis (Figure 1). Among these 172 CLABSIs, 51 were due to *Candida* and 121 due to bacteria.

Median patient age and days with a central line in place (line-days) were similar for CLABSIs caused by *Candida* and bacteria, as were sex and proportion from each facility (Table 1). The median hospital length of stay for patients with *Candida* was 14 days compared to 11 days for bacteria. Charlson Comorbidity Index was similar with a median of 5 (IQR 3-7) for *Candida* and 6 (3-8) for bacteria. There was a slight imbalance in race with the majority of all subjects identifying as “Black”, however the majority of patients with *Candida* identified as “White”.

We compared black race to white and other excluding those patients whose race was unknown and this slight imbalance was not significant (Table 2). There was a significant difference in the proportion of pulmonary disease (OR 2.84) and kidney disease (OR 2.83). There was no significant difference in the presence of multiple central lines of CLABSI due to *Candida* and bacteria (Table 3). There was a significant difference in being in an ICU within seven days of CLABSI (OR 3.09), receiving TPN (OR 2.67), broad spectrum antibiotics (OR 8.78), mechanical ventilation (OR 4.79), use of silver coated needleless connectors (OR 2.47), and blood transfusion (OR 2.28).

Central line type was significant for tunneled dialysis catheter favoring bacteria (OR 0.11) (Table 4). Presence of a non-tunneled dialysis favored *Candida* though it was not significant (p = 0.07), the aggregate of both dialysis catheters was not significant (p = 0.84). The aggregate of all tunneled catheters favored bacteria and was significant (OR 0.22).

Chi square test of patients with multiple catheters versus those with a single catheter was performed to examine for possible imbalances in the exposure of interest. This was significant for hepatic disease, kidney disease, corticosteroids, mechanical ventilation, dialysis, and blood transfusion (Table 5). We then performed multivariate analysis with the following variables: Multiple catheters, pulmonary disease, kidney disease, ICU stay, TPN, broad spectrum antibiotics, mechanical ventilation, silver coated needleless connector, blood transfusion, non-tunneled dialysis catheter use, and tunneled dialysis catheter use. Using backwards selection the final model contained the following significant variables: multiple central lines (OR 0.28 and 95% CI 0.09 - 0.88), pulmonary disease (OR 4.71 CI 1.51 - 14.66), TPN (OR 2.47 CI 1.00 - 6.10), broad spectrum antibiotics (OR 8.15 CI 3.11 - 21.37), mechanical ventilation (OR 2.90 CI 1.15 - 7.32), silver coated needleless connector (OR 2.65 CI 1.09 - 6.49), blood transfusion (OR 2.70 CI 1.18 - 6.54), and non-tunneled dialysis catheter use (OR 3.60 CI 1.01 - 12.82) (Table 6).

Thirty day mortality was higher in CLABSI due to *Candida* spp. with 19 deaths (37%) compared to 23 (19%) for bacteria (OR 2.53 CI 1.22- 4.23 p = 0.01). The Kaplan-Meier curve assessing 30 day mortality visually demonstrated higher mortality for CLABSI due to *Candida* spp. compared to bacteria and the log-rank test was significant

(p= 0.02) (Figure 2). Cox proportional hazard model for 30 day mortality including Charlson Comorbidity Index > 3 in the model was significant (adjusted HR for *Candida* spp. 1.98 p = 0.03), but not when adjusting for ICU stay within 7 days of CLABSI the hazard ratio for *Candida* was no longer significant (HR 1.68, p 0.10) (Table 7).

DISCUSSION

TPN and mechanical ventilation are known risk factors CLABSI but in our study they were stronger predictors of *Candida* when compared to bacteria. TPN was also significant risk factor for bloodstream infection due to *Candida* when compared to bacteria in the case to case analysis performed by Amrutkar et al. (17). Pulmonary disease was strongly associated with bacteremia in that analysis, however in our study it is associated with CLABSI due to *Candida* species rather than bacteria. The reason for this change is not clear, however, our definition of pulmonary disease was broader whereas Amrutkar at al. only included COPD, asthma, and bronchitis.

Previous studies have shown that blood product transfusions increase the risk for CLABSI, nosocomial candidemia, and specifically CLABSI due to *Candida* when compared to uninfected controls (12, 14, 21, 22). We found an increased odds of CLABSI due to *Candida* spp. compared to bacteria. We believe this is the first time that this relationship has been shown in the literature.

Silver coated needleless connectors were used in both hospitals at different times during the study period. In vitro studies of silver nanoparticles used in the construction of the connectors have shown potent bactericidal and fungicidal activity (23-25). However, an in vitro analysis of the silver coated needleless connector product itself showed much stronger bactericidal activity than fungicidal activity (26). A separate analysis of a subset of CLABSIs from the same dataset was performed to assess the impact of silver coated needleless connectors compared to standard needleless connectors (27). This showed a decrease in CLABSI rates among the vast majority of bacteria, specifically gram negative bacteria, *S. aureus*, and *enterococcus* species, but there was not a significant change in

CLABSI rates due to *Candida* spp. Thus our finding that silver coated needleless connectors increase the odds of having a CLABSI due to *Candida* rather than bacteria may best be explained by a protective effect on the vast majority of bacteria and lack of protective effect on *Candida* spp. Another possible explanation for the lack of protection of silver coated needleless connectors against CLABSI due to *Candida* could be an increased proportion of extra-luminal infections compared to bacteria.

Broad spectrum antibiotic use was the single strongest predictor for *Candida* CLABSI compared to bacteria. Previous studies have shown that receipt of antibiotics increase the risk for candidemia (14, 16). While antibiotic use can have profound benefits, they can also cause harm. Examples of harm include infections from *Clostridium difficile,* multidrug-resistant bacteria, and yeast (28, 29). Antibiotic use in the United States is often unnecessary and national efforts are currently increasing the number of antibiotic stewardship programs in place at hospitals across the country (28).

Mortality due to bloodstream infections is significant (3).We have shown that 30 day in-hospital mortality is higher among patients with *Candida* when compared to bacteria, even when accounting for other comorbid conditions. However, it may be that patients with CLABSI due to *Candida* are more acutely ill. This is supported by presence in an ICU prior to CLABSI being a significant risk factor for CLABSI due to *Candida* in both our study and the case to case analysis performed by Amrutkar et al. When we accounted for ICU stay seven days prior to CLABSI the hazard ratio comparing 30 day mortality of CLABSI due to Candida to bacteria is no longer significant.

While we hypothesized that multiple central lines would increase the risk of CLABSI due to *Candida* spp. compared to bacteria, in multivariate analysis multiple

central lines were associated with bacteria relative to *Candida* spp. It is difficult to determine the nature of this finding since we did not compare our patients to negative controls. Since our study is a case to case analysis the OR we calculate in our study is in fact a ratio of the true OR for CLABSI due to *Candida* spp. and the true OR for CLABSI due to bacteria species. This true OR may be protective, harmful, or neutral. However, it does seem unlikely that multiple central lines would be protective for bacteria. Instead, it is more likely that multiple central lines increased the risk of CLABSI due to *Candida* spp. relative to bacteria when controlling for the other parameters in the multivariate analysis.

Our study has several limitations. These data from two academic institutions may not be generalizable to other settings. Our study is retrospective and therefore subject to unmeasured confounding and our exclusion criteria may have biased our results. Furthermore, the NHSN surveillance definition of CLABSI may not be specific allowing some bloodstream infections that are not due to central line to be misclassified as CLABSI when a central line is in place. Our sample size is modest but large compared to similar studies. Finally, we were not able to assess mortality of patients who were discharged from the hospital when assessing 30 day mortality.

Given our findings, future research to assess the impact of antibiotic stewardship programs have on CLABSI rates due to *Candida* should provide additional evidence of their benefit. Despite the poor anti-fungal performance of silver coated needleless connectors when compared to bacteria there is active research involving conjugating antifungals to silver nanoparticles. Incorporation of such a molecule into catheter connectors would be of significant interest (30).

Further studies are needed to understand the risks of having an increasing number of central lines. In particular, a case-case-control study would be ideal, but not within the scope of our current project. Such a study would add a third group of patients (controls) with a central line who did not develop a CLABSI. This should allow for further understanding of the magnitude of underlying odds ratios for each CLABSI type allowing for additional understanding of this important risk factor.

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TABLE 1:

Demographics and Comorbidity score comparing CLABSI due to *Candida* spp. to bacteria among hospitalized patients (N=172)

Variables	Candida N=51 Median (IQR)	Bacteria N=121 Median (IQR)	Total N=172 Median (IQR)
Age	57 (44-65)	58 (48-68)	58 (48-67)
Line-Days	9 (6-24)	10 (7-16)	10 (6-18)
Days to CLABSI	14 (8-25)	11 (7-19)	11 (7-21)
CCI	5 (3-7)	6 (3-8)	6 (3-8)
Categories	**N (%)**	**N (%)**	**N (%)**
Sex			
Male	29 (57)	57 (47)	86 (50)
Female	22 (43)	64 (53)	86 (50)
Facility			
1	29 (57)	63 (52)	92 (53)
2	22 (43)	58 (48)	80 (47)
Race			
Black	21 (41)	65 (54)	86 (50)
White	27 (53)	43 (36)	70 (41)
Other	1 (2)	6 (5)	7 (4)
Unknown	2 (4%)	6 (5)	8 (5)

CLABSI: Central line-associated bloodstream infection
CCI: Charlson Comorbidity Index
Facility 1: Emory University Hospital
Facility 2: Emory University Hospital Midtown

TABLE 2:

Univariate analysis of demographics and comorbidities comparing CLABSI due to *Candida* species to bacteria among hospitalized patients (N=172)

Demographics	Candidemia N=51 N (%)	Bacteremia N=121 N (%)	OR (95% CI)	p value
Male Sex	29 (57)	57 (47)	1.48 (0.77 - 2.86)	0.25
Facility 1	29 (57)	63 (52)	1.21 (0.63 - 2.35)	0.56
Age >55	29 (57)	68 (56)	1.03 (0.53 - 1.99)	0.94
Race = Black ‡	21 (43)	65 (57)	0.57 (0.29 - 1.11)	0.10
Comorbidities:				
CV Disease	32 (63)	85 (70)	0.71 (0.36 - 1.42)	0.30
Hepatic Disease	17 (33)	29 (24)	1.59 (0.77 - 3.25)	0.21
Pulmonary Disease	13 (25)	13 (11)	2.84 (1.21 - 6.67)	0.01
Kidney Disease	40 (78)	68 (56)	2.83 (1.33 - 6.05)	0.01
Diabetes Mellitus	14 (27)	43 (36)	0.69 (0.33 - 1.41)	0.30
HIV	4 (8)	4 (3)	2.49 (0.60 - 10.37)	0.24*
Organ Transplant	4 (8)	4 (3)	2.49 (0.60 - 10.37)	0.24*
CCI > 3	38 (75)	88 (73)	1.10 (0.52 - 2.31)	0.81

* Fisher's exact test utilized
‡ N=49 for *Candida* and 114 for bacteria
CLABSI: Central line-associated bloodstream infection
CV: Cardiovascular
HIV: Human immunodeficiency virus

TABLE 3:

Clinical characteristics comparing CLABSI due to *Candida* species to bacteria among hospitalized patients (N=172)

Characteristic	Candidemia N=51 N (%)	Bacteremia N=121 N (%)	OR (95% CI)	p value
Multiple Central Lines	17 (33)	36 (30)	1.18 (0.59 - 2.38)	0.64
ICU within 7 days	41 (80)	69 (57)	3.09 (1.42 - 6.74)	<0.01
TPN	25 (49)	32 (26)	2.67 (1.35 - 5.29)	<0.01
Abdominal Surgery	7 (14)	14 (12)	1.22 (0.46 - 3.22)	0.69
Corticosteroids	17 (33)	30 (25)	1.52 (0.74 - 3.10)	0.25
Antibiotics	42 (82)	42 (35)	8.78 (3.90 - 19.76)	<0.01
Antifungals	8 (16)	15 (12)	1.31 (0.52 - 3.33)	0.56
Mechanical Ventilator	37 (73)	43 (36)	4.79 (2.34 - 9.84)	<0.01
Dialysis	15 (29)	34 (28)	1.07 (0.52 - 2.19)	0.86
Silver Connector	28 (55)	40 (33)	2.47 (1.26 - 4.81)	0.01
Blood Transfusion	27 (53)	40 (33)	2.28 (1.17 - 4.44)	0.01
Line Days > 10	23 (45)	57 (47)	0.92 (0.45 - 1.74)	0.71
Time to Event > 14	24 (47)	43 (36)	1.61 (0.83 - 3.13)	0.16

CLABSI: Central line-associated bloodstream infection
ICU: Intensive care unit
TPN: Total parenteral nutrition

TABLE 4:

Central line characteristics comparing CLABSI due to *Candida* spp. to bacteria among hospitalized patients (N=172)

Characteristic	Candidemia N=51 N (%)	Bacteremia N=121 N (%)	OR (95% CI)	p value
PICC	22 (43)	38 (31)	1.66 (0.84 - 3.25)	0.14
Tunneled PICC	2 (4)	11 (9)	0.41 (0.09 - 1.91)	0.35
Multilumen	26 (51)	49 (40)	1.53 (0.79 - 2.95)	0.21
Tunneled Multilumen	1 (2)	0 (-)		
Non-tunneled Dialysis	13 (25)	17 (14)	2.10 (0.93 - 4.71)	0.07
Tunneled Dialysis	1 (2)	19 (16)	0.11 (0.01 - 0.83)	<0.01*
Introducer	3 (6)	12 (10)	0.57 (0.15 - 2.10)	0.39*
Port	3 (6)	17 (14)	0.38 (0.11 - 1.37)	0.19*
Femoral	11 (22)	15 (12)	1.94 (0.82 - 4.59)	0.13
Dialysis Catheter	14 (27)	35 (29)	0.93 (0.45 - 1.93)	0.84
Tunneled Catheter	3 (6)	27 (22)	0.22 (0.06 - 0.75)	0.01*

* Fisher's exact test utilized
CLABSI: Central line-associated bloodstream infection
PICC: Peripherally inserted central catheter

TABLE 5:

Demographics, comorbidities, and clinical characteristics comparing CLABSIs having multiple central lines seven days prior to event to those with a single central line (N=172)

Demographics	Multiple N=53 N (%)	One Catheter N=119 N (%)	p value
Male sex	31 (58)	55 (46)	0.14
Facility 1	25 (47)	67 (56)	0.27
Age >55	31 (58)	66 (55)	0.71
Race = Black ‡	24 (50)	62 (54)	0.65
Comorbidities			
Cardiovascular Disease	28 (53)	78 (66)	0.30
Hepatic Disease	24 (45)	22 18%	<0.01
Pulmonary Disease	9 (17)	17 (14)	0.65
Kidney Disease	40 (75)	68 (57)	0.02
Diabetes Mellitus	17 (32)	40 (34)	0.84
HIV	4 (8)	4 (3)	0.23*
Organ Transplant	3 (6)	5 (4)	0.67*
CCI > 3	42 (79)	84 (71)	0.24
Clinical Characteristics			
ICU within 7 days	46 (87)	64 (54)	<0.01
TPN	15 (28)	42 (35)	0.37
Abdominal Surgery	7 (13)	14 (12)	0.79
Corticosteroids	23 (43)	24 (20)	<0.01
Antibiotics	31 (58)	53 (45)	0.09
Antifungals	9 (17)	14 (12)	0.35
Mechanical Ventilation	35 (66)	45 (38)	<0.01
Dialysis	29 (55)	20 (17)	<0.01
Silver Connector	25 (47)	43 (36)	0.17
Blood Transfusion	30 (57)	37 (31)	<0.01
Line Days > 10	28 (53)	52 (44)	0.27
Time to Event > 14	22 (42%)	45 (38)	0.65

* Fisher's exact test utilized
‡ N=49 for *Candida* and 114 for bacteria
CLABSI: Central line-associated bloodstream infection
HIV: Human immunodeficiency virus
CCI: Charlson Comorbidity Index
ICU: Intensive care unit
TPN: Total parenteral nutrition

TABLE 6:

Association of multiple central lines with CLABSI due to *Candida* compared to bacteria among hospitalized patients adjusting for specified parameters (N=172)

Parameter	aOR (95% CI)	p value
Multiple Central Lines	0.28 (0.09 - 0.88)	0.03
Pulmonary Disease	4.71 (1.51 - 14.66)	0.01
TPN	2.47 (1.00 - 6.10)	<0.05
Antibiotics	8.15 (3.11 - 21.37)	<0.01
Mechanical Ventilation	2.90 (1.15 - 7.32)	0.02
Silver Connector	2.65 (1.09 - 6.49)	0.03
Blood Transfusion	2.70 (1.18 - 6.54)	0.025
Non-tunneled Dialysis	3.60 (1.01 - 12.82)	<0.05

CLABSI: Central line-associated bloodstream infection
TPN: Total parenteral nutrition

Multiple central lines was not significant in univariate analysis, however, when accounting for other parameters with univariate analysis p value <0.10 we found that the adjusted odds ratio for multiple central lines was significant at 0.28. We used backwards selection to determine the model, c = 0.87.

TABLE 7:

30 day mortality among CLABSI due to *Candida* versus bacteria, accounting for Charlson Comorbidity Index and ICU stay within seven days of CLABSI event (N=172)

Parameter	Hazard Ratio	p value
Model 1		
Candida	1.98	0.03
Model 2		
Candida	1.98	0.03
CCI > 3	3.26	0.02
Model 3		
Candida	1.68	0.10
ICU within 7 days	2.68	0.03

CCI: Charlson Comorbidity Index
ICU: Intensive care unit

We used three models to assess the impact of CLABSI type on 30 day mortality. Model 1 only examines CLABSI type. We added the Charlson Comorbidity Index (CCI) to model 2 as this a clinical predictor for mortality. Since ICU stay is associated with mortality and ICU stay within 7 days was associated with CLABSI due to *Candida* when compared to bacteria we added this predictor to model 3. While *Candida* remained a significant predictor for mortality when including CCI, it was not significant when including ICU stay within 7 days in the model.

FIGURE1:

Accounting for CLABSI events excluded from study:

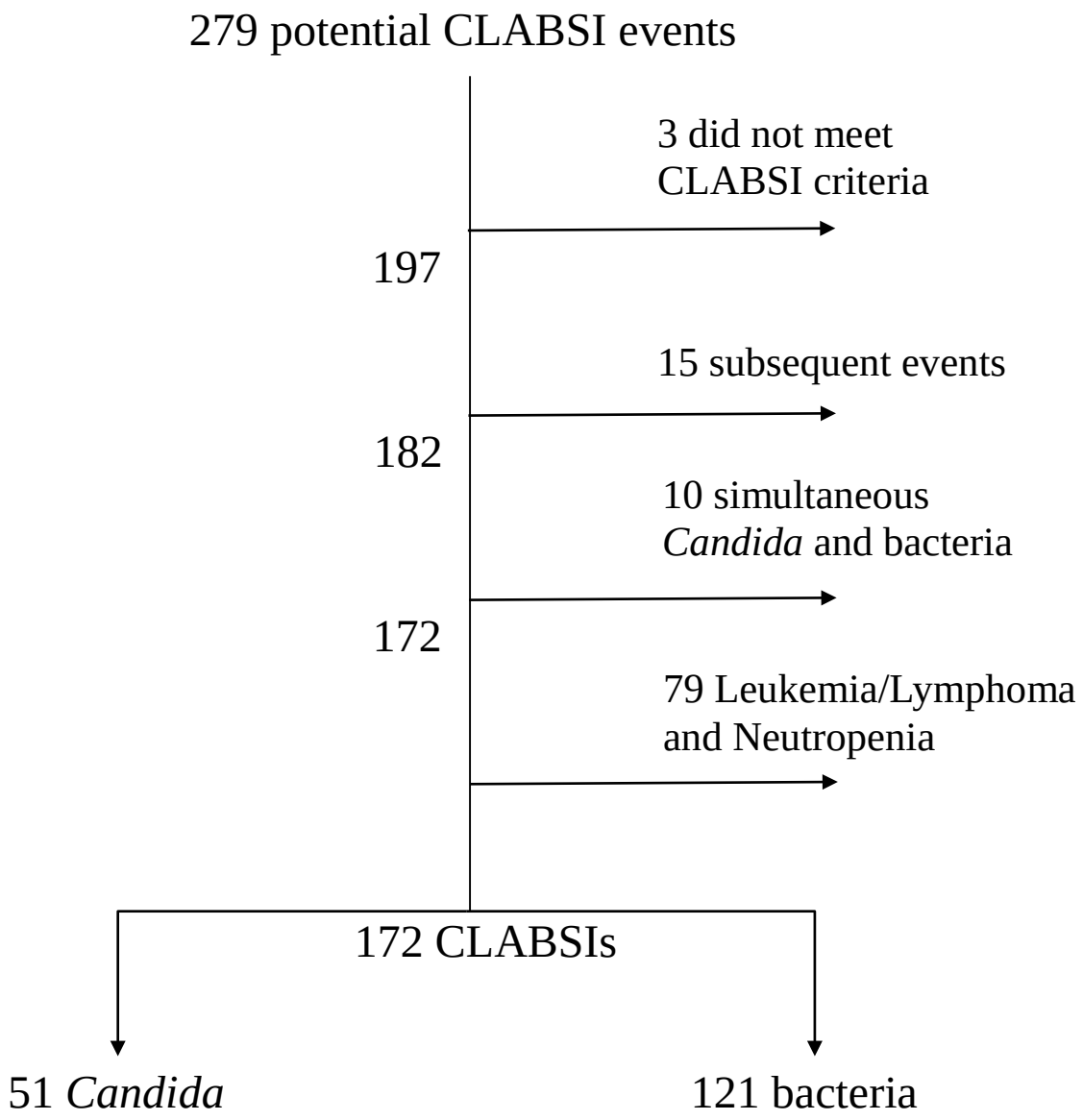

FIGURE 2:

Kaplan-Meier curve comparing 30 day mortality of CLABSI due to *Candida* and bacteria (N=172)