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The Relationship Between Time of Onset of Central Line-Associated Bloodstream Infections and Microbiology

By

William Lee Aurand

Degree to be awarded: Master of Public Health

Epidemiology

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The Relationship Between Time of Onset of Central Line-Associated Bloodstream Infections and Microbiology

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2012

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Abstract

The Relationship Between Time of Onset of Central Line-Associated Bloodstream Infections and Microbiology

By William Lee Aurand

Central lines are important in medical care for the infusion of fluids, medications, and hemodynamic monitoring, but can result in a central line-associated bloodstream infection (CLABSI). Prevention efforts have been effective at lowering the rates of CLABSI, but these insertion event focused changes may have a greater impact on skin-related organisms that cause infection at the time of infection. This study investigated if the time to onset of infection predicted the microbiology of CLABSI (skin organisms compared to organisms not commonly found on the skin).

Data from a previous prospective longitudinal study involving two university hospitals were analyzed. There were 106 CLABSIs due to one or more skin organisms (coagulase-negative staphylococcus, *Staphylococcus aureus*, or *Candida*) or due solely to non-skin organisms: gram-negative bacilli, *Enterococcus*, or other non-staphylococcal gram positive bacteria). The primary predictor, time of onset was dichotomized as early (≤7 days) and late (>7 days). Potential risk factors including sex, hospital, catheter type, subclavian vein insertion site, and infection attributable to the intensive care unit, ICU, were also investigated.

Subclavian vein insertion site was associated less with skin organisms than non-skin organisms (OR 0.25, 95% CI: 0.07, 0.91). Skin organisms were more associated with the hospital with the larger cancer and transplant population (OR 3.10, 95% CI: 1.27, 7.53). Skin organisms were not significantly associated with an early time to onset of infection (OR 1.10, 95% CI: 0.50, 2.44).

The subclavian vein site was found to have a lower OR of a CLABSI from a skin organism compared to other insertion sites, unsurprisingly as sites of the femoral and internal jugular vein have been associated with higher rates of overall CLABSI and tend to have more skin organism colonize at those locations. Early time to onset of infection was not found as a significant difference between the skin and non-skin organisms, possibly because overlap exists where skin organisms also may colonize the hub, leading to infections that are intraluminal and later time to onset.

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Introduction

Central line-associated bloodstream infections (CLABSI) are a cause of much of unnecessary morbidity in U.S. hospitals with an estimated 41,000 occurring annually (1). The infections are also one of the most deadly healthcare acquired infections with an attributed mortality rate of 12%-25% (2). CLABSIs also cause a serious financial burden with an estimated attributable cost of $45,814 (3). Much has been done to prevent CLABSIs which include increased educational awareness to providers, implementing systematic insertion compliance practices, and focusing on removing lines as soon as possible (2, 4-7). These prevention techniques seem to have been effective as CLABSIs in the intensive care unit (ICU) have decreased 58% from 2001-2009 (1). However, because of high mortality rates as well as the financial burden of CLABSIs, continued research is imperative.

CLABSIs occur via two major routes: extraluminally and intraluminally. Extraluminal infections occur when organisms present on the skin surface migrate along the catheter surface to gain access to the bloodstream (8). Intraluminal infections occur when there is a direct contamination of the catheter hub or any part of the fluid system, such as the infusate (8).

Multiple studies have matched organisms found in the blood with organisms found on the skin, hub, or lumen. These studies have found that extraluminal tend to be the dominant route of infection at earlier time intervals of 2.5, 7, and 3.8 days after line matched the organisms in the blood. In contrast, intraluminal tend to be the dominant route of infection at later time intervals at line insertion (9-11). These studies found that organisms attributed to the bloodstream infection more commonly matched those found on the lumen or hub.

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Therefore, it is reasonable to identify organisms that are attributable to CLABSI by where they are found and group them by skin versus non-skin organisms. Some of the common organisms that are responsible for CLABSIs are as follows: coagulase-negative staphylococci, *Staphylococcus aureus*, *Enterococcus* species, *Candida* species, and gram negative species. Those commonly found on the skin include coagulase-negative staphylococci, *S. aureus*, and less commonly *Candida* species (12). Coagulase negative staphylococci are found on the skin of all people, while *S. aureus* is found in nasal passages of adults with an estimate carriage of 20% to 40% and are shed to the skin from the nasal reservoir (12, 13). *Candida* species, or yeasts, are also found on the skin though less frequently (14, 15). In contrast, those organisms less likely to be present as normal skin flora are enterococci and gram negative organisms. Enterococci are commonly found in the intestine (16). Gram negative organisms are also uncommon in skin flora (14). These gram-negative organisms include *Klebsiella*, *Acinetobacter*, *Pseudomonas* and *Escherichia coli* (17).

What is not known is if a time cut-point differentiating early versus late duration from insertion of a central line to documented infection is associated with the organism group of a skin organism versus non-skin organism. Though this time point is not well delineated, from the prior research seven days is a reasonable cut-point. This study will also examine other potential risk factors for CLABSI: sex, insertion site, and infections attributable to the intensive care unit (ICU) (18-22). The study will examine if there is a difference in CLABSIs from organisms that are found commonly occurring on the skin by comparing the total line-days as earlier time to infection, seven days and less, versus later infection time, greater than seven days. It will also examine what other factors may

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be differential between infections from organisms commonly occurring on the skin compared to those that are not.

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Background

A central venous catheter, commonly known as a central line, is defined as an intravascular catheter that terminates at or close to the heart or in one of the great vessels (23). Central lines are used for infusion of fluids, blood products, medications, parenteral nutrition, withdrawal of blood, and/or hemodynamic monitoring (23). Certain types of central lines may be in kept in place for months. The longer the central line remains inserted in the patient, the greater the risk for infection (24).

The Centers for Disease Control and Prevention's (CDC) National Healthcare Safety Network, NHSN, defines a central-line associated bloodstream infection (CLABSI) as a bloodstream infection that develops in a patient with a central line in place for more than 48 hours that is not related to infection at another site (23). This definition is often used by hospitals in the United States for surveillance purposes.

A CLABSI is a form of healthcare acquired infection (HAI) referring to an infection acquired during the course of receiving healthcare treatment (23). An estimated 100,000 deaths per year are associated with HAIs in the US making them the sixth leading cause of death nationally (25). CLABSIs are the cause of much of this mortality, with an attributable mortality rate of 12%–25% (2). Unfortunately, CLABSIs are also moderately common with 41,000 occurring in U.S. hospitals each year (1). This estimate is derived from the CDC multiplying patient-day estimates by central line utilization ratios to estimate the total number of central line-days nationally in each hospital setting (1).

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CLABSIs also cause a serious financial burden with an estimated attributable cost of $45,814 (3). Government programs via the Centers for Medicare & Medicaid Services (CMS) has stated that for discharges occurring on or after October 1, 2008, hospitals will not receive additional payment for cases in which one of the selected conditions was not present on admission and the hospital will have to absorb the cost of caring for the complication (26). CMS has also stated that beginning in January 2011, all hospitals paid under the inpatient prospective payment system, PPS, must submit information on the CLABSI measure or they will lose two percent of the calculated reimbursement 2013 (27). These financial burdens are additional incentives to have continued quality improvements to decrease CLABSI rates to the irreducible minimum.

Prevention Strategies

Because of clinical and financial consequences of CLABSIs along with increasing public demand to reduce HAIs, there are a many national CLABSI prevention efforts. The main strategies for preventing CLABSI include: patient and healthcare worker education, proper hand hygiene, only placing a catheter when necessary, optimize central line insertion practices by use of the central line insertion bundle, insertion as an aseptic procedure by cleaning the area with 2% chlorhexidine gluconate in 70% isopropyl alcohol, uses devices designed to minimize infection risk, and remove catheters as soon as they are no longer needed (4). An intervention designed to decrease CLABSI was found in the following prospective cohort study of 108 intensive care units, ICUs, in hospitals throughout Michigan (5). The ICUs had two strategies for infection prevention. They attempted to improve clinician communication as well as implementing patient-safety interventions. The strategies were compared against controls to assess their

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effectiveness on reducing the rate of CLABSI between March 2004 and September 2005 (5). The patient-safety intervention included educating providers to increase infection awareness, creating a central line insertion cart which kept all the supplies necessary in one sterile area, implementing the habit of asking daily if a central line may be removed, keeping a checklist of guidelines to record compliance with safety measures against infection, and allowing a staff member to have the power to call a stoppage to the insertion if the guidelines were not being followed (6). The median rate of bloodstream infections decreased from 2.7 per 1000 catheter days to 0.0 per 1000 catheter days, 16-18 months after implementation in the ICUs (5). Another study wanted to validate the generalizability of the effect of an educational intervention on CLABSI rates by implementing them in ICUs of six academic medical centers (7). The first element the intervention was to confirm and establish that a standard hospital policy consistent with CDC guidelines (2, 7). The second element involved educating staff with the primary messages being the subclavian vein is the preferred insertion site, sterile barrier precautions should be practiced when inserting catheters, catheter insertion site dressings should be monitored and kept clean, and date all catheter dressings so they are changed on schedule (7). The baseline infection rates were collected for five to seven months prior to the intervention and rates continued to be collected 15 to 18 months after the intervention began in each unit (7). The results found that there was an overall decrease in bloodstream infection rates with a relative rate of 0.79 (95% CI: 0.67 - 0.93) pre-intervention compared to post-intervention (7). It appears that an increase in clinical communication and emphasis on CLABSI as well as bundling prevention techniques

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such as chlorhexidine rinses and decreasing dwell times for the catheter can have a reduction in the infection rates.

These prevention techniques appear to be making a difference on incidence of CLABSI. Pooled data of CLABSIs from NNIS and NHSN has found a 58% reduction in CLABSIs in the ICU between 2001-2009, 43,000 to 18,000 (1). In addition, the NHSN data in 2011, found 41% fewer CLABSIs were reported to NHSN than what was predicted (28).

While the incidence rates of these infections have declined, it is imperative to continue research of CLABSI prevention because of the associated morbidity and financial burden. Incidence of CLABSIs from common organisms attributable to infection have been found to be decreasing individually as well, though at different rates (29). The results suggest that the prevention efforts may be more effective at preventing CLABSIs attributable to some organisms than others (29). Because of this finding, this current study is vitally important as it would be the first to give insight into the organisms of infection in by relation to their time of onset. Enhancing the knowledge of how organisms differ by time of onset will benefit the understanding of how prevention efforts may be improved.

Infection Routes and Causes

Central lines can become contaminated with microorganisms and cause bloodstream infections via two major routes: extraluminal and intraluminal. In the extraluminal route, organisms present on the skin surface migrate along the catheter surface to gain access to the bloodstream (8). The contamination of the surface typically occur at time a of catheter insertion and these infections tend to occur in a short amount

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of time after a catheter is placed (24). Intraluminal infection occurs when the catheter hub or any part of the fluid system, such as the infusate, becomes contaminated, often at the time the catheter is used (8, 24). This type of infection tends to be more common in catheters that have been in place for a longer period of time (24).

Data supporting the claim early infections occur through the extraluminal route and later infections from the intraluminal route are limited. Studies attributing infections to organisms either found on the skin, hub, or lumen do so by laboratory typing the organism found in the blood and matching it to organisms that where collected from cultures at these sites. If the organism found in the blood was matched to the organism found at one of these selected sites than it was counted as the organism attributed to the bloodstream infection. One study of ICU patients found that the patient's skin was the dominant infection source, 80% of infections, for catheters in place from 0.4-8.3 days with an average of 2.5 days (30). Another study investigated adult patients at three hospitals who had catheters placed and found an average of seven line-days until infection (31). The researchers found that all six of their catheter related infections were from contamination of the skin while only two were also from the hub (31). Yet another study used data from two randomized trials to study the pathogenesis of CLABSIs in short term catheters (32). The average duration of line placement to infection was 3.8 days; 45% of the infections were considered extraluminal while only 26% were considered intraluminal (32).

In contrast, a study identifying catheter-related sepsis in patients receiving total parenteral nutrition catheters that were in place for an average of 22 days, 14 of 20 cases of infection were related to the hub, while only two were related to the skin (9). Another

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study which had an average of 26.4 catheter days per line found that all 12 of the infected catheters were from colonization on the lumen (10). Of these 12 infected catheters, four were also infected from the organism that matched the organism recovered on the skin (10). One study quantified 10 days as the cutoff point where infections are defined as early versus late (33). As the previous studies highlighted, there is some overlap in early versus late infections. This relationship is made more complicated because skin organisms have been found to contaminate the hub and may lead to a longer time of onset for the infection. Since is not well known what is considered earlier time versus later time from line insertion to infection, the study used the cut-point of seven days. Earlier time was considered to be zero to seven days after line insertion while eight days and longer represented a later time to infection.

Microbiology

It is important to understand the environmental niche of where the organisms causing CLABSI are found, including colonization on skin, to put the question of which organism groups may be responsible for early or late infections into context. A list of organisms that are responsible for CLABSIs includes coagulase-negative staphylococci, *Staphylococcus aureus*, *Enterococcus* species, *Candida* species, and gram negative bacteria. Of these listed, coagulase-negative staphylococci and *S. aureus* account for 20.5% and 12.3% of reported CLABSIs in the NHSN data from 2009-2010 (34). *Enterococcus* and *Candida* species were also commonly attributed with 18.1% and 14.6% of infections (34). Gram-negative organisms were responsible for approximately 25% of infections (34).

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As previously stated, skin organisms are more likely to be responsible for extraluminal, early line infections. Of the organisms that commonly cause CLABSIs, the ones that commonly are found on the skin include coagulase-negative staphylococci, *S. aureus*, and less commonly *Candida* species (12). Coagulase negative staphylococci are found on the skin of all people (14) while *S. aureus* is found in nasal passages of adults with an estimate carriage of 20% to 40% and are shed to the skin from the nasal reservoir (12, 13). *Candida* species, or yeasts, are also found on the skin though less common (14, 15). *Candida* species are more likely on the skin in patients who have been receiving antibiotics, which includes many hospitalized patients.

In contrast, those organisms responsible for later infections may be less likely to be skin organism, however, the extent to which catheter hub is colonized from skin organisms is unclear. Enterococci are commonly found in the intestine (16). Gram negative species are also uncommon in skin flora (14). Gram-negative organisms include *Klebsiella*, *Acinetobacter*, *Pseudomonas* and *Escherichia coli* (17). Comparing organisms commonly found on the skin versus those that are not will serve as way to determine if these groups are associated with the time that the CLABSI occurred after insertion of the line.

Risk factors for CLABSI

Risk factor analysis has been done on CLABSI and is important when determining what effects covariates may have on the predictor and outcome. A risk factor that has been found in studies involves insertion site of the line. One study investigated insertion site by randomly assigning catheters for ICU patients at either the subclavian or the femoral site (21). The results were that infections were recorded in 19.8% of the

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femoral catheters while only 4.5% of the subclavian inserted catheters recorded infections (21). This would imply that there is a greater risk of infection when using a femoral rather than a subclavian catheter. Another study of a single university hospital examined 93 SICU patients who had catheters inserted (22). After multivariate analysis, internal jugular catheter insertion had an increased odds ratio of 1.83 compared to subclavian catheter insertion (22). Male sex has been shown as a factor associated with increased risk of CLABSI. One study which tracked data of 50 hospital ICUs, found that there was a two-thirds increase risk in developing a CLABSI simply by being male as compared to female (18). Another study also investigated sex in a SICU and found that male sex had an increased odds ratio of 1.93 (19). Another study that has concluded similar findings to this involved a single tertiary hospital system in which there was a hazard ratio of 2.54 for male sex for all patients (20). This same study also found that there was an increased hazard ratio for the patients in the ICU (20). The study collecting data from 50 hospital ICUs also found that there was a decreased risk for patients who had their central line placed outside of the ICU compared to those who had their central line placed while inside the ICU (18). These studies will help dictate biological plausibility when considering variables for multivariate analysis.

The influence of these risk factors for CLABSI will be considered when exploring the relationship between organism type and time of infection in addition to examining other factors with regard to organism type. The above information does not clearly delineate whether or not the organism group attributed to the infection is associated with a defined time period early versus late. Prevention efforts may reduce infections, but be less effective at certain organisms depending on the focus of the intervention strategy.

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Gaining an understanding about this relationship may allow for better assessment of the effectiveness of prevention activities. These factors shape the background and support for the importance of continued research on central line associated bloodstream infections. This study will examine if central line-associated bloodstream infections from organism commonly found on the skin are differential from infections not from organisms commonly found on the skin by earlier infection time versus later infection time CLABSIs as well as what other factors may be differential.

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Methods

This study will investigate the null hypothesis that there is no difference in the relative proportion of CLABSIs attributed to organisms commonly found on the skin comparing infections occurring early (≤7 days) versus late (>7 days) after line insertion. It will also assess what other measured factors may be different in the CLABSIs attributed to organisms commonly found on the skin compared to those attributed to organisms not considered skin organisms. Data previously obtained for a national prospective longitudinal study that compared a silver-coated needleless connector (V-link, Baxter Healthcare) to the standard needleless connector (Clearlink, Baxter Healthcare) will be reviewed for the analysis (35). This previous trial examined whether the silver catheter device lowered rates of CLABSI. The population included patients who were recruited from two university owned hospitals, hospital A and hospital B, in Atlanta, Georgia from the time period November 2009 to August 2011. A CLABSI was defined using the standard NHSN definition (36).

Inclusion/exclusion criteria

All adults admitted to the two hospitals and had a CLABSI, using NHSN definitions, were included (36). Among polymicrobial CLABSIs, only those with either only skin organisms or only non-skin organisms were included. Patients with neutropenic fever, with multiple lines attributed to infection, who had a line inserted prior to admission, and with infections related to dialysis catheters were excluded. Neutropenia was defined as an absolute neutrophil count ≤500 cells/mm^3 on the day blood cultures were collected for patients who had received cytotoxic chemotherapy (36).

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All variables for the study were obtained from electronic record abstraction. The existing study and subsequent analyses were approved by the Emory University Institutional Review Board.

Outcome

The outcome was CLABSI by type of organism (skin bacteria versus non-skin bacteria). This classification was based on typical microbiology. Skin bacteria include coagulase-negative staphylococci (CNS), methicillin susceptible *S. aureus* (MSSA), methicillin resistant *S. aureus* (MRSA), and *Candida* spp. (yeast), while non-skin bacteria include enterococci and gram negative organisms. To confirm the assumption that this grouping was valid, a test for homogeneity was done. A bivariate analysis performed comparing each of the individual skin organisms showed that all were statistically similar by all the predictor covariates; using the chi-squared test, or Fisher's test where appropriate, no significant differences were found.

The primary predictor was time to onset of CLABSI, defined as the period from central line insertion to CLABSI. Covariates included age, sex, ethnicity, facility, central line insertion site, catheter type, needleless connector, and location as ICU at the time of CLABSI. The distribution of time of onset of CLABSI by organism was explored, and then dichotomized into early (≤7 days) versus late (>7 days). Age was measured as a continuous variable. The five categories of central line insertion site (arm, chest, femoral vein, internal jugular vein, and subclavian vein) were dichotomized into subclavian vein versus non-subclavian vein for analysis. Catheter type was separated into five categories: central line, implanted port, introducer/pulmonary artery catheter, non-tunneled peripherally inserted central catheter (PICC), and tunneled central lines/tunneled PICCs.

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The infection was assigned to the ICU location if the infection date was ≥48 hours after ICU admission, or ≤48 hours after ICU discharge.

Statistical Analysis

All statistical analysis was completed using SAS® 9.3 (Cary, NC). A univariate analysis assessed if primary predictor (time of onset to CLABSI) and the other covariates were associated with the outcome variable. Categorical variables were assessed with a chi-squared test or Fisher's test as appropriate. A two sample t-test was used for the single continuous variable, age. A chi-squared test of homogeneity was performed comparing each skin organism to confirm that the skin organisms could be grouped together. The skin organisms were also compared to the referent group of the organisms not commonly found on the skin using a chi-squared test or Fisher's test where appropriate to investigate if any of the skin organisms were different individually from the non-skin organism group by the covariates. The logistic regression assessed crude associations of the skin organisms individually and grouped together for each predictor variables to investigate if any predictor was associated with a single organism and if any predictor was associated with the main outcome of the skin organism group. Exposure variables that were statistically significant crude associations with the outcome, $P<0.05$, by bivariate logistic analysis were examined further using multivariate analysis. The frequency procedure was used to examine for significant differences between the found exposure and all the other predictor variables to determine if any predictors may be effect modifiers of the significant exposure, and thus should be included in the model for possible adjustment. Predictor variables that were statistically significant, $P<0.05$, for the frequency procedure using chi-squared test, Fisher's test, or t-test were included in the

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model for multivariate analysis. In addition, the variables sex, insertion site, needleless connector, catheter type, ICU attributed infections, and facility were *a priori* included in the multivariate analysis because of biological plausibility or because of the dataset being used. The genmod procedure with collinearity option assessed collinearity of all exposure and covariate product terms. High condition indices were defined as those over 30 and variance decomposition proportions of greater than 0.50. To determine the final model, interaction and confounding were examined using the logistic procedure. A chunk test with alpha of 0.05 was used to initially identify interaction followed by backwards elimination to check all interaction terms. The logistic procedure was run with all possible subsets examining models for confounding with the change in estimate approach, using 10% change in the odds ratio (OR) to find the most parsimonious model. The final model was determined by adding biologically plausible covariates and considering precision enhancements to the OR.

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Results

A total of 174 lines resulted in a CLABSI. Among these, 68 were excluded from analysis because the infected patient presented with neutropenia, there were multiple lines which were attributed to infection, and/or the patient had a line inserted prior to admission. This left 106 central lines used for analysis. Out of the study population for analysis, 30.2% of the patients died. The overall average time of onset to CLABSI was 12.2 days, with the skin organisms' average at 11.9 days and the non-skin organisms' average at 12.7 days (Figure 1). The average interval was lowest for infections due to *S. aureus* (7.2 days) (Figure 1). There was a large variation in the number of days within each organism group and the values were not normally distributed (Figure 1). Using, the seven day dichotomous cut-point to separate early versus late time of onset to CLABSI, 38 (35.8%) cases were early and 68 (64.2%) late (Table 1a). There was no significant difference between each skin organism: coagulase-negative staphylococcus, S. *aureus*, and *Candida*, versus the non-skin organism group with regard to time of onset to CLABSI: $P = 0.99$, $P = 0.33$, $P = 0.97$ respectively (Table 1b). None of the other explanatory variables differed by the comparison between a single skin organism and the non-skin organism group, $P>0.05$ (Table 1b). Chi-square test for homogeneity found that the skin organisms did not significantly differ from each other with respect to each explanatory variable, $P>0.05$. For that reason the skin organisms were grouped in addition to examining each on its own for the crude association analysis.

Odds ratios (OR) of the crude association of the grouped skin organisms versus the non-skin organism group, along with comparisons for each skin organism vs. the non-skin organism group, were compiled for each explanatory variable (Table 2a). It was

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found that the proportion of early versus late time of onset of CLABSI was not statistically significant for any of the organisms, differentiating early versus late at 7 days (Table 2a). This also was true for the comparison of the pooled skin organism group with the non-skin organism group, OR 1.10, 95% Confidence Interval (CI): 0.50, 2.44 (Table 2b). There was a significant difference in the skin versus non-skin organism groups by facility; CLABSI attributed to skin organisms were more frequently associated than CLABSI attributed to non-skin organisms when admitted to hospital A (OR 2.28, 95% CI: 1.01, 5.16) (Table 2b). In addition, skin organisms were less frequently associated with CLABSI than non-skin organisms when the catheter was inserted in the subclavian vein (OR 0.33, 95% CI: 0.11, 0.94) (Table 2b).

Differences in distribution of other variables was examined for Hospital A compared to Hospital B to examine if any might affect the crude association found between the hospital variable and the skin organism group. Study patients in Hospital B were older than those in Hospital A, 63.4 years compared to 53.5 years ($P<0.05$) (Table 3a). No statistically significant difference was found for the other variables examined. Likewise, insertion site of subclavian vein was compared to other insertion sites (not in the subclavian vein) for the other study variables. A significant difference, $P<0.05$, was found for the explanatory variables of ethnicity and catheter type (Table 3b). There was also a significantly greater amount of subclavian line placements in the ICU attributed infection group versus the non-subclavian line placements (Table 3b).

Potential interaction of variables was explored using multivariate logistic regression with facility as a predictor for skin vs. non-skin organism groups. The biologically plausible variables of sex, insertion site, catheter type, needleless connector,

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and infection attributable to the ICU were also added. No significant collinearity was found. No significant effect of interaction was found for all two term exposure, facility, and covariate terms. The needleless connector was found to be a confounder with regard to facility, using the 10% change in estimate approach from the fully adjusted model, and thus was adjusted for in the model. The most parsimonious model was determined by including the primary predictor, facility, another significant covariate of insertion site, and the confounder of needleless connector. The final model was constructed by including the variables from the most parsimonious model followed by examining possible subsets with the other biologically plausible variables: sex, catheter type, and infection attributable to the ICU. The final model was determined by which subset created an OR of facility near the fully adjusted OR, within at least 10%, and presented a gain in precision of the confidence interval. Adjusted models showed significant increase in the odds of an infection from a skin organism compared to infection from a non-skin organism in Hospital A compared to the odds of an infection from a skin organism relative to infection from a non-skin organism in Hospital B (Table 4a). The final model OR 3.10 (95% CI: 1.27, 7.53) took into account adjustment for sex, insertion site, needleless connector, and infection attributable to the ICU (Table 4a). This adjusted OR estimate, OR 3.10 (95% CI: 1.27, 7.53), was greater than the crude OR estimate, OR 2.28 (95% CI: 1.01, 5.16), but not significantly. The models also produced an inverse association between insertion site of the subclavian vein with infection from a skin organism, with an OR of 0.27 (Table 4a).

Insertion Site as a predictor for skin vs. non-skin groups was investigated by multivariate logistic regression analysis. The biologically plausible variables of sex and

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needleless connector were also added to the model. No significant collinearity was found between the covariates. No significant effect modification from interaction was found for the two-term exposure, insertion site, and covariate terms. The variables of ethnicity and catheter type were found to be confounders of insertion site, using the 10% change in estimate approach from the fully adjusted model, and were adjusted for in the model. The most parsimonious model was determined by including the primary predictor, insertion site and the confounders of ethnicity and catheter type. The final model was constructed by including the variables from the most parsimonious model followed by examining possible subsets with the other biologically plausible variables: sex, needleless connector, and infection attributable to the ICU. The final model was determined by which subset created an OR of insertion site near the fully adjusted OR, within at least 10%, and presented a gain in precision of the confidence interval. Adjusted models showed a significant inverse association in the odds of a skin organism infection compared to an infection from non-skin organism from an insertion site being subclavian compared to those that were placed elsewhere (Table 4b). The final model which took into account for adjustment with sex, ethnicity, and catheter type gave an OR of 0.25 (95% CI: 0.07, 0.91) (Table 4b). This estimate of the OR was similar to the crude OR found for insertion site.

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Discussion

Skin organisms (coagulase-negative staphylococci, *S. aureus*, and *Candida*) both separately and pooled together, were found to be not statistically significant more frequently associated with early versus late CLABSI using seven days as the cut-point. There was a significant difference in the odds of the grouped skin organisms compared to the non-skin organism group attributable to infection at hospital A compared to B. Specifically, the OR comparing hospital A to Hospital B of an infection from a skin organism than non-skin organisms. Skin organisms were more frequently the organism attributed to CLABSI than non-skin organisms for hospital A compared with hospital B. Lastly, there was a decreased OR for skin organism attributable to the CLABSI if the insertion site was the subclavian vein compared with the line not being in the subclavian vein. Thus skin organisms were less frequently the organism group attributed to infection when the line was inserted in subclavian vein than when the line was inserted in another site.

While skin organisms are more commonly attributed to infections that are extraluminal infections, and extraluminal infections are thought to occur earlier, the route of infection by time from insertion to infection is not well determined. It is believed that skin organisms may be more common to extraluminal infections because those are typically related to contamination at the insertion site where skin organisms are more likely to be present. Using seven days as the cut-point was a reasonable hypothesis from the prior literature. The hypothesis was further supported by the fact that *S. aureus*, one of the organisms found commonly on the skin, was found to have an average of 7.2 days from insertion to infection. However, this was not found in the study, as there was no

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significant difference when examining each skin organism on its own or when pooling them together. As it appears that this is the first study that has investigated for an association of infections attributed to organisms commonly found on the skin by early versus late line-days, it cannot be compared with other literature. The distribution of organisms displays that some overlap exists between infections from skin organisms and infections from non-skin organisms and that some skin organism infections occurred at a later time of onset. One of the reasons why this might have occurred is that skin organisms may contaminate hubs and be associated with late infections occurring through the intraluminal route. A retrospective review of 12 cases of the central lines catheter-related sepsis in a British hospital determined that while all the cases had infections from organisms colonized at the hub there were also four with organisms colonized on the skin (10). Future analyses should look at what time intervals, if any, can differentiate CLABSIs associated with skin organisms from those associated with non-skin organisms.

Infections due to skin organisms were more frequent in hospital A and the odds increased after adjustment (Table 4a) signifying that an unmeasured effect is playing a role in the association. It is unknown what differences between the hospitals would lead to this difference in odds of infection from skin organisms. Further studies will be important to examine what other differences in hospital A contributed to the increased odds of CLABSIs from skin organisms compared to non-skin organisms. These may include the providers responsible for insertion or the setting where insertions are occurring.

The finding that lines placed in the subclavian vein had a lower OR of infections from skin organisms was not unexpected. Insertion site at the subclavian vein has been

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seen as a lower rate for overall infections in other studies. A retrospective review of 232 inserted central lines at a single surgical intensive care unit found that of the 78 cases where an infection occurred, insertion into the subclavian vein had a significantly lower rate compared to those inserted into internal jugular vein, adjusting for catheter use, hospital unit where it was placed, and if the line was a new, guidewire, or replacement type (22). This was also seen in an eight intensive care unit clinical trial where 293 patients were randomized to have either a central lines catheter placed in the femoral vein site or the subclavian vein site (21). Of the 270 patients who were followed up with to examine infection rate differences, it was found that insertion at the femoral site had a hazard ratio of 4.83 (95% CI: 1.96, 11.93) compared to insertion at the subclavian site (21). The subclavian site has also been found to have lower rates of skin colonization compared to other sites. A multi-center randomized clinical trial by Moretti et. al, found that the risk of colonization was significantly lower for subclavian vein inserted catheters compared to internal jugular vein catheters 0.45 (95% CI: 0.29, 0.70) (37). This gives support to what was observed in this study that infections from skin organisms would also be lower at the subclavian vein.

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Strengths and Limitations

The strengths of this current study include a relatively large sample size of CLABSIs. The CLABSIs were identified by a single epidemiologist so a consistent classifying definition of the infection and organism attributed to the infection was being used. While many covariates that would be considered biologically plausible for association with organisms commonly found on the skin were ascertained, there were others that could not be recorded and thus are limitations of the study. These limitations include patient comorbidities, the provider type of the inserter, the hospital location where the line insertion was performed, and details on central line management. Hemodialysis catheters were not included because the dataset was adapted from a study that excluded them. The NHSN CLABSI definition is overly sensitive particularly in patients with chemotherapy induced neutropenia (36). This study excluded patients with neutropenia but the lack of specificity of the NHSN definition may have contributed to the negative study results. One final limitation is that the study did not have skin or hub cultures allowing comparison with the blood isolate and to better pinpoint the source of the organism causing CLABSI.

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Future Directions and Public Health Importance

Investigating other potential factors that could influence the timing of onset to infection and microbiology of CLABSIs could help prevention efforts by determining other modifiable risk factors. These include obesity and problems that result in poor circulation, which may lead to challenging central line insertions and potentially an increased number of insertion attempts and trauma to the skin (38). Similarly, the training of the operator may be important. Internal medicine trained clinicians typically place central lines in the internal jugular using ultrasound (39). In contrast, surgically trained clinicians prefer to insert central lines into the subclavian vein which may require more skill, but is associated with lower rates of infection (39). Radiology trained clinicians have X-ray fluoroscopy to image the insertion of a central line (40). The experience level of the operator and the physical setting of the line insertion (ICU, ward, or emergency department) may also play a role. These two factors have been investigated in other studies for their influence on infection rates and would be important to study further (18). The ICUs with a higher proportion of operators who physicians in training there was an increased rate of CLABSI (18). The study also found insertions that took place outside of the ICU had a lower rate of CLABSI (1818).

The differences between hospitals are also worth exploring, and may be due to unmeasured confounders including the ones discussed above. Another potential line of inquiry is to assess the association of skin organisms and insertion site by sex, comparing the subclavian vein and the internal jugular vein. Sex has been found to have a differential rate of overall CLABSI, and one explanation is that the growth of facial hair on men may lead to greater colonization of the site where the line has been placed, or

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decreased adherence of the occlusive central line dressing, leading to an increased risk of CLABSI.

CMS's action to stop payment for some CLABSIs as well as public reporting have increased pressure on hospitals to decrease CLABSIs. Much progress has been made in the reduction of CLABSI, but the high mortality rates of CLABSI and HAIs in general mean that further prevention efforts are needed. Patients who enter a hospital should not have to have to worry about the threat of acquiring an infection because of their hospital stay. Central lines are and will continue to be a necessary tool for administering care in the hospital, so it is vital to understand what factors influence CLABSIs.

In conclusion, this study found that CLABSIs attributable to skin organisms had a similar distribution by time from central line insertion to infection compared to CLABSIs attributable to non-skin organisms. These study data do not support the hypothesis that skin organisms are more likely to cause infections early after line insertion. These findings may reflect contamination of the catheter hub and needleless connector by skin organisms leading to late onset infections caused by skin organisms. To clarify this origin of the organisms causing CLABSI, it would be necessary to compare the blood isolates to organisms cultured on the catheter hub and skin to attempt to identify the source of the organism of CLABSI. However, this could be done only in a prospective study, and because most lines do not become infected, such studies contain a small sample of CLABSIs. Despite and would be challenging to perform in a study of this size. Despite the failure to reject the null hypothesis, this study has provided further knowledge about the pathogenesis and microbiology of CLABSIs.

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Tables

Table 1a: Demographic and Clinical Characteristics of all Analyzed Central Line-Associated Bloodstream Infection (CLABSI) Cases

N=106		**Overall Mean (SD) or n (%)**
Demographic		
Age, years		57.0 (17.3)
Sex		
	Male	58 (54.7%)
	Female	48 (45.3%)
Ethnicity		
	Black	50 (47.2%)
	White	44 (41.5%)
	Other[¥]	12 (11.3%)
Clinical		
Insertion Site		
	Subclavian Vein	19 (17.9%)
	Not Subclavian Vein	87 (82.1%)
	Arm	45 (42.5%)
	Chest	7 (6.6%)
	Femoral Vein	4 (3.8%)
	Internal Jugular Vein	31 (29.2%)
Catheter type		
	Central Line[†]	41 (38.7%)
	Implanted Port	8 (7.6%)
	Introducer[‡]	6 (5.7%)
	PICC[^]	43 (40.6%)
	Tunneled[§]	8 (7.6%)
Needless Connector		
	Standard	62 (58.5%)
	Silver	44 (41.5%)
Intensive Care Unit Attributable		
	Yes	57 (53.8%)
	No	49 (46.2%)
Facility		
	Hospital A	69 (65.1%)
	Hospital B	37 (34.9%)
Time onset CLABSI,		
days	≤7 days, Early	38 (35.8%)
	>7 days, Late	68 (64.2%)

[¥] includes: 1 Hispanic, 2 not recorded, 5 other, and 4 unknown
[†] Hypothermia Central Line and Multilumen Central Line
[‡] Introducer and Pulmonary Artery Catheter
[^] Peripherally Inserted Central Catheter (PICC) non-Tunneled
[§] Includes: Tunneled Central Line and Tunneled PICC

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Table 1b: Demographic and clinical characteristics of skin organism CLABSI cases from Hospital A and Hospital B from November 2009 to August 2011

N=106		Organism Groups								
		CNS[a]		S. aureus[b]		Candida[c]			Non-Skin[d]	
		n = 12	*P*[1]	n = 12	*P*[1]	n = 32	*P*[1]	*P*[e]	n = 50	*P*[1]
Demographic										
Age, years		61.2(14.8)	0.44	56.7 (11.9)	0.98	55.7(18.3)	0.80		56.8(18.4)	---
Gender										
	Male	5 (41.7%)		7 (58.3%)		21(65.6%)			25(50.0%)	
	Female	7 (58.3%)	0.60	5 (41.7%)	0.60	11(34.4%)	0.16	0.35	25(50.0%)	---
Ethnicity										
	Black	6 (50.0%)	0.81	8 (66.7%)	0.34	11(34.4%)	0.33	0.14	25(50.0%)	
	White	4 (33.3%)		2 (16.7%)		18 (56.2%)			20(40.0%)	
	Other¥	2 (16.7%)		2 (16.7%)		3 (9.4%)			5 (10.0%)	---
Clinical										
Insertion Site										
	Subclavian Vein	2 (16.7%)		1 (8.3%)		13(26.0%)			13(26.0%)	
	Not Subclavian Vein	10(83.3%)	0.71	11 (91.7%)	0.27	29(74.0%)	0.06	0.84	37(74.0%)	---
Catheter type										
	Central Line†	2 (16.7%)	0.28	6 (50.0%)	0.74	11(34.4%)	0.51	0.28	22(44.0%)	
	Implanted Port	1 (8.3%)		2 (16.7%)		1(3.1%)			4(8.0%)	
	Introducer‡	1 (8.3%)		0 (0.0%)		1(3.1%)			4(8.0%)	
	PICC^	6 (50.0%)		3 (25.0%)		17(53.1%)			17(34.0%)	
	Tunneled§	2 (16.7%)		1 (8.3%)		2(6.3%)			3(6.0%)	---
Needless Connector										
	Standard	5 (41.7%)		4 (33.3%)		17(53.1%)			32(64.0%)	
	Silver	7 (58.3%)	0.20	8 (66.7%)	0.99	15(46.9%)	0.33	0.47	18(36.0%)	---
ICU Attributable										
	Yes	4 (33.3%)		4 (33.3%)		21 (65.6%)			28(56.0%)	
	No	8 (66.7%)	0.16	8 (66.7%)	0.16	11(34.4%)	0.39	0.06	22(44.0%)	---
Facility										
	Hospital A	9 (75.0%)		9 (75.0%)		23 (71.9%)			28(56.0%)	
	Hospital B	3 (25.0%)	0.33	3 (25.0%)	0.33	9 (28.1%)	0.17	0.99	22(44.0%)	---
Time onset CLABSI,										
days	≤7 days, Early	4 (33.3%)		6 (50.0%)		11 (34.4%)			17(34.0%)	
	>7 days, Late	8 (66.7%)	0.99	6 (50.0%)	0.33	21(65.6%)	0.97	0.66	33(66.0%)	---

¥ includes: 1 Hispanic, 2 not recorded, 5 other, and 4 unknown

† includes: hypothermia CVC, Multilumen CVC

‡ includes: Introducer, pulmonary artery catheter

^ includes: PICC non-tunneled

§ includes: Trifusion, Tunneled VAD, Tunneled Hickman and PICC Tunneled

[a]: Coagulase Negative Staphylococcus

[b]: Methicillin susceptible or resistant *S. Aureus*

[c]: Candida (Yeast)

[d]: includes: 27 Gram negative, 9 Enterococci, 14 other

[e]: P-value for Chi-square test of homogeneity for skin organisms

[1]: indicates P-value comparing each skin organism to non-skin group, Either Chi-square, Fisher's or t-test

Table 2a: Crude Logistic Analysis of Central Line-Associated Bloodstream Infections (CLABSI) by Individual Skin Organisms for Covariates

N=106

Variable		Organisms: CNS[b] OR[2]	CNS 95% CI	CNS *P*[1]	SA[c] OR[2]	SA 95% CI	SA *P*[1]	*Candida* OR[2]	*Candida* 95% CI	*Candida* *P*[1]
Age, years		1.02	(0.98 - 1.05)		1.00	(0.96 - 1.04)		1.00	(0.97- 1.02)	
Sex										
	Male	0.71	(0.20 - 2.56)		1.40	(0.39 - 5.01)		1.91	(0.76- 4.77)	
	Female	1.00	---		1.00	---		1.00	---	
Ethnicity										
	Black	1.00	---	0.76	1.00	---	0.65	1.00	---	0.31
	White	0.83	(0.21 - 3.36)		0.31	(0.06 - 1.64)		2.05	(0.79- 5.31)	
	Other[¥]	1.67	(0.26 - 10.77)		1.25	(0.20 - 7.74)		1.36	(0.28- 6.74)	
Insertion Site										
	Subclavian Vein	0.57	(0.11 - 2.95)		0.26	(0.03 - 2.21)		0.29	(0.08- 1.13)	
	Non-subclavian Vein	1.00	---		1.00	---		1.00	---	
Catheter type										
	Central Line[†]	1.00	---	0.06	1.00	---	0.60	1.00	---	0.20
	Implanted Port	2.75	(0.12 - 38.00)		1.92	(0.29- 12.75)		0.50	(0.05- 5.03)	
	Introducer[‡]	2.75	(0.12 - 38.00)		0.39	(0.01- 11.36)		0.50	(0.05- 5.03)	
	PICC[^]	3.88	(0.69 - 21.69)		0.69	(0.16- 3.02)		2.00	(0.75- 5.37)	
	Tunneled[§]	7.33	(0.73 - 73.22)		1.48	(0.15- 15.03)		1.33	(0.19- 9.19)	
Needleless Connector										
	Standard	1.00	---		1.00	---		1.00	---	
	Silver	2.49	(0.69 - 8.99)		0.89	(0.24 - 3.37)		1.57	(0.64- 3.87)	
Intensive Care Unit Attributable										
	Yes	0.39	(0.11 - 1.48)		0.39	(0.11 - 1.48)		1.5	(0.60- 3.76)	
	No	1.00	---		1.00	---		1.00	---	
Facility										
	Hospital A	2.36	(0.57 - 9.76)		2.36	(0.57- 9.76)		2.01	(0.78- 5.20)	
	Hospital B	1.00	---		1.00	---		1.00	---	
Time onset CLABSI, days										
	≤7 days, Early	0.97	(0.26 - 3.69)		1.94	(0.54 - 6.94)		1.02	(0.40- 2.59)	
	>7 days, Late	1.00	---		1.00	---		1.00	---	

[¥] includes: 1 Hispanic, 2 not recorded, 5 other, and 4 unknown

[†] Central line hypothermia and Multilumen Central Line

[‡] Introducer and Pulmonary Artery Catheter

[^] Peripherally Inserted Central Catheter (PICC) non-tunneled

[§] Trifusion, Tunneled Central Line, and Tunneled PICC

[b] Coagulase-Negative Staphylococcus

[c] *Staphylococcus aureus*

[1] Test for Trend Mantel Haenszel

[2] The Odds ratio of the skin organism group compared to the non-skin organism group for each covariate.

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Table 2b: Crude Logistic Analysis of Central Line-Associated Bloodstream Infections (CLABSI) by Skin Organism Group for Covariates
N=106

Variable		Group[a] OR[2]	95% CI	*P*[1]
Age, years		1.00	(0.98 - 1.02)	
Sex				
	Male	1.54	(0.71 - 3.33)	
	Female	1.00	---	
Ethnicity				
	Black	1.00	---	0.56
	White	1.32	(0.58 - 2.97)	
	Other[¥]	1.40	(0.39 - 5.01)	
Insertion Site				
	Subclavian Vein	*0.33	(0.11 - 0.94)	
	Non-subclavian Vein	1.00	---	
Catheter type				
	Central Line[†]	1.00	---	0.60
	Implanted Port	1.16	(0.25 - 5.27)	
	Introducer[‡]	0.58	(0.10 - 3.52)	
	PICC[^]	1.95	(0.82 - 4.67)	
	Tunneled[§]	1.93	(0.41 - 9.16)	
Needleless Connector				
	Standard	1.00	---	
	Silver	1.44	(0.66 - 3.15)	
Intensive Care Unit Attributable				
	Yes	0.78	(0.36 - 1.67)	
	No	1.00	---	
Facility				
	Hospital A	*2.28	(1.01 - 5.16)	
	Hospital B	1.00	---	
Time onset CLABSI, days				
	≤7 days, Early	1.10	(0.50 - 2.44)	
	>7 days, Late	1.00	---	

[¥] includes: 1 Hispanic, 2 not recorded, 5 other, and 4 unknown

[†] Hypothermia Central Line and Multilumen Central Line

[‡] Introducer and Pulmonary Artery Catheter

[^] Peripherally Inserted Central Catheter (PICC) non-tunneled

[§] Trifusion, Tunneled Central Line, and Tunneled PICC

[a] includes: Coagulase-Negative Staphylococcus, *Staphylococcus aureus,* and *Candida*

* indicates variables P<0.05

[1] Test for Trend Mantel Haenszel

[2] The Odds ratio of the skin organism group compared to the non-skin organism group for each covariate.

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Table 3a: Bivariate Analysis of Central Line-Associated Infections (CLABSI) by Facility

N=106		Facility		
		A	B	
		N=69	N=37	*P*[1]
Variable				
Age		53.5 (15.9)	63.4 (18.0)	*0.004
Sex				
	Male	38 (55.1%)	20 (54.0%)	
	Female	31 (44.9%)	17 (46.0%)	0.92
Ethnicity				
	Black	28 (40.6%)	22 (59.5%)	0.18
	White	32 (46.4%)	12 (32.4%)	
	Other¥	9 (13.0%)	3 (8.1%)	
Insertion Site				
	Subclavian Vein	15 (21.7%)	4 (10.8%)	
	Non-subclavian Vein	54 (78.3%)	33 (89.2%)	0.16
Catheter type				
	Central Line†	28 (40.6%)	13 (35.1%)	0.74
	Implanted Port	4 (5.8%)	4 (10.8%)	
	Introducer‡	3 (4.3%)	3 (8.1%)	
	PICC^	28 (40.6%)	15 (40.5%)	
	Tunneled§	6 (8.7%)	2 (5.4%)	
Needleless Connector				
	Standard	44 (63.8%)	18 (48.6%)	0.13
	Silver	25 (36.2%)	19 (51.4%)	
Intensive Care Unit Attributable				
	Yes	39 (56.5%)	18 (48.6%)	
	No	30 (43.5%)	19 (51.4%)	0.44
Time onset CLABSI, days				
	≤7 days, Early	22 (31.9%)	16 (43.2%)	
	>7 days, Late	47 (68.1%)	21 (56.8%)	0.25

* indicates variables P<0.05

1: P-value comparing each Hospital A to Hospital B, Either Chi-square, Fisher's or t-test

¥ includes: 1 Hispanic, 2 not recorded, 5 other, and 4 unknown

† Hypothermia Central Line and Multilumen Central Line

‡ Introducer and Pulmonary Artery Catheter

^ Peripherally Inserted Central Catheter (PICC) non-tunneled

§ Trifusion, Tunneled Central Line, and Tunneled PICC

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Table 3b: Bivariate Analysis of Central Line-Associated Infections by Insertion Site

N=106		Insertion Site		
		Subclavian N=19	Non-Subclavian N=87	
	Variable			***P*[1]**
Age		52.6 (18.5)	57.9 (16.9)	0.22
Sex				
	Male	10 (52.6%)	48 (55.2%)	
	Female	9 (47.4%)	39 (44.8%)	0.84
Ethnicity				
	Black	5 (26.3%)	45 (51.7%)	*0.03
	White	9 (47.4%)	35 (40.2%)	
	Other¥	5 (26.3%)	7 (8.1%)	
Catheter type				
	Central Line†	16 (84.2%)	25 (28.7%)	
	Implanted Port	0 (0.0%)	8 (9.2%)	
	Introducer‡	0 (0.0%)	6 (6.9%)	
	PICC^	0 (0.0%)	43 (49.4%)	
	Tunneled§	3 (15.8%)	5 (5.8%)	*<0.001
Needleless Connector				
	Standard	12 (63.2%)	50 (57.5%)	0.65
	Silver	7 (36.8%)	37 (42.5%)	
Intensive Care Unit Attributable				
	Yes	16 (84.2%)	41 (47.1%)	
	No	3 (15.8%)	46 (52.9%)	*0.003
Facility				
	Hospital A	15 (78.9%)	54 (62.1%)	
	Hospital B	4 (21.1%)	33 (37.9%)	0.16
Time onset CLABSI, days				
	≤7 days, Early	6 (31.6%)	32 (36.8%)	
	>7 days, Late	13 (68.4%)	55 (63.2%)	0.66

* indicates variables P<0.05

[1] P-value comparing subclavian vein to non-subclavian vein, Either Chi-square, Fisher's or t-test

¥ includes: 1 Hispanic, 2 not recorded, 5 other, and 4 unknown

† Hypothermia Central Line and Multilumen Central Line

‡ Introducer and Pulmonary Artery Catheter

^ Peripherally Inserted Central Catheter (PICC) non-tunneled

§ Trifusion, Tunneled Central Line, and Tunneled PICC

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Table 4a:

Table 4a: Adjusted Logistic Regression Models of Central Line-Associated Bloodstream Infections (CLABSI): Including Facility and Age and Excluding Ethnicity

N=106

		Models								
		Full Model			Most Parsimonious Model[3]			Final Model[4]		
	Variable	**OR[2]**	**95% CI**	***P*[1]**	**OR[2]**	**95% CI**	***P*[1]**	**OR[2]**	**95% CI**	***P*[1]**
Facility										
	Hospital A	*3.15	(1.23 - 8.07)		*3.06	(1.26 - 7.39)		*3.10	(1.27 - 7.53)	
	Hospital B	1.00	---		1.00	---		1.00	---	
Age		1.01	(0.98 - 1.03)							
Sex										
	Male	1.79	(0.74 - 4.28)					1.59	(0.70 - 3.59)	
	Female	1.00	---					1.00	---	
Insertion Site										
	Subclavian Vein	*0.24	(0.06 - 0.91)		*0.26	(0.09 - 0.78)		*0.27	(0.08 - 0.85)	
	Non-subclavian Vein	1.00	---		1.00	---		1.00	---	
Catheter type										
	Central Line†	1.00	---	0.43						
	Implanted Port	0.78	(0.13 - 4.68)							
	Introducer‡	0.27	(0.04 - 2.07)							
	PICC^	1.33	(0.47 - 3.77)							
	Tunneled§	2.23	(0.39 - 12.71)							
Needleless Connector										
	Standard	1.00	---		1.00	---		1.00	---	
	Silver	1.74	(0.73 - 4.16)		1.71	(0.74 - 3.96)		1.73	(0.74 - 4.03)	
Intenisve Care Unit Attributable										
	Yes	1.12	(0.43 - 2.94)					0.90	(0.38 - 2.10)	
	No	1.00	---					1.00	---	

* indicates variables P<0.05

† Hypothermia Central Line and Multilumen Central Line

‡ Introducer and Pulmonary Artery Catheter

^ Peripherally Inserted Central Catheter(PICC) non-tunneled

§ Trifusion, Tunneled Central Line, and Tunneled PICC

[1] Analysis of Trend

[2] Odds ratio of skin organism group versus non-skin organism group

[3] Includes Only Significant Results and Confounder Needless Catheter

[4] Includes Signficant Results and Confounder: Needleless Catheter. Used accuracy to point estimate of facility in full model and precision gained

Table 4b:

Table 4b: Adjusted Logistic Regression Models of Central Line-Associated Bloodstream Infections (CLABSI): Including Ethnicity and Excluding Facility and Age

N=106

	Models								
	Full Model			**Most Parsimonious Model[3]**			**Final Model[4]**		
Variable	**OR[2]**	**95% CI**	***P*[1]**	**OR[2]**	**95% CI**	***P*[1]**	**OR[2]**	**95% CI**	***P*[1]**
Insertion Site									
Subclavian Vein	*0.24	(0.06 - 0.91)		*0.23	(0.06 - 0.86)		*0.25	(0.07 - 0.91)	
Non-subclavian Vein	1.00	---		1.00	---		1.00	---	
Sex									
Male	1.64	(0.70 - 3.82)					1.63	(0.70 - 3.80)	
Female	1.00	---					1.00	---	
Ethnicity									
Black	1.00	---	0.30	1.00	---	0.18	1.00	---	0.30
White	1.44	(0.57 - 3.60)		1.59	(0.66 - 3.82)		1.43	(0.58 - 3.51)	
Other¥	2.01	(0.46 - 8.81)		2.31	(0.54 - 9.89)		2.04	(0.47 - 8.81)	
Catheter type									
Central Line†	1.00	---	0.40	1.00	---	0.42	1.00	---	0.35
Implanted Port	0.80	(0.15 - 4.34)		0.77	(0.16 - 3.80)		0.81	(0.16 - 4.04)	
Introducer‡	0.29	(0.04 - 2.04)		0.36	(0.05 - 2.37)		0.32	(0.05 - 2.16)	
PICC^	1.22	(0.43 - 3.48)		1.14	(0.42 - 3.12)		1.23	(0.44 - 3.41)	
Tunneled§	2.57	(0.45 - 14.61)		2.38	(0.43 -13.28)		2.56	(0.47 - 13.87)	
Needleless Connector									
Standard	1.00	---							
Silver	1.46	(0.64 - 3.35)							
Intensive Care Unit Attributable									
Yes	1.13	(0.44 - 2.87)							
No	1.00	---							

* indicates variables P<0.05

¥ includes: 1 Hispanic, 2 not recorded, 5 other, and 4 unknown

† Hypothermia Central Line and Multilumen Central Line

‡ Introducer and Pulmonary Artery Catheter

^ Peripherally Inserted Central Catheter (PICC) non-tunneled

§ Trifusion, Tunneled Central Line, and Tunneled PICC

[1] Analysis of Trend

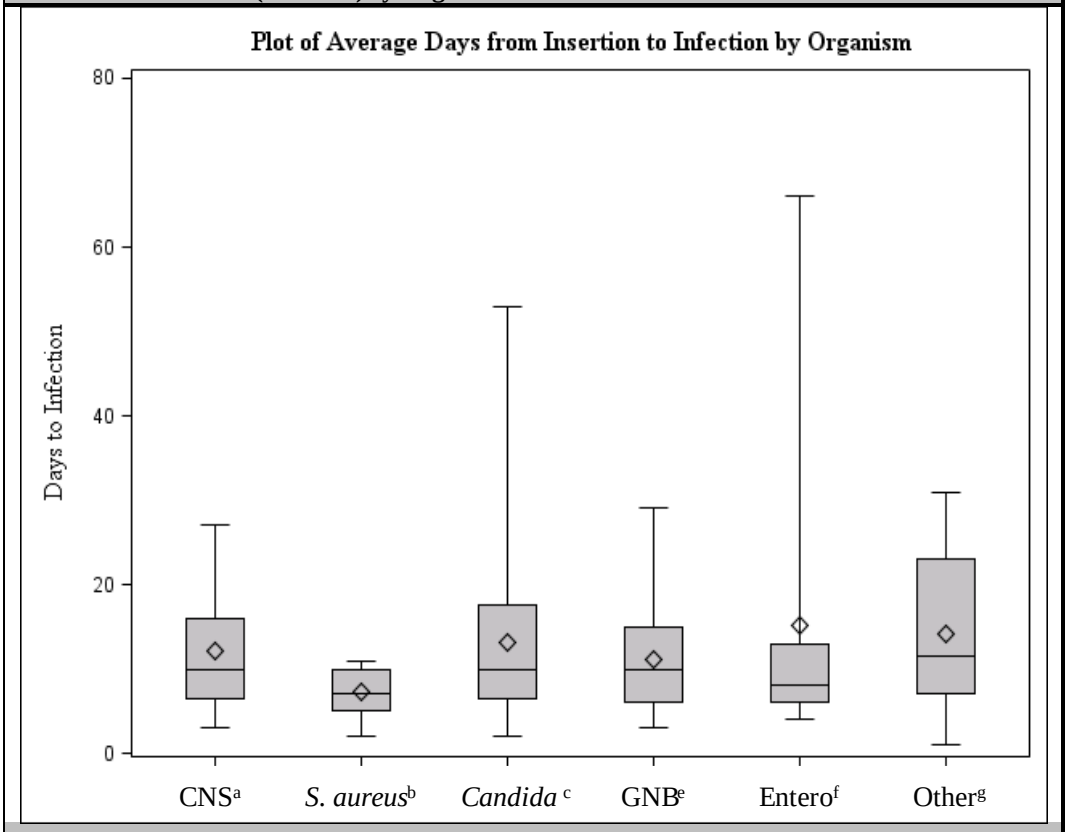
[2] Odds ratio of skin organism group versus non-skin organism group

[3] Includes Only Significant Results and Confounder Needless Catheter

[4] Includes Signficant Results and Confounders: Ethnicity and Catheter Type. Used accuracy to point estimate of Site Subclavian in full model and precision gained.

Figure

Figure 1: Distribution of Time from Line Insertion to Central Line-Associated Bloodstream Infection (CLABSI) by Organism



Organism		Time to Onset Mean	SD	Organism		Time to Onset Mean	SD
CNS[a]	N = 12	12.1	7.4	GNB[e]	N = 27	11.1	7.0
S. aureus[b]	N = 12	7.2	2.8	Entero[f]	N = 9	15.1	19.4
Candida[c]	N = 32	13.2	10.4	Other[g]	N = 14	14.1	9.6
All Skin[d]	N = 56	11.9	9.1	All Nonskin[h]	N = 50	12.7	10.5
				All	N = 106	12.2	9.7

[a] Coagulase Negative Staphylococcus

[b] Methicillin susceptible and resistant *Stapylococcus aureus (S. aureus)*

[c]: *Candida* (Yeast)

[d] includes: CNS, S. *aureus*, and *Candida*

[e] Gram Negative Bacteria

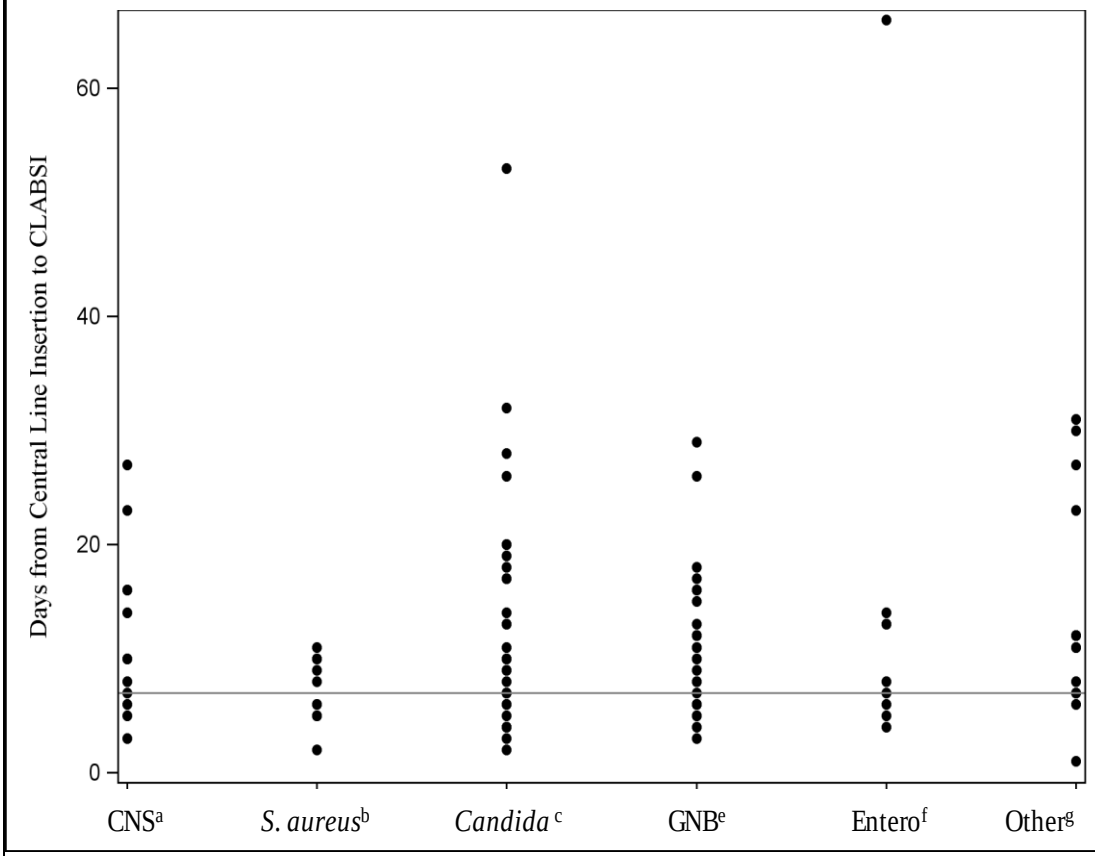
[f] *Enterococcus*

[g] non-staphylococcal gram positive bacteria

[h] Includes: GNB, Entero, Other

Appendix

Figure 2: Dotplot of Time from Central Line Insertion to Central Line-Associated Bloodstream Infection (CLABSI) By Organism



[a]: Coagulase Negative Staphylococcus

[b]: Methicillin susceptible and resistant Staphylococcus Aureus

[c]: Candida (Yeast)

[e]: Gram Negative Bacteria

[f]: Enterococcus

[g]: other non-staphyloccal gram positive bacteria

7 days (Early vs. Late)