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Blood Product Transfusions and Central Line Bloodstream Infections:

A retrospective study of transfusions and their association with central line bloodstream infections

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Master of Public Health

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An abstract of

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Rollins School of Public Health of Emory University

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Abstract

Blood Product Transfusions and Central Line Bloodstream Infections:

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By Kristin Hake, RN

Central line bloodstream infections (CLABSIs) have been an increasing concern in recent years for hospitals, healthcare providers and patients. While some risk factors in the development of CLABSIs have been identified, limited information on blood product transfusion as a risk has been published. Using data from an existing study on CLABSIs, blood product transfusion information was analyzed to determine if blood product transfusion is associated with an increased risk for development of a CLABSI. In multivariate analysis, transfusion of packed red blood cells and transfusion of any type of blood product was significantly associated with development of a CLABSI (OR=1.96; 95% CI 1.25--3.11) and (OR= 2.71; 95% CI 1.71--4.31) respectively, when controlling for short vs. long term period of central line insertion and with receipt of total parenteral nutrition. The risk of CLABSI increased as number of units of PRBCs transfused increased. These results provide insight into the association between blood product transfusions and CLABSIs, however further studies are needed to clarify the relationship.

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Background

Hospital acquired infections (HAIs) are one of the most important healthcare-associated complications, impacting 5% of all hospitalized patients, and deaths from HAIs are among the top ten causes of death in the United States (1, 2). Central line- associated bloodstream infections (CLABSIs) account for approximately 14% of HAIs and the mortality associated with these infections is estimated to be between 12%-25%(1). Increased attention from regulatory agencies, advocacy groups and healthcare organizations aimed at prevention of CLABSIs has led to a decrease in infection rates. However in 2008-2009, there were approximately 60,000 CLABSIs among inpatients and outpatients nationwide(1) indicating there is still progress to be made in reducing these rates.

The Centers for Disease Control and Prevention (CDC) has put forth a standardized definition of CLABSI to aid with surveillance and reporting. According to this standardized definition, a CLABSI is a primary bloodstream infection (BSI) in a patient who had a central line, where the infection is not related to any other site(3). It is important to note though that BSIs secondary to infections at other sites are not always recognizable, so CLABSI surveillance results can sometimes overestimate the number of CLABSIs (3).

There a number of ways in which central lines can cause bloodstream infections, the two most common are contamination of the extraluminal and intraluminal pathways. Extraluminal contamination occurs when skin organisms migrate along the external catheter surface into the bloodstream. (4). This contamination typically occurs at the time of insertion and can be impacted by

adherence to best practices during catheter insertion. Intraluminal contamination occurs when there is contamination of the catheter hub. This can be a result of introduction of organisms from contaminated healthcare workers' hands while the catheter is being manipulated, at the time of connection to fluids or medications and when drawing blood samples (4, 5). The other ways in which central lines can be infected are through contaminated infusate or direct contamination by bacteria already in the bloodstream attaching to the line. Blood product transfusions are thought to increase the susceptibility of the patient to these infections by altering immune response.(6)

Since 2008, the Center for Medicaid Services (CMS) has stopped reimbursing for care needing to treat hospital acquired infections, placing an increased economic burden on hospitals and in turn influencing hospital policy and procedures regarding infection control. Patients who develop CLABSIs require longer hospital stays and additional diagnostic and therapeutic interventions, all at additional costs(7). The estimated economic costs for CLABSIs in the US are approximately $5,500-$23,000 annually and the economic benefits of HAI prevention range from $5.7 to $31.5 billion(8). The increased awareness of CLABSIs did help reduce some of this economic burden; between 2001 and 2009 there was an estimated decrease of 25,000 CLABSIs annually in the US, representing a savings of $414 million in potential excess healthcare costs and an estimated $1.8 billion in cumulative excess healthcare costs since 2001(1).

In addition to financial costs there are also human costs associated with CLABSIs. The crude mortality rate for patients with CLABSIs ranges from 12%-

25%, representing a significant amount of deaths which could be potentially avoided if infection rates are reduced. The previously mentioned reductions in CLABSIs between 2001 and 2009 represents an estimated 3,000-6,000 lives saved annually(1).

Several risk factors for the development of CLABSI have been previously identified and recommendations have been made which are targeted towards these identified risk factors. One of the most commonly investigated risk factors is the type of line used. One systematic review of prospective studies found midline and peripheral catheters had the lowest rate of infections (0.2-0.5 infections per 1000 catheter days) while short-term, non-cuffed central venous catheters and temporary hemodialysis catheters had the highest rates of infection (1.2-4.8 infections per 1000 catheter days)(6). In this same review, long-term hemodialysis catheters, cuffed and tunneled central venous catheters, and implanted ports were associated with significantly lower infection rates (0.1-1.6 per 1000 catheter days) than rates for temporary catheters(6).

In addition to the type of line used, several other risk factors for the development of a CLABSI have been identified, including the location in which the line is placed (a central venous catheter (CVC) placed in femoral sites is at higher risk for infection compared to a peripherally inserted central catheter (PICC) line); duration of line presence, and change of the catheter over a guidewire (9, 10). In response to these identified risk factors, national recommendations have been developed by the CDC to help standardize practice and reduce the number of CLABSIs (3). These recommendations include using aseptic technique throughout the procedure, choosing the line type and location

that minimizes risk of complications, the preferred use of chlorhexidine as an antiseptic during the placement of lines, and use of occlusive dressings throughout the period of maintenance of the lines(3). Interventions aimed at reducing the number of CLABSIs have shown to be the most effective of all HAI prevention measures and show reductions of anywhere from 38% to 71%(8).

While there has been extensive research conducted to identify risk factors associated with CLABSIs, few have studied blood product transfusions as a potential risk factor. Transfusions of blood products are thought to play a role in the likelihood of a patient developing an infection through a process called immunomodulation, which alters the body's immune response and induces suppression of the immune system(11, 12). Studies have indicated those patients who receive transfusions of blood products had higher mortality rates, increased risk of infection and longer stays in the ICU (12-14). A limited number of studies have investigated transfusions of specific types of blood products and their role in increasing risk for nosocomial infections among specific populations(15-18). Several studies investigating the role of packed red blood cells (PRBCs) in BSIs indicate that patients who received this type of blood transfusion were at an increased risk of subsequently developing BSIs and that there was a dose dependent relationship in which an increase in the number of PRBC units a patient receives corresponded to an increased risk of developing a BSI (19-21). In addition to PRBCs, one study concluded that fresh frozen plasma (FFP) also was a risk factor for the development of BSIs and also had a dose-response relationship (21).

Blood product transfusion has been a topic of discussion in the medical community for years, with increased attention starting in the mid-1980s surrounding concerns of transmission of HIV and hepatitis(13). Several risks associated with receiving a blood product transfusion have been identified and that, coupled with the cost of receiving a transfusion and concerns about availability, has led many hospitals to evaluate transfusion practices in hopes of reducing the amount of transfusion and subsequently reducing costs and risks associated with transfusions. In a national, multi-center study, 48% of patients received a transfusion of PRBCs during their hospital stay, with a mean number of 4.8 (± 5.1) units transfused(13). Transfusion practice and complications from other blood products have been investigated as well. Studies looking at FFP transfusion practices have linked FFP transfusions to a higher risk of antibody and protein related complications, such as transfusion related acute lung injury and allergic reactions(22). Studies investigating FFP and risk of infection in critically ill patients showed those who received FFP were at a higher risk for developing BSIs(21). Complications related to platelet transfusions have been less well documented, but there has been some information published. Thrombocytopenia is the main trigger for transfusion of platelets, and it is estimated that 15-30% of critically-ill patients who present with thrombocytopenia will receive a platelet transfusion(22). Transfusion of platelet products have been associated with the development of sepsis and acute respiratory distress syndrome, and have also been theorized to play a role in organ failure and other major morbidities(22).

Transfusions of PRBCs have been shown to be associated with an increased risk of developing any kind of infection, as well as specific infections such as ventilator associated pneumonia (11). In addition to the increased risk of developing an infection, several studies have shown a dose dependent response; as the number of units transfused increases, the risk of developing a BSI increases. One study among trauma patients demonstrated patients receiving a transfusion of PRBCs within 48 hours of admission were at a 1.08 times greater risk of developing an infectious process and also showed a linear correlation between number of units transfused and infection, with an exponential correlation for receipt more than 7 units(11). Other studies showed even higher risks of infection for those receiving transfusions. In one study, the risks of developing pneumonia or sepsis were 1.24 and 1.28 respectively, for patients who received one intraoperative blood transfusion; with an increased risk of 1.25 and 1.53 when there were two units transfused intraoperatively(16). In the same multi-center study mentioned above, 70.3% of patients who received transfusions developed an infection compared to 9.4% of those patients who didn't receive a transfusion(13). Infection risks, with dose-dependent relationships, associated with FFP have also been documented. The relative risk for a bloodstream infection with shock was 3.35 among critically ill surgery patients(21). This same study also showed a dose-dependent response with an OR of infection per unit transfused equal to 1.039(21). Limited information is available for platelet transfusion risks, however, one study investigating the relationship among coronary artery bypass patients showed 20.4% of patients received a platelet transfusion and of those patients, 30.6% developed a postoperative infection(12).

Many previous studies involving blood product transfusions and infections are limited in scope, investigating only a single center as opposed to multiple centers (11, 14, 15, 19), are limited to specific populations such as critically ill or oncology patients(11, 16, 18, 20), or are limited to a single type of blood product(14, 16, 17, 21). An additional limitation of these studies is they do not specifically address CLABSIs, instead looking at sepsis, or bloodstream infections in general. All of these limitations open up the potential for bias or confounding in results. This study attempts to overcome these limitations by investigating the relationship between transfusion of three types of blood products (platelets, FFP and PRBCs) with CLABSIs among all patients admitted during a defined time period.

II. Methods

Null Hypothesis

The rates of CLABSI are the same among patients who receive a blood product transfusion compared to those patients who did not receive a blood product transfusion, after controlling for other important variables.

Patient and Data Collection

This case-control study used data collected from a primary study investigating CLABSIs conducted at Emory University Hospital and Emory University Hospital Midtown in Atlanta, GA. A crossover study design was used to minimize bias and allow each hospital to serve as its own control. Participants included all adult patients admitted to either hospital during the study period of November 2009 through June 2011.

From the data in the initial study, cases of CLABSI were identified and subsequently matched to controls. Cases were identified using CDC's National Healthcare Safety Network's (NHSN) surveillance definitions for CLABSI (23). Patient records were reviewed retrospectively for data not included in the original study. The study received approval from Emory University's Institutional Review Board (#00016682).

For this analysis, a case was defined as an inpatient with an identified CLABSI, using the NHSN definition(23), during the time frame of December 2009-June2011 and whose CLABSI was attributed to the first central line in place during their hospitalization. Patients who were admitted to a hospital unit (either acute care or ICU), regardless of length of stay, were considered

inpatients. A control was defined as an inpatient who had a central line in place during the time frame of December 2009-June 2011 and who had not been diagnosed with a CLABSI during entire hospitalization. To help control for increased awareness and education regarding CLABSIs within the institutions, changes in policies and procedures, as well as changes in staff throughout the study, controls were matched to cases 4:1 based on month and year of admission. 100% of cases had 4 controls matched to them; however no cases were reported for admissions in June 2011, so controls from that month are not present in this analysis. All patient information was gathered retrospectively from electronic medical records.

The primary outcome measure for this analysis was diagnosis of a CLABSI. The primary exposure variable was receipt of any type of blood product transfusion. Blood products included in this analysis were packed red blood cells, fresh frozen plasma and platelet product. In addition to receipt of any type of blood product transfusion, each type of blood product was analyzed individually. Dichotomous variables were created for a transfusion of any type of product, as well as for each individual type of product. Along with these dichotomous variables, variables detailing the number of units transfused were also included. For bivariate analysis, numbers of units received were broken down into four categories: none and then greater than zero by tertiles, which varied for each type of transfusion. In the multivariate analysis, number of units transfused was treated as an interval variable. For controls, any transfusions which occurred throughout the duration of the first catheter placed (line one) were included; with duration of line one considered time at risk for consideration

of other variables in the study. For cases, any transfusions which occurred after line one placement and prior to infection date were included; with duration of line from insertion date to infection date considered time at risk for consideration of other variables in the study. A variable for the hospital in which the admission took places was also included.

For all observations, only the first central line was included in the analysis. Selection of variables to include in analysis was based on risk factors associated with CLABSIs identified in previous research and information available in patient's electronic medical records. Central line types were classified as multilumen central venous catheters (CVC), peripherally inserted central catheters (PICC), dialysis/pheresis catheters, pulmonary artery catheters (PA catheters) and ports/tunneled vascular access catheters. Location of each central line was identified and classified as internal jugular (IJ), subclavian (SC), femoral, arm and chest. The duration of the central line (dwell time), also considered time at risk, was calculated using documented insertion dates and discontinue dates (for controls) or infection dates (for cases). Admission and discharge dates according to the patient's medical record were used to calculate the length of stay throughout the entire hospitalization. A dichotomous ICU variable was created to identify those patients who had any ICU admission during their time at risk. Age was assigned based upon the patient's age at date of admission. Also included in the analysis were dichotomous variables for receipt of hemodialysis, receipt of total parental nutrition (TPN), a procedure taking place in the cardiac catheterization (Cath)/electrophysiology (EP) lab or a procedure in the operating room (OR), during the patient's time at risk.

Hemodialysis, and procedures in the Cath/EP lab or OR, were identified using ICD-9 codes, and in the case of Cath/EP and OR procedures, were assigned to each category based on the location where these procedures take place.

Statistical Analysis

The distribution of clinical and demographic information was compared among cases and controls using χ^2 statistics. Next, the crude associations between blood product transfusions and CLABSI were analyzed using univariate regression for all products combined, and also for each product type individually. Multivariate analysis was conducted, including analysis of interaction and confounding and assessment of collinearity. In the process of developing a model which controlled for important variables, assessment of interaction was performed first. Interaction terms for transfusions and line type, TPN and line type, length of stay and TPN and line type and line site were included. After interaction was assessed, confounding was considered, using variables assessed in univariate analysis. A subsequent model using only those variables which were found to be statistically significant in univariate analysis was considered. Using the results from these models, a final model was built using forward selection, starting with the exposure variable and adding additional variables found to be significant, one at a time. Each model was compared to the previous model using the log likelihood result to determine if there was a significant difference between the two models. If no significant difference between the models was detected, the model with fewer variables was kept for comparison to the subsequent model. At each stage of multivariate analysis, collinearity was also considered using a SAS

macro for collinearity diagnostics; and variables which were determined to have a high degree of collinearity were excluded from the final model. Variance decomposition proportions (VDPs) and condition indices (CDIs) were used to determine if a variable was impacting the reliability of the results secondary to collinearity. A variable with a CDI >30 or two VDPs equal to 0.5 or greater was considered to have a high degree of collinearity. Due to collinearity and low cell counts for central line types, a new variable for central line type was created, classifying central lines as either short-term (CVCs, PA Catheters, and HD Catheters) or long-term (PICC and Port/Tunneled Cath). Interaction terms which were significant but were also found to have a high degree of collinearity were also not considered for the final model. Statistical analysis was completed using SAS 9.2 (SAS Institute, Cary, NC).

III. Results

During the period from December 2009 through June 2011, 152 CLABSIs were identified at both hospitals. Of those, 110 met the inclusion criteria for a case. During that same time period, 18,290 inpatient visits met the inclusion criteria for a control; of those, 440 were randomly selected and matched to cases 4:1 based on admission month and year. Four controls were matched for 100% of the cases.

For the 550 patients in the study population demographic and population characteristics were investigated (Table 1.) For the study population, 291 (53%) were female and 259 (47%) were male; and the mean age was 57.2. The distribution of patients between the two study locations was 216 (39%) at Emory Crawford Long Hospital and 334 (61%) at Emory University Hospital and the mean length of stay of all patients 14.3 days. Of patients in the study, 81 (15%) received dialysis, 80 (15%) received TPN while their central line was in place; and 249 (43%) had a stay in the ICU during their hospitalization. Bivariate analysis of the above variables showed controls were more likely to have received dialysis, while cases were more likely to have received TPN and have had an ICU stay (Table 1). Overall average length of stay was significantly higher among cases. Analysis of effects for central line information between cases and controls (Table 2) showed that patients who had a Multilumen Central Line or PICC were more likely to develop a CLABSI and patients who had a line placed in their arm were also more likely to develop a CLABSI. The average number of days the central line was in place was 10.5 days for cases versus 6 days for controls, a statistically

significant difference ($p<0.0001$). The number of lumens in a central line for cases compared to that for controls was not found to be statistically significant.

For this analysis, the primary exposure was a patient having received any type of blood product transfusion. Crude analysis of blood product transfusions and CLABSIs showed that development of a CLABSI was associated with patients who received a transfusion of any type of blood product (OR 2.62, 95% CI 1.71,4.03) and patients who received transfusions of PRBCs (OR 2.02, 95% CI 1.32, 3.09) (Table 3). However, development of a CLABSI was not associated with receipt of a transfusion of FFP or Platelets (Table 3.). The increased risk of developing a CLABSI when receiving a transfusion of any type of product was driven by the increased risk associated with PRBCs. In addition to crude analysis of an overall effect for transfusions, transfusion amount was investigated to determine if there was an increased risk as the number of units transfused increased. For patients who received a transfusion of any kind, increased risk was found only among those who received between three and six units of blood products. When analyzing transfusion amounts for PRBCs, risk of developing a CLABSI increased as number of units transfused beyond 2 increased; with patients who received greater than six units of PRBCs at highest risk of developing a CLABSI (Table 3). Congruent with the overall results for platelets and FFP, analysis of transfusion amounts for these two products showed no increased risk of developing a CLABSI (Table 3). With the risk of CLABSI associated with any type of blood product transfusion driven mainly by transfusion of PRBCs, further analysis was conducted using transfusion of PRBCs as the main exposure of interest.

Interactions between several variables of interest were assessed and significant interactions were identified (Table 4). A significant interaction was found between the type of central line a patient had and the location of the line, the type of line and the receipt of TPN and the type of line and receipt of a transfusion of PRBCs. Additionally, an interaction between a patient's length of stay and whether they received TPN was identified along with an interaction between a stay in the ICU and receipt of a PRBC transfusion. These interactions indicated that patients who had short term central lines were more likely to have lines placed in their IJ or SC and were also more likely to have received a transfusion of PRBCs while patients who had long term central lines were more likely to have received TPN. In addition to line type, TPN was also associated with length of stay; with patients who had a longer length of stay more likely to have received TPN. Patients who received PRBCs were more likely to have had an admission to the ICU while they were hospitalized. A high degree of collinearity was found among these variables, and their inclusion led to unstable model. Thus, these terms were left out of the final model.

Two initial multivariate models were examined that contained all variables and then statistically significant variables from the univariate analysis. These two initial models yielded unstable results with large standard errors and wide confidence intervals. Although the models were unstable, the point estimates and confidence intervals when assessing the relationship between any type of transfusion and CLABSI did not differ significantly from the crude estimates (Table 5). Once confounding, interaction and collinearity were all addressed for in the multivariate model, the final results modeled the effect of

PRBC transfusions on CLABSIs, controlling for short or long term central line and receipt of TPN while line was in place (Table 6). In addition to the association between PRBC transfusions and CLABSIs, this final model also indicates patients who had a short term central line and who received TPN were at a higher risk of developing a CLABSI (1.9 and 5.9 times more likely, respectively).

IV. Discussion

To our knowledge, this is one of the first studies to look specifically at the relationship between transfusion of specific types of blood products and CLABSIs among all hospitalized patients. The results in this study indicated that FFP and platelet transfusions were not risk factors for developing a CLABSI, whereas PRBC transfusions and overall any transfusion did increase the risk. Most studies looking at individual types of blood products only addressed BSIs or sepsis and not CLABSIs specifically (12, 15, 16, 21) so a direct comparison of results is difficult to make; however, the results from this study seem to correspond with those of previous studies. The increased risk of CLABSI from PRBC transfusion in this study, as well as the increased risk depending on transfusion amount was similar to a study in critically ill patients, looking at PRBC transfusions and BSIs (20). That study indicated patients who received a PRBC transfusion had a 2.23 times greater risk of developing a bloodstream infection; and this risk differed among those who received only 1 or 2 units (OR=1.89) and those who received >4 units (OR=2.63)(20). These estimates are very similar to the estimates of this study. Another study of critically ill trauma patients also showed a significant relationship between PRBC transfusion and bloodstream infection ($p<0.001$) in both univariate and multivariate analysis (19). This study showed no relationship between FFP transfusion and CLABSI, even after adjusting for potential confounders. These differ from a previous study which showed patients who received an FFP transfusion were at a higher risk of developing BSI (21).

In addition to variations between definitions of exposures and outcomes, there was also a difference between this study and others in other variables investigated, with the only variable included in all studies being TPN. Previous studies indicated patients who received TPN were at an increased risk of developing a CLABSI, which the results from this study conclude as well. Previous studies have shown a significant relationship between central line types, central line locations and the amount of time a central line is in place and the development of a CLABSI. Unfortunately, due to the high degree of collinearity present in the variables within this study in regards to central line characteristics, the current study was unable to address this relationship. Even with the limitation of differing outcome definitions, comparisons can be made between study designs. One limitation of this study was that it was retrospective in nature, introducing the possibility of data lost due to follow up. While some previous studies which showed a relationship also had this limitation(16, 21), other studies which showed a relationship were observational studies (11, 14, 15). In this study, data was obtained from electronic medical records through a data collection program and electronic charts were not reviewed individually. The process of data collection opened up the potential for missing and/or inaccurate data due to the information at the source not being documented or being inaccurately documented; or the collection method being flawed. One example of this was BMI; only 62% of the study population had both a height and weight recorded to allow BMI calculation. Likewise, the process of matching in this study might have led to information loss from discarding controls which did not satisfy the matching criteria; for example, there were no cases from June 2011, so

any controls which fell into that month were excluded from sampling. Another limitation is that this study had no measurement to account for either multiple comorbidities or severity of illness. There is often a wide variability in the severity of illness among inpatient hospitalizations, with severe illness and multiple comorbidities being known risk factors for infection and severe illness often requiring transfusions or increased amounts of transfusions compared to those who are not as ill. Previous studies which showed relationships for individual types of blood products were able to use the Acute Physiology and Chronic Health Evaluation (APACHE II) to quantify severity of illness or were able to collect data on presence of known comorbidities, which were shown to be variables of significance in both univariate and multivariate analysis (11, 21).

While this study had its limitations, it does fill a void in current research. The study examined all types of blood product transfusions among all hospitalized patients. The inclusion of all types of transfusions into a single analysis helps provide a broader view of the role transfusions play in the development of CLABSIs. Determining whether the relationship between blood product transfusion and CLABSI is causal would be difficult to answer, but this study provides a starting point to determine strength of association. A large prospective study which includes some of the variables lacking in this study would help to further clarify the results presented here.

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Table 1. Demographic and Clinical Characteristics of Study Population

	Total n=550	**Cases** n=110	**Controls** n=440	**P-value** (**= significant at α= 0.05 level)
		number (%)		
Gender				
Female	291 (53)	61 (55)	230 (52)	
Male	259 (47)	49 (45)	210 (48)	0.55
Age (mean)				
years	57.2	55.9	57.5	0.43
Length of Stay[1]				
days	14.3	28.9	10.6	***p<0.001*
Hospital				
Emory Crawford Long Hospital	216 (39)	42 (38)	174 (40)	0.79
Emory University Hospital	334 (61)	68 (62)	266 (60)	
Dialysis	81 (15)	8 (7)	73 (17)	***p=0.014*
TPN[2]	80 (15)	43 (39)	37 (8)	***p<0.0001*
ICU Stay During Hospitalization	249 (43)	61 (55)	188 (43)	***p=0.017*

[1] Calculated from date of admission to date of discharge
[2] Total Parenteral Nutrition

Table 2. Central Line Characteristics of Study Population

	All n=550	**Cases n=110 number (%)**	**Controls n=440**	**P-value (** significant at α= 0.05 level)**
Central Line Type				
Multilumen Central Line	141 (26)	36 (33)	105 (24)	***p<0.0001**
PICC[3]	167 (30)	52 (47)	115 (26)	
PA Catheter[4]	54 (10)	2 (2)	52 (12)	
Dialysis/Pheresis Catheter	74 (13)	0 (0)	74 (17)	
Implanted Port/ Tunneled VAD[5]	112 (20)	20 (18)	92 (21)	
Central Line Placement Site				
Jugular	176 (32)	26 (24)	150 (34)	***p=0.0031**
Subclavian	97 (18)	14 (13)	83 (19)	
Arm	141 (26)	44 (41)	97 (22)	
Chest	96 (17)	19 (17)	77 (18)	
Femoral	27 (5)	5 (5)	22 (5)	
Number of Lumens				
One	109 (20)	20 (18)	89 (20)	p=0.212
Two	257 (47)	54 (49)	203 (46)	
Three	124 (23)	26 (24)	98 (22)	
Four	22 (4)	8 (7)	14 (3)	
Central Line Days				
# of Days Central Line in Place[6]	6.9	10.5	6	***p<0.0001**

[3] Peripherally inserted central catheter
[4] Pulmonary artery catheter
[5] Tunneled vascular access device
[6] Calculated from documented insertion and discontinue dates

Table 3. Crude Odds Ratios for Blood Product Transfusions

	Odds Ratio (95% CI)
Any Blood Product Transfusion	***2.62 (1.71, 4.03)***
1 or 2 units	1.60 (0.89, 2.89)
3 to 6 units	***3.05 (1.68, 5.53)***
more than 6 units	1.77 (0.96, 3.60)
Packed Red Blood Cell Transfusion	***2.02 (1.32, 3.09)***
1 or 2 units	1.60 (0.91, 2.53)
3 to 6 units	***2.31 (1.26, 4.22)***
more than 6 units	***2.47 (1.29, 4.72)***
Platelet Transfusion	1.37 (0.74, 2.54)
1 or 2 units	0.74 (0.30, 1.81)
3 units	2.41 (0.57, 10.26)
more than 3 units	1.41 (0.51, 4.04)
Fresh Frozen Plasma Transfusion	1.09 (0.58, 2.04)
1 to 4 units	1.17 (0.42, 3.29)
5 to 12 units	1.85 (0.78, 4.38)
more than 12 units	0.97 (0.27, 3.45)

**** significant association at α=0.05 level***

Table 4. Significant Interaction Terms

	χ^2 statistic	p-value
Transfusion*Line Type	4.66	0.031
Length of Stay * TPN[7]	135.69	<0.0001
ICU Stay * Transfusion	18.04	<0.0001
Line Type * Line Site	396.46	<0.0001
Line Type * TPN	11.68	0.0006

[7] Total parenteral nutrition

Table 5. Adjusted Odds Ratios for Blood Product Transfusions

	Odds Ratio (95% CI) (adjusting for all variables included in univariate analysis)	**Odds Ratio (95% CI)** (adjusting for all variables found to be significant in univariate analysis)	**Odds Ratio (95% CI)** (adjusting for TPN and line type)
Any Blood Product Transfusion	***2.54 (1.48, 4.35)**	***2.63 (1.55, 4.45)**	***2.71 (1.71, 4.31)**
1 or 2 units	1.41 (0.70, 2.84)	1.44 (0.73, 2.84)	1.62 (0.87, 3.03)
3 to 6 units	***2.37 (1.13, 4.98)**	***2.34 (1.13, 4.85)**	***2.87 (1.50, 5.47)**
more than 6 units	0.73 (0.31, 1.74)	0.74 (0.32, 1.73)	1.72 (0.87, 3.41)
Packed Red Blood Cell Transfusion	1.37 (0.81, 2.30)	1.34 (0.79, 2.27)	***1.96 (1.25, 3.11)**
1 or 2 units	1.37 (0.70, 2.68)	1.38 (0.72, 2.65)	1.65 (0.90, 3.02)
3 to 6 units	1.56 (0.73, 3.31)	1.53 (0.73, 3.21)	***2.13 (1.10, 4.13)**
more than 6 units	0.97 (0.38, 2.45)	0.99 (0.40, 2.50)	***2.40 (1.15, 5.00)**

**** significant association at α=0.05 level***

Table 6. Final Multivariate Model

BSI= txprbc * short-term * TPN

	Odds Ratio (95% CI)	p-value
Transfusion of PRBCs	1.96 (1.25, 3.11)	0.004
Short Term Central Line	1.88 (1.17, 3.03)	0.009
TPN[8]	5.92 (3.50, 10.00)	<0.0001

[8] Total parenteral nutrition