Central Line Access is Predictive of Diagnostic Blood Loss and Transfusion in the Surgical Intensive Care Unit

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Abstract

Background: Diagnostic laboratory testing (DLT) is a source of blood loss in critically ill patients. Approximately half of patients admitted to the intensive care unit (ICU) present with anemia, with the remainder developing a multifactorial anemia with etiologies including central venous catheter (CVC) placement. Consequently, about a third of ICU patients require red blood cell (RBC) transfusion, a practice associated with poorer clinical outcomes. Our objectives were to characterize DLT blood loss in the surgical intensive care unit (SICU), and its relationship with anemia, RBC transfusion, and CVC placement.

Methods: An observational study was performed by retrospective chart review of patients admitted to a SICU over 1-year. The number of DLT blood draws, average volume of blood drawn, and estimated discard volume were recorded along with clinical and laboratory findings.

Results: A cohort of 292 patients (mean age 62.2 years, male to female ratio 1.5) underwent 299 hospitalizations with an average daily DLT blood loss of 14.3 mL (229.5 mL per admission). Among admissions, 51.2% presented with anemia and 95.3% were anemic at discharge, with 32% of patients receiving an RBC transfusion. Patients with greater DLT-associated blood loss had lower discharge hemoglobin ($p < 0.001$). Admissions requiring CVC (49.8%), demonstrated a significantly greater number of DLT blood draws, increased DLT-associated blood loss, higher rates of RBC transfusion, and an increased length of stay.

Conclusions: Findings from this study suggest that DLT blood loss contributes to anemia in the SICU and the presence and duration of CVC leads to increased testing, blood loss, anemia, and is predictive of RBC transfusion.

Introduction

Diagnostic laboratory testing (DLT) plays an integral role in the clinical management of critically ill patients. While DLT provides invaluable information, helping guide diagnostic, prognostic and therapeutic decisions volume lost due to high testing burden has been shown to contribute to the development of anemia and may lead to an increased rate of transfusion.¹⁻⁴ An estimated 16.2 laboratory tests are collected daily from ICU patients and account for a daily DLT-associated blood loss of 15 to 100 mL.^{2,4-9} In the ICU, blood needed for DLT is frequently collected from a central venous access catheter (CVC). Approximately half of patients in the ICU will undergo placement of a CVC.¹⁰ The ease at which CVC's permit collection of DLT and the clinical acuity of the patients that often require CVC appears to promote increased access, with a an approximately 30% increase in testing and a 40% increase blood volumes collected in patients with CVCs relative to those without CVCs.^{11,12} Ultimately, an increase in DLT and increased DLT-associated blood loss has been shown to correspond with a higher incidence of anemia.¹⁻

Anemia is a common development in the critical care setting, with a reported incidence of anemia in 98% of patients admitted to the ICU.⁹ Suppressed erythropoiesis observed in critically ill patients occurs due to inflammation prompting iron sequestration and decreased erythropoietin activity.^{13–18} Other etiologies include nutritional deficiencies, major surgical interventions, bleeding, LOS, and receipt of care at a teaching institution.^{17,19,20 21–23} Together these factors lead to the development of anemia at discharge in ICU patients, with severe discharge anemia associating with a number of adverse outcomes, including increased 30-day mortality rates and readmissions, representing a significant source of healthcare costs.^{13,21}

The prevalence of anemia in the critically ill often prompts RBC transfusions, occurring in 26.3–50% of ICU patients.^{24–26} The high rate of RBC transfusions is concerning given the observed relationship between liberal RBC transfusions and poor outcomes, such as a higher incidence of serious health-care-associated infections and increased LOS.^{25,27,28} Similarly, mortality rates are appreciably higher in transfused ICU patients relative to non-transfused patients, 30% vs. 19.6%, respectively.²⁶

Measures aimed at mitigating factors that contribute to both the incidence of anemia and the extent of RBC transfusions have the potential to significantly improve patient outcomes in the critically ill. Our study aimed to characterize DLT-associated blood loss, the impact of CVC placement, and their association with anemia and rate of RBC transfusion.

Methods

Design and Setting:

This retrospective study was conducted at the University of Texas Medical Branch (UTMB) in Galveston, Texas, between January 1, 2017, and December 31, 2017, and was approved by the local institutional review board. Data from hospitalization was recorded and no follow-up data was obtained. Cost analysis was performed at University of Texas Southwestern at Parkland Hospital in October of 2021 and did not involve the use of patient data. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were utilized in preparation of this manuscript.²⁹

Study Population:

Our study population comprised consecutive adult patients admitted to the SICU. Patients <18 years of age as well as vulnerable populations were excluded from the study. The study size was a convenience sample derived from the time period reviewed.

Data Collection:

Electronic medical records were manually reviewed with the following data obtained: patient demographics and clinical information (Table 1), laboratory results, progress notes, and discharge

summaries. Data collection was performed by physicians, recorded in standardized de-identified abstraction sheets, and met the requirements of the Health Insurance Portability and Accountability Act. To account for the acuity of illness we calculated the Charlson Comorbidity Index (CCI) for each patient as previously described.³⁰

Table 1
Study Demographic Data

	All Admissions (n=299) +/- SD
Anemia [†] on admission % (n)	51.2% (153)
Anemia [†] on discharge % (n)	95.3% (285)
Charlson Comorbidity Index (CCI), mean	4.4 +/- 2.6
LOS, mean (days)	15.8 +/- 11.2
Admission Hb, mean (g/dL)	12.1 +/- 2.5
Nadir Hb, mean (g/dL)	7.9 +/- 1.7
CVC access % (n)	49.8% (149)
Discharge Hb, mean (g/dL)	9.4 +/- 1.6
Patients requiring RBC transfusion % (n)	32% (95)
RBC units transfused overall	1 (0.73 +/-1.6, range 0-16)
Total number of blood draws	
Per day	5.8 +/- 4.5
Per hospitalization	93.25 +/- 115.5
DLT blood loss per patient (mL)	
Per day	14.3 +/-9.8
Per hospitalization	229.5 +/-253.7
Total iatrogenic blood loss per patient (mL) (including discard)	
Per day	20.0 +/- 16.7
Per hospitalization	346.9 +/- 490.9
CVC, central venous catheter; SD, standard deviation; CCI, Charlson comorbidity index, LOS, Length of stay; Hb, Hemoglobin; RBC, Red Blood Cell unit; DLT, Diagnostic laboratory testing	
[†] Anemia based on based on World Health Organization definitions of Hb <12mg/dL; Male, Hb<13mg/dL	

To estimate the total blood volume collected for a given laboratory tests, tube volumes were confirmed by injecting with water and then measuring final volume into tubes. The number and source (i.e., peripheral

access, CVC) of DLT was identified in the patient's electronic medical records. The product of the average 7-day blood volume and the number of each test type was then calculated to estimate the daily and total blood volumes collected for a given patient. Blood discarded from CVC, arterial lines, and peripherally inserted central catheter (PICC) were estimated based on internal nursing protocol requirements for minimum discard volume.

The following information was also recorded: incidence of anemia (female, Hb <12mg/dL; male, Hb<13mg/dL) based on World Health Organization definitions), frequency of phlebotomy per patient per day, volume of blood loss via phlebotomy per patient per day, number and volume of RBC transfusions, number of RBC units transfused intraoperatively/immediately post-operatively, number of RBC units transfused in the SICU (not immediately post-operatively), SICU admission Hb, pretransfusion Hb (Hb $\leq$ 3 hours pretransfusion), and the primary indication for RBC transfusion, as reported by the ordering provider.³¹

Statistical Analysis:

Statistical analyses were performed using Wizard statistical software, Version 1.9.48. The normality of distribution of continuous variables was tested with the one-sample Kolmogorov-Smirnov test. Frequencies were determined for categorical variables. Continuous variables are expressed as mean with standard deviation. A Fisher's exact test was used for categorical variables. A student's T-test was used for variables with normal distribution and a Mann-Whitney test was used for continuous variables without normal distribution. Statistical significance was assumed at an alpha value of 0.05. A Bonferroni correction was used to account for the multiple testing hypothesis. Hospital charges were obtained from the publicly available fiscal year 2021 Parkland Hospital chargemaster.³² Data was utilized to calculate estimated cost for a single RBC transfusion, bedside CVC placement, and interventional radiology (IR) CVC placement.

Results

Patient Characteristics:

Patient demographics and study outcomes are summarized in Table 1. A total of 291 patients (mean 62.2 years, male to female ratio 1.5) underwent 299 hospitalizations with a LOS of 15.8 days. Comorbidity status as assessed by CCI was 4.4. DLT associated blood loss was 14.3 mL/day (229.5 mL/hospitalization). The overall rate of vascular access was 75.3% (225/299). The rates of vascular access by type were as follows: CVC access 49.8% (149/299), PICC access 17.1% (51/299), and arterial access 69.6% (208/299). Arterial discard blood was felt to be negligible and was counted as 0 ml for discard. Daily discard in patients with CVC only was 16.32 mL (SD=11.0) and daily discard was for patients with PICC only was 13.2 (SD=7.4) ($p=>0.99$). Cumulative blood loss for admissions with CVC and PICC access was greater than CVC alone: 132.2 mL versus 524.1 mL ($p<0.001$). The cumulative admission blood loss was predictive of the magnitude of anemia at discharge, with the largest

diagnostic-associated blood loss group corresponding to a discharge Hb of 8.6 g/dL versus the lowest blood loss group being associated with a Hb of 9.7 g/dl ($p < 0.001$) (Figure 1).

Cvc Vs Non-cvc

Patients with and without CVC had similar length of stay and CCI (Table 2). However, patients with CVC access had significantly higher number of total blood draws, total blood drawn or discarded for access and DLT, and rate of transfusion. Patients with CVC require clearing of access with a discard volume of 204 mL/hospitalization. Rates of anemia on discharge were significantly higher in the CVC group. Also, nadir Hb levels and discharge Hb were significantly lower in patients with CVC placement. The number of total blood draws per day was significantly higher in patients with a longer duration of CVC (Figure 2), and total number of draws was significantly higher in patients with CVC versus those without. The volume of combined DLT-associated blood loss was predictive of receipt of RBC transfusion, independent of a surgical procedure or acuity of illness as complicated by co-morbidities by CCI (Figure 3), though the range of CCI was greater in patients with prolonged CVC access (Figure 4). The majority of patients had concurrent placement of an arterial line (95.3%, 142/149), and fewer had PICC access (17.4%, 26/149)

Table 2
Admissions with CVC access versus patients without CVC access

	CVC (n=149) +/- SD	NO CVC (n=150) +/- SD	<i>p</i> value
Age	63.2 +/- 12.6	60.9 +/- 16.5	<0.001
CCI	4.6 +/- 2.3	4.2 +/- 2.9	<0.001
LOS	17.1 +/- 11.4	14.5 +/- 10.9	0.11
Admission Hb (g/dL)	12.3 +/- 2.7	11.9 +/- 2.3	>0.99
Nadir Hb (g/dL)	7.4 +/- 1.4	8.4 +/- 1.9	<0.001
Discharge Hb (g/dL)	8.9 +/- 1.2	9.8 +/- 1.8	<0.001
Anemia [†] on admission	45.6% (68/149)	56.7% (85/150)	>0.99
Anemia [†] on discharge	100% (149/149)	90% (135/150)	0.004
Rate of RBC transfusion	42.3% (63/149)	22.0% (33/150)	0.010
Number of RBC units transfused	1 +/- 2.1	0.4 +/- 0.9	0.059
Number of Blood Draws Total	121.1 +/- 149.3	60.6 +/- 48	<0.001
per day	7 +/- 5.1	4.6 +/- 3.5	<0.001
Total DLT-associated blood loss (mL)	297.8 +/- 324.3	161.6 +/- 122.6	<0.001
per day (mL)	16.5 +/- 10.7	12.2 +/- 8.3	0.007
Total Discard Volume Per admission (mL)	204 +/- 322		
Duration of CVC Access (mL)	7.4 +/- 5.5		
Total iatrogenic blood loss per patient (including discard) (mL)	501.7 +/- 632.8	193.2 +/- 191.3	<0.001
CVC, central venous catheter; SD, standard deviation; CCI, Charlson comorbidity index, LOS, Length of stay; Hb, Hemoglobin; RBC, Red Blood Cell unit; DLT, Diagnostic laboratory testing			
[†] Anemia based on based on World Health Organization definitions of Hb <12mg/dL; Male, Hb<13mg/dL			

Pre-existing Anemia On Admission Versus Non-anemic On Admission

Patients with and without anemia on admission had similar length of stay and CCI (Table 3). Admission anemia significantly associated with lower Hb nadir, Hb at discharge, and rate of anemia at discharge. Pre-existing anemia was not predictive of transfusion.

Table 3
Patients with anemia on admission versus patients without anemia on admission

	Anemic [†] on admission (n=153) +/- SD	Non-Anemic [†] on admission (n=146) +/- SD	<i>p</i> value
Age	61.7 +/-	62.4 +/- 14.6	>0.99
CCI	4.9 +/-	3.9 +/- 2.3	0.07
LOS	16.5 +/-	15.1 +/- 10.4	>0.99
Admission Hb (g/dL)	10.1 +/-	14.3 +/- 1.3	<0.001
Nadir Hb (g/dL)	7.3 +/-	8.6 +/- 1.9	<0.001
Discharge Hb (g/dL)	8.9 +/-	9.9 +/- 1.8	<0.001
Anemia [†] at Discharge	100% (153/153)	90.4% (132/146)	0.002
Patients requiring RBC transfusion	61% (58/95)	26% (38/146)	>0.99
Number of RBC transfusions	1 (0.8) +/- 1.7	1 (0.7) +/- 1.6	>0.99
CVC access	44% (68/153)	55% (81/146)	>0.99
Duration of CVC Access	3.6 +/- 5.7	3.8 +/- 5.4	>0.99
Blood Draws per Stay	85.8 +/- 102	91.1 +/- 124.2	>0.99
Blood Draws per Day	6.1 +/- 5.1	5.5 +/- 3.8	>0.99
DLT associated blood loss per patient (mL)	214.8 +/- 214	220.3 +/- 284.5	>0.99
Per Day (mL)	15.2 +/- 10.9	13.4 +/- 8.4	>0.99
Total iatrogenic blood loss per patient (including discard) (mL)	361.7 +/- 420.6	331.4 +/- 556.3	0.765
Per Day (mL)	21.6 +/- 18.12	18.4 +/- 14.9	>0.99
CVC, central venous catheter; SD, standard deviation; CCI, Charlson comorbidity index, LOS, Length of stay; Hb, Hemoglobin; RBC, Red Blood Cell unit; DLT, Diagnostic laboratory testing			
[†] Anemia based on based on World Health Organization definitions of Hb <12mg/dL; Male, Hb<13mg/dL			

Surgical Vs Non-surgical Patients

Surgical and non-surgical patients had similar length of stay and CCI (Table 4). Surgical patients had higher rates of CVC placement, lower Hb nadir, and lower Hb at discharge. Receipt of surgery was not predictive of anemia at discharge or non-operative transfusion.

Table 4
Surgical admissions versus non-surgical admissions

	Surgical admissions (n=210) +/- SD	Non-surgical admissions (n=89) +/- SD	<i>p</i> value
Age	62.2 +/- 13.9	61.7 +/- 16.3	>0.99
CCI	4.3 +/- 2.3	4.7 +/- 3.2	>0.99
LOS	16.7 +/- 12.5	13.6 +/- 6.7	>0.99
Admission Hb (g/dL)	12.3 +/- 2.6	11.8 +/- 2.3	>0.99
Nadir Hb(g/dL)	7.6 +/- 1.5	8.6 +/- 2	<0.001
Discharge Hb (g/dL)	9.1 +/- 1.4	9.9 +/- 1.9	0.009
Anemia [†] on admission	49.5% (104/210)	55.1% (49/89)	>0.99
Anemia [†] on discharge	98.1% (206/210)	88.8% (79/89)	0.061
Patients requiring RBC transfusion	35.2 (74/210)	24.7% (22/89)	>0.99
RBC Units Transfused Number	1 (0.8) +/- 1.7	1 (0.6) +/- 1.5	>0.99
CVC Access	60.5% (127/210)	24.7% (22/89)	0.005
Duration of CVC Access	7.2 +/- 5.6	8.7 +/- 6.6	>0.99
Total Number of blood draws	99.6 +/- 124.3	78.3 +/- 89.7	>0.99
per day	5.9 +/- 4.6	5.5 +/- 4.3	>0.99
DLT-associated blood loss per hospitalization (mL)	241.8 +/- 279.8	200.4 +/- 175.7	>0.99
Per day (mL)	142.2 +/- 10.2	14.6 +/- 8.6	>0.99
Total iatrogenic blood loss per patient (including discard) (mL)	375.7 +/- 541.3	279 +/- 337.3	>0.99
Per day (mL)	20.3 +/- 16.7	19.5 +/- 16.6	>0.99
CVC, central venous catheter; SD, standard deviation; CCI, Charlson comorbidity index, LOS, Length of stay; Hb, Hemoglobin; RBC, Red Blood Cell unit; DLT, Diagnostic laboratory testing			

Charge Analysis

Charge analysis was performed comparing CVC placement and the cost of blood transfusion. The cost for CVC and the cost of single RBC transfusion were approximately equivalent (\$1,340 vs. \$1,450). IR placement of CVC is approximately 6 times more expensive than bedside CVC placement (\$1,340 vs. \$7,770).

Discussion

The findings of our study suggest that the total volume of DLT-associated blood loss contributes to both the incidence and magnitude of anemia and was associated with more frequent RBC transfusions in critically ill patients. Likewise, the severity of anemia correlated with the volume of blood drawn (figure 1). Furthermore, CVC access was predictive of increased total blood loss, transfusion, and anemia. The observations of our investigation correspond with those reported in previous studies.^{1,4-9}

CVC placement associated with an increase in blood draws for laboratory testing and a resultant increase in iatrogenic blood loss, both for DLT as well as line clearance blood discards. While the critically ill require extensive DLT to guide therapy, the number of accesses as well as the utilization of blood conserving devices (BCD) to reduce discards represent modifiable factors. BCD use may be especially impactful as there was a significant amount of cumulative blood loss associated with line clearance, 204 mL/admission, which nears the red cell volume of 1 unit of RBCs. A recent meta-analysis by Whitehead et al., demonstrated that utilization of BCDs were associated with a reduction in iatrogenic blood loss as well as the use of pediatric tubes.⁵

While the overall rate of transfusion was 32% (95/299), CVC access was predictive of a higher rate compared to those without CVC access. Transfusion increases morbidity and mortality amongst ICU patients and thus, DLT blood loss represents an area which could be impacted with implementation of common-sense blood saving interventions, such as BCD. We found that CVC line placement >7-days was predictive of a higher rate of RBC transfusions. ICU services often have goals to remove CVCs as quickly as possible, to reduce the risk of central line associated bloodstream infection (CLABSI), which are associated with high mortality, and our findings suggest reduction in DLT blood loss represents a further motive for early CVC removal.³³

One critique of BCDs is an increased cost. A charge analysis performed demonstrated bedside CVC placement was roughly equivalent to the charge for a single RBC transfusion (\$1,340 vs. \$1,450). Though many services place lines at bedside there has been a shift in some centers with the majority being placed by interventional radiology, which we show to be significantly more expensive. Although determining clear pricing information is challenging, utilization of BCDs would prevent doubling the cost of having a bedside CVC if an RBC transfusion is not required.

CVC placement led to lower Hb nadirs and discharge Hb levels. This is impactful, as the body increases cardiac output and shunts blood away from visceral organs through compensatory mechanisms in response to anemia, which may lead to further end organ stress or failure. Also, severe discharge anemia has been shown to be predictive of anemia on long term follow-up for ICU patients, further contributing to readmission, need for transfusion, and poor general health as an outpatient.^{13,16}

Under physiologic conditions the body can readily produce sufficient red cell mass for maintenance of Hb levels, ~10-20 mL per day, and though this number may increase exponentially in states of anemia with adequate iron stores, the critically ill patient has been shown to have reduced red cell production, making any blood loss likely more impactful.^{18,34-37} Many ICU patients are anemic on presentation with nutritional deficiency being a contributing factor in 13% of ICU patients as follows: 2% B12 deficient, 2% folate deficient, and 9% iron deficient.¹⁷ To that end, each ml of blood contains 1 mg of iron, and while patients generally have iron stores of 300-1000 mg, this iron may be rendered inaccessible due to an ongoing inflammatory response.^{34,38,39} Moreover, though healthy blood donors have been shown to have a maximum absorption between 3-5 mg/day iron it is likely that critically ill patients have suboptimal absorption of nutrients.⁴⁰ Erythropoietin is produced predominantly in the kidney with a small percentage produced in the liver, and work shows ICU patients have both reduced production of EPO as well as a blunted response.^{41,42} Ongoing blood draws represent an identifiable loss of red cell mass and iron which the critically ill patient cannot effectively replace, further contributing to iatrogenic anemia.

While we observed a total mean daily loss of blood of 20.0 mL, a volume below that observed ~50-100 mL in other studies, this volume is actually equivalent to steady state RBC production in healthy individuals.^{4-7, 36,43} A mathematical model by Lyon et al. suggested that loss of 53 mL per day in healthy patients with adequate iron stores would lead to anemia in approximately 40 to 70 days.⁴⁴ Conversely, critically ill patients with compromised RBC production would demonstrate anemia in approximately 9 to 14 days.⁴⁴ The observed SICU LOS in our study 15 days, and though 20 mL was significantly less than 53 mL, 95.3% of patients were anemic at time of unit discharge.

One limitation of the study that many patients had both CVC and PICC placement. As such those with only CVC were compared with PICC and those with both PICC and CVC to compare discard volumes. As a single predictor both DLT-associated and total blood loss was significantly lower in those without CVC, and CVC placement alone was predictive of increased blood draws.

As this is a retrospective analysis, we could not actively monitor these patients or obtain additional studies that may have been informative, such as nutritional or inflammatory markers. Moreover, these are complex, critically ill patients and numerous factors, as discussed above, contribute to the incidence of anemia, though we attempt to characterize this with CCI values and by comparing surgical and non-surgical patients. Our group does show a contemporary 'baseline' of iatrogenic blood loss in an SICU setting, which may be generalizable to other SICU services. Likewise, we also showed lower rates of transfusion compared to prior work, showing some movement toward more conservative transfusion

practice. The goal of a “bloodless” ICU admission without transfusion should still be pursued as RBC transfusion in this population is associated with higher rates of mortality, increased LOS, and ongoing anemia as an outpatient.^{13,28} Several limitations including the accuracy of data recorded within the electronic medical records and selection bias. Moreover, the decision to transfuse RBCs was left to the discretion of the treating physician and therefore the rationale for RBC transfusions was not always clear. Finally, chargemaster values were used as opposed to direct costs to the hospital or patient. Chargemaster rates have been shown to have high variability and are likely not predictive of cost to patient, but may provide some insight into billing for these procedures.⁴⁵

Conclusions

While onset or persistence of anemia in this context is multifactorial, an association is clear between DLT, CVCs and hospital acquired anemia. ICU patients especially require numerous laboratory tests given the high acuity of care; however, physicians should be aware that this increased testing associates with higher rates of anemia and the need for RBC transfusion. Given the associated increase in increase morbidity and mortality associated with hospital acquired anemia and transfusion, efforts should be made to reduce unnecessary DLT and associated adverse events to improve quality of care.

Declarations

Conflict of Interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

- Ethics approval and consent to participate
 - IRB approval was obtained for main study. Chargemaster analysis was performed on publicly available data.
- Consent for publication
 - This was a retrospective study and no individual consent was obtained.
- Availability of data and material
 - Data is available and is in the possession of the first and senior author. De-identified data may be provided by contacting the senior author.
- Competing interests
 - There are no relevant competing interests.
- Funding
 - No funding was obtained for this retrospective chart review study.
- Authors' contributions
 - BDA – manuscript preparation and statistical analysis
 - AD - manuscript preparation

- JAT – data collection
- VP – data collection and chargemaster analysis
- AO – manuscript preparation
- SGY – hypothesis generation, manuscript preparation and statistical analysis
- Acknowledgements
 - N/A

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Figures

Figure 1

Discharge hemoglobin level versus volume of diagnostic laboratory blood loss. ($p < 0.001$)

Figure 2

Number of RBC transfusions compared with length of CVC placement (days).

Figure 3

Number of RBC transfusions compared with length of CVC placement (days).

Figure 4

Charlson Comorbidity Index (CCI) comparison amongst patients with CVC placement.